Office of Research Integrity
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Preparing for AAHRPP Re-Accreditation
Guidance for Researchers and Research Staff*

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) 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.

Attached Packet includes:

Question to Consider: *Please note that we DON'T know the exact questions that the Site Visitors will ask. This is just a guide to help you prepare.*

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:

Robin Ginn, MBA, BSN, CHC, CHRC – Team Leader
Assistant Vice President, Research Administration, Executive Director,
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McLaren Health Care Human Research Protection Program (HRPP)

AAHRPP Review Guide for Researchers

MCLAREN HEALTH CARE HUMAN RESEARCH PROTECTION PROGRAM (HRPP)

1. Who is ultimately responsible for the MHC HRPP?
2. How is authority communicated to the research community?
3. What rules or guidelines are you expected to follow?
4. What ethical standards or guides does the IRB follow?
5. What do you do when you need assistance determining applicable laws either in-state or when conducting research in other states (i.e. age of majority, emancipated minors, Legally Authorized Representatives)?
6. Does MHC follow International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines?
7. If you propose research be conducted at an international location, what do you inform the IRB about regarding applicable local regulations, ethics review requirements, or cultural norms?What rules or guidelines are you expected to follow?
8. How does MHC ensure the rights and welfare of participants are protected when the investigator is operating at a non-MHC facility, is conducting collaborative research, or when oversight is shared with or deferred to another organization or IRB?

NEED FOR IRB REVIEW

1. What is the process for determining whether an activity is under the purview of the IRB?

IRB SUBMISSION AND REVIEW TYPE

1. Where do I start when submitting a new application to the IRB?
2. How do I find out general information about the IRB and human research?
3. Where can I learn how to use the iRIS submission system?
4. How do I request IRB approval for changes while conducting the research?

SCIENTIFIC DESIGN AND MINIMIZING RISK

1. What criteria would you consider in evaluating whether your research or a sponsored study is scientifically sound?
2. Who is involved in conducting scientific review at McLaren?
3. How do IRB regulations define minimal risk?
4. What are the kinds and levels of risk?
5. What procedures do you employ to minimize risk or mitigate potential injuries?
6. What additional information privacy regulations apply to select protocols?
7. What is the minimum IRB requirement for maintenance of research records?
8. What is the difference between protecting the privacy interests of participants and maintaining the confidentiality of data?

CONFLICT OF INTEREST

1. What is MHC's policy on Research Conflict of Interest (COI)?
2. How does the IRB manage researcher COI?
3. Who has the ultimate authority regarding management of investigator conflict of interest?

MCLAREN HEALTH CARE HUMAN RESEARCH PROTECTION PROGRAM (HRPP)

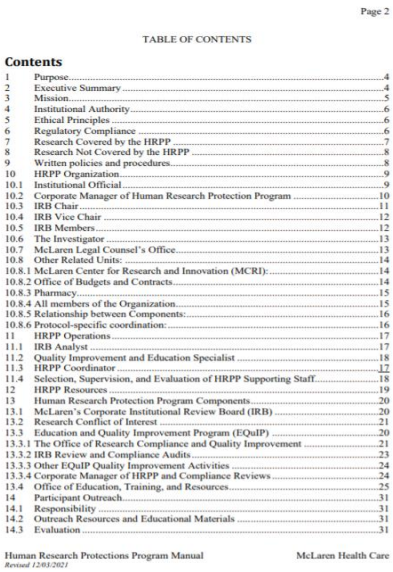
Goal: Investigators are familiar with the institutional Human Research Protection Program, regulatory framework, and ethical standards for protecting human subjects.

1. Who is ultimately responsible for the MHC HRPP?

- **Justin Klamerus, MD,** Executive Vice President/Chief Medical Officer, is the McLaren IRB Institutional Official (IO) of Research.
- Dr. Klamerus is the designated IO responsible for oversight and management of all aspects of MHC research.

