McLaren HEALTH CARE		Policy Title:	Changes to Currently Approved Human Subject Research
Effective Date:	January 16, 2012	**Policy Number:**	MHC_RP0113
Review Date:	August 11, 2020	**Section:**	Research Integrity
Revised Date:	March 22, 2024	**Oversight Level:**	Corporate
Administrative Responsibility:	Corporate Manager of Research Integrity Institutional Official, HRPP		

1. Purpose

1.1. To define the procedures the McLaren Health Care Institutional Review Board (MHC IRB) will follow to ensure prompt reporting to the MHC IRB of proposed changes in approved non-exempt human-subject research.

1.2. To ensure that changes are not initiated without MHC IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subject. [45 CFR 46.103(4)(iii) and 21 CFR 56.108(3)(4)]

2. Scope

2.1. The Human Research Protections Program (HRPP) applies this policy to all proposed activities that meet definitions of "research" and "human subject," the Food and Drug Administration (FDA) definitions of "clinical investigation" and "human subject" and

2.1.1. The research is conducted by or under the direction of an MHC investigator in connection with his/her assignment.

2.1.2. The research is conducted by an investigator employed by MHC or its subsidiary hospitals.

2.1.3. The research is conducted using any property, patient population, or facility of MHC or its subsidiary hospitals.

2.2. Applies to all human subject research requiring changes to currently approved protocol.

3. Definitions

3.1. Refer to Appendix I *"Definitions"*

4. Policy

4.1. PIs are responsible for submitting proposed changes to currently approved research and obtaining IRB approval of the changes prior to implementation.

4.1.1. Changes that are necessary to protect the safety and welfare of subjects can be implemented prior to IRB approval; however, the MHC IRB must be notified within 24 hours of such implementation.

4.1.2. The IRB will then determine whether each change was consistent with ensuring the participant's continued safety and welfare.

4.2. Items that do not constitute a change to the previously approved research should be submitted to the MHC IRB as an information report or at the time of continuing review (i.e., sponsor generated reports, Data and Monitoring Reports provided by the sponsors).

4.3. Study closure prior to the planned completion date must be reported to the IRB promptly. Investigators must submit a completed Final Report Form describing the reason for the premature closure.

4.4. Implementation of changes to research without prior IRB approval, except as described in 4.1.1, is non-compliance and the non-compliance policy will be followed.

5. Procedure

5.1. Mechanism(s) for submission:

5.1.1. An MHC IRB modification application must be submitted via the IRB electronic application system.

5.1.2. If a modification application is submitted by a member of the study team other than the PI, the IRB office must receive a signed and dated copy of the modification application as confirmation that the PI is aware of the changes.

5.1.2.1. The IRB approval letter will not be issued until the appropriate PI signature page has been received by the IRB Office.

5.1.3. Investigators must submit documentation to inform the IRB of changes in the status of the study, including, but not necessarily limited to:

5.1.3.1. Revised protocol (if applicable).

5.1.3.2. Revised consent or parental permission/assent documents (if applicable) or other documentation that would be provided to subjects, including any recruitment materials.

5.1.3.3. Any other documentation relevant to the conduct of the study.

5.2. Submission Process

5.2.1. The IRB staff will check each submission for completeness (e.g., all questions answered completely, any new or modified documents attached).

5.2.2. The staff will make an initial determination whether the proposed change(s) may be reviewed using the expedited process.

5.2.3. Once it is determined that the submission is complete, the IRB staff will assign reviewer(s). If necessary, a consultant will also be assigned to the research study.

5.2.3.1. The reviewer(s) will determine whether the proposed changes may be approved via expedited review procedures or if the submission must be referred to review by the full board.

5.3. How Review is Conducted:

5.3.1. The IRB reviewer(s) determines whether the change is greater than minimal risk.

5.3.1.1. The reviewer(s) may consult with the IRB chair in making the determination.

5.3.2. Changes that are determined to be greater than minimal risk will be sent to additional reviewers and referred to the next convened IRB meeting for review by the full board.

