McLaren HEALTH CARE		Policy Title:	Directed For-Cause Audits
Effective Date:	October 8, 2015	Policy Number:	MHC_RP0303
Review Date:	August 20, 2020	Section:	Research Integrity
Revised Date:	March 22, 2024	Oversight Level:	Corporate
Administrative Responsibility:	Corporate Manager of Research Integrity Institutional Office, HRPP		

1. Purpose

1.1. The purpose of this policy is to establish the process for McLaren Health Care (MHC) Education and Quality Improvement Program (EQuIP) to perform a Directed For-Cause Audit of MHC research studies.

2. Scope

2.1. This policy applies to all industry sponsored, government funded, and investigator-initiated studies conducted at McLaren Health Care and any of its subsidiaries.

3. Definitions

3.1. Refer to Appendix I *"Definitions"*

4. Policy

4.1. As part of the McLaren's AAHRPP Quality Improvement and Quality Assurance Program, EQuIP is authorized to perform a directed for-cause audits requested by the IRB, IRB Chairperson, designee, Institutional Official, or regulatory agency (e.g., FDA, NIH, and OHRP).

4.2. McLaren's Human Research Protection Program (HRPP) is committed to a consistent, proactive effort to continually ensure the human subject research conducted at McLaren occurs in accordance with all applicable federal regulations and/or agency specific requirements, state and local laws, and institutional policies and procedures.

4.3. Directed for-cause audits of MHC research studies will be conducted:

4.3.1. To determine if the rights and welfare of research participants have been properly protected in accordance with federal regulations, local and state laws, and institutional policies.

4.3.2. To ensure the highest degree of research standards are being maintained in regard to the safety of human subject research.

4.3.3. When there are suspicions or allegations of non-compliance.

4.3.4. When there are concerns about whether the rights and welfare of participants enrolled in a particular research protocol are being adequately protected.

4.3.5. When there are concerns about the integrity of the data or research staff misconduct.

4.4. The EQuIP staff has the right to request any study records or records relevant to the research subject eligibility or medical history. Review of study records may include, but are not limited to:

4.4.1. Signed consent documents.

4.4.2. Source documentation.

4.4.3. Logs or checklists.

4.4.4. Narrative forms and/or notes-to-file (when applicable).

4.4.5. Regulatory and IRB binders or files.

4.4.6. Test articles – Drug and device.

4.4.7. Medical records that serve as source documents.

4.4.8. Any other relevant procedures, materials, or documents.

4.5. The Primary Investigator (PI) is expected to fully cooperate with the audit and make available time for discussion, access documents under review, and personnel on stand-by to answer questions or obtain study records.

4.6. Based upon audit results and feedback from the Primary Investigator, it will be determined that there is.

4.6.1. The existence of regulatory non-compliance or lack of subject safety and protection of the research subject.

4.6.2. No evidence of non-compliance.

4.6.3. Need for implementing quality improvement measures or a CAPA plan.

4.7. The IRB will be notified of evidence of suspected serious non-compliance or continued non-compliance audit findings.

4.7.1. The IRB will make the determination of serious or continuing non-compliance and follow up actions (e.g., follow-up review, notification of Sponsor or regulatory authorities, monitoring of informed consent process, suspension, or termination).

5. Procedure

5.1. Request for For-Cause Audit

5.1.1. EQuIP will be notified of a for-cause audit request by the IRB, IRB Chairperson, designee, Institutional Official, or regulatory agency (e.g., FDA, NIH, and OHRP).

5.1.2. The request will name the PI, protocol ID number, reason for the audit, and details of the specific information that is required for the audit.

5.1.3. The audit may focus on a specific area of complaint, or it may extend into other areas if deemed necessary. The request may include, but may not be limited to:

5.1.3.1. Determine the frequency and nature of any alleged non-compliance.

5.1.3.2. Verify serious non-compliance and/or continuing non-compliance with HRPP policies and applicable federal regulations and laws.

