CHAPTER 3: POST APPROVAL PROCEDURES

Authored by:	DLSMHSI-IEC Secretariat
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Approved by:	(original signed) Charles Y. Yu, MD, MSc, FPCP, FPCCP Vice Chancellor for Research

Post Approval Procedures

The objective of this SOP is to describe the review process of the DLSMHSI-IEC related to events reported to the IEC and Principal Investigator (PI) submissions required by the IEC during the conduct of the research. The period covered begins after the approval has been granted by the DLSMHSI-IEC until the completion of the study at the IEC-approved site.

1. Review of Adverse Events (AEs), Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reactions (SUSARs)

1.1 Purpose

To describe the DLSMHSI-IEC review process for Adverse Events (AEs), Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reactions (SUSARs).

1.2 Scope

The SOP applies to the review of Adverse Event (AE), Serious Adverse Events (SAE) and Suspected Unexpected Serious Adverse Reaction (SUSAR) reports submitted by investigators and sponsors to the DLSMHSI-IEC to comply with International Conference on Harmonization – Good Clinical Practice (ICH-GCP). The DLSMHSI-IEC reviews such reports to determine appropriate actions to protect the safety of participants in an approved research.

ICH-GCP E6 defines a SAE or a serious Adverse Drug Reaction (ADR) as any untoward medical occurrence that at any dose:

- results in death
- is life threatening
- requires hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability or incapacity, or
- results in a congenital anomaly or birth defect.

A SUSAR is a serious event, the nature and severity of which, is not consistent with the applicable product information. In the case of an unapproved investigational product, the event is not consistent with the Investigator's Brochure (IB). In the case of a licensed product, the event is not consistent with the approved package insert or summary of product characteristics.

1.3 Responsibilities

1.3.1 The primary responsibility of the DLSMHSI-IEC is to conduct an appropriate review of AE, SAE and SUSAR reports to ensure oversight over the safety of participants enrolled in the study.

1.3.2 The IEC should make sure that researchers are made aware of its policies and procedures concerning SAE reporting.

1.3.3 The DLSMHSI-IEC sets up the necessary mechanisms to receive SAE and SUSAR reports from investigators and sponsors of researches that it has approved.

1.3.4 The primary responsibility of the IEC is to receive and review SAE and SUSAR reports through the appointed SAE Subcommittee members from its own site (on-site or DLSMHSI site[s]) and to take necessary action to ensure the safety of participants in the study.

1.3.5 In multi-center studies, the IEC also receives SAE and SUSAR reports from other sites (off-site or Non-DLSMHSI sites) within and outside the country. It is the responsibility of the IEC to be updated about safety issues related to studies that it has approved.

1.3.6 The DLSMHSI-IEC has the authority to suspend or terminate approval of research at its site when the safety of participants is no longer assured. When the IEC takes such action, it is required to provide the reasons for its action and to promptly report such decision to the investigator, the sponsor, the institution and relevant regulatory authorities.

1.4 Process Flow

	ACTIVITY	RESPONSIBILITY
Step 1	Document and report SAE and SUSAR	Principal Investigator
Step 2	Receive the completely accomplished SAE Report, log in Submissions logbook and enter in SAE database	Secretariat
Step 3	Refer the SAE reports to SAE Subcommittee for review and evaluation and forward recommendation to IEC chair	Secretariat
Step 4	Appraise and discuss the recommendations of the SAE Subcommittee in full board meeting for decision and appropriate action	Chair/Members
Step 5	Inform the Principal Investigator about the IEC's decision, whenever it is necessary	Secretariat
Step 6	File all the pertinent SAE and SUSAR documents in the SAE File Folder	Secretariat

1.5 Description of Detailed Procedures

1.5.1 The Principal Investigator documents and reports SAE and SUSAR.

- It is a requirement from the Principal Investigators to document and report AEs, SAEs and SUSARs to the IEC for all studies approved by

the IEC through the prescribed SAE Report form (FORM 3A-V3-2019).

The following are the guidelines in reporting Serious Adverse Events by the PI to the DLSMHSI-IEC:

- Any SAE that result to death
  - On-site: Submission Timeline by the site to IEC: Within 24 hours that Principal Investigator/site is informed of the event.
  - Off-site: Submission Timeline by the site to IEC: Within 24 hours that Principal Investigator/site receives report from the Sponsor.
  - SAEs occurring on weekends/holidays may be reported to the Independent Ethics Committee via email to iec@dlshsi.edu.ph**.** The duly accomplished Form 3A/V3/2019 may be submitted on the next working day.

- Serious Adverse Event (SAE) Reports
  - On-site SAEs that are related and expected: Submission Timeline by the site to IEC: Within 7 working days from date that Principal Investigator/site is informed of the event.
  - Off-site SAEs that are related and expected: Submission Timeline by the site to IEC: Within 7 working days from date that Principal Investigator/site receives report from Sponsor.

- Suspected Unexpected Serious Adverse Reaction (SUSARs):
  - On-site: Submission Timeline by the site to IEC: Within 7 working days from date that Principal Investigator/site is informed of the event
  - Off-site: Submission Timeline by the site to IEC: Within 7 working days from date that Principal Investigator/site receives report from Sponsor

- SAEs or SUSARs that are determined to change study risks, and necessitate modification of the IEC-approved protocol/ICF
  - On-site and Off-site: Submission Timeline by the site to IEC: Within 7 working days from date that Principal Investigator/site receives report from the Sponsor

1.5.2 The Secretariat receives the completely accomplished SAE Report (FORM 3A-V3-2019), log in Submissions logbook and enter in SAE database.

1.5.3 The Secretariat refers the SAE reports to SAE Subcommittee for review and evaluation and forward recommendation to IEC Chair.

- The DLSMHSI-IEC Secretariat shall be responsible for receiving, logging and encoding reports and forwarding the AE, SAE and SUSAR reports within two (2) working days to the SAE Subcommittee for review and recommendations.

- To review SAE reports, the SAE subcommittee should use the SAE Subcommittee Recommendation Form, Form 3J/V1/2012 accomplished by the subcommittee reviewers that recommends appropriate action to be done by the IEC. The review and assessment process may result in the following recommendations:

  - No modification required and the study is allowed to continue.
  - More information needed. The report is forwarded to the chair with request for information that is needed and for further review and evaluation if the report shall be reviewed at the convened meeting by full board.
  - Modification(s) needed. The report is forwarded to the chair with the recommended modifications in specific areas of the protocol (ie. Inclusion-exclusion criteria, informed consent, etc.) and is added to the agenda for review at a convened meeting by full board.
  - Implementation of additional procedures. The report is forwarded to the chair with the recommended additional procedures (ie. screening, additional labs, monitoring, etc.) and is added to the agenda for review at a convened meeting by full board.
  - Suspension of enrollment, research procedure among current participants or of entire study. The report is forwarded to the chair with recommendations and is added to the agenda for review at a convened meeting by full board.

1.5.4 The Chair and IEC members appraise and discuss the recommendations of the SAE Subcommittee in full board meeting for decision and appropriate action.

- On-site AE, SAE and SUSAR reports are reviewed regularly and recommended at the next board meeting while off-site AE, SAE and SUSAR reports are analyzed as trends and report to the IEC board meeting twice a year.

- For off-site SAE/SUSAR reporting, it is generally not necessary to report events that are considered unrelated to the study procedure/investigational medicinal product.

- The SAE Reports and SUSAR submission shall be classified according to their origin or site of occurrence: off-site (foreign site or local site)

and on-site (DLSMHSI site). Based on the site of occurrence, the SAE subcommittee members shall formulate an appropriate response:

- For off-site multicenter international studies, note the trend of occurrence of SAE/SUSAR in foreign and local study site.
- For off-site multicenter national studies, note the nature of the SAE/SUSAR as either related or expected.
- For SAEs that occur onsite, the IEC shall evaluate the investigator/sponsor assessment as to related or unexpected and may need to recommend some form of action to the investigator to ensure the safety of participants. The chair of the SAE subcommittee should inform the IEC chair about their recommendations for appropriate IEC action.

