The quarterly newsletter from Human Research Protections Program | ***Summer 2015***

HRPP Outlook

Corporate IRB ▪ Office of Research Education, Training and Resources ▪ Office of Research Compliance and Quality Improvement

McLaren HEALTH CARE

Full Accreditation — Association for the Accreditation of Human Research Protection Programs, Inc.

EQuIP Corner

Nuts & Bolts of a Quality Assurance Review or Audit *by Patricia Ivery*

In the previous issue, we discussed quality assurance (QA) and quality improvement (QI) in clinical research. This issue will focus on the details of a quality assurance review or audit. Both reviews and audits utilize the same assessment tools, however, the purpose and focus of each are different.

Audits versus Reviews

Audits are directed or ordered by the IRB for a specific reason(s), also known as "for-cause" audits. The audit request is generally prompted by the IRB being made aware of an allegation of serious or continuing non-compliance concerning the primary investigator of a research trial. The reviewer will focus the evaluation on the specific allegation and other study conduct areas as deemed necessary.

Routine quality assurance reviews, on the other hand, are part of a McLaren Health Care institution-wide research education initiative. This initiative is designed to help investigators identify standards of excellence and potential areas for improvement in order to enhance the quality of human subject research throughout the McLaren research community. Studies are randomly selected for a quality assurance review from a list of all open studies at McLaren. The Office of Research Compliance modifies the random selection process based on subject enrollment numbers, experience of the PI, risk level of the study, and use of vulnerable subjects. During a quality assurance review, the reviewer is not necessarily looking for a needle in the haystack, but for systemic problems requiring correction.

Situations do occur that may prompt a routine, not necessarily random quality assurance review. These include, but are not limited to, failure to comply with federal regulations, a continuing review submission that suggests changes have been made without IRB approval, complaints from study subjects or members of study staff, numerous study deviations, or lapse in IRB approval.

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EQuIP Corner

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Preparing for an Audit or Review

Prior to the review both the PI and his/her research clinical coordinator will receive an email notification that their study has been selected for a random review or for-cause audit. The PI and reviewer will work together to select a date amenable to both parties. (Routine random reviews are generally scheduled within 2-3 weeks of notification. For-cause audits should take place within 7-10 days of notification, if not sooner.) Once the appointment has been set, a confirmation letter and preparation guidelines will be emailed and sent via US mail to the PI.

There are a few things you can do to ensure you are prepared for a review. HINT: It's all about the documents and proper documentation. Ensuring that all documents are present and documentation is complete and accurate is essential. Keeping them organized and up to date regularly will make the review process that much easier and less stressful. While consenting subjects, review each consent form to ensure the correct version is used, and that each is signed/dated properly by the subject. Prior to the reviewer's visit, take the time to carefully examine your documentation. If you identify a problem with a consent form, make a note in the study file and correct it as soon as possible, ensuring that you notify the IRB. It is also important to review your regulatory binders (IRB, FDA, etc.) prior to the visit. Make sure that you have all IRB, sponsor, and FDA correspondence regarding your study; and that the Regulatory File and study files are in order.

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The Process

Quality assurance reviews can last anywhere from 4 hours to all day, depending on the nature of the study. The review and audit procedures begin with an introductory interview, followed by review of the records, and end with a close out discussion of pertinent findings. During the close out session, you will be given the opportunity to ask questions, share concerns about the HRPP office, and the reviewer will take time to provide informal education.

Key to the actual review of records, is the standards used to judged or measure the research site, and which records will be evaluated. The yardstick by which study conduct is measured, is the culmination of HRPP policies, the Health Insurance Portability and Accountability Act (HIPPA), all applicable federal regulations and Good Clinical Practice (GCP) guidelines, and state and local laws and regulations. Please note that the HRPP policies are based on federal regulations or rules (you may review these policies at any time on our website http://www.mclaren.org/Main/IRBPoliciesProcedures.aspx).

