McLaren HEALTH CARE		**Policy Title:**	Changes to Currently Approved Human Subject Research
Effective Date:	January 16, 2012	**Policy Number:**	MHC_RP0113
Review Date:	April 14, 2016	**Section:**	Human Research Protections Program (HRPP)
Revised Date:	February 12, 2016	**Oversight Level:**	Corporate
Administrative Responsibility:	Corporate Director, HRPP Institutional Official, HRPP		

1. Purpose

1.1. The purpose of this policy is:

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

1.1.2. 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 a MHC investigator in connection with his/her assignment.

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

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

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

3. Definitions

3.1. Refer to Appendix I “*Definitions”*

4. Policy

4.1. PIs are responsible for submitting changes to currently approved human subject research which requires review and approval of the MHC IRB prior to the initiation of changes.

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 implementing the change.

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

4.2. Items that do not constitute a change to the previously approved research will not require a modification and 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. Premature closure of a study (closure prior to the planned completion date) must be reported to the IRB promptly. Investigators should submit a completed Final Report/Study Closure Form describing the reason for the premature closure.

5. Procedure

5.1. Mechanism(s) for Submission:

5.1.1. MHC IRB Amendment application must be submitted via the e-Protocol online system.

5.1.2. If an Amendment application is not submitted by the PI, the IRB office must receive a signed amendment page as a way of PIs confirmation as she/he is aware of the changes.

5.1.2.1. IRB approval letter will not be issued until the IRB Office receive signed/dated signature page.

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

5.1.3.1. Revised Investigator's Protocol or Sponsor's Protocol (if applicable).

5.1.3.2. Revised approved 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 relevant documents provided by the Investigator.

5.2. Submission Process

5.2.1. The IRB staff checks for completeness (e.g., all questions answered, any new or modified documents attached). The IRB Staff will determine whether the

proposed changes may be approved through an expedited review process, if the changes are minor, or whether the modification warrants full board review.

5.2.2. The IRB staff will assign a reviewer(s) and if needed a consultant to the research study.

5.2.2.1. The reviewer(s) has the ultimate responsibility to determine that the proposed changes may be approved through the expedited review procedure and, if not, must refer to the submission for full board review.

5.3. How Review is Conducted:

5.3.1. The IRB reviewer(s) makes the determination on whether the change is greater than minimum risk.

5.3.2. The IRB Chair may be consulted to determine if the revision qualifies as greater than minimum and therefore needs to be sent to additional reviewers and be reviewed at the convened IRB meeting.

5.3.3. For research studies in which it is not clear if the change is greater than minimum, the study will be sent directly to the convened IRB.

5.3.4. Expedited Review of Protocol Modifications:

5.3.4.1. An IRB may use expedited review procedures to review minor changes in ongoing previously approved research during the period for which approval is authorized. An expedited review may be carried out by the IRB Chair and/or designee(s) among the IRB members.

5.3.4.2. IRB Chair or designated experienced reviewer serve as the primary reviewer for expedited submissions and has the authority to approve, or require modifications to expedited submissions. The Chair or designated experienced reviewer does not have the authority to disapprove expedited proposals but must refer these for consideration by the fully convened IRB.

5.3.4.3. Reviewer(s) provided with all the material submitted by the PI in order to conduct their review. All of the modification documents will be provided using e-protocol system.

5.3.4.4. The reviewer(s) complete the “Modification Review” checklist to determine whether the modification meets the criteria allowing review of the amendment using expedited procedure, and if so, whether the research with the proposed modifications continues to meet the regulatory criteria for approval.

5.3.4.5. The 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.

5.3.4.6. Reviewer(s) will determine whether the proposed human subjects research meet the federal criteria's for approval, per Policy *MHC_RP106 "Expedited Review of Human Subject Research".* The IRB Chair or designated experienced reviewer completes the reviewer checklist for applications meeting the criteria for expedited review.

5.3.5. Full Board Review of Protocol modifications:

5.3.5.1. When a proposed change in a research study is more than minimum risk (e.g., procedures involving increased risk or discomfort are to be added), then the IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the subjects' continued welfare.

5.3.5.2. All IRB members are provided with all the modification documents provided by the investigator.

5.3.5.3. At the meeting, the Primary Reviewer and/or Presenter present an overview of the changes and lead the IRB through the completion of the regulatory criteria for approval. The IRB will determine whether the research with the proposed modifications continues to meet the regulatory criteria for approval.

5.3.5.4. When the IRB reviews modifications to previously approved research, the IRB 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.

5.4. IRB Member Considerations:

5.4.1. The IRB member(s) is 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 must be met to approve or recommend approval of the application.

5.4.2. When reviewing modifications to an approved research study (revisions, amendments), the criteria for IRB approval must be met to approve the requested revision. The IRB member(s) should determine how the change may affect the IRB approval criteria (e.g., change in recruitment may affect the selection of subject criteria for approval). The IRB member(s) should refer to Policy *MHC_RP109 "Criteria for IRB Approval of Research and Possible IRB Actions"* to review the proposed change as needed.

5.4.3. The IRB member(s) should, in particular, consider the following:

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

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

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

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:

5.4.3.8.1. Use of an information sheet vs. re-consent.

5.4.3.8.2. If provided, the adequacy of information sheet or re-consent document.

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

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. Complete and submit the applicable forms (e.g., modification and all applicable addendums, amendment, or information report);

6.1.3. When adding co-investigator(s) or key personnel ensuring co-investigator(s) and key personnel have current human subject protection education certification;

6.1.4. Copies of the modified document(s) that clearly indicate the changes that have been made (e.g., a "tracked changes") and a final version of the modified document(s) to be approved;

6.1.5. Any other relevant study documentation which will allow the MHC IRB to make a determination regarding approval;

6.1.6. Providing 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 for incomplete submissions, clarifications or minor changes to allow complete review by the fully convened IRB or the IRB Chair or their designee.

6.2.5. Confirm study 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, or information report) to the next available convened MHC IRB meeting.

6.2.7. Assign full board submission(s) to a primary reviewer(s).

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

6.2.9. Assign expedited submission for to the IRB Chair or another qualified reviewer for review.

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

6.2.11. Assign expedited and exempt applications to the IRB Chair or another qualified reviewer for review.

6.2.12. Include approval of submissions on the agenda of a fully convened IRB.

6.2.13. Prepare IRB correspondence to the investigator using eProtocol.

6.3. IRB:

6.3.1. Determines whether the proposed human subjects research meet the federal criteria's for approval through 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 or educationally disadvantaged persons.

6.3.1.2. Have the authority and should make recommendations to the fully convened IRB. 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. Have 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 subjects;

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 promptly.

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: November 19, 2012, November 16, 2015

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

10. Approvals:

MHC Institutional Review Board initial review: February 17, 2012

MHC Institutional Review Board acknowledgement: December 4, 2015, April 14, 2016

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Institutional Official of Research

Date