5.1.3.3. Determine if and how subjects were harmed by non-compliance.

5.1.3.4. Determine the root cause(s) of non-compliance.

5.1.3.5. Assess the integrity of the research data.

5.1.3.6. Assess adherence to protocol.

5.1.3.7. Assess accurate record keeping.

5.1.3.8. Assess a protocol involving an investigator unresponsive to IRB requests.

5.1.3.9. Investigate breach of HIPAA.

5.1.3.10. Investigate for unauthorized access by individuals not approved by the IRB.

5.1.3.11. Determine if there have been informed consent violations.

5.1.3.12. Evaluate a study with high volume of subject enrollment.

5.1.3.13. Evaluate an investigator study with significant unanticipated problems or events and serious adverse events.

5.1.3.14. Evaluate an investigator with significant number of protocol violations.

5.1.3.15. Evaluate the subject or sponsor complaints.

5.1.3.16. Evaluate concerns from government agencies (e.g., FDA, NIH, and OHRP).

5.1.3.17. Assess for suspected fraud.

5.1.3.18. Review drug/device accountability.

5.1.3.19. Determine if and what type of corrective/remedial actions need to occur.

5.2. Pre-Audit Preparation:

5.2.1. The QI and Education Specialist will conduct the audit within the time frame of the requestor.

5.2.2. The QI and Education Specialist will notify the Principal Investigator and Research Coordinator via email and/or phone:

5.2.2.1. That there is a request for a directed for-cause audit.

5.2.2.2. Reason for the audit.

5.2.2.3. Any IRB determinations (i.e., suspension).

5.2.2.4. Time frame audit will take place.

5.2.2.5. Request for list of all subject IDs.

5.2.3. Additional email notifications will be sent to:

5.2.3.1. Corporate Manager of Research Integrity.

5.2.3.2. McLaren Center for Research and Innovation (MCRI) will be notified if they have oversight over the study.

5.2.3.3. Academic Advisor and Director of Medical Education will be notified if the PI is a resident or student.

5.2.4. Once an appointment date and time has been agreed upon, an official Audit Notification Letter is emailed to the Primary Investigator and Research Coordinator. The letter will contain:

5.2.4.1. The reason(s) for the directed for-cause audit.

5.2.4.2. Date and time of audit.

5.2.4.3. Personnel that should be present.

5.2.4.4. Request for adequate space for the audit.

5.2.4.5. Any hold that the IRB has placed on the research.

5.2.4.6. All documents including complete subject files.

5.2.4.7. Interviews that will be conducted.

5.2.4.8. Planned inspection of the facilities (data storage, drug, and device storage, etc.).

5.2.4.9. Whether or not the IRB has requested that the auditor observe the informed consent process with potential participants.

5.2.4.10. Contact number for questions.

5.3. Review of IRB Files

5.3.1. The QI and Education Specialist may study the IRB files in order to become familiar with the protocol and to identify any additional issues that should be focused on during the audit. The following may be reviewed:

5.3.1.1. Initial IRB electronic application.

5.3.1.2. Subsequent IRB electronic submissions:

5.3.1.2.1. Amendments, revisions, or modifications.

5.3.1.2.2. Continuing reviews.

5.3.1.2.3. Reports.

5.3.1.3. All correspondence to and from IRB including approval letters and notifications.

5.3.1.4. Training records.

5.3.1.5. Clinical Trial Agreements, if applicable.

5.3.1.6. IRB meeting minutes.

5.4. Onsite Audit Activities:

5.4.1. **Audit tools and methods** may include, but not be limited to:

5.4.1.1. Interview questions.

5.4.1.2. Review of any study records, subject files, source documents, binders, etc.

5.4.1.3. The QI and Education Specialist will audit the selected study using EQuIP compliance worksheets.

5.4.2. Debriefing Interview

5.4.2.1. The QI and Education Specialist will cover the impetus behind the audits and audit process with the PI and research staff.

5.4.2.2. The PI and research staff will have an opportunity to explain or respond to issues that instigated the directed for-cause audit.

5.4.3. Audit of Records

5.4.3.1. The PI does not need to be present during the entire audit. A designated member of the study team must be available via phone/page or nearby for questions and retrieval of additional material.