The records that the reviewer will examine will depend on whether the review is comprehensive or targeted. Figure 1 gives a snap shot, not exhaustive, list of all potential items that may be reviewed or audited.

Findings and Final Wrap-up

If serious non-compliance is discovered, or if subject safety is found to be in immediate jeopardy, the IRB chairperson and corporate director of HRPP are immediately notified. Any further actions taken by the IRB chairperson and the board will be based on HRPP policy. In the event that no serious non-compliance is identified and / or it is found that there is no immediate jeopardy to subjects, the research team will be notified within 15 days. They will be provided with a formal written report that outlines the site visit observations, comments, request(s) for clarification, recommendations, and/or required corrective actions. If no response is required back from the PI, the review is closed and the final report is filed with the Office of Research Compliance.

POTENTIAL AREAS OF REVIEW

- Study Team: training, delegation of duty, CV, licensure
- Subject Files:
- Consents/Consenting Process/HIPAA
- Documentation Practices
- Eligibility
- AE capture and reporting
- Drug Accountability
- Protocol Procedures
- Regulatory Documents: Sponsor and IRB Communications
- Logs (enrollment, screening)
- Contracts and Agreements
- Study Safety Evaluations, Protocols, IB
- Sponsor Monitoring Reports
- External audits
- Comparison to IRB files at HRPP office

If a response is required from the study team, it is due within 30 days.

When a response from the study team is received, the HRPP Corporate Director and reviewer will examine the response and confirm that all issues have either been resolved, or whether they require additional clarification. Consultation with the IRB Chairman will be sought as necessary. When the site process is complete, the research team will be provided with a close out letter.

Internal audits and routine reviews are part of HRPP internal system of quality assurance and improvement. All report letters and CAPA records are kept confidential and are not available to external reviews or the IRB. However, serious non-compliance events and continued non-compliance events will be reported to IRB and regulatory authorities, per HRPP policies.

What Else

The office of research compliance has created a self-assessment tool for researchers and their staff. This assessment tool is designed for use by investigators and research staff to assess compliance with federal regulations and guidance's, MHC HRPP policies, ICH GCP guidelines and overall conduct of study activities. It follows the basic principles and procedures of a QA/QI audit one would expect from an internal or external auditor. This self-assessment form can be requested from the Office of Research Compliance.

Resident's Corner

Protocol Document? What's THAT?

The HRPP office receives a number of resident submissions which contain no protocol document. Nine times out of ten when the protocol document is requested, the same question is asked – "What is a protocol document?". The answer is not as daunting as you might think. A protocol document, in its simplest form, is a comprehensive overview of your research project and why you think it is relevant. It is important to keep in mind that the electronic application you are submitting through eProtocol is merely a snap shot of your research project, designed to give the reviewer the 'basics' of what you are attempting to accomplish. Your protocol document should include, but is not limited to:

- Study Title
- Study Summary
- Study Objective
- Study Design
- Study Methods
- Confidentiality
- Data Management and Storage
- Consent
- Risk and Benefit Assessment
- References

In an effort to simplify protocol writing, the HRPP has developed two protocol templates, both of which are available on our website (http://www.mclaren.org/Main/ProtocolTemplateirb.aspx). There is a general Protocol Template to be utilized for prospective investigator-initiated studies, and a Record Review Protocol Template to be utilized for chart review projects. In the event that you are conducting a prospective investigator-initiated study, you should also contact the McLaren Center for Research and Innovation (MCRI) for assistance with protocol writing and statistical considerations. MCRI can be reached at (810) 342-1025.

Common Protocol Errors

It is a common conception among researchers that the process of developing and submitting a research protocol for review and approval by an IRB is tedious,

A thorough and compliant protocol submission can improve the efficiency and turn-around time of IRBs review.

lengthy and complicated. It does not have to be! However, an insufficient protocol can lead to substantial delays. It is important to remember that you are very familiar with your project; the IRB is seeing it for the first time. The clearer and more concise your application and protocol document are, the less questions the IRB reviewer will have. A protocol with missing, incomplete or incorrect information makes it difficult for an IRB to understand your project, thus leading to questions and subsequent protocol revisions which ultimately lead to delays in approval. It is important to remember that you can also keep the approval process moving by ensuring that you address their questions / concerns in a timely fashion. The longer it takes for the IRB to get the information they

need, the longer the approval process will be.