5.3.3. If it is not clear if a change is greater than minimal risk, the study will be sent directly to the convened IRB for review.

5.3.4. Expedited Review of Protocol Modifications:

5.3.4.1. Expedited IRB review procedures may be used to review minor changes to previously IRB approved research that is normally subject to convened board review following previously approved research, during the period for which approval is authorized. An expedited review may be carried out by the IRB chair and/or designated IRB members.

5.3.4.2. Proposed changes to research eligible for expedited review may be reviewed using expedited procedures unless the modification will result in the research no longer qualifying for expedited review.

5.3.4.3. The IRB chair or a designated experienced IRB reviewer will serve as the primary reviewer for expedited submissions and has the authority to approve or require modifications to expedited submissions.

5.3.4.4. The primary reviewer does not have the authority to disapprove expedited submissions. If the reviewer feels that a submission is not fit for approval, it must be referred to the fully convened IRB for consideration.

5.3.4.5. Reviewer(s) will be given access to all materials submitted with the application via IRB electronic application system in order to conduct their review.

5.3.4.6. Reviewer(s) will complete the "Modification Review" checklist to determine whether the modification meets the criteria for expedited review procedures and whether the research continues to meet the regulatory criteria for approval with the modifications as proposed.

5.3.4.7. Reviewer(s) will also consider whether information about those modifications might relate to participants' willingness to continue to take part in the research and, if so, whether to provide that information to participants.

5.3.5. Administrative Review Procedures

5.3.5.1. IRB staff may approve a modification submission as an administrative change if the request only involves adding study personnel, without removing or replacing other personnel, or making any other changes to the protocol, since the IRB made the initial determination that the number of staff listed on the study is adequate and the credentials and/or described qualifications are representative of the appropriate expertise needed to conduct the study.

5.3.6. Full Board Review of Protocol Modifications:

5.3.6.1. When a proposed change in a research study normally subject to convened board review is more than minimum risk (e.g., procedures involving increased risk or discomfort are to be added), the IRB must review and approve the proposed change at a convened meeting, prior to implementation.

5.3.6.1.1. The only exception to this requirement is a change that is necessary to eliminate apparent immediate hazards to research subjects. In such a case, the IRB should be promptly informed of the change following its implementation and will review the change to determine if is consistent with ensuring the subjects' continued welfare.

5.3.6.2. All IRB members are given access to the modification and supporting documentation via the IRB electronic application system.

5.3.6.3. The primary reviewer and/or presenter will present an overview of the changes at a convened IRB meeting and lead the IRB through the regulatory criteria for approval. The IRB will determine whether the research with the proposed modifications continues to meet the regulatory criteria for approval.

5.3.6.4. The IRB will consider whether submitted modifications might relate to participants' willingness to continue to take part in the research and, if so, whether information must be provided to participants.

5.4. IRB Member Considerations:

5.4.1. IRB members are required to review and approve protocols using the criteria at federal regulations 45 CFR 46 and, for FDA research studies, 21 CFR 56. The criteria for IRB approval must be met to approve the application.

5.4.2. IRB members will determine how the change may affect the criteria for IRB approval (e.g., change in recruitment may affect the selection of subject criteria for approval), referring to policy *MHC_RP109 "Criteria for IRB Approval of Research and Possible IRB Actions"* as needed.

5.4.3. Particular consideration will be given to the following:

5.4.3.1. The type of change (modification vs. addition).

5.4.3.2. Whether there is a change in the level of risk.

5.4.3.3. Whether the change alters the review level and/or category of the research study.

5.4.3.4. Overall effect of change on research study.

5.4.3.5. Whether change requires a modification to the consent process.

5.4.3.6. Whether the change involves:

5.4.3.6.1. Vulnerable populations.

5.4.3.6.2. Addition of sensitive questions.

5.4.3.6.3. Privacy and/or confidentiality considerations.

5.4.3.7. Effect of the change on subjects' willingness to continue the study.

5.4.3.8. Whether information should be provided to past or currently enrolled subjects. If so:

5.4.3.8.1. Whether use of an information sheet is appropriate to relay information to the subject or if re-consenting is necessary.

