McLaren HEALTH CARE		Policy Title:	Non-Compliance in Human Subject Research
Effective Date:	January 16,2012	**Policy Number:**	MHC-RP0123
Review Date:	August 17, 2020	**Section:**	Research Integrity
Revised Date:	March 22, 2024	**Oversight Level:**	Corporate
Administrative Responsibility:	Corporate Research Integrity Manager Institutional Official, HRPP		

1. Purpose

1.1. Establish guidelines for identifying and reporting all allegations of noncompliance in human subjects' research, including but not limited to, allegations of serious and/or continuing noncompliance.

1.2. Describe how the Institutional Review Board (IRB) and the Research Integrity Department follow for handling allegations of noncompliance.

2. Scope

2.1. This policy applies to all faculty, staff, and students of MHC and its subsidiary hospitals, our affiliate researchers, or other individuals who are involved in human subjects' research which has been reviewed and approved by the MHC IRB and under the jurisdiction of the McLaren Human Research Protections Program.

3. Definitions

3.1. Refer to Appendix I *"Definitions"*

4. Policy

4.1. The ethical conduct of research is a shared responsibility. It requires cooperation, collaboration, and trust among the institution, investigators and their research staff, the participants who enroll in research, IRB members, and Research Integrity Department staff.

4.2. As part of its commitment to protecting the rights and welfare of human subjects in research, McLaren Health Care Institutional Review Board (MHC IRB) reviews allegations of noncompliance with IRB requirements and/or federal regulations governing the conduct of human research and takes any necessary action to ensure the ethical conduct of research.

4.1. IRB members do not participate in alleged noncompliance reviews if they have a conflict of interest. (See the COI and IRB Members SOP.)

4.2. All investigators and other study personnel involved in human subjects' research are required to comply with all laws and regulations governing their research activities, as well as with requirements and determinations of the MHC IRB.

4.2.1. Study personnel includes the principal investigator and any staff members directly involved with participants or the informed consent process.

4.3. Non-compliance with human subject protection requirements (e.g., U.S. Department of Health and Human Services (DHHS) regulations, institutional review board (IRB) requirements) is a violation of McLaren Healthcare Corporation policy.

4.4. Non-compliance presents a serious challenge to the IRB and to McLaren Health Care.

4.5. Regardless of investigator intent, unapproved research activities involving human subjects places those subjects at an unacceptable risk.

4.6. Investigators and their study staff are required to report instances of possible non-compliance. The principal investigator is responsible for reporting any possible non-compliance by study personnel to the IRB.

4.6.1. Common reports to the IRB that are not serious or continuing are typically protocol violations. However, any individual or employee may report observed or apparent instances of noncompliance to the MHC IRB Office. In such cases, the reporting party is responsible for making these reports in good faith, maintaining confidentiality, and cooperating with any MHC IRB and/or institutional review of these reports.

4.7. If an individual is uncertain whether there is cause to report noncompliance, he or she may contact the IRB chair directly to discuss the situation informally.

4.8. Failure to report a protocol violation in a timely manner may be considered serious and/or continuing noncompliance as outlined in policy MHC_RP123 "Non-Compliance in Human Subject Research".

4.9. Failure to report protocol deviations (an occurrence that does not meet the definition of exception or violation) by the investigator and submitted to the MHC IRB at the time of the continuing review may be considered serious and/or continuing noncompliance as outlined in policy MHC_RP123 "Non-Compliance in Human Subject Research".

4.10. Reports of non-compliance must be submitted directly to the MHC IRB within 7 working days of discovery of the noncompliance. The report must include the personnel involved and a description of the non-compliance.

4.11. Allegations of non-compliance should remain confidential to the extent possible. Generally, complainants decide if they wish to remain unidentified or have their

identity known. However, for a respondent involved in an allegation of non-compliance to have a meaningful opportunity to be heard, it may be necessary to identify the complainant. If the complainant is a subordinate of the respondent, the IRB will, to the best of its ability, protect the identity of the complainant while conveying the substance of the allegations and information gained to the respondent. The IRB cannot guarantee the anonymity of the complainant.

4.12. No entity, may override determinations or corrective actions related to the investigator's human subject research protocols imposed by the MHC IRB that limits, imposes conditions or in any way restricts an investigator's privileges, or imposes conditions or restrictions upon an investigator's research protocols.