2. How is authority communicated to the research community?

- **Available on the McLaren Research website,** the MHC HRPP Manual establishes the authority and independence as well as the level and scope of responsibility for the IRB and describes the organizational structure for human research protection.
- McLaren's HRPP operates under the authority of the Organization policy "MHC_RP0201_Human Research Protection Program."



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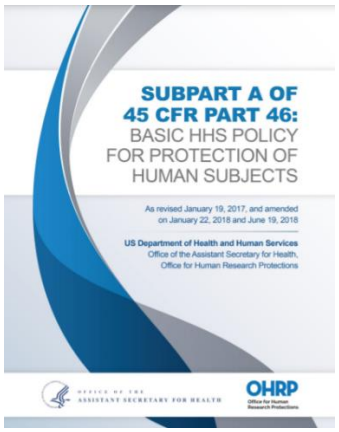
Revised 12/03/2021

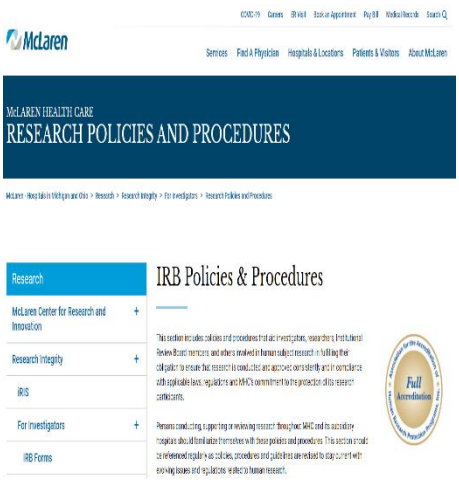
3. What rules or guidelines are you expected to follow?

- Federal Regulations that Apply to All MHC Human Subject Research:
  [Department of Health and Human Services (DHHS) 45 CFR 46]
  - Subpart A – "Common Rule" IRB Operations, Approval Criteria, Informed Consent
  - Subpart B - Fetuses/Pregnant Women/Neonates
  - Subpart C – Prisoners
  - Subpart D – Children
- Regulations that are Applicable to Select Protocols:
  - Food and Drug Administration regulations
  - Health Insurance Portability Accountability Act (HIPAA), Family Educational Rights and Privacy Act (FERPA), or General Data Protection Regulation (GDPR)



- Funding Agency Requirements
  - Department of Defense (DoD)
  - US Department of Education (DoED)
  - Environmental Protection Agency (EPA)
  - US Department of Justice (DOJ); National Institute of Justice (NIJ); Bureau of Prisons (BOP)
  - Department of Energy (DOE)
- State Law or Local Policy
  - State laws regarding legally authorized representatives
  - Department of Corrections (DOC) consent requirements
  - School District Research Review requirements

- McLaren Policies, Procedures, and Regulations
  - Where can I find them?
  - https://www.mclaren.org/main/research-policies-procedures
- Corporate Level Administrative Regulations:
  - MHC_CC0109: Conflict of Interest Disclosures and Business Integrity
  - MHC_CC1101: Use and Disclosure of Protected Health Information (PHI) – General
  - MHC_CC1111: HIPAA – Uses and Disclosures of PHI for Research



4. **What ethical standards or guides does the IRB follow?**

- The Nuremberg Code
- The Declaration of Helsinki
- The Belmont Report
  - **Respect for persons** involves recognition of the personal dignity and autonomy of individuals and special protection of those persons with diminished autonomy.
  - **Beneficence** entails an obligation to protect persons from harm by maximizing anticipated benefits and minimizing possible risks of harm.
  - **Justice** requires that the benefits and burdens of research be distributed fairly.

5. **What do you do when you need assistance determining applicable laws either in-state or when conducting research in other states (i.e. age of majority, emancipated minors, Legally Authorized Representatives)?**

- Prior to IRB review, the PI is responsible for determining applicable state laws relative to the conduct of their research.
- The McLaren HRPP relies on the MHC Corporate Counsel
- If assistance is needed, the PI may consult a Corporate Attorney with McLaren Risk Management at (810) 342-5408.