▪ SAE and SUSAR reports are reviewed and discussed during IEC meetings for appropriate actions on the following points:

- The results of the reviewed on-site SAE and SUSAR reports by the SAE Subcommittee are recommended to the Chair and reported in the next IEC board meeting for discussion.
- The consolidated trend analyses of off-site SAE and SUSAR reports by the SAE Subcommittee are presented to the IEC board meeting twice a year for discussion.
- After the discussion, the chair may call for a consensus to send notification to the PI and communicate the decision to:
  - Uphold original approval with no further action and the study is allowed to continue.
  - Recommend further action with recommendations and the response is processed by full board review
  - Request for further information and the response is processed by full board review.
  - Have a pending decision with major clarifications and the response is processed by full board review.

1.5.5 The Secretariat informs the Principal Investigator about the IEC's decision, whenever it is necessary.

▪ The Secretariat writes a formal letter (FORM 4G-V2-2019) to notify the investigator of the action they should take according to the IEC decision. The chair approves signs and dates the letter which is logged/recorded and eventually given to and received by the PI.

1.5.6 The Secretariat files all the pertinent SAE and SUSAR documents in the SAE File Folder.

2. Review of Amendment

2.1 Purpose

To describe the DLSMHSI-IEC review process for amendments of the protocol and related documents.

2.2 Scope

This SOP applies to previously approved study protocols and related documents that have been amended and now being submitted for approval by the DLSMHSI-IEC. Any amendment of the study related documents may not be implemented until reviewed and approved by the IEC.

2.3 Responsibility

2.3.1 It is the responsibility of the DLSMHSI-IEC Secretariat to manage a protocol amendment packages submitted by the PI.

2.3.2 It is the responsibility of the original primary reviewers to review the amendments and recommend appropriate action.

2.3.3 It is the responsibility of the IEC Chair to determine whether the amendment goes to expedited of full board review. The IEC approves the final decision for amendments submitted by the PI to the IEC.

2.4 Process Flow

	ACTIVITY	RESPONSIBILITY
Step 1	Submit application for amendment	Principal Investigator
Step 2	Check and receive the completely accomplished amendment form (FORM 3B-V2-2015) and package, log in Submissions logbook and enter in IEC database	Secretariat
Step 3	Refer the amendment documents to the primary reviewers for review and evaluation and forward recommendation to IEC chair who determines whether amendment should be referred to full board review and approval	Secretariat
Step 4	Evaluate the amendment documents which will be presented or discussed in full board meeting, if necessary, for decision and appropriate action	Primary Reviewers/Chair
Step 5	Inform the Principal Investigator about the IEC's decision	Secretariat
Step 6	Maintain a copy of all amendment related documents in the protocol file	Secretariat

2.5 Description of Detailed Procedures

2.5.1 The Principal Investigator submits application for amendment.

- It is a requirement from the Principal Investigators to submit an amendment application whenever there are changes regarding the composition of the study team, the study site and the protocol and related documents for approvals previously granted by the IEC through the prescribed Protocol Amendment form (FORM 3B-V2-2015).

2.5.2 The Secretariat checks and receives the completely accomplished amendment form (FORM 3B-V2-2015) and package, log in Submissions logbook and enter in IEC database. Receive and manage complete amendment package.

2.5.3 The Secretariat refers the amendment documents to the primary reviewers for review and evaluation and forward recommendation to IEC chair who determines whether amendment should be referred to full board review and approval.

- Whether amendment review is expedited or full board the following decision points apply:
  - Approval with no further modifications required.
  - Minor modifications, subsequent approval of which could be expedited.
  - Major modifications, subsequent approval of which requires full board.
  - Disapproval, study cannot be allowed to proceed further.

2.5.4 The primary reviewers evaluate the amendment documents which will be presented or discussed in full board meeting, if necessary, for decision and appropriate action.

- The primary reviewers check the amended documents and compare them with the previously IEC-approved documents in the protocol file.
- The primary reviewers check if the amendments would alter the risk-benefit ratio of the study and make appropriate recommendations using FORM 3B-V2-2015. Amendments that may potentially alter the risk-benefit ratio of a study are referred to full board for further discussion.
- Protocol amendments that increase the risk to study participants may include, but is not limited to the following:
  - A change in study design
  - Additional treatments or the deletion of treatments
  - Any change in the inclusion and exclusion criteria
  - Change in mode of drug intake or route of drug intake

- Significant change in the number of subjects, increase or decrease in sample size that alters the fundamental characteristics of the study
- Significant increase or decrease in dosage amount

2.5.5 The Secretariat informs the Principal Investigator about the IEC's decision.

- The Secretariat prepares a communication letter on modifications (FORM 2H-V2-2019) or approval (4E-V1-2012) to inform the investigator about the committee decision. The Secretariat forwards the letter to the investigator for proper action and logs receipt of letter by the investigator.

    - If only minor changes are involved in the amendment and are administrative in nature, the review is expedited and the reviewer's recommendation become the basis for the final decision of the IEC. A letter granting approval is prepared by the IEC Secretariat.
    - If major changes are involved in the amendment, the amendment is referred to full board after review of the primary reviewers. The members discuss the issues related to the amendments to arrive at a decision.

2.5.6 The Secretariat maintains a copy of all amendment related documents in the protocol file.

3. Review of Progress Reports, Final Reports and Close-Out Forms

3.1 Purpose

To describe the DLSMHSI-IEC review process for Progress Reports, Final Reports and Close-Out Forms.

3.2 Scope

3.2.1 This SOP provides instructions for the review of Progress Reports, Final Reports and Close-out Forms that are required by the DLSMHSI-IEC to be submitted by the PI to monitor the safety of participants enrolled in a study. The annual progress report serves as the basis for continuing review of protocols whose approval needs to be renewed every year. The Final Report includes an updated information of the Close-out Form along with data analysis completion, submission of the final results and relevant publications/ conference presentations of the study findings that are submitted by the PI upon completion of participant enrollment and all follow-up procedures. The Close-out Form is submitted to notify the DLSMHSI-IEC that the study accrual and other protocol procedures have ended. The form summarizes the completion of post-approval reports, study duration and number participants enrolled/withdrawn in the study.

3.2.2 This SOP applies to conducting any continuing review of study protocols involving human participants at interval appropriate to the degree of risk but not less than once a year. Depending upon the degree of risk to the participants and the duration of the study, the IEC may choose to review or monitor the protocols more frequently.

3.2.3 This SOP describes the follow-up of Progress and Final Reports by the IEC Secretariat and the review of such reports and Close-out Forms submitted by the Principal Investigator by designated members of the IEC in compliance with ICH-GCP requirements.

3.3 Responsibility

3.3.1 It is the responsibility of the DLSMHSI-IEC Secretariat to remind investigators to submit the Progress and Final Reports before the due date, to forward the reports to the original primary reviewers for evaluation, to communicate with the investigators if there is any need for further information or action, and to submit to full board a list of Progress Reports and Final Reports for evaluation.

3.3.2 It is the responsibility of the primary reviewers to evaluate the reports to check completeness of information and ensure that the date is in accordance with the protocols and other related documents approved by the IEC.

3.4 Process Flow

	ACTIVITY	RESPONSIBILITY
Step 1	Reminds through a notification letter (FORM 4L-V1-2012) the Primary Investigators to submit Progress Report using the Continuing Review Application Form (FORM 3C-V2-2015) and Final Report (FORM 3D-V2-2015) prior to due date	Secretariat
Step 2	Submit Progress Report using Continuing Review Application Form 3C/V2/2015) and Final Report (Form 3D/V2/2015) on or before due date.	Principal Investigator
Step 3	Check the completeness of the information in the report and form and forward to them to the primary reviewers for evaluation	Secretariat
Step 4	Review and evaluate the Progress Report, Final Report and Close-Out Form if it is in accordance with the IEC-approved protocol and related documents and subsequently recommend appropriate action	Primary Reviewers
Step 5	Forward the recommendation to the IEC Chair who determines whether Progress Report should be referred to full board review and approval. The Final Reports are also presented to full board	Secretariat
Step 6	Evaluate and discuss in full board meeting the Progress Report and Final Report, if necessary, for decision and appropriate action to be communicated to the Principal Investigator	Chair/Members
Step 7	Maintain a copy of all the Progress Reports, Final Reports and Close-Out Forms submission along with the related documents in the protocol file	Secretariat

3.5 Description of Detailed Procedures

3.5.1 The Secretariat reminds through a notification letter (FORM 4L-V1-2012) the Primary Investigators to submit Progress Report using the Continuing Review Application Form (FORM 3C-V2-2015) and Final Report (FORM 3D-V2-2015) prior to due date.

