Supersedes:	Previous NCH-IRB SOPs
Prepared by:	2017 NCH-IRB SOP Committee
Reviewed by:	**NATIONAL CHILDREN'S HOSPITAL INSTITUTIONAL REVIEW BOARD (NCH-IRB)**
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Approval Date:	

3. MONITORING PROCEDURES

3.1. Review of Protocol Amendment
3.2. Review of Progress Report
3.3. Review of Final Report
3.4. Review of Serious Adverse Event
3.5. Review of Protocol Violation/Deviation
3.6. Responding to Participant's Request/Query
3.7. Study Site Visit
3.8. Review of Early Protocol Termination

See Appendix C

Form 3.1 Protocol Amendment Application Form
Form 3.2 Progress Report
Form 3.3 Closure/Final Report
Form 3.4 Onsite Serious Adverse Event Report
Form 3.5 Protocol Violation/Deviation Report
Form 3.6 Query/Complaint Record
Form 3.7 Study Visit Site Report
Form 3.8 Early Study Termination Application

3.1. REVIEW OF PROTOCOL AMENDMENTS

3.1.1. Purpose

To describe the NCH-IRB review procedure for amendments of the protocol and related documents

3.1.2. Scope

This SOP applies to previously approved study protocols and related documents that are being amended later and submitted for approval to the NCH-IRB. Any amendment of the study related documents may not be implemented until reviewed and approved by the NCH-IRB.

3.1.3. Responsibilities

It is the responsibility of the NCH-IRB Secretariat to manage protocol amendment package submitted by the PI.

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

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

3.1.4. Process Flow/Steps

NO.	ACTIVITY	PERSON/S RESPONSIBLE	TIMELINE
1	Receive the protocol amendment package and check its completeness Verify NCH-IRB approval of the initial protocol submission.	Staff	Review of protocol amendments should be completed within 14 days when done through expedited review of minor protocol amendments. It may take longer for major amendments
2	Determine type of review and identify primary reviewers	Chair and Secretariat	
3	Forward amendment package to primary reviewers	Staff	
4	Discuss major amendment or report the expedited review results to the NCH-IRB during full board meeting	Members	
5	Communicate NCH-IRB decision to PI	Secretariat	
6	File documents & update protocol file index and the protocol database	Staff	

			depending on the schedule of full board meeting.

3.1.5. Detailed Instructions

3.1.5.1. Receive the protocol amendment package and check its completeness

- The NCH-IRB should properly inform the principal investigator to submit an application for amendment whenever there is any change regarding the composition of the study team, the study site, the protocol and related documents that it previously approved using the Protocol Amendment Submission Form.
- The NCH-IRB Staff verifies NCH-IRB approval of the initial protocol submission
- The NCH-IRB Staff checks the completeness of the protocol amendment package submitted by the PI. Staff also verifies whether the Protocol Code No. and forms used are correct.
- The NCH-IRB Staff records the submission in the protocol database.

3.1.5.2. Determine type of review & identify primary reviewers

- NCH-IRB Chair/Member Secretary reviews document to determine whether amendment is major or minor.
- Major protocol amendments: increased risk to study participants and require full board review. These include but are not limited to the following:
  - Modification of treatment – addition or reduction of treatments
  - Any changes in inclusion/exclusion criteria
  - Change in study design
  - Additional treatment/s or the deletion of treatment/s
  - Change in method of dosage formulation, such as, oral to intravenous
  - Significant change in the number of subjects
  - Significant decrease or increase in dosage amount
  - Any other changes that will entail more than minimal risk.

- Minor protocol amendments: those which are unlikely to compromise the integrity of the research or the welfare and rights of the participants and present no new ethical issues; and changes that are administrative in nature can be expedited.
- NCH-IRB Staff identifies the Primary Reviewers who did the initial review.

- If Primary Reviewers are not available to do the review, NCH-IRB Chair and/or Member-Secretary do the review provided they do not have COI. Otherwise the Chair designates qualified members to do the review.

3.1.5.3. Forward amendment package to primary reviewers

- NCH-IRB Staff prepares protocol amendment package; photocopies relevant documents of previous review/s of the protocol that will provide the Primary Reviewers with background information that will facilitate the assessment of the proposed amendment/s.
- Better still, the Primary Reviewers should go to the NCH-IRB office to review the pertinent documents in the protocol file and determine whether the proposed changes in the protocol will cause a change in the risk-benefit ratio of the approved protocol.
- NCH-IRB Staff records the protocol amendment package in the Log for Outgoing Documents
- NCH-IRB Staff sends the protocol amendment package and relevant documents of previous review/s with the Notice of Review to the Primary Reviewer/s at least 14 days before the full board meeting.
- The Primary Reviewer or his/her alternate reviews the amended documents and compares them with the previously NCH-IRB - approved documents in the protocol file folder to assess if the proposed amendment/s would alter the risk/benefit ratio and to make appropriate recommendations using the NCH-IRB-part of Protocol Amendment Submission Form
- Major protocol amendments are reviewed by full board while minor protocol amendments are reviewed by expedited review by the Primary Reviewers/Chair/Member-Secretary.