6. **Does MHC follow International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines?**

- **Yes.** When applicable, MHC subsidiaries follow ICH-GCP guidelines as adopted by the FDA.
- MHC **does not** apply International Conference on Harmonization/Good Clinical Practice (ICH/GCP) requirements to **all** human research.

ICH
harmonisation for better health

7. **If you propose research be conducted at an international location, what do you inform the IRB about regarding applicable local regulations, ethics review requirements, or cultural norms?**

- **Identify Applicable Requirements/Protections: If research is to be conducted at an international location, the investigator identifies local regulations, laws, or standards for human subject protection.**
- **Cultural Consultation: The IRB obtains a cultural consultant to provide comments, concerns, translations, in writing to the IRB on protocols involving non-English speaking subjects, and/or subjects from a foreign culture.**

8. **How does MHC ensure the rights and welfare of participants are protected when the investigator is operating at a non-MHC facility, is conducting collaborative research, or when oversight is shared with or deferred to another organization or IRB?**

- **In iRIS: Investigators are required to submit a "Request to use an External IRB" application and all the applicable supporting documents to the McLaren IRB before a protocol can be submitted to the external IRB.**
- **If research involves collaboration with any sites and/or personnel outside McLaren, then it is considered multi-site research and IRB reliance issues will need to be addressed.**
- **MHC IRB will evaluate whether the external IRB has equivalent human subject protections in place.**

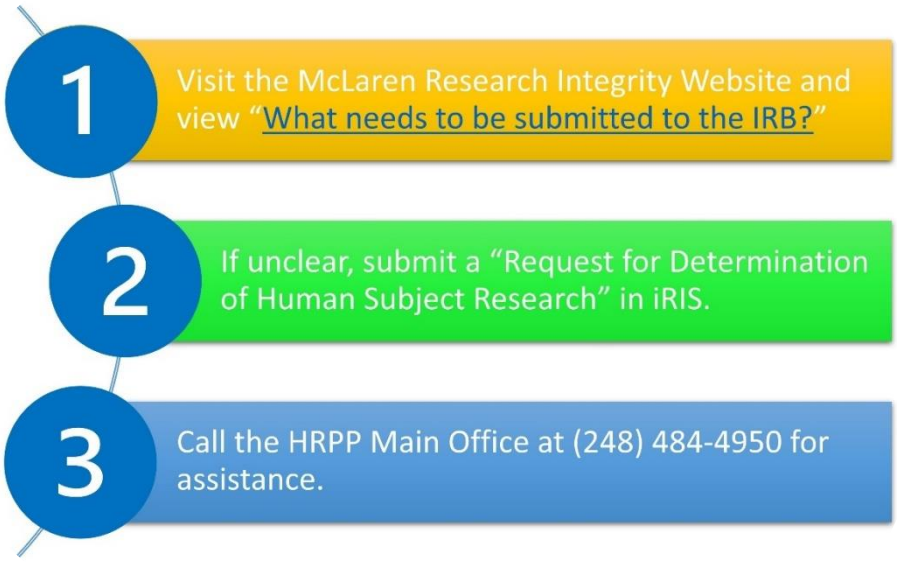
See policy MHC_RP0128 Relying on an external IRB as an IRB of record.

- **McLaren has procedures to define the responsibilities of collaborating institutions and to coordinate communication among responsible IRBs.**
- **IRB Authorization Agreement (IAA): Required before MHC may rely on an external IRB for review.**
- **Federal policies require review by a single IRB for select multi-site research.**
- **Studies using an external IRB MUST submit to the MHC IRB.**

NEED FOR IRB REVIEW

Goal: Investigators understand the definition of human research and seek guidance when determining if an activity requires IRB review.