A thorough and compliant protocol submission can improve the efficiency and turn-around time of IRBs review. As a resident conducting research, it is vital that you thoroughly review your project with your Academic Advisor to ensure the best possible protocol submission.

The primary responsibility of the IRB is to safeguard human subject protection. To that end, the IRB reviews protocols in the context of adhering to principles of ethical research (respect for persons, beneficence, and justice), applicable laws, regulations and the institution's policies.

Generally speaking, most IRB submission errors fall into these categories:

- Incomplete submission
- Missing documentation
- Inconsistent information

By far, the most commonly cited submission error is incomplete information and documentation. The most missed documentation in resident submissions here at McLaren are a formal protocol document, Confirmation of Scholarly Review or Validity signed by the Academic Advisor, and Project Impact Statements (remember, even if you are conducting a chart review, you are impacting the Medical Records department by gaining access to those records).

In the context of the protocol document, researchers often provide an inadequate description of the research question or the background information required to support the need for the research. The HRPP office receives numerous protocols that specify, in great detail, procedures that will be followed, but omit an adequate description of the research question and/or the background information to support the need for the research. It is important to know procedures, and equally as important to know the hypothesis for your project. There must be sufficient justification for exposing subjects to risk when conducting research. It is important to remember, that 'risks' are not limited to physical risks, a subject's privacy is also at risk when you are accessing their PHI. A scientifically sound research hypothesis provides the basis for this justification. If you do not provide the necessary information, the IRB will have difficulty determining whether risks to subjects are minimized or are reasonable in relation to the anticipated benefits.

Did you know...?

The protocol must include an adequate description of the research question and/or background information to support the need for the research.

The IRB wants to proceed as efficiently as possible in reviewing and approving research protocols just as much as the researcher. The IRB, however, has particular compliance and regulatory requirements that necessitate the careful scrutiny of protocols to ensure completeness. By carefully constructing the protocol and understanding the necessary information required, an investigator can mitigate the risk of rejection or delays by the IRB.

Did you know?

The role of the IRB member involves much more than a meeting once a month. In addition to attending regularly scheduled IRB meetings, our IRB members:

- **Review all study submissions scheduled for full board review**
- **Perform reviews of expedited study submissions, as assigned**
- **Keep current on local and federal regulations and policies regarding human subjects research**
- **Participate in educational activities**
- **Maintain current human subjects assurance training via Collaborative Institutional Training Initiative (CITI)**

Getting to know the MHC IRB

Meet Soe Maunglay, MD

In this edition we would like to introduce you to one of the newest members of our team! Dr. Soe Maunglay, MD joined the MHC IRB in April 2015. He is a Hematologist / Oncologist at the Karmanos Cancer Center in Lapeer. Dr. Maunglay is board certified in medical oncology. Welcome, Dr. Maunglay!

New Primary Member...

Dr. David Cook, a long-standing alternate member of the MHC IRB, has become a primary member. Thank you, Dr. Cook!

"Under FDA regulations, an IRB is an appropriately constituted group that has been formally designated to review and monitor biomedical research involving human subjects. In accordance with FDA regulations, an IRB has the authority to approve, require modifications in (to secure approval), or disapprove research. This group review serves an important role in the protection of the rights and welfare of human research subjects.

