McLaren HEALTH CARE		Policy Title:	Criteria for IRB Approval of Research
Effective Date:	July 20, 2012	**Policy Number:**	MHC_RP0109
Review Date:	August 11, 2020	**Section:**	Research Integrity
Revised Date:	January 16, 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 outline the federal criteria to be applied by the McLaren Health Care Institutional Review Board (MHC IRB) when considering approval of research involving human subjects.

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) are subject to this policy.

3. Definitions

3.1. Refer to Appendix I "Definitions"

4. Policy

4.1. This policy is to ensure that IRB approval is based on the specific criteria set forth in the federal regulations found at 45 CFR 46.111 (Department of Health and Human Services (DHHS), also known as the Common Rule) and 21 CFR 56.111 (Food and Drug Administration (FDA)).

4.2. The IRB Chair, designee, 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, modifications or continuing studies, no matter whether these fall into the expedited or convened IRB category, in accordance with 45 CFR 46.111 and 21 CFR 56. 111.

4.2.1. 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.

4.3. In order for the MHC IRB to approve human subjects research, either through expedited review or by the full IRB, it must determine that the following requirements are satisfied:

4.3.1. Risks to subjects are minimized:

4.3.1.1. (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and

4.3.1.2. (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

4.3.2. Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.

4.3.2.1. In evaluating risks and benefits, the IRB will consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research).

4.3.2.2. The IRB will not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

4.3.3. Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research, the setting in which the research will be conducted,` and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disable persons, or economically or educationally disadvantaged persons.

4.3.4. Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by the Federal Regulations.

4.3.5. Informed consent will be appropriately documented, in accordance with, and to the extent required by the Federal Regulations.

4.3.6. When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

4.3.7. When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

4.3.8. When some or all the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.

4.4. In addition to evaluation of the risks in the research, the IRB determines, based on the materials submitted by the investigator, that research studies have:

4.4.1. The resources necessary to protect participants, such as adequate time for the researchers to conduct and complete the research.

4.4.2. Adequate number of qualified staff and adequate facilitates.

4.4.3. Access to a population that will allow recruitment of the necessary number of participants.
4.4.4. Availability of medical and psychosocial (when applicable) resources that participants might need as a consequence of the research.

4.5. These criteria must be satisfied for each review (initial, continuing, and modifications) for both expedited review and review by the convened IRB.

5. Procedure

Risk/Benefit Assessment

5.1. The goal of the assessment is to ensure that the risks to research subjects posed by participation in the research are justified by the anticipated benefits to the subjects or society. Toward that end, the IRB must:

5.1.1. Judge whether the anticipated benefit, either of new knowledge or of improved health for the research subjects, justifies asking any person to undertake the risks;

5.1.1.1. Disapprove research in which the risks are judged unreasonable in relation to the anticipated benefits.

5.1.2. The assessment of the risks and benefits of proposed research involves a series of steps:

5.1.2.1. Identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research;

5.1.2.2. Determine whether the risks will be minimized to the extent possible by evaluating the necessity of procedures that impact risk and whether the data could be gained by procedures that are already being performed for other purposes or by alternative procedures that impact less risk;

5.1.2.3. Identify the probable benefits to be derived from the research, both direct benefits to subjects and possible benefits to society, science and others;

5.1.2.4. Determine whether the risks are reasonable in relation to the benefits to subjects, if any, and assess the importance of the knowledge to be gained;

5.1.2.5. Ensure that potential subjects will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits;

5.1.3. **Risks to subjects are minimized**:

5.1.3.1. By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk; and

5.1.3.2. Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

5.1.4. **Risks to subjects are reasonable in relation to anticipated benefits**, if any, and to the importance of the knowledge that may reasonably be expected to result.

5.1.4.1. In evaluating risks and benefits, the IRB will consider only those risks and benefits that may result from the research - as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research.

5.1.4.2. The IRB will not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

5.1.5. Scientific Merit:

5.1.5.1. In order to assess the risks and benefits of the proposed research, the IRB must determine that:

5.1.5.1.1. The research uses procedures consistent with sound research design;

5.1.5.1.2. The research design is sound enough to reasonably expect the research to answer its proposed question; and

5.1.5.1.3. The knowledge expected to result from this research is sufficiently important to justify the risk.

5.1.5.2. In making this determination, the IRB may draw on its own knowledge and disciplinary expertise, or the IRB may draw on the knowledge and disciplinary expertise of others, such as reviews by a funding agency, or departmental review.

5.1.5.3. When scientific review is conducted by an individual or entity external to the MHC IRB, documentation must be provided to the IRB for review and consideration.

5.1.5.4. Scientific and Scholarly Validity Review:

5.1.5.4.1. Scientific validity is one of the basic expectations of human subject research and is an integral part of the IRB review.

