McLaren HEALTH CARE		Policy Title:	Additional Consideration during IRB Review and Approval of Research
Effective Date:	January 18, 2013	**Policy Number:**	MHC_RP0110
Review Date:	August 11, 2020	**Section:**	Research Integrity
Revised Date:	January 12, 2023	**Oversight Level:**	Corporate
Administrative Responsibility:	Corporate Manager of Research Integrity Institutional Official, HRPP		

1. Purpose

1.1. The purpose of this policy is to describe actions that the IRBs may take during review of research conducted at McLaren Health Care (MHC) and its subsidiary hospitals.

2. Scope

2.1. This policy applies to all members who serve on MHC IRB as well as the MHC IRB Staff and Administration.

2.2. Non-exempt human subject research and clinical investigations reviewed by the McLaren Health Care Institutional Review Board (MHC IRB) at a convened meeting are subject to this policy.

3. Definitions

3.1. Refer to Appendix I “Definitions”

4. Policy

4.1. The convened IRB shall conduct a systematic review of the study materials and in accordance with 45 CFR 46.111 and 21 CFR 56. 111.

5. Procedure

Lead Investigator/Coordinating Center

5.1. When the IRB is reviewing multi-site research where the investigator is responsible for the overall conduct of the research, AAHRPP standards (Element II.2.I) require that the investigator provides, and the IRB reviews, procedures for the management and communication of information that is relevant to the protection of human subjects. The language in this section is designed to satisfy these requirements but may be customized to the organization.

5.2. The same policies will be followed when MHC investigator is the Lead site or Coordinating Center.

5.3. Determination of Risk

5.3.1. At the time of initial and continuing review, the IRB will make a determination regarding the risks associated with the research protocol. Risks associated with the research will be classified as either “minimal” or “greater than minimal”.

5.3.2. Risk determination may vary over the life of a research plan depending on the procedure and risks that subjects will be exposed to as the research progresses.

5.3.2.1. The level of risk associated with the research influences eligibility for expedited review.

5.3.3. The meeting minutes will reflect the committee’s determination regarding risk levels.

5.4. Period of Approval

5.4.1. At the time of initial review and at continuing review, when continuing review is required, the IRB will make a determination regarding the frequency of review for each protocol. All protocols will be reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year.

5.4.2. Calculation of IRB Approval and Expiration Dates

5.4.3. An IRB may not approve a research study for more than one year. Typically, the approval period is 364 days.

Calculation of Initial Approval Date

5.4.4. The IRB calculates the date of initial IRB approval in the following manner:

5.4.4.1. When a research study is approved at a convened meeting, the date of the convened meeting is the date of IRB approval.

5.4.4.2. When the research study is approved subject to stipulations at a convened meeting, once the stipulations have been verified by the IRB Chair or designee the date of IRB approval is the date of the convened IRB meeting.

5.4.4.3. When a research study is reviewed and approved through an expedited review process, the date the submission is approved by the IRB Chair or designee is the date of IRB approval.

Calculation of Expiration Date

INITIAL APPROVAL

5.4.5. The IRB calculates the date of expiration in the following manner:

5.4.5.1. When a research study is fully approved at a convened meeting, the date of expiration is based on the date of the convened meeting (minus one day).

5.4.5.2. When a research study is approved subject to stipulations, the date of expiration is one year from the date of the convened meeting (minus one day). It is not calculated from the date that the IRB chair or designee verifies the requested changes and grants final approval.

5.4.5.3. The approval period expires at 11:59 p.m. on the expiration date set forth in the IRB approval letter.

MODIFICATION DATES

5.4.6. The IRB calculates the date of modification approval in the following manner:

5.4.6.1. When a modification is approved through an expedited review mechanism, the modification approval date is the date that the IRB chair or designee reviews and approves the modification.

5.4.6.2. When a modification is reviewed at a full board meeting and is approved at the meeting, the modification approval date is the date of the IRB meeting.