The purpose of IRB review is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in the research. To accomplish this purpose, IRBs use a group process to review research protocols and related materials (e.g., informed consent documents and investigator brochures) to ensure protection of the rights and welfare of human subjects of research." – FDA.gov

NEW Active Research Projects

New studies open to enrollment at McLaren since December 2014. ***For a complete list of studies please visit our website at: http://www.mclaren.org/Main/ClinicalTrialsHRPP.aspx***

GEMINI ACS 1

A Randomized, Double-blind, Double-dummy, Active-controlled, Parallel-group, Multicenter Study to Compare the Safety of Rivaroxaban versus Acetylsalicylic Acid in Addition to Either Clopidogrel or Ticagrelor Therapy in Subjects with Acute Coronary Syndrome
– McLaren Macomb

INTREPID

Investigating TicagRElor treatment in Patients with myocardial Injury post non-cardiac surgery
– McLaren Macomb

BIOFLOW-V - BIOTRONIK

A Prospective Randomized Multicenter Study to Assess the Safety and Effectiveness of the Orsiro SiroLimus Eluting Coronary Stent System in the TReatment Of Subjects With up to Three De Novo or Restenotic Coronary Artery Lesions- V
– McLaren Bay Region

Mitroflow DL PAS

Mitroflow Aortic Pericardial Heart Valve with Phospholipid Reduction Treatment Post Approval Study
– McLaren Bay Region

ARTEMIS

Affordability and Real-world Antiplatelet Treatment Effectiveness After Myocardial Infarction Study
– McLaren Bay Region, McLaren Flint, McLaren Macomb

INTREPID

A Multinational, Randomised, Double-Blind, Placebo-Controlled Trial to Evaluate the Effect of Ticagrelor 90 mg twice daily on the Incidence of Cardiovascular Death, Myocardial Infarction or Stroke in Patients with Type 2 Diabetes Mellitus [THEMIS - effect of Ticagrelor on Health outcomes in diabetes Mellitus patients Intervention Study]
– McLaren Macomb, McLaren Northern Michigan

Upcoming Education

2015 BROWN BAG SESSIONS ANNOUNCED!

The Education Quality Improvement Program (EQuIP) has begun offering Brown Bag education sessions. These sessions are provided in a webinar format and take place around the noon lunch hour. Sessions are open to all research professionals, coordinators, residents, students, staff or faculty. Keep an eye on your email for registration information.

Privacy and Confidentiality

September 8, 2105

HUDs and Emergency Research

December 8, 2015

DON'T FORGET

Research CANNOT begin until the proposed study has been approved by the IRB. If you are conducting human subject research without IRB approval, you are in violation of Federal Regulations and subject to non-compliance.

Assistance for Researchers:

Do you have questions related to eProtocol, IRB forms, policies, or review procedures?

Our Office of Research Education, Training and Resources holds office hours to help Researchers, including graduate students and residents, who are preparing Institutional Review Board (IRB) submissions and exemption requests. Sessions are intended to help researchers, students and their advisors navigate eProtocol (electronic IRB submission system) and learn about policies and review procedures.

No appointment is necessary. Please contact Jodi Reetz at (810) 342-1003 or (810) 342-1024 or via e-mail at Jodi.Reetz@mclaren.org for questions or more information.

Assistance for IRB Members:

Do you have questions related to eProtocol, IRB member checklists, policies, IRB review process or IRB criteria for approval?

Our Office of Research Education, Training and Resources holds office hours to help IRB Members to navigate eProtocol (electronic IRB submission system) and learn about policies and review procedures, including newly developed checklists. Sessions could be done either in person or via telephone.

No appointment is necessary. Please contact Jodi Reetz at (810) 342-1003 or (810) 342-1024 or via e-mail at Jodi.Reetz@mclaren.org for questions or more information.

Question: Who are investigators required to notify of complaints from subjects? HINT: this can be found in an HRPP policy!

Submit your answer to HRPP@mclaren.org . The first person to submit the CORRECT answer to the following question will receive a $10 Starbucks gift card!

McLaren HEALTH CARE

Mission statement: McLaren Health Care, through its subsidiaries, will be the best value in health care as defined by quality outcomes and cost.

If you have ideas for stories that you'd like to see in a future issue of ***HRPP Outlook***, lana.gevorkyan@mclaren.org.

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