Preparing for AAHRPP Re-Accreditation
Guidance for Key Personnel

All McLaren Investigators/Researchers, Administrators, HRPP Staff, and IRB Members are **essential** components of the Human Research Protection Program (HRPP) throughout the corporation and its subsidiary hospitals. The McLaren Human Research Protections Program (HRPP), under the oversight of the Research Integrity Department, is currently seeking re-accreditation. AAHRPP accreditation is a gold standard that will contribute to increased interest in the research being performed at McLaren and publicly affirms McLaren as a top-tier institution in ethical and regulatory conduct of human subject research.

The AAHRPP site review team will be at the McLaren Healthcare Corporation on February 16th and 17th. You have been chosen as an individual to be interviewed. The HRPP re-accreditation largely depends on successful completion of these interviews. We are counting on the commitment you make and solicit your help in this endeavor.

We have created materials to help you succeed.

This guidance is not intended to be memorized; it is intended to focus your thinking as you prepare for the interview. You may be familiar with the information included, however, it is important that you refresh your understanding. Interviews are very collegial and supportive.

AAHRPP Site Visitors:

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Associate Chair for Academic Affairs, Medical Manager HRPP, Chair IRB Pediatrics
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Areas of Focus

In addition to using this guidance, the following items have been identified by other institutions as likely areas of focus by the site review team:

- ✓ Know your role(s) as a Key Personnel in the Human Research Protection Program
- ✓ Know the roles of other members of the HRPP [e.g., IRBs, Office of Research Compliance and Quality Improvement, Office of Research Education, Dr. Justin Klamerus - Executive Vice President/Chief Medical Officer (Institutional Official)]
- ✓ Know how to access HRPP's Policies and Procedures
- ✓ Understand what constitutes Financial Conflict of Interest
- ✓ Understand the Research Conflict of Interest Review Committee's mechanism to review Investigator COI and how the information is communicated to the Investigator and to the IRB for consideration. See the Research Conflict of Interest Committee Policy and COI Review Process Table

Questions to Consider

Please note that some of the questions might not apply to your role directly.

1. **Do you know HRPP's structure?**
2. **Do you know what AAHRPP accreditation is and why McLaren is seeking accreditation?**
3. **Who holds ultimate responsibility for the oversight of the HRPP at McLaren? (or who is the institutional official (IO)?)**
4. **Who holds direct responsibility for the day-to-day functions of the HRPP and IRB?**
5. **Who has the authority to approve human subject research at McLaren?**
6. **Can you describe the leadership and composition of the IRB?**
7. **In general, how long does it take to achieve IRB approval?**
8. **May an Investigator appeal a decision made by the IRB?**
9. **Who determines whether an activity is human subject research (HSR)?**
10. **Who determines whether a human subjects research project is exempt from the requirement for IRB review and oversight?**
11. **Who is responsible for the overall conduct of the research?**
12. **Are finders' fees and bonus payments allowed at McLaren?**
13. **Can you describe the Conflict-of-Interest review process at McLaren?**
14. **What training and basic education is required to ensure McLaren researchers are qualified to complete a human subjects project?**
15. **Are there categories or types of research that McLaren does not participate in?**
16. **Other Related Units**
17. **At McLaren, is there a Research Pharmacy? Describe the Pharmacy Relationship with the IRB**
18. **Describe the responsibilities of Legal Counsel to the IRB**
19. **Who is responsible for negotiating contracts? What is the process of ensuring that all required human protections language is in contracts?**
20. **Who is responsible for Research Compliance and Quality Improvement at McLaren?**

1. Do you know HRPP's structure?

Important: MHC is committed to protecting the rights and welfare of subjects in Human Research. Protecting research participants is the responsibility of everyone within McLaren and is not limited to the Institutional Review Board (IRB).

McLaren's Human Research Protection Program is a centralized system to ensure the protection of the rights and welfare of subjects and compliance with the highest legal and ethical standards in Human Research.