5.4.3.2. The documents reviewed will focus on the reason for the audit request and may include, but not limited to:

5.4.3.2.1. Informed consent: forms, process, observation of consenting process.

5.4.3.2.2. Confirmation of subject eligibility.

5.4.3.2.3. Confirmation of protocol procedures and interventions.

5.4.3.2.4. Collecting and reporting adverse events and UPIRSOs.

5.4.3.2.5. Protocol violations or deviations.

5.4.3.2.6. Confidentiality and security measures.

5.4.3.2.7. Subject recruitment, screening, and compensation.

5.4.3.2.8. Subject study and source files.

5.4.3.2.9. IRB, Sponsor, Regulatory Agencies correspondences.

5.4.3.2.10. Monitoring reports.

5.4.3.2.11. Storage facilities for devices, drugs, and biologic.

5.4.3.2.12. Training files.

5.4.3.2.13. Discussion with any individuals involved in study activities.

5.4.3.3. Other documents will be reviewed at the discretion of the QI and Education Specialist.

5.4.3.4. Once the audit is complete, the designated study team member will return study files/records.

5.4.3.5. The length of the audit is dependent on many factors such as the reason for the audit, the type of study, the number of subjects, how long the study has been open, etc.

5.4.3.6. The QI and Education Specialist documentation of findings will be a based on:

5.4.3.6.1. The information contained in the IRB electronic application approved by the IRB.

5.4.3.6.2. Review of written study records reflecting study conduct.

5.4.3.6.3. Verbal report from the PI and research personnel.

5.4.3.6.4. Applicable policies, regulations, and ICH GCP guidelines.

5.4.3.7. Audit findings will be documented on the EQuIP compliance worksheets.

5.4.4. Preliminary Findings

5.4.4.1. The QI and Education Specialist will meet with the PI and/or designee to discuss preliminary findings and to allow an opportunity to correct, explain, and/or ask questions.

5.4.4.2. Feedback will be sought regarding the IRB process, educational/training programs, as well as other aspects of the human research protections program at MHC.

5.4.4.3. The QI and Education Specialist will provide recommendations and describe the next set of steps in the process.

5.4.4.4. The exit interview occurs upon completion of the audit but may be deferred if there is a conflict in scheduling (i.e., PI is in surgery).

5.4.4.4.1. A deferred discussion may occur via the phone or email.

5.5. Post Audit Activities

5.5.1. If the findings reveal an immediate threat to subject rights, safety and welfare, the IRB chair and Corporate Manager of Research Integrity will be notified.

5.5.1.1. When appropriate, the policy *MHC_RP111_Study Suspension, Termination and Investigator Hold* will be followed.

5.5.1.2. A follow-up report will be created as in section 5.5.2.

5.5.2. Written Audit Report

5.5.2.1. Upon completion of the audit, the information collected will be analyzed and a Post Audit Summary Report will be generated within 5 business days. The report will address:

5.5.2.1.1. Report on findings specific to the request.

5.5.2.1.2. All other findings where the investigator did not adhere to applicable federal regulations, MHC HRPP policies, ICH GCP guidelines or the protocol.

5.5.2.1.3. Corrective Action Preventative Action Plan, if applicable (see 5.5.3 for CAPA plan procedures).

5.5.2.2. If there are indications of serious or continuing non-compliance, the IRB will be notified.

5.5.2.2.1. The IRB will make the determination of serious or continuing non-compliance and follow up actions (e.g., follow-up review, notification of Sponsor or regulatory authorities, monitoring of informed consent process, suspension, or termination).

5.5.3. Primary Investigator CAPA Plan Procedures

5.5.3.1. If the PI must complete a CAPA Plan, the PI will have 30 days from submission of the Post Audit Summary Report Letter.

5.5.3.2. In the event the PI requires more than 30 days to develop, document and submit the CAPA plan, or has questions or concerns regarding the process, the PI or coordinator must contact the EQuIP Office.

5.5.3.3. The PI will then have the opportunity to respond in writing to each find in the audit, either challenging the finding or offering additional supporting evidence.

5.5.3.4. If the CAPA Plan is not received by the given deadline, the QI and Education Specialist will send an email reminder to the PI and coordinator.

5.5.3.5. Once the responses to the CAPA plan are received, the Corporate Manager of Research Integrity will review the response.