1. **What is the process for determining whether an activity is under the purview of the IRB?**



- **Remember/Consider:**

  Private information is considered a human subject if you:
  - **can see identifiers**
  - **have access to a code linking identifiers**
  - **know who provided the private information**
  - **can readily figure out who provided the private information**

IRB SUBMISSION AND REVIEW TYPE

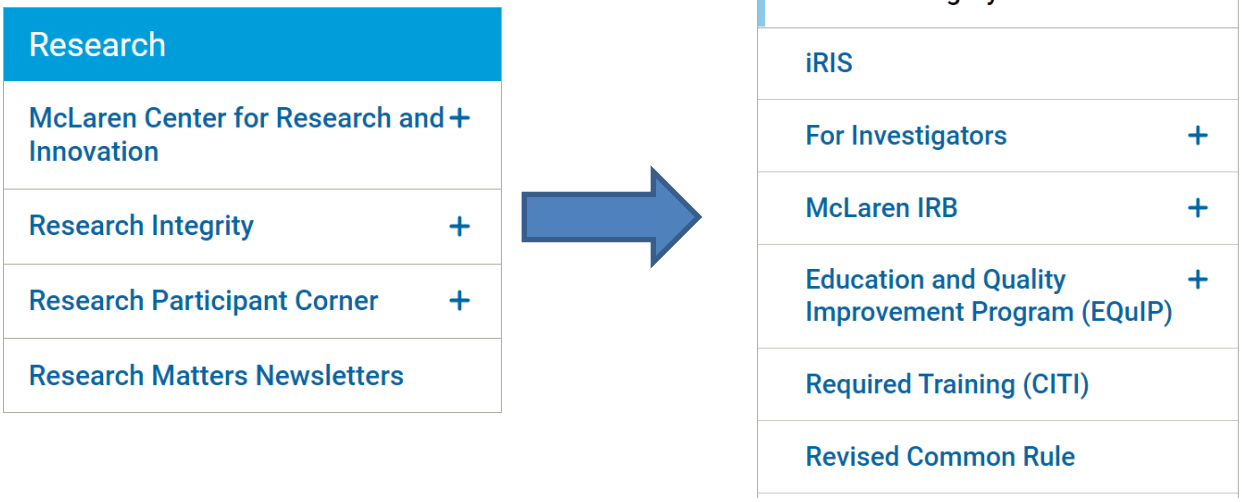
Goal: Investigators understand how to submit an application in iRIS and are familiar with the MHC IRB review process.

1. Where do I start when submitting a new application to the IRB?

Is the project human subjects research?	•Complete Request for Determination of Human Subject Research Form via iRIS.
Complete required training.	•All KSP: CITI Human Subject Research training •PI's and Co-I's: CITI Conflict of Interest training
Review MHC research policies, regulations, and templates.	•https://www.mclaren.org/main/research-integrity
Submit form via iRIS.	•https://www.mclaren.org/main/iris-research
Obtain department, committee, or other approvals.	•Prospective interventional studies: Protocol Review Committee. •Some studies: Service Agreements, DUA, or CIA.
Gather and complete required IRB submission materials.	•Email hrpp@mclaren.org with questions.

2. How do I find out general information about the IRB and human research?

- **The McLaren Research Integrity website:**
  - **https://www.mclaren.org/main/research**



3. Where can I learn how to use the iRIS submission system?

- https://www.mclaren.org/main/iris-research
- iRIS technical support helpdesk: research.informatics@mclaren.org
- Non-technical iRIS application issue questions: hrpp@mclaren.org
- Training: Susmita.Jain@mclaren.org

4. How do I request IRB approval for changes while conducting the research?

- Modification Form: Submit for any change to a protocol from what was previously IRB-approved.
    - Includes proposed changes to the current IRB approved protocol or changes which impact an individual subject, but does not change the overall protocol (i.e., Exception or Deviation)
- Exception: One-time enrollment of a research subject in a protocol that fails to meet current IRB approval
- Deviation: One-time departure from the current IRB-approved protocol once a subject has been enrolled
- Changes may not be initiated without IRB review and approval, except where necessary to eliminate immediate hazard!

Review policy MHC_RP0113 Changes to Currently Approved Research!