- The Secretariat checks the database and tracks the due dates of Progress and Final Reports of Study protocols approved by the IEC:
  - Continuing Review Application (FORM 3C/V2/2015) – must be filed 60 days prior to expiry date of current IEC approval
  - Final Report (FORM 3D/V2/2015) – must be filed within 90 days after study completion

- The Secretariat reviews the completeness of the submitted report and forms and forwards them to the primary reviewers.
- Close-out Form (FORM 3K-V2-2019) is submitted by the Principal Investigator once the study site has completed close-out procedures where data on final study duration and number participants enrolled/withdrawn are summarized.

3.5.2 The Principal Investigators submit Progress Report using Continuing Review Application Form 3C/V2/2015 and Final Report (Form 3D/V2/2015) on or before due date.

- The Close-Out Form (Form 3K/V2/2019) is submitted prior to the Final Report to notify about the study site close-out information.

3.5.3 The Secretariat checks the completeness of the information in the report and form and forward to them to the primary reviewers for evaluation.

3.5.4 The Primary Reviewers review and evaluate the Progress Report, Final Report (Form 3D/V2/2015) and Close-Out Form (Form 3K/V2/2019) if it is in accordance with the IEC-approved protocol and related documents and subsequently recommend appropriate action.

- The primary reviewers refer to the protocol file to check compliance with approval given by the IEC during initial review and, if applicable, upon submission of amendments.
- The primary reviewers recommend approval of the Progress Report and Final Report (Form 3D/V2/2015) if there is no deviation or violation of IEC approvals and decide whether there is further action needed for Close-Out Form submissions.
- If there are any deviations or violations of approvals given by the IEC or unanticipated problems such as unresolved adverse events (AEs) or protocol deviations that were not previously reported to the IEC, the primary reviewers recommend the appropriate action to be taken by the Principal Investigator. For summary of AEs, use FORM 3H/V1/2012 and for protocol deviations use FORM 3E/V1/2012.
- Approval or other recommendations by the primary reviewers of the Progress Report and Final Report (Form 3D/V2/2015) are reported to the committee meeting by the Secretariat.

- Approval of the annual progress report is necessary to renew the initial approval of the protocol and allow the investigator to continue the conduct of the research. Approval of the Final Report (Form 3D/V2/2015) enables the IEC Secretariat to close the protocol file while response to the Close-Out Form (Form 3K/V2/2019) submission is essential whether there is further action needed for the site close-out information.
- Related issue or recommendations associated to the Progress reports and Final reports are included in the agenda for discussion during the committee meeting in order to arrive at a decision for appropriate action. Response to the Close-Out Form (Form 3K/V2/2019) submissions that are needed further action or information is decided upon the Chair whether to be included in the agenda of the meeting.
- The Secretariat takes note of the decision and/or discussion during the committee meeting in the minutes and communicates with the PI if further action is required.

3.5.5 The Secretariat forwards the recommendations to the IEC Chair who determines whether Progress Report should be referred to full board review and approval. The Final Reports are also presented to full board.

3.5.6 The Chair and IEC members evaluate and discuss in full board meeting the Progress Report and Final Report, if necessary, for decision and appropriate action to be communicated to the Principal Investigator through a notification letter (FORM 4G-V2-2019), approval letter for Final Report (FORM 4J-V1-2012) and approval letter for Progress Report (FORM 4R-V1-2012).

- The IEC Secretariat accepts the reports and notifies the investigator about its decision:
  - Uphold original approval with no further action with the renewal of approval of the protocol and related documents to enable the PI to continue the conduct of the research.
  - Request for further information, specifying information that is required prior to renewal of approval.
  - Recommend further action, specifying action required prior to renewal of approval.
- The IEC Secretariat accepts the Final Report and considers the study Completed with prior submission of the study Close-Out Form (Form 3K/V2/2019).
- The IEC Secretariat maintains a copy in the protocol files of the Progress and Final Reports and Close-Out Forms signed by the primary reviewers and the Chair or Member-Secretary.
- The IEC Secretariat marks the folder of the completed protocol and archives the entire study protocol.

3.5.7 The Secretariat maintains a copy of all the Progress Reports, Final Reports and Close-Out Forms submission along with the related documents in the protocol file.

4. Review of Protocol Violation or Deviation

4.1 Purpose

To describe the DLSMHSI-IEC review process for protocol violation or deviation.

4.2 Scope

This SOP provides instructions for taking action and maintaining records of various types of protocol deviations or violations.

4.2.1 It includes investigators who fail to comply with the procedures in the IEC-approved protocol or to comply with national or international guidelines for the conduct of human research, including those who fail to respond to the DLSMHSI-IEC's requests for information or action.

4.2.2 It also covers the action taken by the IEC related to the protocol violation or deviation reports submitted by the PI related to any event at the site that is not in compliance with the protocol documents previously approved by the IEC.

4.3 Responsibility

4.3.1 It is the responsibility of the IEC Secretariat to receive protocol violation or deviation reports submitted to the IEC.

4.3.2 It is the responsibility of the committee members or designated members to take action related to protocol violation of deviation.

4.4 Process Flow

	ACTIVITY	RESPONSIBILITY
Step 1	Receive the completely accomplished protocol violation or deviation reports submitted through Non-Compliance (Deviation/Violation) Report Form (FORM 3E-V1-2012)	Secretariat
Step 2	Discuss and evaluate at full board meeting for decision and appropriate action of the reported protocol violations or deviations	Chair/Members
Step 3	Inform the Principal Investigator about the IEC's decision through a notification letter (FORM 4G-V2-2019)	Secretariat
Step 4	Maintain a copy of all Non-Compliance (Violation/Deviation) reports in the protocol file	Secretariat

4.5 Description of Detailed Procedures

4.5.1 The Secretariat receives the completely accomplished protocol violation or deviation reports submitted through Non-Compliance (Deviation/Violation) Report Form (FORM 3E-V1-2012).

- The Secretariat shall receive protocol violation or deviation reports (FORM 3E-V1-2012) from investigators and other parties related to any event in the site that is not in compliance with previously IEC-approved protocol and related documents.
- The Secretariat secures full information about the event and includes the report in the next full committee meeting agenda.

4.5.2 The Chair and IEC members discuss and evaluate at full board meeting for decision and appropriate action of the reported protocol violations or deviations.

- Whenever a protocol non-compliance, deviation or violation has been observed:
  - Ensure that the issues as well as the details of the non-compliance involving research investigators are included in the agenda of the DLSMHSI-IEC meeting.
  - Maintain a file that identifies investigators who are found to be non-compliant with national or international regulations or who fail to follow protocol approval stipulations of fail to respond to the IEC's request for information or action.
  - The IEC may elect to suspend or terminate approval of current or ongoing studies or refuse subsequent applications from the investigators cited. Such decisions are documented or recorded in the minutes.

- Basis of IEC decision and action for a prior study approval to be withdrawn:
  - SAE directly or indirectly attributed to the research
  - Breach of previously approved conduct of the research
  - Major changes, deviations or amendments to the approved protocol without another approval by the IEC.
  - Revisions in the informed consent form

4.5.3 The Secretariat informs the Principal Investigator about the IEC's decision through a notification letter (FORM 4G-V2-2019).

- The PI is notified of the IEC's decision which may be:
  - Uphold original approval with no further action required.

- Request for further information, specifying information that is required prior to upholding original approval.
- Recommend further action, specifying action required prior to upholding original approval.