5. Procedure

Submission and Screening of Allegations of Noncompliance:

5.1. Anyone may report or submit allegations of noncompliance or continuing noncompliance involving human subjects research to the Research Integrity Department verbally or in writing. Research Integrity staff or the IRB may also identify concerns during the review process. The Office of Research Compliance and QI (EQuIP) will submit to the Research Integrity Manager and IRB Chair routine review or audit findings suggestive of serious or continuing non-compliance.

5.1.1. When the Research Integrity Office or MHC IRB receives an allegation of noncompliance regarding a study that is under the oversight of an external IRB, the allegation will be investigated and managed in accordance with the terms of the reliance agreement/procedures.

5.2. Investigators are required to promptly report to the IRB all findings and allegations of apparent serious or continuing Non-compliance, including major protocol violations, subject complaints, and changes to the protocol made without IRB approval to eliminate apparent immediate harm to subjects. The timeframe for reporting is within 5 working days of becoming aware of the event.

5.3. All complaints of non-compliance, written or verbal (including telephone complaints), regardless of point of origin, are recorded in writing and forwarded to the IRB chair and Corporate Manger of Research Integrity.

5.4. The MHC IRB chair or designee will promptly address (or delegate staff to address), and if necessary, investigate any and all complaints or concerns of non-compliance, and appeals received by the MHC IRB.

5.5. Upon receipt of the complaint, the chair, in consultation with the Corporate Manger of Research Integrity, will make a preliminary assessment whether the complaint of non-compliance warrants immediate suspension of the research project.

If a suspension is warranted, procedures in policy MHC_RP0111_Study Suspension, Termination, Investigator Hold will be followed.

Assessment of Allegations of Non-compliance

IRB Chair or Designee Review

5.5.1. All Allegations of non-compliance will be reviewed by the IRB chair, who will review:

5.5.1.1. All documents relevant to the allegation.
5.5.1.2. The last approval letter from the IRB.
5.5.1.3. The last approved IRB application and protocol.
5.5.1.4. The last approved IRB application and protocol.
5.5.1.5. The grant, if applicable; and
5.5.1.6. Any other pertinent information (e.g., questionnaires, DSMB reports, etc.).

5.6. The IRB Chair will review the allegation and make a determination as to the truthfulness of the allegation.

5.7. The IRB Chair may gather more information through discussions or correspondence with the principal investigator.

5.8. The IRB Chair may request review by others (e.g., IRB member(s) or the IRB). If the IRB Chair determines that such review is necessary, the individual will receive all relevant materials (e.g., IRB file, communications, relevant research materials [e.g., survey, consent], and audit reports). If any individual feels that he/she is not qualified to review the research study, the IRB staff should be notified.

5.9. The IRB Chair will be consulted to determine an appropriate replacement.

5.10. The investigator(s) may submit in writing his/her account and explanation of the events possibly constituting noncompliance. At his/her request, the investigator(s) may also appear before the IRB. Investigator(s) under investigation for noncompliance may choose to be accompanied, or represented, by faculty or legal counsel in presenting to the convened IRB. The investigator must notify the IRB in advance if this is the case. Or, the investigator(s) may have a member of the IRB, typically the representative from his/her college, institution, or the Chair of the IRB, present on their behalf to the convened IRB.

5.11. The IRB Chair, alone or in consultation with the IRB, determines whether the allegation is substantiated or has a basis in fact (incident involved noncompliance).

5.12. If the IRB Chair determines that noncompliance did not occur because the incident was within the limits of an approved protocol for the research involved, the determination is reported in writing to the PI and, if applicable, the reporting party.

5.13. If in the judgment of the IRB Chair, any allegation, or findings of non-compliance warrants suspension of the research before completion of any review or investigation to ensure protection of the rights and welfare of participants the Chair may initiate a suspension in accordance with MHC_RP0111 Suspension Termination and Investigator Hold.

5.14. The Chair may determine that additional expertise or assistance is required to make these determinations and may form an ad hoc committee to assist with the review and fact gathering process. When an ad hoc committee assists in the review process, the Chair is responsible for assuring that minutes of the meeting are generated and kept helping support any determinations or findings made by the ad hoc committee.

5.15. If the IRB Chair (or designee) determines that the allegation of noncompliance has no basis in fact, then no further action will be taken under this policy. If the IRB Chair (or designee) determines that the allegation of noncompliance is confirmed noncompliance, then Section 5.17 will be followed.

5.16. Review of Findings of Non-compliance

IRB Chair Determination that non-compliance is not serious or continuing:

5.16.1. When the chair determines that noncompliance occurred but does not meet definition of serious or continuing noncompliance, the determination is reported in writing to the PI and the reporting party (if applicable).