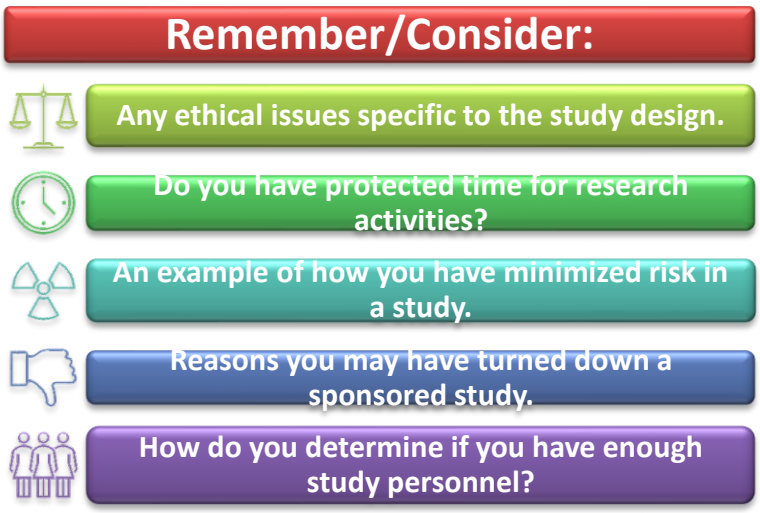
SCIENTIFIC DESIGN AND MINIMIZING RISK

Goal: Investigators design scientifically sound research that is likely to develop or contribute to generalizable knowledge. Investigators judge the design and validity of sponsored research before participating or enrolling subjects. Investigators understand and apply procedures to minimize risk.

1. **What criteria would you consider in evaluating whether your research or a sponsored study is scientifically sound?**

   - **The IRB application forms mirror the regulations so that the IRB gets the answers or justifications they need to make determinations.**

   - **The Criteria for Approval Checklist includes informed consent elements and the federally required criteria for approval:**
     - **Risks to subjects are reasonable in relation to anticipated benefits;**
     - **Subject selection is equitable;**
     - **Adequate provisions are in place for seeking informed consent (including required and applicable additional elements);**
     - **The provisions for documenting informed consent/assent are appropriate;**
     - **Adequate provisions for protecting the privacy and confidentiality of subjects;**
     - **Safeguards included to protect rights and welfare of vulnerable subjects; and**
     - **Data & safety monitoring – Greater than minimal risk research or NIH funded/FDA regulated clinical investigations, adequate provisions are in place for monitoring the data collected.**
     - **potential risk/benefit ratio**
     - **potential contribution to generalizable knowledge**
     - **demographic illustrative of real patient/subject population**
     - **enrolment criteria to rule out 'at risk' participants**
     - **specific indicators for diagnostic criteria study design, (e.g., intervention or outcomes; comparative or placebo)**
     - **controls, blinding, deception**
     - **statistical plan & methods to minimize bias**
     - **certificate of confidentiality to protect sensitive information against compulsory legal demands**
     - **subject safety monitoring**