4.5.4 The Secretariat maintains a copy of all Non-Compliance (Violation/Deviation) reports in the protocol file.

5 . Participant's Requests/Queries

5.1. Purpose

To describe the DLSMHSI-IEC process related to participant requests and queries**.**

5.2. Scope

This SOP applies to all queries and requests related to the rights and well-being of the research participants in studies approved by the De La Salle Health Sciences Institute-Independent Ethics Committee (DLSMHSI-IEC).

5.3. Responsibility

A designated member of the secretariat is responsible for receiving participant queries and requests related to their participation, refers relevant issues to the DLSMHSI-IEC Chair or members for the IEC to take appropriate action. The Secretariat keeps records of all action taken by the IEC.

5.4. Process Flow

	ACTIVITY	RESPONSIBILITY
Step 1	Receive and document the request or query (Form 3I/V1/2012)	Secretariat
Step 2	Assess the nature of the request and refer to the appropriate person	Chair
Step 3	Take action and refer to full board if necessary, the recommendations of the assigned member to review	Chair/Members
Step 4	Communicate the decision to the person who made the query	Secretariat
Step 5	Maintain documents in protocol file	Secretariat

5.5 Description of Detailed Procedures

5.5.1 The Secretariat receives and documents the request or query (FORM 3I-V1-2012).

- The Secretariat receives the inquiry or requests from research participants/patients or the community through various forms of communication (email, telephone call, letter, etc.).

5.5.2 The Chair assess the nature of the request and refer to the appropriate person.

5.5.3 The Chair and IEC member take action and refer to full board if necessary, the recommendations of the assigned member to review.

- The Chair and member investigate the fact/s about the request or query, record the request and information and any action or follow-up taken in the request record form (FORM 3I-V1-2012), sign and date the form and forward to the Secretariat for filing and report to full board about the action taken and the outcomes.

5.5.4 The Secretariat communicates the decision to the person who made the query.

- The Secretariat replies to the request or query, if it is within the authority of the Secretariat or refer to the Chair or DLSMHSI-IEC member for appropriate action where a corresponding letter will be given for the decision.

5.5.5 The Secretariat maintains documents in protocol file.

- The Secretariat keeps the record form in the “response” file, keeps a copy in the protocol folder and store the file in the appropriately labeled shelf.

6. Site Visits

6.1. Purpose

To describe the De La Salle Health Sciences Institute-Independent Ethics Committee (DLSMHSI-IEC) process related to the conduct of site visits.

6.2 Scope

This SOP applies to any visit made in any study site, on behalf of the DLSMHSI-IEC, to check compliance with Good Clinical Practice (GCP) and DLSMHSI-IEC approved protocol and related documents.

6.3 Responsibility

6.3.1 It is the responsibility of the DLSMHSI-IEC to review periodically the database files for Post Approval monitoring reports of protocols and to perform or designate some members to perform on its behalf on-site visit of the research projects it has approved.

6.3.2 The DLSMHSI-IEC members or Secretariat in consultation with the Chair may initiate an on-site evaluation of a study site for cause or for a routine audit.

6.4. Process Flow

	ACTIVITY	RESPONSIBILITY
Step 1	Select the study sites and inform the Principal Investigator about the planned visit	Chair/Members
Step 2	Check the approval given by the IEC from the protocol files and collect relevant information about the study site	Members
Step 3	Check the onsite documents and compare with the documents in the protocol files; interview the principal investigator and/or research staff	Members
Step 4	Write a report and make a recommendation utilizing the Site Visit Report (Form 3G-V1-2012)	Members
Step 5	Present the findings to the Full Board which adopts an appropriate action	Members
Step 6	Communicates the committee's decision to the Principal Investigator through a notification letter (FORM 4L-V1-2012)	Secretariat
Step 7	The Principal Investigator implements the recommendations and reports the action to the committee	Primary Investigator
Step 8	Maintain copies of the documents in	Secretariat

	protocol file	

6.5 Description of Detailed Procedures

6.5.1 The Chair and designated members select the study sites and inform the Principal Investigator about the planned visit.

Selection of study sites

- Review periodically the database files of the submitted/approved study protocols.
- Selects study site needed to be monitored based on the following criteria:
  - New study sites or new principal investigators
  - Reports of remarkable serious adverse events
  - Big number of studies carried out at the study site
  - Frequent protocol submission for DLSMHSI-IEC review
  - Non-compliance or suspicious conduct
  - Frequently fail to submit final reports
  - Frequent protocol violations

6.5.2 The designated IEC members check the approval given by the IEC from the protocol files and collect relevant information about the study site.

Before the visit

- Contact the site to notify them about the site visit.
- Coordinate a time for the site evaluation visit.
- Make the appropriate travel arrangements.
- Review the DLSMHSI-IEC files for the study and site.
- Make appropriate notes, or
- Copy some parts of the files for comparison with the site files.

6.5.3 The designated IEC members check the onsite documents and compare with the documents in the protocol files; interview the Principal Investigator and/or research staff.

During the visit

- Use the Site visit checklist (Form 3G/V1/2012)
- Review the informed consent document to make sure that the site is using the most recent version,
- Review randomly the subject files to ensure that subjects are signing the correct informed consent,
- Check if the files are orderly and confidentiality is maintained
- Debrief the principal investigator about site visit findings and comments.
- Get immediate feedback.

6.5.4 The designated IEC members shall write a report and make a recommendation utilizing the Site Visit Report (FORM 3G-V1-2012).

After the visit

- Write a report/comment (use Form 3E/V1/2012) within 1 week describing the findings during the audit.
- Forwards a copy of the site visit to the Secretariat for inclusion in the next board meeting.
- Sends a copy of the report to the site for their files, and
- Places the report in the correct site files.

6.4.5 The designated IEC members present the findings to the Full Board which adopts an appropriate action.

Presentation of the site findings

- Present the site visit report to Full Board.
- Board makes a decision about appropriate action.

6.4.6 The IEC Secretariat communicates the committee's decision to the Principal Investigator through a notification letter (FORM 4L-V1-2012).

6.4.7 The Principal Investigator implements the recommendations and reports the action to the committee.

6.4.8 The IEC Secretariat maintains copies of the documents in protocol file.

7. Early Protocol Termination

7.1 Purpose

To describe the DLSMHSI-IEC process related to early termination or withdrawal of protocol implementation.

7.2 Scope

This procedure describes how the DLSMHSI-IEC proceeds and manages the premature or early termination or withdrawal of a protocol when subject enrollment is discontinued before the scheduled end of the study. Protocols are usually terminated at the recommendation of the Data Safety Monitoring Board (DSMB), the Scientific Director, sponsor, Principal Investigator, by the IEC itself or other authorized bodies.

7.3 Responsibility

It is the responsibility of the IEC to act on any early protocol termination application. It is also the responsibility of the IEC to withdraw approval for any previously approved protocol when the safety or benefit of the study participants is doubtful or at risk. All applications are reviewed at full board for appropriate action.

7.4. Process Flow

	ACTIVITY	RESPONSIBILITY
Step 1	Receive the application for early termination utilizing the Early Study Termination Form (FORM 3F-V1-2012)	Secretariat
Step 2	Check approval given by the IEC from the protocol files and collect relevant information	Primary Reviewers
Step 3	Review the termination package or issues and make recommendations	Primary Reviewers
Step 4	Discuss at full board for the appropriate decision	Primary Reviewers
Step 5	Communicate the board decision to the principal investigator through a notification letter (FORM 4G-V2-2019)	Secretariat
Step 6	Maintain copies of the forms and related documents in protocol file	Secretariat

7.5 Description of Detailed Procedures

7.5.1 The IEC Secretariat receive the application for early termination utilizing the Early Study Termination Application Form (FORM 3F-V1-2012).

Receive application or recommendation for early study termination.

- Receive recommendation and comments from the Sponsor, DSMB, IEC members, Scientific Director, or other authorized bodies for study protocol termination.
- Inform the principal investigator to prepare and submit a protocol termination package.
- Receive the study protocol termination package prepared and submitted by the principal investigator.
- Check the completeness of the contents of the package to include the Early Study Termination Form 3F/V1/2012.
- The request for termination memorandum should contain a brief written summary of the protocol, its results, and accrual data.