The HRPP Mission:

- To safeguard and promote the health and welfare of human research subjects by ensuring that their rights, safety and well-being are protected.
- To provide timely and high-quality education, review and monitoring of human research projects; and
- To facilitate excellence in human subjects research.

The McLaren HRPP is composed of both centralized and de-centralized components.

The Corporate Manager of the Research Integrity (Patricia Ivery), the VP of Clinical Excellence and Reserch is Chandan Gupte and the Institutional Official of Research (Dr. Justin Klamerus) all collaborate closely in leading the program. The HRPP is comprised of the following components:

(1) MHC IRB
(2) Office of Research Education, Training and Resources
(3) Office of Research Compliance and Quality Improvement/Assurance
(4) Research Conflict of Interest Review Committee

The components listed below are essential to the successful and ethical conduct of research, but not are necessarily housed within the HRPP:

(1) Individuals such as the Legal Counsel to the IRB (Ann Hollenbeck), the Corporate Compliance Officer (Dan Gillett), Managers of Medical Education, Investigators, Research Staff, and Research Participants.
(2) Other research units and administrative offices such as the McLaren Center for Research and Innovation (MCRI), , McLaren pharmacies handling investigational products.
(3) Committees such as the Protocol Review Committee

Remember: ***Human Research Protection is a shared institutional responsibility which encompasses diverse units and personnel crossing the three domains: Organizations, IRB and Researchers.***

The Human Research Protections Program (HRPP) - it is NOT all about the IRB

2. Do you know what AAHRPP accreditation is and why McLaren seeking re-accreditation?

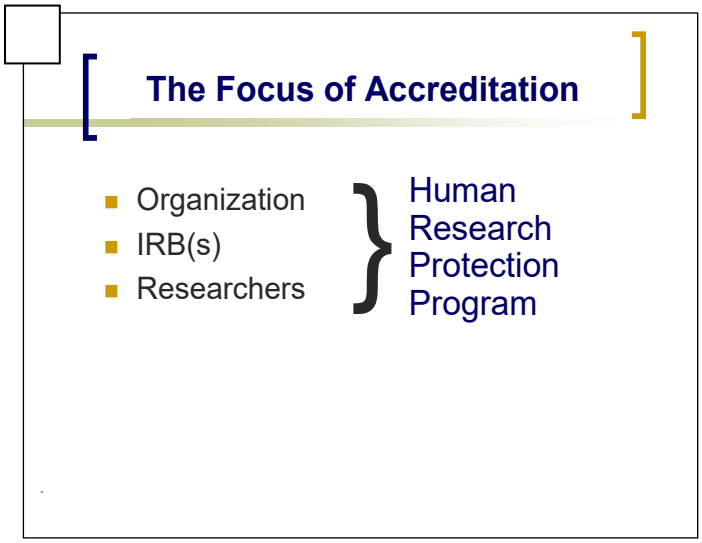
The Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRP) (www.aahrpp.org) accreditation process is voluntary, peer-driven, is educationally focused, and aims to foster a culture of conscience and responsibility within institutions seeking its services.

AAHRPP works to protect the rights and welfare of research participants and promote scientifically meritorious and ethically sound research by fostering and advancing the ethical and professional conduct of persons and organizations that engage in research with human participants. AAHRPP achieves its mission by using an accreditation process based on self-assessment, peer review, and education.

AAHRPP standards go "above and beyond" and recognize additional requirements that must be met, should research be supported by other entities. Through the self-assessment process, the McLaren HRPP continues to develop effective and efficient processes. Written policies and procedures have been developed to reduce the need for the IRB to make decisions on a case-by-case basis, and to provide guidance to investigators.

Points of Interest:

- ✓ The Office for Human Research Protections (OHRP) and the FDA recognize the value of accreditation.
- ✓ AAHRPP accreditation will enhance McLaren's reputation, giving us a competitive edge with sponsors.



3. Who holds ultimate responsibility for the oversight of the HRPP at McLaren? (or who is the institutional official (IO)?)