3.1.5.4. Discuss the amendment or report the review result to the NCH-IRB during full board meeting

FOR MAJOR PROTOCOL AMENDMENT

- The Primary Reviewer or his/her alternate presents the results of the review to the NCH-IRB during full board meeting.
- The NCH-IRB decides whether or not there is a need for the PI to clarify, elaborate or explain further the amendment/s. The following are possible review decisions of the Board:
  - Approval
  - Recommend major changes to the protocol/Informed Consent Form
  - Recommend minor changes to the protocol/Informed

Consent Form
- Disapproval

FOR MINOR PROTOCOL AMENDMENT

- The Primary Reviewer or his/her alternate submits the results of the review using the for-NCH-IRB portion of the Application Form for Amendment.
- The review decision is reported to the NCH-IRB during the meeting.

3.1.5.5. Communicate NCH-IRB decision to PI

- Refer to SOP on Communicating NCH-IRB Decision to PI
- NCH-IRB Staff prepares Notification of NCH-IRB Decision/ Approval for Protocol Amendment, for signature of NCH-IRB Chair.
- If the amendment is approved, the PI is requested to submit an amended copy of the study protocol or protocol related document with an updated version no. and date.
- NCH-IRB Staff sends the notification to the PI.

3.1.5.6. File documents and update protocol file index and the protocol database

- NCH-IRB Staff ensures that the version no. and date marked on the amended document are correct.
- NCH-IRB Staff stamps the amended protocol or protocol-related document "AMENDMENT-APPROVED" with the approval date.
- NCH-IRB Staff keeps a copy of all protocol amendment related documents in the protocol file folder and updates the protocol file index.

3.2. REVIEW OF PROGRESS REPORTS

3.2.1. Purpose

To describe the NCH-IRB review procedures for progress report for renewal/continuing review of NCH-IRB approval.

3.2.2. Scope

This SOP provides instructions for the review of progress reports that are required by the NCH-IRB to be submitted by the principal investigator to monitor the safety of participants enrolled in a study.

The annual report becomes the basis for continuing review of protocols the approval of which needs to be renewed every year.

This SOP applies to the conduct of any continuing review of study protocols involving human subjects at intervals appropriate to the degree of risk but not less than once a year. Depending upon the degree of risk to the participants, the nature of the studies, and the vulnerability of the study participants and duration of the study, the NCH-IRB may require more frequent submission of progress report.

3.2.3. Responsibility

It is the responsibility of the NCH-IRB Secretariat to remind investigators two months before to submit the progress reports one month before the due date, to forward the reports to the primary reviewers for review, and to communicate NCH-IRB decision to the PI.

It is the responsibility of the Primary Reviewers to review the reports to check completeness of the information and ensure that it is in accordance with the protocol and related documents approved by the NCH-IRB.

3.2.4. Process Flow/Steps

NO.	ACTIVITY	PERSON/S RESPONSIBLE	TIMELINE
1	Receive the progress report package and check its completeness	Staff	Review of protocol progress reports should be completed within 14 days when done through expedited review. It may take longer for full board review depending on the schedule of
2	Determine type of review and identify primary reviewers	Chair/ Member-Secretary	
3	Forward progress report to primary reviewers for review	Staff	
4	Discuss the progress report or report expedited review result to the NCH-IRB during full board meeting	Members	

5	Communicate NCH-IRB decision to PI	Staff	the full board meeting.
6	File documents and update protocol file index and protocol database		

3.2.5. Detailed Instructions

3.2.5.1. Receive the progress report package and check its completeness

- The NCH-IRB Staff periodically checks the protocol database to track due dates of progress reports of study protocols approved by the NCH-IRB.
- The NCH-IRB Staff prepares and sends reminder letter addressed to the PI two months before the due date of the report.
- For studies of long term duration *(more than 3 years)*, the PI and the rest of the study team are required to submit evidence of updated Good Clinical Practice (GCP) Training.
- The continuing review application package shall include the accomplished Progress Report Form with the informed consent document currently in use.
- The NCH-IRB Staff checks the completeness of submitted application for review package and whether the Protocol Code No. and the form used are correct.
- The NCH-IRB Staff records the submission in the protocol database.