7.5.2 The Primary Reviewers check approval given by the IEC from the protocol files and collect relevant information.

7.5.3 The Primary Reviewers review the termination package or issues and make recommendations.

- The primary reviewers review the safety data. It is important for the termination package to contain a plan to follow up the participants who are still active in the study.

7.5.4 The Primary Reviewers discuss at full board for appropriate decision.

7.5.5. The IEC Secretariat communicates the board decision to the Principal Investigator through a notification letter (FORM 4G-V2-2019).

7.5.6. The IEC Secretariat maintains copies of the forms and related documents in protocol file.

8. Version History

Version No.	Authors	Reviewer/s	Approved Date	Approved By	Effectivity Date
1	Dr. Frias	NA	22 Oct 2012	IEC Committee	22 Oct 2012
2	Dr. Frias & Ms. Bayas	PHREB	15 Jun 2016	PHREB	15 Jun 2016
3	Dr. Frias	PHREB			

SERIOUS ADVERSE EVENT REPORT (FORM 3A/V3/2019)

To the Principal Investigator, use this form to report the following adverse events, according to the recommended submission timelines:

- ***All SAEs that result to death***
  - ***On-site, within 24 hours that Principal Investigator/site is informed of the event***
  - ***Off-site, within 24 hours that Principal Investigator/site receives report from the Sponsor***
    Note: SAEs that occur on weekends/holidays may be reported to the IEC via email to iec@dlshsi.edu.ph.
    The duly accomplished Form 3F/V2/2014 may be submitted on the next working day.

- ***Other on-site SAEs must be reported within 7working days that Principal Investigator/site is informed of the event***
  - ***SAEs that are related and expected***
  - ***Adverse events that are serious, related and unexpected (SUSARs)***

- ***All SAEs that change the study risks and necessitate modification of the IEC-approved protocol /ICF must be reported within 7 working days from date that Principal Investigator/site receives report from the Sponsor***

Use the ADVERSE EVENT SUMMARY REPORT (Form 3G/V1/2012) for adverse events that are not covered by the foregoing reporting criteria.

Please obtain an electronic copy of this Form, fill-out the requested information, and make your submission both in electronic version and hard copy. Print in letter-sized paper with printer default set at A4.

I. PROTOCOL INFORMATION	**IEC Protocol Tracking No.**
Study Protocol No.	Protocol Approval Date: <dd/mm/yy>
Study Initiation Date: <dd/mm/yy>	Expected End Date: <dd/mm/yy>
Title:	Version Number, Date
Name of Principal Investigator	Contact Nos.:
Sponsor/CRO	
Study Site	
Type of Review (*To be determined by IEC*)	

☐ Full Board
☐ Expedited

1. What Is Being Reported? ☐ SAE ☐ SUSAR ***Seriousness Criteria:*** ☐ Death ☐ Life-threatening ☐ In-patient hospitalization/ prolongation ☐ Persistent/significant disability/incapacity ☐ Congenital anomaly/birth defect	2. Report Type ☐ Initial ☐ Follow-Up Follow-up Report No. ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ ____
3. Has the Sponsor been notified? ☐ No ☐ Yes (explain/give reasons)	3. Number of similar SAEs that occurred previously at: 3.1. DLSMHSI site <number> 3.2. Other site(s) <number>

4. In the opinion of the PI, will amendments be required to:	Study Protocol?	Informed Consent Form?	Participant Information?
	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No

5. If Yes, will already enrolled patients be re-consented?
☐ Yes (*If YES, append revised document*)
☐ No (*If No, why not?)*

II. INFORMATION REQUIRED	**SAE REPORT SUBMISSION DATE** <dd/mm/yy>

1. PATIENT INFORMATION

Patient Case No.	Date of Birth <dd/mm/yy>	Age	Gender	Weight <kg/lbs>: Height: <cm/in>
			☐ Male ☐ Female	

2. EVALUATION OF EVENT

2.1. Event/Reaction	2.2 Serious? ☐ Yes ☐ No	2.3. Expected? ☐ Yes ☐ No
2.4. Date PI became aware of SAE/SUSAR <dd/mm/yy>	2.5. Date of Experience <dd/mm/yy>	2.6. End of Experience <dd/mm/yy>

2.6. Causality/Relatedness Assessment by PI ☐ Certainly ☐ Probably ☐ Possibly ☐ Unlikely ☐ NOT RELATED	2.7. Rationale for the Causality Assessment
2.8. Action taken with investigational drug ☐ Continued unchanged ☐ Withdrawn ☐ Interrupted ☐ Dose reduced ☐ Dose increased ☐ Others (specify)	2.9. Did the event/reaction abate after stopping the investigational drug? ☐ Yes ☐ No ☐ Not Applicable
2.10. Did the event/reaction reappear after reintroduction of the drug? ☐ Yes ☐ No ☐ Not Applicable	2.11 Have urgent safety measures implemented? I ☐ Yes (*give details*) ☐ No (*explain/give reasons*) ☐ Not Applicable
2.12. Describe the event/reaction (*Summary of s/s, diagnosis. treatment start and stop dates, hospitalization start and stop dates, other relevant laboratory tests and findings, and medical history including concurrent and pre-existing conditions*)	

3. CONCOMITANT MEDICATION PRIOR TO EVENT/REACTION

Drug (*to include route of administration*)	**Daily Dose**	**Date Begun**	**Date Stopped**	**Reason for Use**

4. Is there a reasonable possibility that other medications contributed to the event/reaction?
   - ☐ Yes (*specify*)
   - ☐ No

5. Are there other possible contributory factors?
   - ☐ Yes (*specify*)
   - ☐ No

6. OUTCOME OF EVENT/REACTION

6.1. Outcome of the SAE
- ☐ Recovered/Resolved
- ☐ Recovered with sequelae (*specify*)
- ☐ Improving//Recovering/Resolving
- ☐ Deteriorating
- ☐ Not recovered/ Not resolved
- ☐ Death
- ☐ Unknown
- ☐ Others (specify)

6.2. If patient died, was an autopsy performed?
- ☐ Yes (*If Yes, provide date of autopsy <dd/mm/yy>*)
- ☐ No
- ☐ Unknown

6.3. Primary cause of death as determined by the autopsy (*if performed*)

I declare that the above information/statements are true and correct to the best of my knowledge.

_____

_____

Signature Over Printed Name of Principal Investigator *Date*

III. IEC RECOMMENDATION	Specifics
☐ NO FURTHER ACTION REQUIRED ☐ REQUEST INFORMATION *(indicate Information)* ☐ RECOMMENDED FURTHER ACTION *(indicate Action)* ☐ PENDING WITH MAJOR CLARIFICATION	
Reviewer ☐ Primary ☐ Secondary	_____ *Reviewer's Signature Over Printed Name* _____ *Date*

PROTOCOL AMENDMENT SUBMISSION (FORM 3B/V2/2015)

To the Principal Investigator:

An IEC approval must be secured before any protocol amendment can be implemented. It is important to complete and submit this form to fully evaluate its effect on the ethical and/or scientific acceptability of the study.

All amended documents must have the changes tabbed and highlighted, and must contain the revised version numbers and dates. A summary or tabulated detail of the changes, together with the page number or section where the changes can be found is further required.

Please obtain an electronic copy of this Form, fill-out the requested information, and make your submission both in electronic version and hard copy. Print in letter-sized paper with printer default set at A4.

I. PROTOCOL INFORMATION	**IEC Protocol Tracking No.**
Study Protocol No.	Protocol Approval Date: <dd/mm/yy>
Study Initiation Date: <dd/mm/yy>	Expected End Date: <dd/mm/yy>
Title:	Version Number, Date
Name of Principal Investigator	Contact Nos.:
Sponsor/CRO	
Study Site	
Type of Review (*To be determined by IEC*) ☐ Full Board ☐ Expedited	

NUMBER OF AMENDMENTS <number>	**AMENDMENT SUBMISSION DATE** <dd/mm/yy>
Amendment Summary	

I declare that the above information/statements are true and correct to the best of my knowledge.

