McLaren HEALTH CARE		**Policy Title:**	**QA/QI Routine Review**
Effective Date:	October 8, 2015	**Policy Number:**	MHC_RP0302
Review Date:	October 8, 2015	**Section:**	Human Research Protections Program
Revised Date:		**Oversight Level:**	Corporate
Administrative Responsibility:		Corporate Director, HRPP Institutional Official, HRPP	

1. Purpose

1.1. The purpose of this policy is to establish the process for the EQuIP Office to perform QA/QI Routine Reviews 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. Continuing Non-Compliance: A pattern of non-compliance that indicates a deficiency likely to result in further non-compliance or circumstance in which an investigator fails to cooperate with investigating or correcting non-compliance.

3.2. Corrective Action Preventative Action Plan (CAPA): A systematic plan to align research conduct in line with federal regulations, laws, and institutional policies.

3.2.1. Corrective Action is the action taken to eliminate the causes of an existing non-compliance issue or other undesirable situation in order to prevent recurrence.

3.2.2. Preventative Action is action taken to eliminate the cause of a potential non-compliance or other undesirable situation in order to prevent occurrence.

3.3. Education and Quality Improvement Program (EQuIP): A program that encompass the HRPP Offices of Research Compliance and Quality Improvement with the Office of Education, Training, and Resources.

3.4. Good Clinical Practice (GCP): Good clinical practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and wellbeing of the trial subjects are protected; consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data is credible.

3.5. Minor Non-Compliance: Any non-compliance that is not serious or continuing. The non-compliance does or did not:

3.5.1. harm or pose an increased risk to a participant.

3.5.2. result in a detrimental emotional or clinical change in the participant or

3.5.3. have a substantive effect on the value of the data collected.

3.5.4. Examples of minor non-compliance may include, but are not limited to, lapses in continuing IRB approval, failure to obtain a prospective exempt determination from the IRB, minor changes in or deviations from an approved protocol, or administrative error.

3.6. Non-Compliance: Failure to follow the regulations, requirements, or determinations of the IRB.

3.7. QA/QI Routine Reviews: A quality assurance and quality improvement effort to ensure optimal conduct of human subject research within the framework of institutional policy and regulatory requirements and to provide educational resources to Investigators and members of the study team.

3.8. Quality Assurance (QA): An evaluation of whether or not activities meet defined standards. In the context of research, QA is a retrospective, objective, and systematic review of trial related activities to ensure that the trial is performed in compliance with federal regulations, MHC institutional policies, and Good Clinical Practices.

3.9. Quality Improvement (QI): Systematic efforts or activities aimed at improving human subject research conduct through analysis and interpretation of performance demonstrated through QA/QI reviews and audits.

3.10. QA/QI Routine Review Preparation Overview: An informational document that provides an overview of the review process and instructions on how to prepare for the review.

3.11. Serious Non-Compliance: Non-compliance that adversely affects the rights and welfare of subjects.

3.12. Refer to Appendix I "Definitions" for additional definitions.

4. Policy

4.1. As part of the McLaren's AAHRPP Quality Improvement and Quality Assurance Program, the Office of Research Compliance and Quality Improvement, through EQuIP, is authorized to conduct QA/QI routine site visits to review research records, observe ongoing research projects, and the consenting process as well as continually educating and updating MHC researchers' regarding human subject protection.

4.2. McLaren's 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. QA/QI Routine Reviews of MHC research studies will be conducted to:

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

4.3.2. Ensure the highest degree of research standards are being maintained in regards to the safety of human subject research.

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. Based upon the results of routine reviews and feedback from investigators, quality improvement measures, a CAPA plan, or both may be implemented.

4.6. If non-compliance in the conduct of research is determined, the PI will be responsible for complying with a Corrective Action Preventative Action (CAPA) plan initiated by the EQuIP Office.

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

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

5. Procedures

5.1. Selection of Protocol/Primary Investigator:

5.1.1. The total number of protocols reviewed in a year and focus of the QA/QI Routine Review will be determined by the QI and Education Specialist in consultation with the Corporate Director of HRPP. This information will be listed in the QA/QI Plan.

5.1.2. Each quarter the QI and Education Specialist will create of list of potential protocols that meet the following criteria:

5.1.2.1. Active studies that have not undergone previous EQuIP review.

5.1.2.2. All active studies using an investigational drug or device.

5.1.2.3. All active studies regardless of category of IRB review: Chart Review, Expedited, Exempt, HUD, or Full-Board Review.

5.1.2.4. All active studies with currently enrolling subjects.

5.1.3. Protocols selected for review are either:

5.1.3.1. Selected randomly by assigning a number to each protocol and running a random function in the Microsoft Excel program.