2. Who is involved in conducting scientific review at McLaren?

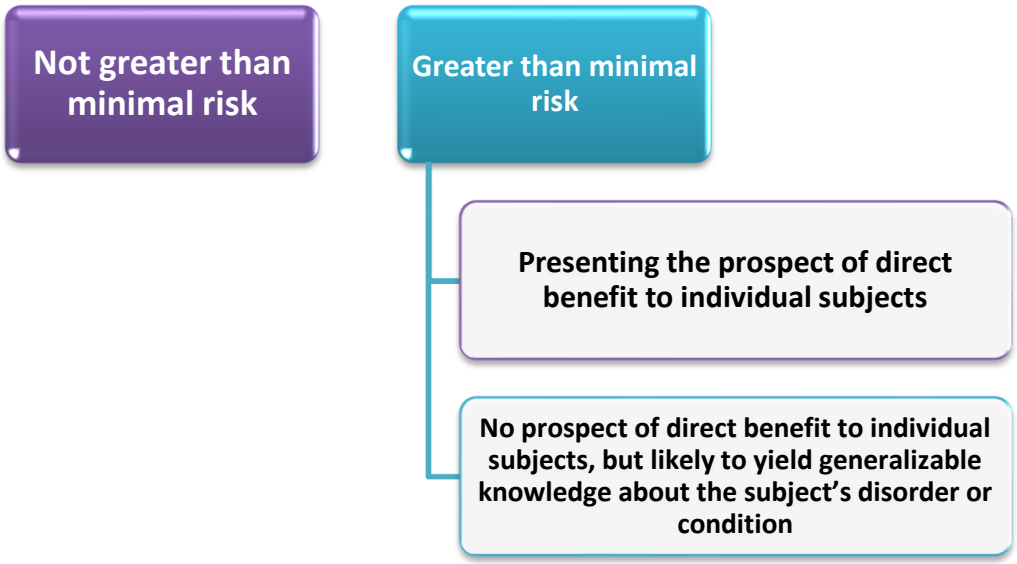
- The Scientific Reviewer's signature confirms the soundness of the research design and the ability of the research to achieve its aims.
- The Scientific Reviewer must be someone other than the Principal Investigator (PI).
- For Medical Resident and Fellows that are part of MHC Graduate Medical Education Program, the Scientific Reviewer must be:
  - Program Director
  - Assistant Program Director (if Program Director is the PI)
  - Chief Medical Officer (if Assistant Program Director is the PI or if no Assistant Program Director)
- The IRB considers the scientific study design **within the context of human subject protection.**

3. How do IRB regulations define minimal risk?

- The Department of Health and Human Services defines minimal risk to mean "the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests' [45 CFR 46.102(2)(i)].

4. What are the kinds and levels of risk?

- A risk is a potential harm or injury associated with the research that a reasonable person in the subject's position would likely be considered injurious.
- May be physical, psychological, sociological, economic, and legal.
- Ultimately, the IRB designates the risk-benefit category.
- The IRB considers 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. What procedures do you employ to minimize risk or mitigate potential injuries?

- Potential protections include:
  - Using procedures already being conducted for non-research reasons
  - Incorporating criteria to exclude "at risk" subjects
  - Choosing least intrusive design that yields valid data (outcomes vs. randomized intervention; comparative drug vs. placebo)
  - Conducting safety monitoring including safety labs and other assessments
  - Planning for responding to clinically significant abnormalities including withdraw of study product and re-challenge with product if appropriate
  - Including provisions for medical services or professional intervention (e.g., counseling) in the event of adverse events
  - Ensuring protections to secure confidential or private identifiable information
  - Establishing data and safety monitoring

6. What additional information privacy regulations apply to select protocols?

- Health Insurance Portability and Accountability Act (HIPAA) is a federal regulation designed to protect the use and disclosure of Protected Health Information or PHI.
  - PHI is defined as any of the 18 HIPAA identifiers in combination with health information transmitted or maintained in any form (electronic, paper, or oral) that relates to the past, present or future physical or mental health or conditions of an individual.

- Family Educational Rights and Privacy Act (FERPA) is a federal law that protects the privacy of personally identifiable information contained within a student's educational record.