3.2.5.2. Determine type of review & identify primary reviewers

- The continuing review of protocol initially reviewed at full board is again reviewed at full board.
- The NCH-IRB Staff identifies the primary reviewers who did the initial review.
- If Primary Reviewers are not available to do the review, the NCH-IRB Chair and/or Secretary may review provided they do not have COI. Otherwise, the Chair designates qualified members to do the review.

3.2.5.3. Forward progress report to primary reviewers for review

- NCH-IRB Staff photocopies relevant documents of previous review/s of the protocol such as current approved versions of the protocol, informed consent forms (ICF), protocol amendments, protocol deviations and on-site SAEs/SUSARs since the last continuing review. They will provide the Primary Reviewer/s with background information to facilitate the assessment of risk-benefit ratio. Better still, the Primary Reviewers should go to the NCH-IRB

office to review pertinent documents in the protocol file folder and determine whether there is a change in the risk-benefit ratio.

- The NCH-IRB Staff sends the Progress Report package for full board review to the primary reviewers and other members at least 14 days before full-board meeting.
- Primary reviewers conduct continuing review of progress/annual report if they are in accordance with the protocol and related documents approved by the NCH-IRB.
- Primary reviewers refer to documents in the protocol file folder to check compliance with the latest NCH-IRB approved protocol and ICF.
- In the review of the progress/annual report, the following are the key evaluation points:
- Risk Assessment
  i. The risks to the subjects are minimized
  ii. The risks to the subjects are reasonable in relation to anticipated benefits, if any, and the importance of the knowledge that may be expected to be gained from the study.

- Adequacy of Informed Consent
  i. Informed consent/Assent forms *(current or most recent)*
  ii. Appropriate, new significant findings since the last continuing review that may be related to the subjects' willingness to continue participation provided to enrolled subjects *(e.g., important toxicity or adverse event information)*

- Local Issues
  i. Changes in the investigator's situation or qualifications *(e.g., suspension of hospital privileges, medical license; involvement in numerous clinical trials)*
  ii. Evaluation, investigation and resolution of complaints related to the research, if any
  iii. Changes in the acceptability of the proposed research in terms of institutional commitments *(e.g., personnel and financial resources, adequacy of facilities) and regulations, applicable national law, or standards of professional conduct of practice.)*
  iv. Report from third party observation of the research *(including the informed consent process)* carried out
  v. Investigator concerns about trial conduct at the local site *(e.g., study coordinator ineffectiveness, inability of subjects to understand sections of the informed consent document required by institutional policies)*, if any.

- Trial Progress
  i. Start date of the study and expected duration
  ii. Total subject enrollment
    a. Expected enrollment
    b. Actual enrollment
    c. Enrollment issues

  iii. Subject withdrawal
    a. Number of subjects who withdrew
    b. Lost to follow-up
    c. Summary of reasons for withdrawal at local site

- The NCH-IRB may also request the Principal Investigator to provide additional information, when necessary.
- The Primary Reviewer/s must complete the review within 14 days prior to the NCH-IRB meeting.

3.2.5.4. Discuss the progress report or report expedited review results to the NCH-IRB during full board meeting

FOR FULL BOARD REVIEW OF PROGRESS REPORT:

- The NCH-IRB Secretariat collates the comments of the Primary Reviewers and includes the application for renewal of NCH-IRB approval in the agenda.
- The protocol file folder for continuing review, including relevant NCH-IRB meeting minutes, should be made available during the meeting.
- During the meeting, the Primary Reviewers present a summary of the progress of the research, any significant issues and their recommendation to full-board.
- The NCH-IRB members determine the need for the investigator to elaborate, explain or clarify any aspect of the progress/annual report as deemed necessary.
- The following are the possible NCH-IRB decisions for continuing review:
  - Renew approval
  - Request additional information
  - Recommend modification
  - Suspend:
    - enrollment of new subjects
    - research procedures in currently enrolled subjects
    - entire study

  - Disapprove renewal

- Approval of progress report reviewed by the Primary Reviewers by expedited procedure is reported to the board meeting by the Chair/Member-Secretary.

3.2.5.5. Communicate NCH-IRB decision to PI

- The NCH-IRB Secretariat takes note of the decision and/or discussion during the board meeting in the meeting minutes and communicates with the PI if further action is required.
- NCH-IRB Staff prepares Notification of NCH-IRB Decision– Progress/Annual Report for signature of NCH-IRB Chair.
- NCH-IRB Staff sends the notification to the PI

3.2.5.6. File documents and update protocol file index and protocol database

- NCH-IRB Staff keeps the continuing review application package together with the review comments of the primary reviewer/s in the protocol file folder and updates the protocol file index.
- NCH-IRB Staff updates the protocol database.