5.1.3.2. Selected purposely based on the following criteria;

5.1.3.2.1. Studies that involve vulnerable populations.

5.1.3.2.2. Investigators who conduct studies that involve a potential high risk to subjects.

5.1.3.2.3. A new PI and/or Clinical Research Coordinator.

5.1.3.2.4. Past clinical trial non-compliance/problems.

5.1.3.2.5. Studies involving various waivers.

5.1.3.2.6. Protocols with lapses of IRB approval.
5.1.3.2.7. High enrolling studies.
5.1.3.2.8. Resident or student PI.
5.1.3.2.9. Involvement of multiple departments, i.e. cancer, cardiology, neurology, etc.
5.1.3.2.10. Investigators who conduct studies that involve large numbers of subjects.

5.2. Pre-audit Preparation

5.2.1. The QI and Education Specialist will notify the Principal Investigator (PI) and Coordinator that their study has been selected for routine review.

5.2.1.1. An email notification is sent approximately 4 weeks prior to the review. The PI will be asked to respond within 1 week of email notification.

5.2.1.2. If the EQuIP Office does not receive the PI's response within one week of the initial notification, a *Reminder Routine Review Notification* will be sent by email.

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

5.2.1.4. If the PI is a resident or student, the academic advisor and Director of Medical Education will also be notified.

5.2.1.5. The HRPP Director will be copied on the notification.

5.2.2. Once the PI confirms availability for the routine review, the PI or designee will be asked to forward a list of all consented subject IDs, not names, no later than 2 weeks prior to the scheduled review date.

5.2.2.1. Once received, the QI and Education Specialist will randomly select a percentage of subjects for review and notify the PI prior to the review date which complete subject files should be available for review.

5.2.2.2. In addition to selected subjects' research files, the PI will be informed to have available for review all the signed consent forms.

5.2.2.3. If the study has no subjects consented or if the study has been completed, terminated, closed to enrollment (data analysis only), or otherwise deemed ineligible for review, the study will be withdrawn from the review.

5.2.3. After the appointment date and time along with subject selections are confirmed, a *Routine Review Notification Confirmation Letter* is emailed to the primary investigator and research coordinator.

5.2.3.1. A QA/QI Routine Review Preparation Overview form will be included in the confirmation notification.

5.2.3.2. The primary investigator will be encouraged to complete the QA/QI Review Self-Assessment Form.

5.3. Review of IRB Files

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

5.3.1.1. Initial eProtocol application

5.3.1.2. Subsequent eProtocol 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 correspondences 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 Review Activities:

5.4.1. QA/QI Routine Review 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.

5.4.2. Debriefing Interview

5.4.2.1. The QI and Education Specialist will meet with the PI and/or designee to discuss:

5.4.2.1.1. Purpose and activities of the routine review.

5.4.2.1.2. Problems or issues regarding study conduct.

5.4.3. Review of Records:

The PI does not need to be present during the entire review; however, a designated member of the study team must be available via phone/page or nearby for questions and retrieval of additional material.

5.4.3.1. The QI and Education Specialist may review the following, but not limited to:

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

5.4.3.1.2. Confirmation of subject eligibility

5.4.3.1.3. Confirmation of protocol procedures and interventions
5.4.3.1.4. Collecting and reporting adverse events and UPIRSOs
5.4.3.1.5. Protocol violations or deviations
5.4.3.1.6. Confidentiality and security measures
5.4.3.1.7. IRB, Sponsor, Regulatory Agencies correspondences
5.4.3.1.8. Subject recruitment, screening, and compensation
5.4.3.1.9. Subject study and source files
5.4.3.1.10. Monitoring reports
5.4.3.1.11. Storage facilities for devices, drugs, and biologic
5.4.3.1.12. Training files
5.4.3.1.13. Discussion with any individuals involved in study activities

5.4.3.2. Once the review is complete, the designated study team member will return study files/records.

5.4.3.3. The length of the review is dependent on many factors such as the type of study, the number of subjects, how long the study has been open, etc.

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

5.4.3.4.1. The information contained in the eProtocol application approved by the IRB
5.4.3.4.2. Review of written study records reflecting study conduct
5.4.3.4.3. Verbal report from the PI and research personnel
5.4.3.4.4. Applicable policies, regulations, and ICH GCP guidelines

5.4.3.5. Audit findings will be documented on EQuIP compliance worksheets.

5.4.4. Preliminary Findings Discussion

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 routine review activities but may be deferred if there is a conflict in scheduling.

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

5.5. Post Review Activities

5.5.1. After the review, the EQuIP staff will complete a review summary report. Possible outcomes will usually fall into 1 or 2 of 4 categories, which will determine post-review follow-up activities:

5.5.1.1. PI is conducting the research study in compliance with federal regulations, HRPP policies, and approved protocol.