5.4.6.3. When a modification is reviewed at a full board meeting and is approved subject to stipulations, the modification approval date is the date that the response is verified by the IRB chair or designee.

5.4.6.4. Expiration dates on modifications are maintained as the date assigned upon initial or continuing review unless the IRB determines that there has been a significant change to the risk/benefit ratio which would require a more frequent continuing review. If this change occurs, the IRB will notify the principal investigator of the study of the new expiration date. The new date must never exceed the original expiration date. In the event that a study was released from continuing review and a determination is made to change that determination, the expiration date will be one year from the approval of the modification.

5.4.7. In some circumstances, a shorter review interval (e.g., semi-annually, quarterly, or after accrual of a specific number of participants) may be required (see below).

5.4.8. The meeting minutes will reflect the IRB's determination regarding review frequency.

5.5. Review More Often Than Annually

5.5.1. Unless specifically waived by the IRB, research that meets any of the following criteria will require review more often than annually:

5.5.1.1. Significant risk to research subjects (e.g., death, permanent or long-lasting disability or morbidity, severe toxicity) without the possibility of direct benefit to the subjects.

5.5.1.2. The involvement of especially vulnerable populations likely to be subject to coercion (e.g., terminally ill).

5.5.1.3. A history of serious or continuing non-compliance on the part of the PI.

5.5.2. The following factors will also be considered when determining which studies require review more frequently than on an annual basis:

5.5.2.1. The probability and magnitude of anticipated risks to subjects.

5.5.2.2. The likely medical condition of the proposed subjects.

5.5.2.3. The overall qualifications of the PI and other members of the research team.

5.5.2.4. The specific experience of the Responsible Investigator and other members of the research team in conducting similar research.

5.5.2.5. The nature and frequency of adverse events observed in similar research at this and other institutions.

5.5.2.6. The novelty of the research making unanticipated adverse events more likely.

5.5.2.7. The nature of and any risks posed by the research.

5.5.2.8. The degree of uncertainty regarding the risks involved.

5.5.2.9. The vulnerability of the participants.

5.5.2.10. The experience of the clinical investigator in conducting the type of research.

5.5.2.11. The IRB's or EC's previous experience with that researcher or sponsor (e.g., compliance history, previous problems with the researcher obtaining informed consent, prior complaints from participants about the researcher).

5.5.2.12. The projected rate of enrollment.

5.5.2.13. Whether the study involve novel therapies

5.5.2.14. Any other factors that the IRB deems relevant.

5.5.3. In specifying an approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of subjects (either studied or enrolled).

5.5.3.1. If a maximum number of subjects studied or enrolled is used to define the approval period, the following are understood:

5.5.3.1.1. The approval period can, in no case, exceed one year.

5.5.3.1.2. The number of subjects studied or enrolled determines the approval period only when that number of subjects is studied or enrolled in less than one year.

5.5.3.2. If an approval period of less than one year is specified by the IRB, the reason for more frequent review must be documented in the minutes.

5.6. Independent Verification That No Material Changes Have Occurred

5.6.1. The IRB recognizes that protecting the rights and welfare of subjects sometimes requires that the IRB verify independently that that no material changes occurred during the IRB-designated approval period. This may involve utilizing sources other than the investigator.

5.6.2. Independent verification from sources other than the investigator may be necessary at times, for example, in cooperative studies, or other multi-center research.

5.6.3. The IRB will determine the need for verification from outside sources on a case-by-case basis, according to the following criteria:

5.6.3.1. Protocols where concerns have been raised regarding possible material changes occurring without IRB approval based on information provided in continuing review reports or from other sources.

5.6.3.2. Protocols conducted by principal investigators who have previously failed to comply with federal regulations and/or the requirements or determinations of the IRB.