3.3. REVIEW OF FINAL REPORT

3.3.1. Purpose

To describe the NCH-IRB review procedures for final reports.

3.3.2. Scope

This SOP provides instructions for the review of final reports that are required by the NCH-IRB to be submitted by the principal investigator when the approved study is completed or when the study site is closed. The final report, when approved by the NCH-IRB, becomes the basis for initiation of the archiving procedure. This SOP applies to the review of final/closure report of a study protocol approved by the NCH-IRB.

3.3.3. Responsibility

It is the responsibility of the NCH-IRB Staff to identify study protocols whose final reports are due.

It is the responsibility of the Primary Reviewers to review the reports to check completeness of information and to ensure that the data are in accordance with the protocol and other related documents approved by the NCH-IRB.

3.3.4. Process Flow/Steps

NO.	ACTIVITY	PERSON/S RESPONSIBLE	TIMELINE
1	Receive the final report package and check its completeness	Staff	Review of final report should take place within 14 days except when there is a delay due to the schedule of the full board meeting
2	Identify primary reviewers	Chair/Secretary	
3	Forward final/closure report to primary reviewers for review	Staff	
4	Approve the final/closure report during NCH-IRB full board meeting	Members	
5	Communicate NCH-IRB decision to PI	Secretariat	
6	File documents & update protocol file index and protocol database	Staff	

3.3.5. Detailed Instructions

3.3.5.1. Receive the final report package and check its completeness

- The submission shall include the accomplished Progress Report and the Final Report forms.
- The NCH-IRB Staff verifies the completeness of the submission and whether the Protocol Code No. and the forms used are correct.

3.3.5.2. Identify primary reviewers

- The NCH-IRB Staff identifies the Primary Reviewers of the protocol from the protocol database.
- If the Primary Reviewer is not available, the review is done either by the NCH-IRB Chair/Member-Secretary, or qualified Member/s designated by the Chair/Member-Secretary.

3.3.5.3. Forward final/closure report to primary reviewers for review

- The NCH-IRB Staff records the Closure/Final Report package together with the Notice of Review and a copy of the latest version of the protocol in the Log of Outgoing Documents.
- The Closure/Final Report package is forwarded to the primary reviewer/s at least 14 days before the full board meeting.
- The Primary Reviewer/s accomplish the review by commenting and recommending appropriate action on the Closure/Final Report form.
- Primary Reviewer signs and dates the form and returns the Closure/Final Report package to the NCH-IRB Staff.

3.3.5.4. Approve the final/closure report during full board meeting

- The Primary Reviewer presents the results of the review.
- The NCH-IRB decision can be any of the following:
  - Acknowledged/Accepted
  - Request for further information, specify
  - Recommend further action, specify

3.3.5.5. Communicate NCH-IRB decision to PI

- The Secretariat takes note of the decision and/or discussion during the board meeting in the meeting minutes and communicates with the PI if further action is required.
- The NCH-IRB Staff prepares Notification of NCH-IRB Decision – Review of Closure/Final Report for signature of the REC Chair.
- The NCH-IRB Staff sends the notification to the PI

3.3.5.6. File documents and update protocol file index and protocol database

- The NCH-IRB Staff files the accomplished, signed and dated Closure/Final Report and other related document in the protocol file folder and updates the protocol file index.
- Upon approval of the Closure/Final Report, the study protocol is classified as inactive, the Protocol Code No. is updated and the protocol file folder re-labelled and transferred to storage cabinet for inactive files
- NCH-IRB Staff updates the protocol database.

3.4. REVIEW OF SERIOUS ADVERSE EVENTS

3.4.1 Purpose

To describe the NCH-IRB review procedures for serious adverse events

3.4.2 Scope

This SOP applies to the review of SAE and SUSAR reports submitted by investigators and sponsors to the NCH-IRB to comply with ICH GCP. The NCH-IRB reviews such reports to determine appropriate action to protect the safety of participants in an approved study.

ICH-GCP E6 defines a serious adverse event (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 suspected unexpected serious adverse reaction (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.

3.4.3 Responsibilities

The Chair assigns the Primary reviewers and designate other members to conduct an appropriate review of onsite SAE and SUSAR reports to ensure oversight over the safety of participants enrolled in the study. The NCH-IRB should also:

- Make sure that researchers are made aware of its policies and procedures concerning SAE reporting.
- Set up the necessary mechanisms to receive SAE and SUSAR reports from investigators of researches that it has approved.
- Review SAE and SUSAR reports from other sites within and outside the country to be updated about safety issues related to the protocols that it has approved.