5.1.5.4.1.1. It is unethical to put subjects in harms way or expose them to risk when a study cannot generate any valid results.

5.1.5.4.2. In addition to reviewing research proposals for the protection of human subjects, proposals will be reviewed by the MHC IRB for the scientific or scholarly validity review.

5.1.5.4.3. When evaluating the scientific and scholarly validity of a protocol, the MHC IRB relies on the review provided by different entities, as follows:

5.1.5.4.3.1. For federally sponsored research, the respective peer review process (e.g., NIH, NCI) provides a scientific and scholarly review.

5.1.5.4.3.2. For research subject to FDA review, the FDA conducts a rigorous scientific design review during IND or IDE evaluation. Most industry-sponsored research falls within this category.

5.1.5.4.3.3. The Karmanos Cancer Institute Protocol Review Monitoring Committee (PRMC) reviews all local and national research protocols involving cancer patients treated at McLaren for scientific merit, feasibility as well as to define the data safety monitoring plan in the protocol.

5.1.5.4.3.4. When applicable, some of the McLaren's local Committees review research proposal for the scientific merit, feasibility and/or operational impact.

5.1.5.4.3.4.1. MHC IRB will require confirmation provided by the PI or Academic Advisor. The PI will complete and submit the form "***Confirmation of Scientific or Scholarly Validity Review"*** in the IRB electronic application system. The form has to be submitted to the IRB:

5.1.5.4.3.4.1.1. For research that has departmental funding, McLaren foundation funding, or that has not otherwise gone through a scientific and scholarly review as described above.

5.1.5.4.3.4.1.2. For ***all*** research conducted by students, including residents and fellows a "Confirmation of Scientific or Scholarly Validity Review" worksheet must be signed either by the Academic Advisor or someone other than the PI who can confirm that the study is scientifically valid and can generate valid results.

5.1.5.4.4. If no scientific validity review is done before IRB submission, the MHC IRB will conduct its own review as stated in Section 5.1.5.1 of this policy.

5.1.5.5. When ICH-GCP (E6) applies:

When ICH-GCP (E6) applies - Policies and procedures include the evaluation of available nonclinical and clinical information on an investigational product is adequate to support the proposed clinical trial.

5.2. Equitable Selection of Subjects:

5.2.1. The IRB determines by viewing the application, protocol, and other research project materials that the selection of subjects is equitable with respect to gender, age, class, etc.

5.2.2. The IRB will not approve a study that does not provide adequately for the equitable selection of subjects or has not provided an appropriate scientific and ethical justification for excluding classes of persons who might benefit from the research.

5.2.3. In making this determination, the IRB evaluates:

5.2.3.1. the purposes of the research;

5.2.3.1.1. the setting in which the research occurs;

5.2.3.1.2. the inclusion/exclusion criteria;

5.2.3.1.3. whether prospective participants will be vulnerable to coercion or undue influence; the proposed recruitment and enrollment procedures;

5.2.3.1.4. the potential influence of any payments to participants;

5.2.3.1.5. scientific and ethical justification for including vulnerable populations; and the scientific and ethical justification for excluding classes of persons who might benefit from the research.

5.2.4. At the time of the continuing review the IRB will determine that the PI has followed the subject selection criteria that he/she/originally set forth at the time of the initial IRB review and approval.

5.3. Recruitment of Subjects:

5.3.1. The investigator will provide the IRB with all recruiting materials to be used in identifying participants including recruitment methods, advertisements, and payment arrangements.

5.4. Informed Consent

5.4.1. The IRB will ensure that informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20.

5.4.2. In addition, the Committee will ensure that informed consent will be appropriately documented in accordance with, and to the extent required by 45 CFR 46.117 and 21 CFR 50.27.

See policy: MHC_RP0115 Obtaining Informed Consent from Research Subjects

5.5. Safety Monitoring

5.5.1. For all research that is more than minimal risk, the investigator must submit a safety monitoring plan.

5.5.1.1. The initial plan submitted to the IRB should describe the procedures for safety monitoring, reporting of unanticipated problems involving risks to subjects or others, descriptions of interim safety reviews and the procedures planned for transmitting the results to the IRB.

5.5.1.2. DSM may be performed by a researcher, medical monitor, safety monitoring committee, or other means.

5.5.2. The IRB reviews the safety monitoring plan and determines if it makes adequate provision for monitoring data to ensure the safety of subjects and for addressing problems that may arise over the course of the study. If a plan was not submitted, the IRB determines whether a plan is required, and, depending on the circumstances, what the plan should include. The overall elements of the monitoring plan depend on the potential risks, complexity, and nature of the research study.