5.16.1.1. IRB Chair may determine the event represents non-serious and non-continuing non-compliance and no action is required.

5.16.1.2. The event represents non-serious and non-continuing non-compliance and corrective action / preventative action plan is required.

5.16.1.2.1. The chair will work with the PI to develop a corrective action / preventative action plan.

5.16.1.2.2. The report of noncompliance and corrective action will be reported to the IRB in writing.

5.16.1.2.3. If the PI refuses to cooperate with the corrective action plan the matter will be referred to a convened meeting of the IRB with notification to the IO and the Corporate Compliance Department.

IRB Chair Determination of Potential Serious or Continuing Noncompliance:

5.16.2. When the chair or designee determines that noncompliance may meet the definition of serious or continuing noncompliance (or make the initial

determination), the report is referred for review by the IRB at the next convened meeting as described below:

Potential Serious or continuing non-compliance referred to the Convened IRB

5.16.3. All findings of potential serious or continuing non-compliance referred to by the IRB will be reviewed at a convened meeting.

5.16.4. The chair may use discretion and call an emergency IRB meeting, should the circumstances warrant such an urgent meeting.

5.16.5. All IRB members will receive all documents relevant to the allegation and:
5.16.5.1. The last approval letter from the IRB.
5.16.5.2. The last approved IRB protocol; and
5.16.5.3. The last approved consent document,

5.16.6. At this stage, the IRB may:

5.16.6.1. Find that there is no issue of non-compliance.

5.16.6.2. Find that there is noncompliance that is neither serious nor continuing and an adequate corrective action plan is in place.

5.16.6.3. Find that there is noncompliance that is neither serious nor continuing that requires additional action and require such actions.

5.16.6.4. Find that there is serious or continuing non-compliance and approve or modify any changes proposed by the chair and/or ad hoc committee.

5.16.6.5. Find that there may be serious or continuing non-compliance and direct that a formal inquiry (described below) be held; or

5.16.6.6. Request additional information.

The determination may be made by the IRB that an inquiry is necessary.

Inquiry Procedures

5.16.7. A determination may be made by the IRB that an inquiry is necessary based on several issues that may include, but are not limited to:

5.16.7.1. Subject complaint(s) that rights were violated.
5.16.7.2. Report(s) that investigator is not following the protocol as approved by the IRB.
5.16.7.3. Unusual and/or unexplained adverse events in a study.
5.16.7.4. Repeated failure of investigator to report required information to the IRB.

5.16.8. A subcommittee consisting of IRB members and non-members will be appointed, if appropriate, to ensure fairness and expertise. The subcommittee is charged by the IRB to do any or all the following:

5.16.8.1. Review protocol(s) in question.
5.16.8.2. Review sponsor audit report of the investigator.
5.16.8.3. Review of any relevant documentation, including consent documents, case report forms, subjects' investigational and/or medical files etc., as they relate to the investigator's execution of her/his study involving human subjects.

5.16.8.4. Interview appropriate personnel, if necessary.

5.16.8.4.1. The IRB representative interviews the complainant or, in cases where the complainant requests anonymity, the individual who received the original allegation/concern interviews the complainant. In some cases, the complainant may have already submitted a written complaint. Either the IRB representative or the RCO or designee may request additional information from the complainant.

5.16.8.4.2. The convened IRB, the IRB Chair, or a designated IRB representative (e.g., RCO or designee) interviews the respondent and gives him/her the opportunity to comment on the allegation/concern and provide information. The respondent may submit a written rebuttal to the complaint. Either the IRB or the RCO may request additional information from the respondent.

5.16.8.5. Prepare either a written or oral report of the findings, which is presented to the full IRB at its next meeting:

5.16.8.5.1. The report may consist of a summary of the allegations/concerns, interview summaries, and copies of pertinent information or correspondence. The report may or may not include recommendations for IRB action. (In some cases, the IRB representative simply provides the IRB with a summary of the allegations/issues, the interview summaries, and copies of pertinent information without an accompanying written report from the review team.)

5.16.8.6. Recommend actions.

Review Procedures for Potential Serious or Continuing Noncompliance

Final Review

5.17. The IRB reviews the material presented by the review team at a convened meeting at which a quorum is present. The materials provided include the summary report of the noncompliance, the protocol if applicable and the informed consent document if applicable. The convened IRB determines whether to request additional

information or whether to interview additional witnesses. The IRB may give the respondent the opportunity to meet with the convened IRB before it takes final action.