_____ _____

Signature Over Printed Name of Principal Investigator *Date*

IEC RECOMMENDATION:	**Justification for the Recommendation:**
☐ APPROVAL ☐ MINOR MODIFICATIONS ☐ MAJOR MODIFICATIONS ☐ DISAPPROVAL	

Reviewer: ☐ Primary ☐ Secondary	_____ _____ *Reviewer's Signature Over Printed Name* *Date*

CONTINUING REVIEW APPLICATION (FORM 3C/V2/2015)

To the Principal Investigator:

To ensure continued protection of study participants, the IEC conducts a continuing review of previously approved protocols at intervals appropriate to the degree of risk involved, but at least annually.

Please be advised that no research-related activities may continue after the IEC approval has expired. To avoid lapse in approval, applications for continuing review must be filed 60 days prior to the expiry date of the current IEC approval.

Please obtain an electronic copy of this Form, fill-out the requested information, and make your submission both in electronic version and hard copy. Print in letter-sized paper with printer default set at A4.

I. PROTOCOL INFORMATION	**IEC Protocol Tracking No.**
Study Protocol No.	Protocol Approval Date: <dd/mm/yy>
Study Initiation Date: <dd/mm/yy>	Expected End Date: <dd/mm/yy>
Title:	Version Number, Date
Name of Principal Investigator	Contact Nos.:
Sponsor/CRO	
Study Site	
Type of Review (*To be determined by IEC*) ☐ Full Board ☐ Expedited	

II. INFORMATION REQUIRED	**CONTINUING REVIEW APPLICATION SUBMISSION DATE <dd/mm/yy>**
1 Status of the Study ☐ On-going ☐ Still open to additional enrollment ☐ Closed to additional enrollment, protocol-related interventions/treatments completed, study still active for long-term follow-up ☐ Remaining research activities limited to data analysis ☐ Others (specify)	

☐ Not started/Not Initiated (*state reasons*)
☐ Suspended (*state reasons*)
☐ Terminated/Canceled/Aborted (*PI should submit instead an Early Study Termination Application [DLSMHSI-IEC Form 3F/V1/2012]*))
☐ Closed/Completed (*PI should submit instead Final Report [DLSMHSI-IEC Form 3D/V1/2012])*

2. Since the last IEC review, have there been any amendments in the research design, methodologies, interventions, data analysis, participant population, recruitment procedures?
   ☐ No
   ☐ Yes (*explain/give reasons for the amendments, indicate dates of Protocol Amendment Submission and Approval, and append the IEC-approved amendments)*

3. Since the last IEC review, have any participating investigators been added or deleted?
   ☐ No
   ☐ Yes *explain/give reasons for the changes, provide the names of the study personnel, and indicate dates of Protocol Amendment Submission and Approval, and append the updated version)*

4. Since the last IEC review, have any new collaborating sites been added or deleted?
   ☐ No
   ☐ Yes (*explain/give reasons for the changes, enumerate the sites, and indicate dates of Protocol Amendment Submission and Approval, and append the updated version)*

5. Since the last IEC review, have there been any changes in the Informed Consent process/document?
   ☐ No
   ☐ Yes (*explain/give reasons for the changes, indicate dates of Protocol Amendment Submission and Approval, and append the updated version)*

6. Since the last IEC review, have all Informed Consents/Assents obtained from all research participants?
   ☐ No (*explain/give reasons)*
   ☐ Yes

7. Since the last IEC review, have any participants withdrawn from the study?
   ☐ No
   ☐ Yes (*append a summary describing the number and reasons for each of the participant's withdrawals)*

8. Summary of Protocol Participants

8.1. Accrual ceiling set by IEC	<number>
8.2. New participants accrued since last review/approval	<number>
8.3. Total participants accrued since study began	<number>
8.3.1. Active Patients	<number>
8.3.2. Patients Who have Completed the Study	<number>
8.4. Number of drop-outs	<number>
8.5. Withdraw	<number>
8.6. Death	<number>
9. Accrual Exclusions ☐ None ☐ Male ☐ Female ☐ Others (specify)	
10. Impaired Participants ☐ None ☐ Male ☐ Female	

☐ Others (specify)	

11. Since the last IEC review, have there been any SAEs that were not previously reported to the IEC?
    - ☐ No
    - ☐ Yes (*append a summary describing the number and nature of the SAEs)*

12. Since the last IEC review, have there been any unanticipated problems such as unresolved adverse events or deviations that were not previously reported to the IEC?
    - ☐ No
    - ☐ Yes (*append a summary describing the number and nature of the problems, adverse events, and minor deviations)*

13. Since the last IEC review, have there been any participant complaints that were not previously reported to the IEC?
    - ☐ No
    - ☐ Yes (*append a summary describing the number and nature of the complaints, and state whether they have been resolved or if not, specify the aspect(s) of the compliant that have not been resolved*

14. Since the last IEC review, has any new information emerged either from your study or from other sources that could alter IEC's previous risk-benefit assessment?
    - ☐ No
    - ☐ Yes (*append a summary of the new information)*

15. Since the last IEC review, have any changes been made in the data safety monitoring plan?
    - ☐ No
    - ☐ Yes (*append a summary of the changes, and state whether the changes are likely to affect*

16. Since the last IEC review, has there been new/additional investigational drug/device registrations associated with this study?
    - ☐ No
    - ☐ Yes (*indicate the registration information*)
        - ☐ IND
        - ☐ IDE

17. Since the last IEC review, have there been other changes that have not been mentioned?
    - ☐ No
    - ☐ Yes (*explain/give reasons for the changes, indicate dates of Protocol Amendment Submission and Approval, and append the updated version)*

18. Since the last IEC review, have there been any changes in the financial/non-financial interests of the study personnel which may be considered as Conflict of Interest?
    - ☐ No
    - ☐ Yes (*append a statement of disclosure)*

I declare that the above information/statements are true and correct to the best of my knowledge.

_____

_____

Signature Over Printed Name of Principal Investigator ***Date***

III. IEC RECOMMENDATION	Justification for the Recommendation
☐ UPHOLD ORIGINAL WITH NO FURTHER ACTION ☐ REQUEST INFORMATION (*specify information*) ☐ RECOMMEND FURTHER ACTION (*specify action*)	
Reviewer ☐ Primary ☐ Secondary	_____ _____ *Reviewer's Signature Over Printed Name* *Date*

FINAL REPORT
(FORM 3D/V2/2015)

To the Principal Investigator:

Please be advised that upon study completion or site closure, a Final Report must be submitted for review and approval. IEC retention period of study files is three (3) years following study closure.

Please obtain an electronic copy of this Form, fill-out the requested information, and make your submission both in electronic version and hard copy. Print in letter-sized paper with printer default set at A4.

I. PROTOCOL INFORMATION	**IEC Protocol Tracking No.**
Study Protocol No.	Protocol Approval Date: <dd/mm/yy>
Study Initiation Date: <dd/mm/yy>	Expected End Date: <dd/mm/yy>
Title:	Version Number, Date
Name of Principal Investigator	Contact Nos.:
Sponsor/CRO	
Study Site	
Type of Review (*To be determined by IEC*) ☐ Full Board ☐ Expedited	

II. INFORMATION REQUIRED	**FINAL REPORT SUBMISSION DATE** <dd/mm/yy>
	Response/ Comments
1. Continuing Review Application submission date and IEC recommendation	
2. Protocol Amendments, if any, and date(s) of approval	
3. Study Objectives	
4. Duration of the study	
5. Number of study arms	
6. Total number of participants approved for recruitment	

7. Total number of participants recruited	
8. Number of patients withdrawn, if any, and reason(s) for their withdrawal	
9. Number and nature of protocol deviations/violations, if any	
10. Were all SAEs reported to IEC? ☐ Yes ☐ NO (*provide a summary describing the number and nature of the unreported SAEs*)	
11. Summary of participant's queries, complaints/grievances, if any, regarding conduct of the study	
12. Difficulties encountered during the study (ie. unresolved/problematic AEs), if any	
13. Is data analysis complete? ☐ Yes ☐ NO (*explain/give reasons why data analysis is not yet complete*)	
14. Are the final results attached? ☐ Yes ☐ NO (*when will they be made available to IEC?)*	
15. Have there been any relevant publications/ conference presentations of study findings? ☐ No ☐ Yes (*provide details of the publications/presentations*)	
I declare that the above information/statements are true and correct to the best of my knowledge. _____ _____ ***Signature Over Printed Name of Principal Investigator*** ***Date:***	

III. IEC RECOMMENDATION	**Specifics**
☐ APPROVAL ☐ REQUEST INFORMATION ☐ RECOMMENDED FURTHER ACTION	
Reviewer ☐ Primary ☐ Secondary	_____ _____ ***Reviewer's Signature Over Printed Name*** ***Date***

NON-COMPLIANCE (Deviation/Violation) REPORT (FORM 3E/V1/2012)

To the Principal Investigator:

All major non-compliance with the conditions of IEC approval of the Protocol must be submitted not later than 7 days of discovery. Reports of minor/administrative deviations can be submitted with the Continuing Review Application. Failure to report major protocol deviations/violations promptly is in itself an instance of non-compliance.

