4.3.5.3.1. The study protocol is classified as INACTIVE.
4.3.5.3.2. Ethical clearance is expired effective on the day of the IRB meeting.
4.3.5.3.3. Study protocol records will be made available for three **(3) years in the archives.**

4.4.6. Files management

4.4.6.1. The IRB Chair shall sign **MDH IRB FORM 3(C)2021: FINAL REPORT FORM.**

4.4.6.2. The Secretariat stores the signed final report documents in the study protocol file folder, upon approval of the final report, when no further action is expected from the PI.

4.4.6.3. The Secretariat highlights in grey the study protocol data in the Study Protocol Database to signify the end of study and update relevant fields on the date of termination and status.

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

4.5. Study Protocol Non-compliance (Deviation/Violation) Report

4.5.1. Management of the Study Protocol Non-compliance Reports upon submission

4.5.1.1. The investigator should document, explain and report to the MDH IRB any non-compliance from the approved protocol, whether major or minor, within 7 working days upon knowledge of the Protocol Deviation.

4.5.1.2. The investigator may implement a deviation from the protocol to eliminate an immediate hazard(s) to study subjects without prior MDH IRB approval, but must

submit as soon as possible, a report of deviation or change, the reasons for it, and if appropriate, a necessary study protocol amendment(s).

4.5.1.3. Reporting of study protocol non-compliance is facilitated through the submission of an electronic copy and 1 hard copy of **MDH IRB FORM 3(D) 2021: STUDY PROTOCOL NON-COMPLIANCE (DEVIATION OR VIOLATION) REPORT,** together with documents deemed relevant by the investigator to clarify information indicated in the report. This comprises the study protocol non-compliance report package.

4.5.1.4. The Secretariat checks the submission for completeness, requests the PI or his representative to log details of submission in the submissions logbook, and gives a receiving copy of **MDHIRB FORM 3(D)2021: STUDY PROTOCOL NON-COMPLIANCE (DEVIATION OR VIOLATION) REPORT** to the PI or his/her representative stamped received by MDH IRB.

4.5.2. Classification of Review by the IRB Chair

4.5.2.1. The IRB Chair classifies the submission as either full board or expedited review.

4.5.2.2. Minor or administrative deviations that do not affect the scientific soundness of the study protocol or compromise the rights, safety, or welfare of human participants in the study are classified under expedited review e.g. missed visits or out of window visits without safety concerns, non-submission of diaries, etc, Each of these deviations must be reported within 7 working days upon knowledge.

4.5.2.3. Major deviations or protocol violations that consist of persistent protocol non-compliance with potentially serious consequences that could critically affect data analysis or put patients' safety at risk are classified under full board review, e.g. incorrect medications, noncompliance with inclusion and exclusion criteria, non-maintenance of IP storage requirements, etc. Each of these deviations must be reported within 7 working days upon knowledge.

4.5.3. Review by IRB Chair and Primary reviewers

4.5.3.1. For submissions under expedited review, action is finalized at the level of the IRB Chair within **seven (7)** calendar days.

4.5.3.2. Study protocol noncompliance report packages subject to full board review received within the cut-off period of **fifteen (15)** days before the IRB meeting are uploaded **ten (10) to twelve (12)** calendar days before the IRB meeting.

4.5.3.3. The Secretariat places the study protocol noncompliance report on the agenda for the next IRB meeting.

4.5.3.4. The primary reviewers accomplish the review using **MDH IRB FORM 3(D)2021 STUDY PROTOCOL NON-COMPLIANCE (DEVIATION OR VIOLATION) REPORT** within three (3) working days prior to the MDH IRB meeting.

4.5.4. Full board review of study protocol non-compliance report

4.5.4.1. The Secretariat uploads the following Study Protocol Non-compliance Report Package for IRB Members along with the meeting agenda:

4.4.4.1.1. **MDH IRB FORM 3(D)2021: STUDY PROTOCOL NON-COMPLIANCE (DEVIATION OR VIOLATION) REPORT**

4.4.4.1.2. Documents related to the deviation

4.5.4.2. The documents are presented to IRB members when study protocol non-compliance reports are deliberated on. The IRB deliberates on both the type and degree of non-compliance and takes the appropriate action: For detailed information on full board review of study protocol non-compliance report, see **SOP II-5.8.5.** The MDH IRB Chair calls on the MDH IRB Members to recommend any of the following actions:

a. Uphold original approval with no further action
b. Request information
c. Recommend further action
    - Site Retraining
    - Site Visit
    - Suspension until Site Visit has been completed
    - Withdraw approval

4.5.4.3. The MDH IRB can suspend approval or subject recruitment until non-compliance issues are addressed.

4.5.4.4. The MDH IRB may opt to withdraw approval under the following circumstances:

4.4.4.4.1. Fraud

4.4.4.4.2. Unresolved serious safety issues

4.5.5. Communication of results

4.5.5.1. The PI is notified of the IRB decision, referring to IRB action on the study protocol noncompliance report, through an action letter, at least 7 working days after the IRB meeting.

4.5.5.2. The PI may be requested to provide additional information, submit additional documents, or implement corrective action at least 7 working days after the receipt of the IRB decision.

4.5.6. Files management

4.5.6.1. The IRB Chair signs the **MDH IRB FORM 3(D)2021: STUDY PROTOCOL NON-COMPLIANCE (DEVIATION OR VIOLATION) REPORT**.

4.5.6.2. The Secretariat stores the signed study protocol non-compliance report documents in the study protocol file folder.

4.6. Early Study Termination Application

4.6.1. Management of the early study termination application upon submission

4.6.1.1. An application for early study termination is submitted when a study approved by the MDH IRB is being recommended for termination before its scheduled completion. This is done when the safety of the study participant is doubtful or at risk and also upon the request of the PI or the sponsor.

4.6.1.2. Early study termination is facilitated through the submission of an electronic copy and 1 hard copy of **MDH IRB FORM 3(E)2021: EARLY STUDY TERMINATION APPLICATION FORM,** together with documents deemed relevant by the investigator to support or clarify information indicated in the application. This comprises the early study termination application package.

4.6.1.3. The Secretariat checks the submission for completeness, requests the PI or his representative to log details of submission in the submissions logbook, and gives a receiving copy of **MDH IRB FORM 3(E)2021: EARLY STUDY TERMINATION APPLICATION FORM** to the PI or his/her representative stamped received by MDH IRB.

4.6.2. Classification of Review by IRB Chair

4.6.2.1. The IRB Chair classifies the submission as either full board or expedited review.