5.6.3.3. Protocols subject to internal audit.

5.6.3.4. Whenever the IRB deems verification from outside sources is relevant.

5.6.4. The following factors will also be considered when determining which studies require independent verification:

5.6.4.1. The probability and magnitude of anticipated risks to subjects.

5.6.4.2. The likely medical condition of the proposed subjects.

5.6.4.3. The probable nature and frequency of changes that may ordinarily be expected in the type of research proposed.

5.6.5. In making determinations about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period or may retrospectively require such verification at the time of continuing review, review of modifications and/or unanticipated problems.

5.6.6. If any material changes have occurred without IRB review and approval, the IRB will decide the corrective action to be taken.

5.7. Consent Monitoring

5.7.1. In reviewing the adequacy of informed consent procedures for proposed research, the IRB may on occasion determine that special monitoring of the consent process by an impartial observer (EQuIP Office Staff) is required to reduce the possibility of coercion and undue influence.

5.7.2. Such monitoring may be particularly warranted where the research presents significant risks to subjects, or if subjects are likely to have difficulty understanding the information to be provided.

5.7.3. Monitoring may also be appropriate as a corrective action when the IRB has identified problems associated with a particular investigator or research project.

5.8. Investigator Conflicts of Interest

5.8.1. The IRB application asks protocol-specific questions regarding conflict of interest for the investigators and key personnel.

5.8.2. As part of its review process, the IRB will make a final determination as to whether a conflict of interest exists about the research under review.

5.8.3. If a conflict of interest exists, final IRB approval of a protocol cannot be given until an approved conflict management plan is in place to adequately protect the human subjects in the protocol.

5.9. Significant New Findings

5.9.1. When significant new knowledge or findings about the medication or test article and/or the condition under study develop during research, the PI is required to report such findings to the IRB.

5.9.2. The IRB will review the findings with regard to the impact rights and welfare of subjects.

5.9.3. During the ongoing review process, the IRB may require that the PI contact currently enrolled subjects to inform them of the new information, as it may affect the risks or benefits to subjects or their willingness to continue in the research.

5.9.3.1. The informed consent should be updated to reflect new findings.

5.9.3.2. The IRB may require that currently enrolled subjects be re-consented, acknowledging receipt of this new information and affirming their continued participation.

5.9.3.3. The IRB will communicate any such requirements to the PI in writing.

5.10. Advertisements

5.10.1. The IRB must approve any and all advertisements for studies that are conducted under the purview of MHC IRB, prior to their posting and/or distribution. The IRB will review:

5.10.1.1. Information contained in the advertisement.

5.10.1.2. Mode of communication.

5.10.1.3. Final copy of printed advertisements.

5.10.1.4. Final audio/video taped advertisements.

5.10.2. This information is to be submitted to the IRB with the initial application or as a modification to the protocol.

5.10.3. The IRB will review the material to ensure it is accurate, not coercive, or unduly optimistic, and does not unduly influence subjects to participate. Undue influence includes, but is not limited to:

5.10.3.1. Statements implying a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.

5.10.3.2. Explicit or implicit claims that the drug, biologic, or device is safe or effective for the purposes under investigation.

5.10.3.3. Explicit or implicit claims that the test article is known to be equivalent or superior to any other drug, biologic, or device.

5.10.3.4. Use of terms such as “new treatment,” “new medication,” or “new drug” without an explanation that the test article is investigational.

5.10.3.5. Promising “free medical treatment” when the intent is to indicate that participants will not be charged for taking part in the investigation.

5.10.3.6. Emphasis on payment or the amount to be paid, such as bold type or larger font on printed media.

5.10.3.7. The inclusion of exculpatory language.

5.10.4. Advertisement to recruit subjects should be limited to the information needed for prospective subjects to determine their eligibility and interest in participation. When appropriately worded, the following items may be included:

5.10.4.1. Name and address of the clinical investigator and/or research facility.

5.10.4.2. Condition being studied and/or the purpose of the research.

5.10.4.3. A summary of criteria that will be used to determine eligibility for the study.

5.10.4.4. Time or other commitment required of the subjects.

5.10.4.5. Location of the research and the person or office to contact for further information.

5.10.4.6. A clear statement that it is research and not treatment.

5.10.4.7. A brief list of potential benefits (e.g., no cost of health exam).

5.10.5. Advertisements for a trial offered by a sponsor may not include the use of a coupon for a discount on the purchase price of the product once it has been approved for marketing.