3.4.4 Process Flow/Steps

NO.	ACTIVITY	PERSON/S RESPONSIBLE	TIMELINE
1	Receive SAE/SUSAR Report	Staff	14 days
2	Determine type of review and forward SAE Reports to	Chair/Member-Secretary	

	appropriate reviewers		
3	Assign the primary reviewers and designate members to conduct the review	Chair	
4	Review on-site and off-site SAEs	Primary Reviewers/ Designated Members	
5	Discuss on-site SAE reports at full board to ensure patient safety	Members	
6	Communicate decision to PI	Secretariat	
7	File documents in protocol file folder and update SAE database	Staff	

3.4.5. Detailed Instructions

3.4.5.1 Receive SAE/SUSAR Report

- The NCH-IRB Staff checks submitted documents for completeness and whether Protocol Code Number and form used are correct.
- The NCH-IRB Staff classifies the SAE/SUSAR reports according to their origin or sites where they happened: on-site or off-site *(within or outside the country).*

3.4.5.2. Determine type of review and forward SAE Reports to appropriate reviewers

- On-site SAEs and SUSARs are reviewed by the Primary Reviewer/s or by SAE Committee or by suitable members designated by the Chair/Member-Secretary if the Primary Reviewer is not available to do the review.
- Off-site SAEs are reviewed through expedited process by an NCH-IRB designated member *(preferably, a pharmacist or a pharmacologist)* or SAE Committee to note the trends in SAE occurrence.
- NCH-IRB Staff identifies the Primary Reviewer of the protocol and prepares the SAE Report package with Notice to Reviewer for forwarding to the Primary Reviewer/s.
- The NCH-IRB forwards the SAE Report to the Primary Reviewer/s or designated Member/s at least 14 days before the full board meeting.
- Primary Reviewer or designated Member recommends appropriate action to be done by the NCH-IRB.

3.4.5.3. Assign the primary reviewers and designate members to conduct the review

The NCH-IRB Chair assigns the primary reviewers and designate members to conduct the review.

3.4.5.4. Review on-site and off-site SAEs

- The NCH-IRB should adopt appropriate response depending on the site where the SAE/SUSAR happened.
- For SAEs that occur onsite, the NCH-IRB should analyze the investigator/sponsor's assessment *(related, unexpected):*
  - Assessment of the SAE is unlikely or unrelated to the study drug or article: The report is forwarded to the Chair for review and determination if the report should be reviewed at the convened meeting by full board.
  - Assessment of the SAE is definitely, possibly, or probably related to the study drug or article: The report is added to the agenda for review at a convened meeting by full board meeting.
  - Assessment of the SAE is unexpected/unanticipated and definitely, possibly, or probably related to the study drug or article: The report is added to the agenda for review at a convened meeting by full board meeting.

- For multicenter, international studies, note the trend of occurrence of SAE/SUSAR in study sites in foreign counties and other local sites. For multicenter, national studies, note the nature (related or expected) of the SAE/SUSAR.

3.4.5.5. Discuss on-site SAE reports at full board to ensure patient safety

- Primary reviewers or designated member/s present the results of review to full-board.
- Full-board discusses on-site SAEs and its impact to patient safety.
- After deliberation NCH-IRB decides on appropriate action as follows:
- Request an amendment to the protocol or consent form
- Request further information
- Suspension of:
  - Enrollment of new research participants until further review by the NCH-IRB
  - All trial-related procedures *(except those intended for the safety and well-being of the participants)* until further review by the NCH-IRB

- Termination of the study

- Take note and continue monitoring
- Conduct Study Site Visit
- Designated member reports trends in off-site SAEs for full board information. This will be reported on a quarterly basis to full board.

3.4.5.6. Communicate decision to PI

- NCH-IRB Staff prepares Notification of NCH-IRB Decision about SAE Report, for NCH-IRB Chair's signature**.**
- Forward the notice to the PI.

3.4.5.7. File documents in protocol file folder and update SAE database

- NCH-IRB Staff files the documents in the protocol file folder and updates the protocol file index.
- NCH-IRB Staff encodes the SAE or updates the SAE Database.

3.5 REVIEW OF PROTOCOL VIOLATION/PROTOCOL DEVIATION

3.5.1 Purpose

To describe the NCH-IRB review procedures for protocol violation/deviation

3.5.2 Scope

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

- It includes investigators who fail to comply with the procedures in the approved protocol or to comply with national/ international guidelines for the conduct of human research, including those who fail to respond to the NCH-IRB's requests.
- It also covers action taken by the NCH-IRB related to protocol violation/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 NCH-IRB.