If changes are made to the IEC-approved Protocol, such changes must be submitted as Protocol Amendment, and not as Protocol Deviation/Violation.

Please obtain an electronic copy of this Form, fill-out the requested information, and make your submission both in electronic version and hard copy. Print in letter-sized paper with printer default set at A4.

I. PROTOCOL INFORMATION	**IEC Protocol Tracking No.**
Study Protocol No.	Protocol Approval Date: <dd/mm/yy>
Study Initiation Date: <dd/mm/yy>	Expected End Date: <dd/mm/yy>
Title:	Version Number, Date
Name of Principal Investigator	Contact Nos.:
Sponsor/CRO	
Study Site	
Type of Review (*To be determined by IEC*) ☐ Full Board ☐ Expedited	

II. INFORMATION REQUIRED	**NON-COMPLIANCE REPORT SUBMISSION DATE** <dd/mm/yy>
1. Nature of the Report: ☐ **Minor Protocol Deviation -** A non-compliance with defined procedures, as described in the IEC-approved protocol, that poses no conceivable threat to participant safety or data integrity. This includes deviations that are administrative in nature. ☐ **Major Protocol Deviation/ Violation:** A non-compliance with defined procedures, as described in the IEC-approved protocol that impacts participant safety or data integrity. .	

2. Date of Protocol Deviation/ Violation: <dd/mm/yy>	Date Resolved: <dd/mm/yy>
3. Details of Protocol Deviation/Violation	
4. Details of corrective/preventive action taken by PI/ Sponsor	
5. Risk Assessment (*include impact on safety of participants, and on scientific/ ethical acceptability of the protocol*)	

I declare that the above information/statements are true and correct to the best of my knowledge.

I declare that the study is being conducted in keeping with the conditions of IEC approval of the Protocol.

_____ _____

Signature Over Printed Name of Principal Investigator ***Date:***

III. IEC RECOMMENDATION	**Specifics**
☐ UPHOLD ORIGINAL APPROVAL WITH NO FURTHER ACTION ☐ REQUEST INFORMATION ☐ RECOMMENDED FURTHER ACTION	
Reviewer ☐ Primary ☐ Secondary	_____ _____ ***Reviewer's Signature Over Printed Name*** ***Date***

EARLY STUDY TERMINATION APPLICATION (FORM 3F/V1/2012)

To the Principal Investigator:

Where the study is terminated/suspended before the expected end date, this Form must be submitted together with other relevant documents for consideration of the IEC.

Please obtain an electronic copy of this Form, fill-out the requested information, and make your submission both in electronic version and hard copy. Print in letter-sized paper with printer default set at A4.

I. PROTOCOL INFORMATION	**IEC Protocol Tracking No.**
Study Protocol No.	Protocol Approval Date: <dd/mm/yy>
Study Initiation Date: <dd/mm/yy>	Expected End Date: <dd/mm/yy>
Title:	Version Number, Date
Name of Principal Investigator	Contact Nos.:
Sponsor/CRO	
Study Site	
Type of Review (*To be determined by IEC*) ☐ Full Board ☐ Expedited	

II. INFORMATION REQUIRED	**EARLY STUDY TERMINATION APPLICATION SUBMISSION DATE** <dd/mm/yy>
INFORMATION REQUIRED	**RESPONSE/ COMMENTS**
1. Date of Last Continuing Review /Progress Report submitted to IEC	<dd/mm/yy>
2. Summary of Protocol Participants	
2.1. Accrual ceiling set by IEC	<number>
2.2. Total participants since the study begun	<number>
2.2.1. Active patients	<number>
2.2.2. Patients who have completed the study	<number>
2.3. Number of drop-outs	<number>

3. Summary of Results To Date
4. Reason for Termination/Suspension with Justification
I declare that the above information/statements are true and correct to the best of my knowledge. _____ _____ *Signature Over Printed Name of Principal Investigator* *Date*

III. IEC RECOMMENDATION	**Specifics**
☐ APPROVAL WITH NO FURTHER ACTION ☐ REQUEST INFORMATION ☐ RECOMMENDED FURTHER ACTION	
Reviewer ☐ Primary ☐ Secondary	_____ _____ *Reviewer's Signature Over Printed Name* *Date*

SITE VISIT REPORT (FORM 3G/V1/2012)

To the IEC Member:

Routine/for cause monitoring is part of the continuing oversight to ensure compliance with the conditions of the IEC approval of the protocol.

Please obtain an electronic copy of this Form, fill-out the requested information, and forward to the Secretariat both in electronic version and hard copy. Print in letter-sized paper with printer default set at A4.

I. PROTOCOL INFORMATION	**IEC Protocol Tracking No.**
Study Protocol No.	Protocol Approval Date: <dd/mm/yy>
Study Initiation Date: <dd/mm/yy>	Expected End Date: <dd/mm/yy>
Title:	Version Number, Date
Name of Principal Investigator	Contact Nos.:
Sponsor/CRO	
Study Site	

II. DATE OF SITE VISIT <dd/mm/yy> **DURATION OF VISIT** <hours> **START OF VISIT** <hh/mm> **END OF VISIT** <hh:mm>	**SITE VISIT REPORT SUBMISSION DATE** <dd/mm/yy>
INFORMATION REQUIRED	**RESPONSE/ COMMENTS**
1. Summary of Protocol Participants	
1.1. Accrual ceiling set by IEC	<number>
1.2. Total participants since the study begun	<number>
1.2.1. Active Patients	<number>
1.2.2. Patients who have completed the study	<number>
1.3. Number of drop-outs	<number>
2. Are site facilities appropriate? ☐ Yes ☐ NO (*explain/comment)*	
3. Was the latest IEC-approved version of the protocol used? ☐ Yes ☐ NO (*explain/comment)*	
4. Was the latest IEC-approved version of the ICFs used? ☐ Yes	

☐ NO (*explain/comment*)	
5. Were all other documents (e.g. data collection forms) used in accordance with the conditions of the IEC approval? ☐ Yes ☐ NO *explain/comment*)	
6. Were consent/assent obtained from the participants? ☐ Yes ☐ NO (*If No, explain/comment*)	
7. Were there any SAEs not previously reported to IEC? ☐ Yes ☐ NO (*explain/comment*)	
8. Were the SAEs reported to IEC within 7 working days and SAE resulting in death within 24 hours? ☐ Yes ☐ NO (*explain/comment)*	
9. Were there any protocol non-compliance (deviations/violations) not previously reported to the iEC? ☐ Yes ☐ NO (*explain/comment)*	
10. Were there any unanticipated problems, adverse events and minor deviation not previously reported to the IEC? ☐ Yes ☐ NO (*explain/comment)*	
11. Were there any participant complaints not previously reported to the IEC? ☐ Yes ☐ NO (*explain/comment)*	
12. Are study documents and investigating product(s) kept safe and secure? ☐ Yes ☐ NO (*explain/comment)*	
13. Overall, are participant's rights, safety and welfare adequately protected? ☐ Yes ☐ NO (*explain/comment)*	
14. Any outstanding result of the visit? ☐ Yes (*give details*) ☐ NO (*explain/comment)*	

I declare that the above information/statements are true to the best of my personal knowledge and belief.