5.10.6. The IRB will review advertising to ensure that it does not make claims, either explicit or implicit, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling.

5.10.6.1. Once approved by the IRB, an advertisement cannot be altered or manipulated in any way without prior IRB approval.

5.11. Payment to Research Subjects

5.11.1. Payment to research subjects may be an incentive for participation or a way to reimburse a subject for travel and other experiences incurred due to participation.

5.11.1.1. Payment for participation is not considered a research benefit.

5.11.2. Regardless of the form of remuneration, investigators must take care to avoid coercion of subjects.

5.11.3. Payments should reflect the degree of risk, inconvenience, or discomfort associated with participation. The amount of compensation must be proportional to the risks and inconveniences posed by participation in the study.

5.11.4. Investigators who wish to pay research subjects must indicate justification for such payment in the research application. Justification should:

5.11.4.1. Substantiate that proposed payments are reasonable and commensurate with the expected contributions of the subject.

5.11.4.2. State the terms of the subject participation agreement and the amount of payment in the informed consent form; and

5.11.4.3. Substantiate that subject payments are fair and appropriate, and that they do not constitute (or appear to constitute) undue pressure on the patient to volunteer for the research study.

5.11.5. The IRB must review both the amount of payment and the proposed method of disbursement to assure that neither entails problems of coercion or undue influence.

5.11.6. Credit for payment should accrue and not be contingent upon the participant completing the entire study.

5.11.7. Any amount paid as bonus for completion of the entire study should not be so great that it may unduly influence participants to remain in the study when they otherwise would have withdrawn.

5.11.8. All information concerning payment, including the amount and schedule of payments, and the conditions under which participants would receive partial or no payment (e.g., if they withdraw partway through the study) is set forth in the consent document.

5.12. Non-Monetary Gifts and Incentives

5.12.1. Similar to financial incentives, non-monetary gifts or incentives can also present problems of undue influence or coercion that impact a potential subject's ability to consider participation fully and freely in research.

5.12.2. If subjects will be provided with non-monetary gifts or tokens of appreciation, such as totes, books, toys, or other such materials, the approximate retail value must be described to the IRB and the IRB will be provided with a description, photo, or sample product to review.

5.12.3. Investigators should carefully structure incentives and methods of disbursement so that, while they may serve as a factor in a subject's decision to participate, they do not serve to unduly influence or coerce participation.

5.13. Payments to Research Personnel and Physicians

5.13.1. The MHC IRB does not approve and prohibits *finder's fees* in research studies. Finder's fees are any payments to physicians or other professional for referring individuals to research studies. Finder's fees for subject referral may compromise the integrity of a research study by giving an appearance of affecting the judgment of the investigator/research team.

5.13.2. The MHC IRB does not approve and prohibits recruitment bonus as an additional payment from sponsor to the *individual researcher or research staff* based on rate or timing of recruitment. This may place potential subjects at risk of coercion or undue influence or cause inequitable subject selection.

5.13.3. The MHC IRB believes that *finder's fees and individual recruitment payment* to investigators and study staff create a *potential conflict of interest*. Specifically, the investigator may be motivated by financial interest to refer a patient when such referral might not be of any benefit to, or in the best interest of the subject.

6. References

6.1. 21 CFR 56

6.2. 21 CFR 50

6.3. 45 CFR 46

6.4. Appendix I "*Definitions"*

7. Previous Revisions: 1/18/13, 12/5/21

8. Suspended Policy: None

9. Approvals:

MHC Institutional Review Board initial approval:1/18/13

MHC Institutional Review Board acknowledgement: 3/18/13, 11/20/15

Signature on File *1/31/23*

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