3.5.3 Responsibility

It is the responsibility of the NCH-IRB Staff to receive protocol violation/deviation reports submitted to the NCH-IRB. It is the responsibility or the NCH-IRB Chair or Member-Secretary or Primary Reviewer to take action related to protocol violation/deviation.

3.5.4 Process Flow/Steps

NO.	ACTIVITY	PERSON/S RESPONSIBLE	TIMELINE
1	Receive Protocol Violation/Deviation Report	Staff	14 days
2	Forward Protocol Violation/Deviation Report to Primary Reviewers		
3	Discuss/report during full board meeting for decision/information	Members	
4	Communicate decision to PI	Staff	
5	File documents in protocol file folder and update protocol database		

3.5.5. Detailed instructions

3.5.5.1. Receive Protocol Violation/Deviation Report

- Reports of protocol deviation/violation may come directly from the PI, or as result of study site monitoring by the Clinical Monitor/Sponsor or the NCH-IRB Site Visit Team, or from related documents received by the NCH-IRB.
- The NCH-IRB Members performing monitoring of the research

study at the trial site may detect protocol violation/deviation if the implementation of the research is not conducted as per approved protocol or institutional, national or international standards.

- It is the responsibility of the Principal Investigator to determine whether a protocol violation/deviation is major or minor, and ensure proper reporting to NCH-IRB. If the PI is unsure whether the variance is a violation or deviation she should seek advice from the sponsor to ensure appropriate action is taken.
- The NCH-IRB Staff checks submitted documents for completeness and whether Protocol Code Number and form used are correct.
- The NCH-IRB Staff records the report in the Log of Incoming Documents.

3.5.5.2. Forward Protocol Violation/Deviation Report to Primary Reviewers

- Major protocol violation/deviation is a persistent protocol noncompliance with potentially serious consequences that could put patients' safety at risk or critically affect data analysis
- Minor protocol deviation is a non-systematic protocol noncompliance with minor consequences, in terms of its effect on the participant's/subject's rights, safety or welfare, or the integrity of study data; includes deviations that are administrative in nature
- Protocol violation in a research study should be discussed at Full Board meeting.
- The NCH-IRB Secretariat includes the Protocol Violation/Deviation Report in the meeting agenda for the month.
- The NCH-IRB Chair refers the Protocol Violation/Deviation Report to the Primary Reviewers at initial review.

3.5.5.3. Forward Protocol Violation/Deviation Report to appropriate NCH-IRB Member/s

- The NCH-IRB Staff records the report and forwards the package to the Primary Reviewer/s within 14 days before the full board meeting.
- Primary Reviewer/s assess if the protocol violation/deviation impacts on patient safety or the integrity of the data.
- The assigned primary reviewer/s complete their review and recommend corrective actions, if any within 14 days after receipt.
- Forward their assessment to the Secretariat.
- The result of the review decision is reported to full board for discussion.

3.5.5.4. Discuss/report to full board for information or appropriate action

- The Primary Reviewers present the result of their assessment to full board that deliberates the effects of the protocol violation/deviation on the rights and safety of research participants or integrity of data.
- Possible decisions are as follows:
  - Acknowledged – no further information or action required
  - Additional information required – additional information is needed in order to properly evaluate the violation
  - Correction and/or corrective actions are required. The NCH-IRB must specify the corrective measures to prevent harm to current and future research participants.

3.5.5.5. Communicate decision to PI

- NCH-IRB Staff prepares the Notification Letter for signature of the NCH-IRB Chair.
- If correction and/or corrective action are required from the PI, the PI is requested to provide the information within two weeks.
- A site visit may also be required by the NCH-IRB.

3.5.5.6. File documents in protocol file folder and update protocol database

- NCH-IRB Staff checks if Protocol Violation/Deviation Report is completely accomplished, signed and dated by Primary Reviewers and file the document in the protocol file folder, and updates the protocol file index.
- Filed documents should also include the Study Site Monitoring Visit Report, if a post-review study site visit was conducted.
- Record the protocol violation/deviation in the protocol violation/deviation database to facilitate tracking of repetitive violations/deviations of the same nature.

3.6. RESPONDING TO PARTICIPANTS' REQUESTS/QUERIES

3.6.1. Purpose

To describe the NCH-IRB procedures related to research participants' requests and/or queries

3.6.2. 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 NCH-IRB.

3.6.3. Responsibility

A NCH-IRB Staff is responsible for receiving participant queries and requests related to their participation, refers relevant issues to the NCH-IRB Chair to take appropriate action. The Secretariat keeps records of all action taken by the NCH-IRB.