_____ _____

Signature Over Printed Name of Visiting IEC Member ***Date***

ADVERSE EVENT SUMMARY REPORT (FORM 3H/V1/2012)

To the Principal Investigator:

Use this Form for adverse events that do not fall under the 7-working day reporting criteria (i.e. on-site adverse events that are <u>expected</u>, related and consistent with the frequency and severity listed in the protocol, informed consent and/or investigator's brochure, and for off-site adverse events that do not affect the safety profile of the study or will not result in any modification to the current risk section of the Protocol and Informed Consent)

This Form should be submitted as an attachment to the Continuing Review Application or, if applicable, Final Study Report.

Please obtain an electronic copy of this Form, fill-out the requested information, and make your submission both in electronic version and hard copy. Print in letter-sized paper with printer default set at A4.

I. PROTOCOL INFORMATION	**IEC Protocol Tracking No.**
Study Protocol No.	Protocol Approval Date: <dd/mm/yy>
Study Initiation Date: <dd/mm/yy>	Expected End Date: <dd/mm/yy>
Title:	Version Number, Date
Name of Principal Investigator	Contact Nos.:
Sponsor/CRO	
Study Site	
Type of Review (*To be determined by IEC*) ☐ Full Board ☐ Expedited	

COUNTRY/SITE	**DATE OF ONSET**	**ADVERSE EVENT**	**OUTCOME OF THE EVENT**	**WAS EVENT REPORTED DURING THE PAST APPROVAL PERIOD? IF *YES*, PROVIDE DATE OF REPORT**	**SPONSOR NOTIFICATION DATE (REQUIRED FOR IND/IDE STUDIES)**	**REMARKS**

I declare that the above information/statements are true and correct to the best of my knowledge.

_____ _____

Signature Over Printed Name of Principal Investigator *Date*

III. IEC RECOMMENDATION	**Specifics**
☐ UPHOLD ORIGINAL APPROVAL WITH NO FURTHER ACTION ☐ REQUEST INFORMATION ☐ RECOMMENDED FURTHER ACTION ☐ FORWARD TO SAE SUB-COMMITTEE	
Reviewer ☐ Primary ☐ Secondary	_____ _____ *Reviewer's Signature Over Printed Name* *Date*

QUERIES OR COMPLAINTS REPORT (FORM 3I/V1/2012)

To the IEC Member and Staff:

Please accomplish this Form to provide information on any queries or complaints concerning the conduct of an IEC-approved study and/or its investigators.

Please obtain an electronic copy of this Form, fill-out the requested information, and forward to the Secretariat both in electronic version and hard copy. Print in letter-sized paper with printer default set at A4.

I. PROTOCOL INFORMATION	**IEC Protocol Tracking No.**
Study Protocol No.	Protocol Approval Date: <dd/mm/yy>
Study Initiation Date: <dd/mm/yy>	Expected End Date: <dd/mm/yy>
Title:	Version Number, Date
Name of Principal Investigator	Contact Nos.:
Sponsor/CRO	
Study Site	
Type of Review (*To be determined by IEC*) ☐ Full Board ☐ Expedited	

II. QUERY/COMPLAINT INFORMATION	**RECEIVING DATE** <dd/mm/yy>
1. Query/Complaint received via: ☐ Telephone/Fax (<dd/mm/yy>) ☐ Mailed letter (<dd/mm/yy>) ☐ E-mail (<dd/mm/yy>) ☐ Walk-in (<dd/mm/yy> and <hh:mm>) ☐ Others (*specify*)	2. Relation to Study Protocol ☐ Study Participant ☐ Participant's Parent ☐ Participant's Legal Guardian/LAR ☐ Others (*specify*)

3. Information on Person Lodging the Query/Complaint		
3.1. Name	<Title, Name, Surname>	
3.2. Address		
3.3. Telephone	3.4. Mobile	3.5. E-mail.

4. What is raised?
   - ☐ Query (specify)
   - ☐ Complaint (specify)
   - ☐ Problem (specify)
   - ☐ Others (*specify*)

I declare that the above information/statements are true and correct to the best of my knowledge.

_____ _____

Signature Over Printed Name of IEC Member/Staff *Date*

III. IEC RECOMMENDATION	Specifics
☐ UPHOLD ORIGINAL APPROVAL WITH NO FURTHER AACTION ☐ REQUEST INFORMATION ☐ RECOMMENDED FURTHER ACTION	
Reviewer ☐ Primary ☐ Secondary	_____ _____ *Reviewer's Signature Over Printed Name* *Date*

CLOSE-OUT FORM (3D/V1/2015)

To the Principal Investigator:

Please be advised that upon study completion or site closure, a Close-out Report must be submitted for review and approval. IEC retention period of study files is three (3) years following study closure.

Please obtain an electronic copy of this Form, fill-out the requested information, and make your submission both in electronic version and hard copy. Print in letter-sized paper with printer default set at A4.

I. PROTOCOL INFORMATION	**IEC Protocol Tracking No.**
Study Protocol No.	Protocol Approval Date: <dd/mm/yy>
Study Initiation Date: <dd/mm/yy>	Expected End Date: <dd/mm/yy>
Title:	Version Number, Date
Name of Principal Investigator	Contact Nos.:
Sponsor/CRO	
Study Site	
Type of Review (*To be determined by IEC*) ☐ Full Board ☐ Expedited	

II. INFORMATION REQUIRED	**Close-Out REPORT SUBMISSION DATE** <dd/mm/yy>
	Response/ Comments
1. Continuing Review Application submission date and IEC recommendation	
2. Protocol Amendments, if any, and date(s) of approval	
3. Study Objectives	
4. Duration of the study	
5. Number of study arms	
6. Total number of participants approved for recruitment	

7. Total number of participants recruited	
8. Number of patients withdrawn, if any, and reason(s) for their withdrawal	
9. Number and nature of protocol deviations/violations, if any	
10. Were all SAEs reported to IEC? ☐ Yes ☐ NO (*provide a summary describing the number and nature of the unreported SAEs*)	
11. Summary of participant's queries, complaints/grievances, if any, regarding conduct of the study	
12. Difficulties encountered during the study, if any	

I declare that the above information/statements are true and correct to the best of my knowledge.

_____ _____

Signature Over Printed Name of Principal Investigator *Date:*

III. IEC RECOMMENDATION	**Specifics**
☐ NO FURTHER ACTION REQUIRED ☐ REQUEST INFORMATION ☐ RECOMMENDED FURTHER ACTION	
Reviewer ☐ Primary ☐ Secondary	_____ _____ *Reviewer's Signature Over Printed Name* *Date*

SAE SUBCOMMITTEE RECOMMENDATION FORM (FORM 3J/V1/2012)

I. PROTOCOL INFORMATION

IEC Protocol Tracking No:		Drug/Intervention:	
Study Protocol No:		Studies included:	
Study Initiation Date:		Phase of Study:	
Title:		Date of Report:	
Name of Principal Investigator:		Date of Meeting:	

II. SAE REPORT

Event no.	Event	Offsite/Onsite	Onset/Stop of AE	Date drug started/stopped	Age	Sex	Country/ Race	Co-morbid	CAI	CAS	Action	Reviewer's Causality Assessment

III. STUDY SAE STATISTICS

Total number of SAE	
No. of certain	
No. of probable	
No. of possible	
No. of unlikely	
No. of conditional	
No. of unclassifiable	
No. of deaths	
Item(s) in need of follow-up	

REVIEWERS:

NAME	SIGNATURE

IV. SAE SUBCOMMITTEE RECOMMENDATION(S)

AE SUBCOMMITTEE RECOMMENDS THE FOLLOWING ACTION(S):	REMARKS / COMMENTS / SPECIFICATIONS
☐ More information needed	
☐ No modification required, study to continue	
☐ Modification(s) needed in the following areas:	
o Inclusion/exclusion criteria for study participants	
o Informed consent to include a description of newly found risk	
o Other:	
☐ Implementation of additional procedure(s):	
o Screening procedure prior to start of new participant(s)	
o Monitoring procedure during the study period	
o Monitoring procedure after the study period	
o Other:	
☐ Suspension of:	
o enrolment of new participants	
o research procedure among current participants	
o entire study	