5.5.1.2. PI is conducting the research study with potential issues of minor non-compliance.

5.5.1.3. PI is conducting the research study with potential issues of serious or continuing non-compliance.

5.5.1.4. Routine review results indicate IRB non-compliance.

5.5.2. Follow-Up of Research Conducted in compliance with federal regulation, IRB policies, and approved protocol

5.5.2.1. No CAPA plan is required.

5.5.2.2. A QA/QI Routine Review Summary Letter will be sent to the PI via email within 10 business days of the review.

5.5.2.3. The PI and Coordinator will review the findings and forward any comments to the EQuIP Office.

5.5.3. Follow-Up on Potential issue of minor non-compliance

5.5.3.1. A CAPA plan is created (see 5.5.6. for CAPA plan procedures)

5.5.3.2. A QA/QI Routine Review Summary Letter with a CAPA Plan will be emailed within 10 business days of the review.

5.5.3.3. If additional investigation is required after the site review, the turnaround timeline will change accordingly.

5.5.4. Follow-up on Potential issues of serious or continuing non-compliance

5.5.4.1 If the findings reveal an immediate threat to subject rights or safety and welfare, the IRB chair and Corporate Director of HRPP will be notified immediately. If this occurs, the *MHC_RP111_Study Suspension, Termination, and Investigator Hold* policy will be followed.

5.5.4.2. The IRB will make the formal determination of serious or continued non-compliance following the policies

MHC_RP0123_ Complaints and Non-Compliance in Human Subject Research and *MHC_RP0124_Reporting to Regulatory Agencies and Institutional Officials*.

5.5.4.3. A CAPA plan will be created (see 5.5.6 for CAPA plan procedures)

5.5.4.4. A QA/QI Routine Review Summary Letter with a CAPA Plan will be emailed within 10 business days of the review.

5.5.4.5. If additional investigation is required after the site review, the turnaround timeline will change accordingly.

5.5.5. Follow-Up on Routine review results in which there are IRB non-compliance findings

5.5.5.1. If the findings are relevant to IRB non-compliance, a separate IRB QA/QI Routine Review Summary Letter with recommendations will be emailed to the IRB Chair within 10 business days of the review.

5.5.5.2. If corrective actions are required, the Corporate Director of HRPP will initiate a CAPA Plan.

5.5.6. Primary Investigator CAPA Plan Procedures

5.5.6.1. The PI will have 30 days from submission of the QA/QI Routine Review Summary Letter to submit a response to the CAPA Plan.

5.5.6.2. 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 QI and Education Specialist.

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

5.5.6.4. Once the responses to CAPA Plan are received, the Corporate Director of HRPP will review the responses.

5.5.6.5. If the CAPA Plan is approved the EQuIP Office will email a Closeout Letter.

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

5.5.6.7. If the CAPA Plan is not approved:

5.5.6.7.1. The EQuIP Office will return the CAPA Plan with a cover letter.

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

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

5.5.6.8. 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.

5.6. Dissemination of the QA/QI Routine Review Summary and Closeout Letter:

5.6.1. Primary Investigator.

5.6.2. Corporate HRPP Director.

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

5.6.4. McLaren Center for Research Innovation (MCRI) management will be notified if they have oversight over the involved MHC site.

5.6.5. QA/QI reviews are confidential and will not be submitted to the IRB unless there is evidence of serious or continuing non-compliance.

5.7. Retention of Review Documents

5.7.1. The PI's electronic audit files will be stored on a password-protected computer in the Office of Research Compliance and Quality Improvement.

5.7.2. Paper review files will be locked in a file cabinet of the Office of Research Compliance and Quality Improvement.

5.7.3. The audit documents will be stored for 3 years at the Office of Research Compliance and Quality Improvement.

6. Responsibilities

6.1. Quality Improvement and Education Specialist:

6.1.1. Responsible for conducting QA/QI Routine Reviews 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 identified strengths, deficiencies, or deviations from federal regulations, local laws, institutional policies, and Good Clinical Practice.

6.1.3. Responsible for preparing and presenting reports to the Corporate HRPP Director.

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 right, 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 Director of HRPP

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 CFR 46.109(e) IRB Review of Research
7.2. 21 CFR 56.109(f) IRB Review of Research
7.3. 21 CFR 56.108(a) IRB Functions and Operations
7.4. 45 CFR 46.103(b)(4) Assuring compliance with this policy
7.5. OHRP Guidance on Written Procedures, January 2007
7.6. Terms of the Federalwide Assurance, #4 on written procedures
7.7. MHC_RP111_Study Suspension, Termination and Investigator Hold
7.8. MHC_RP0123_Complaints and Non-Compliance in Human Subject Research
7.9. MHC_RP0124_Reporting to Regulatory Agencies and Institutional Officials
7.10. MHC_RP0125_Investigator Responsibilities
7.11. MHC_RP301_Education and Quality Improvement Program – EQuIP
7.12. EQuIP Compliance Worksheets

8. Previous Revisions: None

9. Supersedes Policy: None

10. Approvals:

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