3.6.4. Process Flow/Steps

NO.	ACTIVITY	PERSON/S RESPONSIBLE	TIMELINE
1	Receive the complaint or inquiry	Staff	14 days
2	Review the complaint/inquiry	Chair/ Member-Secretary	
3	Discuss in convened meeting or report the decision/action taken to full board	Members	
4	Communicate NCH-IRB's response	Staff	
5	File pertinent documents		

3.6.5. Detailed Instructions

3.6.5.1. Receive the complaint or inquiry

- Study protocol-related complaints and inquiries may come from research participants, or other parties.
- The NCH-IRB Staff receives the complaint.
- The NCH-IRB Staff may assist to put the complaint in writing especially if the complainant or inquiring party is a research participant.
- The NCH-IRB Staff refers the complaint or inquiry to the Chair/Member-Secretary for appropriate action.
- NCH-IRB Staff records the submitted document in the Log of Incoming Documents.

3.6.5.2. Review the complaint/inquiry

- The NCH-IRB Chair or Member-Secretary reviews the complaint.
- The PI may be contacted to provide clarification or further

information.

3.6.5.3. Discuss in a convened meeting or report the decision/action taken to full board

- The Chair presents a serious complaint to full board for discussion.
- The NCH-IRB members discuss to take appropriate actions.

3.6.5.4. Communicate NCH-IRB's response

The NCH-IRB Staff Secretariat prepares response to inquiry complaint within 14 days from the time of review.

3.6.5.5. File pertinent documents

- The NCH-IRB Staff files the accomplished **Form 3.6** together with the letter of inquiry/complaint and excerpts of the meeting minutes when this was deliberated or reported in the protocol file folder.
- The NCH-IRB Staff updates the protocol file index.

3.7. SITE VISITS

3.7.1. Purpose

To describe the NCH-IRB procedures related to the conduct of site visits

3.7.2. Scope

This SOP applies to any visit made in any study site, on behalf of the NCH-IRB, to check compliance with NCH-IRB approved protocol and related documents, and national and international standards.

3.7.3. Responsibility

It is the responsibility of the NCH-IRB to conduct study site monitoring for cause or routine.

NCH-IRB Members may recommend that a particular study site be visited.

The NCH-IRB Chair/Member-Secretary selects members of the study site visit team.

3.7.4. Process Flow/Steps

NO.	ACTIVITY	PERSON/S RESPONSIBLE	TIMELINE
1	Recommend study site to visit	Members	
2	Select study site to visit	Chair	7 days
3	Create Study Site Visit Team	Chair/ Member-Secretary	
4	Prepare Study Site Visit Plan	Study Site Visit Team	
5	Notify PI of date of site visit	Staff	
6	Conduct site visit and debrief study team	Study Site Visit Team	14 days
7	Present findings during full committee meeting		
8	Communicate results of site visit and recommended actions, if any to PI	Staff	
9	File pertinent documents		

3.7.5. Detailed Instructions

3.7.5.1. Select study site to visit

- The NCH-IRB Members may recommend to visit study sites for any of the following reasons: frequent occurrence of SAE, protocol violations, failure to submit progress reports, complaints about PI performance.

- Visits may also be conducted to monitor implementation of risky protocols, PI with many ongoing studies or inexperienced PIs.
- Study site visit may be conducted upon recommendation of Primary Reviewers.

3.7.5.2. Create Study Site Visit Team

- The NCH-IRB Chair/Member Secretary selects members of Study Site Visit Team and designates the Team Leader. Members should include the Primary Reviewers.
- The Site Visit Team members are formally informed of their assignment.
- The NCH-IRB Staff prepares the Study Site Visit package consisting of the latest version of the approved protocol and informed consent documents, and other relevant documents, *(like protocol deviation reports, on-site SAEs/SUSARs - initial and follow-up reports)* and a copy of the Study Site Visit Report Form.

3.7.5.3. Prepare Study Site Visit Plan

- The Study Site Visit Team prepares the Study Site Visit Plan that includes the following:
  - Date and time of the planned visit
  - Members of the Study Site Visit Team
  - Objectives of the Visit
  - Documents to be reviewed
  - Persons to be interviewed

- The Study Site Visit Team, in consultation with the NCH-IRB Chair, is given access to documents in the protocol file folder of a study for monitoring. The Team may also photocopy some parts of the files *(like advertisement materials, the informed consent form (ICF), case report form)* for comparison with the documents used in the study site.

3.7.5.4. Notify PI of date of site visit

The NCH-IRB Staff prepares the letter informing the PI of the planned study site visit for signature by the NCH-IRB Chair. Attached to the letter is the Study Site Visit Plan and the Study Site Visit Report form.