		Who must comply?	Protected information	Permitted disclosures[1]
FERPA	The **Family Educational Rights and Privacy Act (FERPA)** is a federal law enacted in 1974 that protects the privacy of **student education records.** The Act serves two primary purposes: 1. Gives parents or eligible students more control of their educational records 2. Prohibits educational institutions from disclosing "personally identifiable information in education records" without written consent 	• Any public or private school: – Elementary – Secondary – Post-secondary • Any state or local education agency Any of the above must receive funds under an applicable program of the US Department of Education	**Student Education Record:** Records that contain information directly related to a student and which are maintained by an educational agency or institution or by a party acting for the agency or institution	• School officials • Schools to which a student is transferring • Specified officials for audit or evaluation purposes • Appropriate parties in connection with financial aid to a student • Organizations conducting certain studies for or on behalf of the school • Accrediting organizations • Appropriate officials in cases of health and safety emergencies • State and local authorities, within a juvenile justice system, pursuant to specific state law • To comply with a judicial order or lawfully issued subpoena
HIPAA	The **Health Insurance Portability and Accountability Act (HIPAA)** is a national standard that protects sensitive **patient health information** from being disclosed without the patient's consent or knowledge. Via the Privacy Rule, the main goal is to • Ensure that individuals' health information is properly protected while allowing the flow of health information needed to provide and promote high quality health care and to protect the public's health and well-being. 	• Every healthcare provider who electronically transmits health information in connection with certain transactions • Health plans • Healthcare clearinghouses • Business associates that act on behalf of a covered entity, including claims processing, data analysis, utilization review, and billing	**Protected Health Information[2]:** Individually identifiable health information that is transmitted or maintained in any form or medium (electronic, oral, or paper) by a covered entity or its business associates, excluding certain educational and employment records	• To the individual • Treatment, payment, and healthcare operations • Uses and disclosures with opportunity to agree or object by asking the individual or giving opportunity to agree or object • Incident to an otherwise permitted use and disclosure • Public interest and benefit activities (e.g., public health activities, victims of abuse or neglect, decedents, research, law enforcement purposes, serious threat to health and safety) • Limited dataset for the purposes of research, public health, or healthcare operations

7. What is the minimum IRB requirement for maintenance of research records?

- **In accordance with the Common Rule and FDA regulations (45 CFR 46.115(b) and 21 CFR 56.115(b)), IRB records are retained for at least three years after the completion of the research, either electronically or as hard copy.**
- **In accordance with federal HIPAA privacy regulations, IRB records pertaining to those containing protected health information (PHI) are retained for at least six years after the completion of the research.**
- **It is MHC's policy to retain records for the greatest amount of mandated time. Thus, all research records, including investigator study files and including records for studies cancelled without participant enrollment must be retained for at least 7 years.**

8. **What is the difference between protecting the privacy interests of participants and maintaining the confidentiality of data?**

- **Privacy** is the freedom from unauthorized intrusion – the right to be left alone.
- **Confidentiality** is the ability to keep something secret.

Individuals/PEOPLE **vs.** **Their information/DATA**

CONFLICT OF INTEREST

Goal: Investigators and research staff should understand the organization's conflict of interest policy in order to follow it. For example, investigators should know what interests the organization requires to be disclosed. Investigators and research staff should know how, when, and to whom to disclose interests.

1. What is MHC's policy on Research Conflict of Interest (COI)?

- McLaren has multiple policies on conflict of interest:
  - Review and Management of Conflict of Interest in Research
  - IRB Members
  - Institutional
- A **conflict of interest (COI)** occurs when any financial arrangement, situation, or action affects or is perceived to exert inappropriate influence on the design, review, conduct, results, or reporting of research activities or findings.

- Examples of **financial conflict of interest (FCOI)** may include:
  - The receipt of personal compensation for consulting activity
  - Ownership of equity in publicly or privately held businesses
  - Income from intellectual property rights held by the researcher

- A **significant financial interest** is:
  - Anything of monetary value,
  - Whether or not the value can be readily determined;
  - Relates to the "Investigator's professional responsibilities on behalf of the Institution;" or
  - Belongs to the Investigator or their spouse or dependent children.

Significant Financial Interests (SFI)
Publicly Traded Entities

- **Aggregate value ≥ $5,000 or 5% ownership (income, stock, or a combination of the two)**
- **During the past 12 months prior to the disclosure**
- **Not McLaren salary!**

Significant Financial Interests(SFI)
Non-Publicly Traded Entities

- **Aggregate value ≥ $5,000 (income payments only)**
- **During the past 12 months prior to the disclosure**
- ***Any* amount of equity (stock, stock options, or other ownership interest) in an entity such as a start-up company**
- **Threshold = $0**

Physician Payments Sunshine Act of 2010
Open Payments Database

- **Part of the Affordable Care Act**
- **Manufacturers of drugs, devices, and biologicals that participate in federal healthcare programs (i.e. Medicare & Medicaid)**
- **Track and report annually to Centers for Medicare & Medicaid Services (CMS)**