The authority and responsibility to establish, maintain and oversee the McLaren HRPP was delegated to the Executive Vice President/Chief Medical Officer, Dr. Justin Klamerus. Dr. Klamerus serves as the IO of the McLaren HRPP. Dr. Klamerus was granted this authority by a vote of each subsidiary hospital's Board of Trustees. Likewise, the Board of Trustees approved and authorized the development and implementation of the Corporate HRPP, including policy-making, and charged the MHC IRB with the authority to approve, require modifications in, or disapprove human subject research. Each subsidiary's Board of Trustees agreed with this decision which is reflected in the Letter of Resolution for each hospital.

The IO delegation includes, but is not limited to:

- Overseeing the protection of human participants, regulatory compliance and implementation of the HRPP
- Setting the level of the institutional culture of the ethical obligations of compliance
- Instilling respect for human research participants and ensuring effective system-wide communication and guidance on human subject research
- Ensuring that HRPP has the resources and support necessary to comply with all institutional policies and with federal regulations and guidelines that govern human subject research
- Ensuring that the HRPP is functional, adequately staff and funded, and respected in the research community
- Assuring that all investigators are appropriately knowledgeable to conduct research in accordance with ethical standards and applicable regulations
- Ensuring the independence of the IRB, including the authority to act without undue influence

The IO is also the signatory of Federal-wide Assurance (FWA) for McLaren Health Care and assumes the obligations of McLaren's FWA. ***NOTE: McLaren has 1 FWA that covers all subsidiary hospitals conducting federally funded research***

The IO is ultimately responsible for overseeing the protection of human subjects participating in research conducted at each hospital, by MHC employees or agents, and research approved by the MHC IRB. Additionally, the IO is legally authorized to execute documents and instruments with respect to the MHC IRB and with respect to the human subject research conducted at each subsidiary hospital.

The Corporate Manager of Research Integrity and VP of Clinical Excellence meet weekly to discuss the HRPP and address any concerns or questions that arise. Resources available to the HRPP are evaluated by VP of Clinical Excellence and Research in conjunction with the IO as needed and at least on an annual basis.

4. Who holds direct responsibility for the day to day functions of the HRPP and IRB?

Patricia Ivery was delegated the responsibility of the day-to-day functions, oversight and management of the Corporate HRPP, including MHC IRB. Patricia Ivery serves as an expert resource on matters of regulations and policies and provides the day-to-day administration of the HRPP. Dr. M. Ammar Hatahet is a seasoned investigator and IRB Chair and collaborates with McLaren's HRPP in the development and implementation of the HRPP, including educational programs, policies, and other resources.

The Corporate Manager of HRPP is involved with the centralized components and facilitates communication and coordination among all components to ensure protection in human subject research.

5. Who has the authority to approve human subject research at McLaren?

McLaren has one Corporate IRB (***MHC IRB***). MHC IRB has the authority to approve human subject research at McLaren and its subsidiary hospitals. MHC IRB has been charged by the Board of Trustees of each subsidiary hospital with the authority to approve, require modifications to secure approval, or disapprove human subjects research at McLaren and its subsidiary hospitals.

Other individuals or components of the organization may disallow a research study, but they cannot overturn a disapproval by the IRB or approve research that the MHC IRB has not approved. The IRB may, on occasion, cede IRB review and oversight in full or in part to another IRB through a formal arrangement established between the 2 IRBs. Such requests must be approved by the Corporate Manager of HRPP and the IO. McLaren might rely upon the IRB of another organization, provided one of the following is true:

- The IRB is the IRB of an AAHRPP accredited organization.
- McLaren's investigator is conducting research with another organization and has a written agreement between the 2 IRBs.

- For review of collaborative research on a case-by-case basis. When this occurs, a single project reliance agreement is executed by the parties. This is done through the Corporate Manager of HRPP.

In general, the McLaren IRB (MHC IRB) chooses to maintain local oversight as the local IRB, as it is in the best position to evaluate the circumstances of the local research plan and protections for our participants.