5.18. When the non-compliance is determined by the convened IRB to be serious and/or continuing, the IRB considers whether to implement one or more of the following actions:

5.18.1. Suspension of research approval (refer to MHC_RP0111 Suspension Termination and Investigator Hold).

5.18.2. Termination of research approval (refer to MHC_RP0111 Suspension Termination and Investigator Hold.

5.18.3. Notification of currently enrolled subjects when information related to the non-compliance issue may relate to the subject's willingness to continue to participate in the research.

5.19. When the non-compliance is determined by the convened IRB to be serious and/or continuing, the IRB may take a variety of possible other actions depending on the outcome of the review that include, but are not limited to:

5.19.1. Request a corrective action plan from the investigator.

5.19.2. Verification that participant selection is appropriate and monitoring of the actual informed consent.

5.19.3. An increase in data and safety monitoring of research activity.

5.19.4. Request a directed audit of targeted areas of concern and/or monitoring of research by Office of Research Compliance and QI (EQuIP).

5.19.5. Request a status report after each participant receives intervention.

5.19.6. Modify the continuing review or annual assessment cycle.

5.19.7. Require additional investigator and staff education.

5.19.8. Provide additional information provided to past participants.

5.19.9. Require modification of the research protocol.

5.19.10. Modification of the continuing review schedule.

5.19.11. Require modification of the information disclosed during the consent process.

5.19.12. Require inspections of other active protocols of the investigator.

5.19.13. Require the PI to re-consent participants for continued participation.

5.19.14. Determine that the investigator may not use the data collected for this research study for publication.

5.19.14.1. Request that investigator inform publishers and editors if he/she has already submitted or published manuscript emanating from this research study.

5.19.15. Referral to other Organizational entities (e.g., legal counsel, risk management, institutional official).

5.19.15.1. The Institutional Official can suspend/terminate the researchers and/or research at any McLaren subsidiary hospital.

5.19.16. Other actions appropriate for the local context.

5.19.17. The investigator is informed of the IRB determination and the basis for the determination in writing and is given a chance to respond.

5.19.18. For all incidents determined by the fully convened IRB to be serious or continuing noncompliance, the IRB will notify the following individuals within seven (7) days of such determination:

5.19.19. The IRB informs the following additional individuals of the allegation/issue, the review process, and the findings of the review, if appropriate, depending upon the outcome of the review, the external sponsor, or the requirements of the applicable regulatory agency:

5.19.19.1. Principal Investigator

5.19.19.2. Complainant.

5.19.19.3. The department chair.

5.19.19.4. Vice President of Clinical Excellence and Research

5.19.19.5. Sponsor, if appropriate.

5.19.19.6. Other administrative personnel as appropriate

5.19.19.7. If the IRB determines that the non-compliance was serious or continuing, the results of the final review will be reported as described Policy MHC_RP124 “Reporting to Regulatory Agencies and Institutional Officials”.

Appeal of IRB Decision

5.20. Appeals of IRB decisions should be made in writing to the IRB. The IRB will review the appeal at the next regularly convened meeting (same 1st or 3rd Friday group). Should a researcher wish, the appeal may be made in person.

6. Responsibility

6.1.1. Execution of SOP: Research Integrity Department Staff, IRB Chair, IRB Members, Research Compliance Officer (RCO), VP of Clinical Excellence and Research, Principal Investigator (PI)/Study Personnel.

7. References

7.1. 21 CFR 50
7.2. 21 CFR 56.123
7.3. 45 CFR 46.112
7.4. MHC_RP0124 *"Reporting to Regulatory Agencies and Institutional Officials"*
7.5. MHC_RP0126 COI and IRB Members
7.6. MHC_RP0129 Concerns, Questions and Complaints About Human Research Studies
7.7. OHRP Guidance on Reporting Incidents to OHRP
7.8. Appendix I "Definitions"

8. Previous Revisions: 12/20/12, 3/22/13, 12/15/21, 1/16/23

9. Supersedes Policy: MHC_RP0117 Non-Compliance in Human Subject Research

10. Approvals:

MHC Institutional Review Board Initial Review: 2/17/12

MHC Institutional Review Board acknowledgement:12/18/15

Signature on File *3/22/2024*

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Justin Klamerus, MD, MMM Date
Executive Vice President/Chief Clinical Officer
Institutional Official of Research