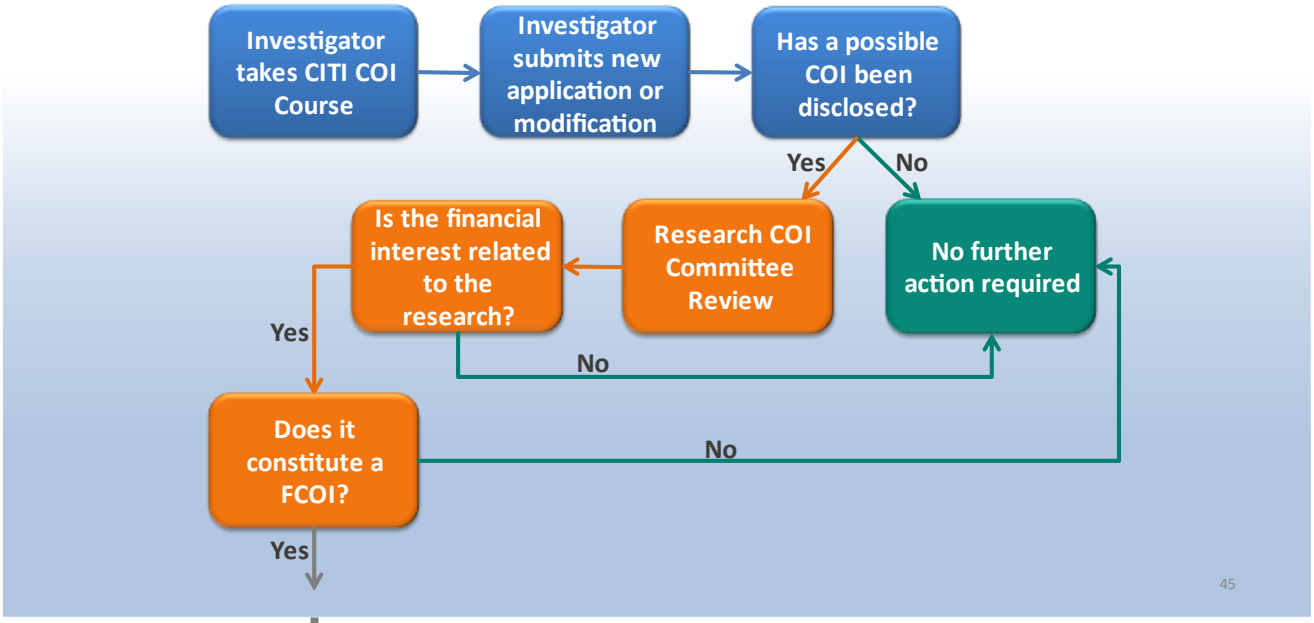
2. How does the IRB manage researcher COI?

- With mandatory education and training
  - CITI COI Course
- With disclosure of SFIs when the Investigator submits a new protocol to the MHC IRB
  - IRB application asks protocol-specific questions regarding COI
- All Investigators are required to adhere to the McLaren Research policy of Review and Management of Conflict of Interest in Research (MHC_RP0202) and must complete Financial Conflict of Interest training.
- The Research Conflict of Interest Committee
  - Is the financial interest related to the research?
  - If yes, does it constitute a FCOI?

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

McLaren HEALTH CARE

2. How does the IRB manage researcher COI?



1. COI Committee develops a Management Plan and forwards to the IRB for review and approval prior to

2. Management Plan is incorporated into the IRB approval letter. PI is notified of management plan at the time of approval and acknowledged plan.

3. Who has the ultimate authority regarding management of investigator conflict of interest?

- **After reviewing a significant financial interest in research, the Research Conflict of Interest Committee will communicate its conclusions, along with any management plan to be imposed, to the MHC IRB.**
- **For human subject research, the IRB has the final authority to decide whether the conflict of interest and approved management plan, if any, allows the research to be approved.**
- **The IRB may impose further restrictions on the protocol or disapprove the protocol.**
- **The IRB does not have the authority to disapprove the final approved management plan but may require additional protections.**