6. Can you describe the leadership and composition of the IRBs?

MHC IRB has a designated Chair and Vice-Chair. Dr. Hatahet, is a Board certified physician in Internal Medicine with research experience and serves as the IRB Chair to MHC IRB. Michael Laeder serves as the Vice-Chair to MHC IRB. Michael Laeder is an MHC retired employee who worked as Director of Pharmacy Services. He served several years as an IRB member.

The MHC IRB is composed of physicians, nurses, pharmacists, privacy and compliance officers, and other disciplines with a breadth of specialty expertise and knowledge of vulnerable populations. The IRB is composed of both scientific and non-scientific members and members affiliated and unaffiliated (commonly referred to as Community Representatives) with McLaren. When the MHC IRB requires expertise beyond its membership, it seeks consultation from others internally, or from others external to the organization. MHC IRB meets twice a month.

7. In general, how long does it take to achieve IRB approval?

** Note: This is something that site visitors will be looking at closely. Please review this section carefully.*

*Often the delay in approval is due to incomplete application as well as delayed responses to reviewers' questions.

Review Type	Number of days from receipt of a complete submission to Approval
EXEMPT	10 - 20 *
EXPEDITED	7 - 14 *
FULL Board	15 - 25 *

8. May an investigator appeal a decision made by the IRB?

Yes, investigators are welcome to submit a request for reconsideration to the IRB and to personally present their case. An investigator can request reconsideration by submitting a written response to the IRB via e-mail at hrpp@mclaren.org.

9. Who determines whether or not an activity is human subjects research (HSR)?

Investigators are asked to contact the MHC IRB office with any questions regarding whether an activity constitutes research and/or a clinical investigation involving human subjects. The investigators will be asked to complete the "Request for Determination of Non-Human Subject Research" form and send it to MHC IRB via e-mail. The MHC IRB staff and/or MHC IRB Chair will determine whether the activity meets the definition of human subject research based on federal regulatory definitions, 45 CFR 46.102(d), 21 CFR 50, or 21 CFR 56.

The investigator shall not make the determination.

10. Who determines whether or not a human subject's research project is exempt from the requirement for IRB review and oversight?

Determinations of exemption should be made by persons well-versed in the regulations, but not personally involved in the investigation or otherwise conflicted. At McLaren, determination of whether human subject research can be exempt is made by the MHC IRB Chair or IRB Analyst who is also a member of the IRB, acting on behalf of MHC IRB. Investigators or others within the organization may not make exemption determinations.

11. Who is responsible for the overall conduct of the research?

The Principal Investigator (PI).

12. Are finders fees and bonus payments allowed at McLaren?

Although research sponsors may offer to pay researchers and research staff an additional fee to encourage participant recruitment efforts and the timely or accelerated opening of research studies, these payments are strictly prohibited.

- ✓ It is not permissible to pay or accept a "finder's fees."
- ✓ It is not permissible to accept bonus payments. McLaren employees or students cannot accept personal payments from sponsors or other researchers in exchange for accelerated recruitment or referrals of patients. Cash or cash-equivalent payment to health care providers for referral of subjects or potential subjects is not permitted.
- ✓ Other types of compensation (e.g., books, other non-cash gifts) are also prohibited.

13. Can you describe the COI review process at McLaren?

**Note: It is important that interviewees provide the same answers for how the process works. Please review this section carefully.*

McLaren maintains a Research Conflict of Interest Committee (RCOI). The purpose of the RCOI is to establish an effective process to identify, report, and resolve conflicts of interest. The specific functions and authority of the RCOI Committee is to handle matters that present potential conflicts of interest with respect to institutional interests and with respect to all researchers and research personnel at McLaren.

1. All research personnel (Principal Investigator (PI), Sub-Investigators, Coordinators, etc.) are required to disclose any potential conflict of interest on the application for IRB Review. The IRB application asks protocol-specific questions regarding conflict of interest for the investigators, personnel and their immediate families. Moreover, the PI is prompted to update the COI Questionnaire while completing any submissions to the MHC IRB.