3.7.5.5. Conduct site visit and debrief study team

- The Study Site Visit Team conducts the site visit as per the Study Site Visit Plan. Additional guide in the conduct of the visit is the Study Site Visit Report Form
- At the end of the visit, the Study Site Visit Team presents the findings to the Study Team and solicits feedback.

- The Study Site Visit Team completes the Study Site Visit Report Form
- Conflicting findings should be resolved by consensus.
- The report is submitted to the NCH-IRB Staff within 14 calendar days from the date of the visit.
- NCH-IRB Staff logs the submission in the Log of Incoming Documents.
- The NCH-IRB Secretariat includes the presentation of the study site visit report in the meeting agenda.

3.7.5.6. Present findings during full committee meeting

- The Study Site Visit Team presents the report during the full committee meeting.
- The NCH-IRB makes a determination whether the rights, safety and welfare of research participants are compromised and appropriate recommendations to the PI, if any.

3.7.5.7. Communicate results of site visit and recommended actions, if any to PI

- Based on the minutes of the meeting, the NCH-IRB Staff prepares the Notification Letter – Study Site Visit for signature of the NCH-IRB Chair.
- The PI may be requested to provide additional information or documents or implement corrective actions.

3.7.5.8. File pertinent documents

The NCH-IRB Staff files the Study Site Visit Report, excerpt of the minutes of the meeting when report was discussed and the Notification Letter *(including the response from the PI, if any)* in the protocol file folder and update the protocol file index.

3.8. EARLY PROTOCOL TERMINATION

3.8.1. Purpose

To describe the NCH-IRB procedures related to early termination of protocol implementation

3.8.2. Scope

This procedure describes how the NCH-IRB proceeds and manages the premature or early termination 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, PI, by the NCH-IRB itself or other authorized bodies

3.8.3. Responsibility

It is the responsibility of the NCH-IRB to act on any early protocol termination application. It is also the responsibility of the NCH-IRB 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 committee for appropriate action.

The NCH-IRB Secretariat is responsible for the receipt and management of the termination documentation. The primary reviewers review the reasons for early termination and make a recommendation to full committee.

3.8.4. Process Flow/Steps

NO.	ACTIVITY	PERSON/S RESPONSIBLE	TIMELINE
1	Receive application for early study termination	Staff	7 days
2	Refer Notice of Early Termination to Primary Reviewers	Chair/ Member-Secretary	
3	Review the Submission	Members	
4	Deliberate decision during full board meeting		
5	Communicate NCH-IRB decision to PI	Staff	
6	File pertinent documents and update protocol database		

3.8.5. Detailed Instructions

3.8.5.1. Receive application or recommendation for early study termination

- An application for early termination is submitted when an NCH-IRB -approved study protocol is being recommended for termination

before its scheduled completion. This is done when the rights, safety and welfare of participants are threatened or upon the request of the PI or sponsor due to operational problems.

- Recommendation for early termination may come from the Sponsor, DSMB, Scientific Director, NCH-IRB members, or other authorized bodies.
- NCH-IRB Staff receives the study protocol termination package prepared and submitted by the principal investigator and verifies whether the Protocol Code Number and form used are correct, and the completeness of the Early Study Termination Form
- Check approval given by the NCH-IRB and type of review from the protocol data base.

3.8.5.2. Forward Notice of Early Termination to Primary Reviewers

NCH-IRB Staff forwards the document package to the Primary Reviewer/s.

3.8.5.3. Review the submission

- Assess the termination issues and make recommendation. 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.
- For submission to full board review, the NCH-IRB Secretariat includes the review of the study for early termination in the meeting agenda.

3.8.5.4. Discuss decision during full committee meeting

- The NCH-IRB deliberates on the effects of the early study termination on the safety and welfare of study participants.
- Final decision of the application are as follows:
  - Approval
  - Acknowledgment
  - Further information required

3.8.5.5. Communicate NCH-IRB decision to PI

- Based on the minutes of the meeting, the NCH-IRB Staff prepares the Notification Letter – Early Study Termination for signature of the NCH-IRB Chair.
- The PI may be requested to provide additional information or documents or implement actions to ensure the safety and welfare of subjects still active in the study.

3.8.5.6. File pertinent documents and update protocol database

- The NCH-IRB Staff files the Study Site Visit Report, excerpt of the

minutes of the meeting when report was discussed and the Notification Letter *(including the response from the PI, if any)* in the protocol file folder and update the protocol file index.

- Upon approval of the Early Study Termination application, the study protocol is classified as inactive, the Protocol Code No. is updated and the protocol file folder re-labelled and transferred to storage cabinet for inactive files.
- NCH-IRB Staff updates the protocol database and labels the protocol "INACTIVE-EARLY TERMINATION".