5.5.3.5.1. If the CAPA Plan is approved, EQuIP will email a Closeout Letter.

5.5.3.5.2. The Closeout Letter will include a statement on future follow-up visits, if deemed necessary, to ensure adherence to the CAPA Plan.

5.5.3.5.3. If CAPA Plan is not approved:

5.5.3.5.3.1. EQuIP will return the CAPA Plan with a cover letter.

5.5.3.5.3.2. The cover letter will explain the deficiencies in the response and request a revision.

5.5.3.5.3.3. The PI will have 2 weeks to revise and correct the CAPA plan.

5.5.3.6. The time between receipt of the CAPA Plan and Closeout Letter will depend upon request for additional information or revision of response by the PI.

5.5.4. Dissemination Post Audit Summary Report and Closeout Letter will be sent to:

5.5.4.1. Primary Investigator.

5.5.4.2. Requestor of the Audit.

5.5.4.3. Corporate Manager of Research Integrity.

5.5.4.4. Academic Advisor and Director of Medical Education if PI is a resident or student.

5.5.4.5. McLaren Center for Research Innovation (MCRI) management if they have oversight over the involved MHC site.

5.5.5. Verbal Audit Report

5.5.5.1. The QI and Education Specialist may present the audit findings at a convened IRB meeting.

5.5.6. Retention of Audit Documents

5.5.6.1. The PI's electronic audit files will be stored on a password-protected computer in the EQuIP offices.

5.5.6.2. Paper audit files will be locked in a file cabinet in the EQuIP offices.

5.5.6.3. The audit documents will be stored for 3 years in the EQuIP offices.

6. Responsibilities

6.1. Quality Improvement (QI) and Education Specialist:

6.1.1. Responsible for conducting directed for cause audits of MHC research studies to ensure compliance with applicable federal regulations and/or agency specific requirements, state or local laws, and institutional policies and procedures.

6.1.2. Generate written reports with results of site review and identify strengths and deficiencies or deviations from federal regulations, local laws, institutional policies, and Good Clinical Practice (GCP).

6.1.3. Responsible for preparing and presenting reports to the Corporate Manager of Research Integrity.

6.2. Principal Investigator (PI):

6.2.1. Responsible for the conduct and oversight of their research study, including oversight of personnel and for protecting the rights, safety, and welfare of the subjects enrolled in the research.

6.2.2. Responsible for making available study documents for review or audit and addressing concerns or deficiencies via interview and/or CAPA plan.

6.3. IRB:

6.3.1. Responsible for assuring that research studies are approved in accordance with federal, state, and local regulations as well as the HRPP policies and procedures.

6.3.2. Responsible for making available time as well as addressing concerns or deficiencies via interview and/or CAPA plan.

6.4. Corporate Manager of Research Integrity

6.4.1. Responsible for developing, managing, and evaluating policies and procedures that ensure compliance with all state and federal regulations governing research.

6.4.2. Responsible for developing and implementing needed improvements and ensuring follow-up of actions, as appropriate, for the purpose of managing risk in the research program.

6.4.3. Instituting Corrective Action Plans based upon audit findings.

7. References

7.1. 45 CRF 46.113 Suspension or termination of IRB approval of research

7.2. 21 CFR 56.113 Suspension or termination of IRB approval of research

7.3. 45 CFR 46.109(e) IRB Review of Research

7.4. 21 CFR 56.109(f) IRB Review of Research

7.5. 21 CFR 56.108(a) IRB Functions and Operations

7.6. 45 CFR 46.103(b)(4) Assuring compliance with this policy.

7.7. OHRP Guidance on Written Procedures, January 2007

7.8. Terms of the Federalwide Assurance, #4 on written procedures

7.9. MHC_RP111_Study Suspension, Termination and Investigator Hold"

7.10. MHC_RP0123_Complaints and Non-Compliance in Human Subject Research

7.11. MHC_RP0124_Reporting to Regulatory Agencies and Institutional Officials

7.12. MHC_RP301_Education and Quality Improvement Program – EQuIP

7.13. EQuIP Compliance Worksheets

8. Previous Revisions: 11/28/21, 1/20/23

9. Supersedes Policy: None

10. Approvals:

Signature on File *3/22/2024*

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