5.5.3. The principles the IRB applies in evaluating the adequacy of a proposed DSM plan include:

5.5.3.1. Monitoring should be commensurate with the nature, complexity, size, and risks of the research.

5.5.3.2. Monitoring should be timely. Frequency should be commensurate with risk. Conclusions are reported to the IRB.

5.5.3.3. For low-risk studies, continuous, close monitoring by the study investigator or an independent party may be an adequate and appropriate format for monitoring, with prompt reporting of problems to the IRB, sponsor, and regulatory bodies, as applicable.

5.5.3.4. For greater than minimal risk studies that do not include a plan for monitoring by a Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC), and that are blinded, multi-site, involve vulnerable populations, or involve high-risk interventions or procedures, the IRB will carefully evaluate the proposed DSM plan and may require establishment of a DSMB, DMC, or other methods to enhance the monitoring and management of participant safety.

5.5.3.5. Data and Safety Monitoring plans should specify:

5.5.3.6. The entity or person(s) who will perform the monitoring, and the independence or affiliation that the entity or person(s) has with the sponsor or investigator.

5.5.3.7. The safety information that will be collected and monitored, including serious adverse events and unanticipated problems

5.5.3.8. The frequency or periodicity of review of safety data.

5.5.3.9. The procedures for analysis and interpretation of the data.

5.5.3.10. The procedures for review of scientific literature and data from other sources that may inform the safety or conduct of the study

5.5.3.11. The conditions that trigger a suspension or termination of the research (i.e., stopping rules), when appropriate.

5.5.3.12. The procedures for reporting findings to the IRB, including a summary description of what information that will be provided For a Data Safety Monitoring Board. The plan:

5.5.3.12.1. Should also describe the composition of the board or committee. Generally, a DSMB or DMC should be composed of experts in all scientific disciplines needed to interpret the data and ensure subject safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease/condition and treatment under study should be part of the monitoring group or be available if warranted.

5.5.3.12.2. The National Institutes of Health (NIH) requires the establishment of DSMBs for multi-site clinical trials involving interventions that entail potential risk to the participants.

5.5.3.12.3. When DSMBs or DMCs are used, IRBs conducting continuing review of research may rely on a current statement, or the most recent report, from the DSMB or DMC which indicates that it has and will continue to review study-wide adverse events, study wide interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

5.6. Privacy and Confidentiality:

5.6.1. The IRB will determine whether adequate procedures are in place to protect the privacy of subjects and to maintain the confidentiality of the data.

5.6.2. Privacy

5.6.2.1. The IRB must determine whether the activities in the research constitute an invasion of privacy. In order to make that determination, the IRB must obtain information regarding how the investigators are getting access to subjects or subjects' private, identifiable information and the subjects' expectations of privacy in the situation.

5.6.2.2. Investigators must have appropriate authorization to access the subjects or the subjects' information.

5.6.2.3. In developing strategies for the protection of subjects' privacy, consideration should be given to:

5.6.2.3.1. Methods used to identify and contact potential participants.

5.6.2.3.2. Settings in which an individual will be interacting with an investigator.

5.6.2.3.3. Appropriateness of all personnel present for research activities.

5.6.2.3.4. Methods used to obtain information about participants and the nature of the requested information.

5.6.2.3.5. Information that is obtained about individuals other than the "target participants," and whether such individuals meet the regulatory definition of "human participant" (e.g., a subject provides information about a family member for a survey).

5.6.2.3.6. How to access the minimum amount of information necessary to complete the study.

5.6.3. Confidentiality

5.6.3.1. Confidentiality and anonymity are not the same. If anyone, including the investigator, can readily ascertain the identity of the subjects from the data, then the research is not anonymous, and the IRB must determine if appropriate

protections are in place to minimize the likelihood that the information will be inappropriately divulged.

5.6.3.2. The level of confidentiality protections should be commensurate with the potential of harm from inappropriate disclosure.

5.6.3.3. At the time of initial review, the IRB ensures that the privacy and confidentiality of research subjects is protected.

5.6.3.4. The IRB assesses whether there are adequate provisions to protect subject's privacy and maintain confidentiality. The IRB does this through the evaluation of methods used to obtain information:

5.6.3.4.1. About subjects,

5.6.3.4.2. About individuals who may be recruited to participate in studies.

5.6.3.4.3. The use of personally identifiable records and;

5.6.3.4.4. The methods to protect the confidentiality of research data.

5.6.4. The PI will provide the information regarding the privacy and confidentiality of research subjects at the time of initial review through the completion of the application, any necessary HIPAA Forms, research protocol, and/or other submitted, applicable materials.

5.6.4.1. The IRB will review all information received from the PI and determine whether or not the privacy and confidentiality of research subjects is sufficiently protected.

5.6.4.2. In reviewing confidentiality protections, the IRB will consider the nature, probability, and magnitude of harms that would be likely to result from a disclosure of collected information outside the research.