Studies with a potential COI will be forwarded to the Corporate Manager of HRPP who will review the disclosures and the study and obtain further information as needed. The potential COI is forwarded to the RCOI.

NOTE: A Financial Conflict of Interest exists if the Committee determines that the interest could *directly and significantly* affect the design, conduct or reporting of the research. In making this determination, the Committee will consider—and may ask the Investigator to provide—additional information related to the following factors:

- Nature of the interest (e.g., consulting, equity interest, speaking fee, travel, etc.)
- Value or amount of the Financial Interest
- The Investigator's role in the project,(e.g., consenting/enrolling patients, data analysis, publication & reporting, etc.0
- Risk profile of the project (i.e., to project participants, to the organization, etc.)
- Additional information regarding the relationship of the Financial Interest to the particular research project or program

If the Committee determines that an FCOI exists, the Committee will develop a Management Plan.

The Corporate Manager of HRPP will make a report to the MHC IRB that includes a summary of the facts, the conclusion as to whether an actual or potential conflict exists and may include recommendations for a proposed management plan to address the circumstances, which may include management and/or disclosure of the conflict.

The IRB reviews the report and recommendations of the Research Conflict of Interest Review Committee. The IRB will make a final determination as to whether a conflict of interest exists with regard to the specific protocol under review and the actions to take in regards to management and/or disclosure. If a conflict of interest exists, final IRB approval cannot be given until an approved conflict management plan is in place or determined to be unnecessary.

Annually, all McLaren leaders are required to complete a COI Survey. The survey includes questions related to research. If institutional potential conflict is disclosed, it will be forwarded to the FCOI for review and determination. If an institutional conflict exists in relation to research, appropriate actions will be taken to eliminate or minimize the risk to business decision.

14. What training or basic education is required to ensure McLaren researchers are qualified to complete a human subjects project?

Currently, all individuals conducting research at McLaren are required to complete the CITI Human Subjects Research Tutorial for credit. McLaren has implemented the CITI Conflict of Interest Course which is available to all Researchers to take.

All individuals involved in **conducting** human subject research are required to successfully complete training in ethical principles on which human research is to be conducted and accepted Good Clinical Practices. HRPP has an oversight mechanism to ensure that all individuals involved in conducting human subject research are up-to-date with their required training.

15. Are there categories or types of research that McLaren does not participate in?

McLaren does not currently engage in:

- planned emergency research (research in which an intervention must be administered before consent from subjects or permission from their representatives can be obtained),
- international research,
- research funded by or otherwise subject to Department of Defense regulations,
- research funded by or otherwise subject to Department of Justice regulations,
- research funded by or otherwise subject to Department of Education regulations,
- research funded by or otherwise subject to Veteran Administration regulations and
- research that plans to or is likely to involve prisoners as subjects.

In the event that an investigator wanted to pursue research within one of these categories, additional policies and processes would need to be put into place in order to ensure that the research was conducted and reviewed in accordance with ethical standards and regulations governing such research. The decision on whether to apply the resources necessary to move forward with such research would be made by the Institutional Official (IO).

16. Other Related Units:

McLaren Center for Research and Innovation (MCRI) has a centralized clinical trial infrastructure which streamlines operations while maintaining efficiencies and conducting research in compliance with federal and state regulations and HRPP policies. MCRI and HRPP work closely together to ensure transparency within the departments.

Feasibility Review Committee is responsible for reviewing all non-oncology research conducted at McLaren for operational impact, contract and budget.

Protocol Review Committee (PRC) is charged with the responsibility to review all research conducted at McLaren through the MCRI. Exception applies to oncology research conducted through Karmanos. Approval from the PRC is provided to the MHC IRB at the time of IRB submission.

Protocol Review Monitoring Committee (PRMC) is charged with the review of the scientific merit for all oncology research conducted at McLaren, study prioritizing and monitoring accrual status/goal. Approval from the PRMC is provided to the MHC IRB at the time of IRB submission.