5.4.3.8.2. Whether the information sheet or re-consent document is adequate.

5.4.3.9. Whether there are any significant new findings that arise from the review process that might relate to subjects' willingness to continue participation.

6. Responsibilities:

6.1. Principal Investigator (PI):

6.1.1. Is expected to provide the IRB with all relevant information regarding the conduct of the research, including:

6.1.2. All applicable forms and supporting documentation (e.g., modification and all applicable addendums, amendments, or information report).

6.1.3. Assurance that co-investigator(s) or other key personnel be added to the study have current human subject protection education certification.

6.1.4. Copies of all modified document(s) with submitted changes clearly tracked (i.e., "tracked changes") and a final version of the modified document(s) to be approved.

6.1.5. Provide any other relevant study documentation which will assist the MHC IRB in deciding regarding approval.

6.1.6. Provide any additional information or clarification requested by the fully convened IRB, IRB Chair, or designee, in a timely fashion, to assist in the determination of approval.

6.2. IRB Staff

6.2.1. Advise PI and research staff in preparation and completion of the submission process.

6.2.2. Conduct a pre-review of the submission and supporting documents to identify non-scientific issues.

6.2.3. Ensure all applicable documents have been provided.

6.2.4. Submit concerns to the study team regarding incomplete submissions, clarifications, or minor changes to allow complete review by the fully convened IRB, IRB chair, or their designee.

6.2.5. Confirm review type (e.g., expedited, or full board) is appropriate as submitted by the PI and request changes in accordance with federal regulations, state and local laws and institutional policies and procedures.

6.2.6. Schedule full board submissions (e.g., modification and all applicable addendums, amendment, reports) to the next available convened MHC IRB meeting.

6.2.7. Assign full board submissions to appropriate reviewers.

6.2.8. Ensure IRB has adequate representation during the evaluation of the proposed human subjects' research.

6.2.9. Assign expedited and exempt submissions to the IRB chair or other designated IRB member(s) for review.

6.2.10. Ensure MHC IRB members with a conflict of interest are not present during the discussion and vote.

6.2.11. Include approval of submissions on the agenda for the fully convened IRB.

6.2.12. Prepare IRB correspondence to the investigator using IRB electronic application system.

6.3. IRB:

6.3.1. Determines whether the proposed human subjects research meets the federal criteria for approval via the reviewer checklist.

6.3.1.1. Ensures additional safeguards have been included in the study to protect the rights and welfare of subjects that are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically and educationally disadvantaged persons.

6.3.1.2. IRB reviewers will make recommendations to the fully convened IRB and should do so. These recommendations can be accepted as presented, modified, or rejected by a motion and passed by a majority.

6.3.2. Have the authority to vote on the final determinations of those recommendations. Request the motion, for each submission, by the IRB primary reviewer, if applicable.

6.3.3. The IRB has the authority to require notification to current or previous research subjects of any significant new findings that may affect the subjects' willingness to continue participation and the re-consent of study subjects.

6.3.3.1. Notification can occur by:

6.3.3.1.1. Letter to subject.

6.3.3.1.2. Phone call to subjects (promptly); and/or

6.3.3.1.3. Re-consent of subjects at next study visit or sooner.

7. References:

7.1. 45 CFR 46

7.2. 21 CFR 56

7.3. MHC_RP106 “Expedited Review of Human Subject Research”

7.4. MHC_RP109 “Criteria for IRB Approval of Research and Possible IRB Actions”

7.5. Appendix I “Definitions”

8. Previous Revisions: 11/19/12, 11/16/15, 12/14/21, 1/12/23

9. Supersedes Policy: MHC_RP0119_Changes to Currently Approved Human Subject Research

10. Approvals:

MHC Institutional Review Board initial review: 2/17/12

MHC Institutional Review Board acknowledgement: 12/4/15, 4/14/16

Signature on File *3/22/2024*

Justin Klamerus, MD, MMM Date
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Institutional Official of Research