5.7. IRB will evaluate the effectiveness of proposed de-identification techniques, coding systems, encryption methods, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections.

5.8. Vulnerable Populations:

5.8.1. At the time of initial review, the IRB will consider the scientific and ethical reasons for including vulnerable subjects in research.

5.8.2. The IRB may determine and require that, when appropriate, additional safeguards be put into place for vulnerable subjects, such as those without decision-making capacity.

5.9. Possible IRB Determinations:

The IRB, IRB chair or designee makes the following determinations and PIs are notified via IRB electronic application system:

5.9.1.1. Approved Without Stipulations: The study is approved as submitted. The PI is not required to change any aspect of the protocol or informed consent document. The approval date is the date of the IRB meeting. The approval is

valid for one year unless the IRB committee, IRB chair or designee designates a shorter period due to the risk in the study.

5.9.1.2. Approved with Contingencies: Occurs when the stipulations are minor or prescriptive. May not be used for substantive changes, requirements or requests for more information that are necessary for the IRB to be able to determine whether the criteria for approval are satisfied.

5.9.1.2.1. The IRB may vote to authorize the IRB chair or designee to approve the response submitted by the PI unless the investigator does not provide the minor revisions requested.

The approval date:

5.9.1.2.2. 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.

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

5.9.1.2.4. Should the IRB chair or designee feel that the response is not adequate or requires review by the fully convened IRB, the study would be added to the next available agenda for the committee that originally reviewed the application.

5.9.1.2.5. The PI may not make additional changes until full IRB approval is granted.

5.9.1.3. Moved: Occurs when IRB Chair, member or designee has determined that further information regarding the protocol is needed for the IRB to decide.

5.9.1.3.1. Moved studies will be transferred to the next convened IRB meeting

5.9.1.4. Not Approved: The IRB has determined that the research cannot be conducted at MHC and its subsidiary hospitals or by employees or agents of MHC and its subsidiary hospitals or otherwise under the auspices of MHC.

5.9.1.4.1. Once a study has been disapproved, it can be submitted as a new application to the IRB for re-consideration.

5.9.1.4.2. A new submission of previously disapproved protocols must be reviewed by the fully convened IRB.

5.9.1.4.3. A new application must address all previous concerns outlined by the IRB for the previously disapproved protocol.

5.9.1.5. Suspension of IRB Approval: An action of the IRB or Organizational Official to withdraw IRB approval of some temporarily or permanently or all research procedures.

5.9.1.5.1. Suspended studies remain open and are subject to continuing review.

5.9.1.6. Tabled: The study might be tabled when the quorum was lost during the convened IRB meeting,

5.9.1.7. Termination: A directive of the convened IRB to permanently cease all activities in a previously IRB-approved research protocol.

5.9.1.7.1. Terminated protocols are considered closed and no longer require continuing review.

5.9.1.7.2. Termination of protocols approved under expedited review must be made by the convened IRB.

5.9.1.8. Withdrawn: Occurs when the IRB analyst removes a study from the IRB electronic application system when the PI requests to remove a submission.

5.9.1.8.1. Withdrawn studies will be removed from the IRB electronic application system at the request of the PI, IRB Analyst, and/or by the IRB chair or designee.

5.9.1.8.2. No further action will be taken unless the PI resubmits the protocol.

6. Responsibilities:

6.1. Principal Investigator:

6.1.1. Must outline how all of the criteria for approval of research are met in their application for initial and currently approved research for review and approval by the MHC IRB.

6.1.2. Must respond to any concerns or comments received from the MHC IRB to address each of the federal criteria for approval of research.

6.2. Convened IRB, IRB Chair, or designee:

6.2.1. Must review each application for initial and continuing review of research using the criteria outlined in this policy.

6.2.2. Must clarify any questions or concerns regarding the criteria outlined above prior to the approval of research involving human subjects.

6.3. IRB Staff and Administrators:

6.3.1. Ensure that applications for initial and continuing review of research include documentation that each of the above referenced criteria are met.

6.3.2. Document that each of the above referenced criteria are met in the meeting minutes of the fully convened IRB.

7. References:

7.1. 21 CFR 56

7.2. 21 CFR 50

7.3. 45 CFR 46

7.4. Appendix I “Definitions”

8. Previous Revisions: 12/12/12, 9/18/13, 8/10/15, 12/6/21

9. Supersedes Policy:

9.1. MHC_RP0107_Evaluation Criteria

9.2. MHC_RP0115_Possible IRB Actions

10. Approvals:

MHC Institutional Review Board Initial Approval: 7/20/12

MHC Institutional Review Board acknowledgment: 9/20/13, 8/21/15, 11/20/15

Signature on File *1/31/23*

_____ _____

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