Feasibility Review Oncology Committee is responsible for reviewing all oncology research conducted at McLaren for operational impact, contract and budget.

McLaren Flint Research Advisory Board (RAB)reviews Graduate Medical Education investigator-initiated studies that are proposed to be conducted at McLaren Flint. The Board is charged with the review of the scientific merit.

17. At McLaren, is there a Research Pharmacy? Describe the Pharmacy Relationship with the IRB.

McLaren's pharmacies typically do not engage in the ordering/providing, dispensing, or compounding of drugs used in research, unless the drug is a controlled substance or administered on an inpatient basis, in which case the item is ordered/received by the Pharmacy and re-issued in appropriate quantities to researchers for human studies, pursuant to a study-specific and patient-specific medication order developed by the pharmacy in collaboration with the researcher.

PIs are typically responsible for the accountability of medications and drugs used in their clinical investigation but may delegate these duties to an appropriate McLaren Pharmacy. When using McLaren's Pharmacy, the Manager of Pharmacy is primarily responsible for the accountability of all investigational drugs; however, all pharmacies are authorized to dispense according to policy and procedure. PI works closely with the Pharmacy Staff to ensure that protocol procedures are followed.

All McLaren pharmacies are available to provide guidance to investigators in relation to the management of the study drugs.

18. Describe the responsibilities of Legal Counsel to the IRB

The McLaren HRPP relies on the MHC Corporate Counsel for the interpretations and applications of State law and the laws of any other jurisdiction where research is conducted as they apply to human subject research.

Legal Counsel at MHC advises on human-subjects research issues and legal requirements; research compliance matters; research integrity and related misconduct investigations; conflicts of interest questions; intellectual property; technology transfer and licensing. Their work related to human subject protection includes, for example, drafting IRB Authorization Agreements, Letters of Resolutions, Investigator Agreements, advising on project-specific issues (e.g., informed consent, confidentiality), counseling on privacy requirements, assisting in investigations of alleged noncompliance, advising on liability issues, and generally interpreting and advising on new and existing legal requirements and conflicts between applicable laws.

19. Who is responsible for negotiating contracts? What is the process of ensuring that all required human protections language is in contacts?

It is McLaren HRPP's Policy that any research conducted under the auspices of the Institution is conducted in accordance with federal guidelines and ethical standards. Certain research agreements with federal, foundation, or non-profit sponsors (except registries and exempt studies) conducted at or through MHC subsidiaries will be reviewed by the Office of Budgets and Contracts through the McLaren Center for Research and Innovation (MCRI). MCRI staff and/or assigned attorney uses a specific checklist to ensure that all AAHRPP required elements are included in the contract.

Certain contracts are reviewed by another entity in which the Investigator reports. Investigators are also required to use the specific checklist to ensure that all AAHRPP required elements are included in the contract.

As part of its quality improvement program, McLaren's HRPP requests a copy of the contract to ensure that the protocol, consent form and contract is consistent and meet AAHRPP's standards.

IRB application will ask a set of questions to ensure that no subjects are enrolled unless CTA and the MHC IRB approved consent form are in agreement.

20. Who is responsible for the Research Compliance and Quality Improvement at McLaren?

The Corporate Manager of HRPP is responsible for the Office of Research Compliance and Quality Improvement at McLaren. The QI and Education Specialist works closely with the Corporate Manager of HRPP to ensure that research at McLaren is reviewed and conducted according to the highest ethical standards, in compliance with federal, state and organizational regulations.

The QI and Education Specialist conducts QA/QI reviews of human subject research studies. Directed ("for cause") audits and periodic (not "for cause") compliance reviews are being conducted to assess investigator compliance with federal, state, and local law, and Organization policies, and to identify areas for improvement, and suggest recommendations based on existing policies and procedures.

The Office of Research Compliance and Quality Improvement is separate from the IRB and falls under the HRPP.