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:	November 20, 2015	**Section:**	Human Research Protections Program
Revised Date:	November 4, 2015	**Oversight Level:**	Corporate
Administrative Responsibility:	Corporate Director, HRPP 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 IRB chair, IRB-designees and convened IRB shall conduct a systematic review of the study materials and shall consider the same principles and criteria in its deliberations of all new or continuing studies, no matter whether these fall into the exempt, expedited or convened IRB category, in accordance with 45 CFR 46.111 and 21 CFR 56. 111.

4.1.1. Exempt research is not subject to these regulations however the reviewer of exempt research will determine if there any additional ethical requirements which must be met.

5. Procedure

5.1. Determination of Risk

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

5.1.2. 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.

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

5.1.3. The meeting minutes will reflect the Committee's determination regarding risk levels.

5.1.3.1. Expedited reviewers will document the determination risk level on the reviewer's checklist.

5.2. Period of Approval

5.2.1. At the time of initial review and at continuing review, the IRB will make a determination regarding the frequency of review of the research protocols. All protocols will be reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year.

5.2.2. 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).

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

5.2.3.1. Expedited reviewers will document the review frequency on the reviewer's checklist.

5.2.4. Review More Often Than Annually

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

5.2.4.1.1. 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;

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

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

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

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

5.2.4.2.2. The likely medical condition of the proposed subjects.

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

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

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

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

5.2.4.2.7. Any other factors that the IRB deems relevant.

5.2.5. 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.

5.2.5.1. If a maximum number of subjects studied or enrolled is used to define the approval period, it is understood that the approval period in no case can exceed one year and that 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.

5.2.5.2. 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.

5.3. Independent Verification That No Material Changes Have Occurred

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

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

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

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

5.3.3.2. Protocols conducted by Principal Investigators who have previously failed to comply with federal regulations and/or the requirements or determinations of the IRB.

5.3.3.3. Protocols subject to internal audit.

5.3.3.4. Whenever else the IRB deems verification from outside sources is relevant.

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

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

5.3.4.2. The likely medical condition of the proposed subjects.

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

5.3.5. 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 amendments and/or unanticipated problems.

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

5.4. Consent Monitoring

5.4.1. 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 in order to reduce the possibility of coercion and undue influence.

5.4.2. 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.

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

5.5. Investigator Conflicts of Interest

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

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

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

5.6. Significant New Findings

5.6.1. During the course of research, significant new knowledge or findings about the medication or test article and/or the condition under study may develop.

5.6.2. The PI must report any significant new findings to the IRB and the IRB will review them with regard to the impact on the subjects' rights and welfare.

5.6.3. Since the new knowledge or findings may affect the risks or benefits to subjects or subjects' willingness to continue in the research, the IRB may require, during the ongoing review process, that the PI contact the currently enrolled subjects to inform them of the new information.

5.6.3.1. The IRB will communicate this to the PI.

5.6.3.2. The informed consent should be updated and the IRB may require that the currently enrolled subjects be re-consented, acknowledging receipt of this new information and for affirming their continued participation.

5.7. Advertisements

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

5.7.1.1. The information contained in the advertisement.

5.7.1.2. The mode of its communication.

5.7.1.3. The final copy of printed advertisements.

5.7.1.4. The final audio/video taped advertisements.

5.7.2. This information should be submitted to the IRB with the initial application or as an amendment to the protocol.

5.7.3. The IRB reviews the material to assure that the material is accurate and is not coercive or unduly optimistic, creating undue influence to the subject to participate which includes but is not limited to:

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

5.7.3.2. Claims, either explicitly or implicitly, that the drug, biologic or device was safe or effective for the purposes under investigation.

5.7.3.3. Claims, either explicitly or implicitly, that the test article was known to be equivalent or superior to any other drug, biologic or device.

5.7.3.4. Using terms like “new treatment,” “new medication,” or “new drug” without explaining that the test article was investigational.

5.7.3.5. Promising “free medical treatment” when the intent was only to say participants will not be charged for taking part in the investigation.

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

5.7.3.7. The inclusion of exculpatory language.

5.7.4. Any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest. When appropriately worded, the following items may be included:

5.7.4.1. The name and address of the clinical investigator and/or research facility.

5.7.4.2. The condition being studied and/or the purpose of the research.

5.7.4.3. In summary form, the criteria that will be used to determine eligibility for the study.

5.7.4.4. The time or other commitment required of the subjects.

5.7.4.5. The location of the research and the person or office to contact for further information.

5.7.4.6. A clear statement that this is research and not treatment.

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

5.7.4.8. Advertisements will not include compensation for participation in a trial

offered by a sponsor to involve a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

5.7.5. The IRB reviews advertising to ensure that advertisements do not make claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling.

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

5.8. Payment to Research Subjects

5.8.1. 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.

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

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

5.8.3. 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.

5.8.4. Investigators who wish to pay research subjects must indicate in their research application the justification for such payment. Such justification should:

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

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

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

5.8.5. 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.

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

5.8.7. The IRB does not allow the entire payment to be contingent upon completion of the entire study.

5.8.8. Any amount paid as bonus for completion of the entire study should not be so great that it becomes coercive.

5.8.9. The consent form must describe the terms of payment and the conditions under which subjects would receive partial payment or no payment (e.g., if they withdraw from the study before their participation is completed).

5.9. Non-Monetary Gifts and Incentives

5.9.1. 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 fully and freely consider participation in research.

5.9.2. 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.

5.9.3. Investigators should carefully structure incentives and methods of disbursement so that while the incentives may serve as a factor in a subjects decision to participate, that they have not served to unduly influence or coerce participation.

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: January 18, 2013

8. Supersedes Policy: None

9. Approvals:

MHC Institutional Review Board initial approval:	January 18, 2013
MHC Institutional Review Board acknowledgment:	March 18, 2013 November 20, 2015

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Michael McKenna, MD — Date
Executive Vice President/Chief Medical Officer
Institutional Official of Research