Updated 01/22/2024

Risk-Based Quality Monitoring Framework

Pre-Submission Services

The Research Operations Director role is incorporated into the Quality Program. This position is a liaison between the CW HRPP and the research community conducting research at CW. This role is important for help in pre-submission work with teams with things like onboarding new staff, familiarizing them with the resources and tools available through the CW HRPP, assisting with feasibility assessments, etc.

Services and resources for investigators and teams as a research project is being planned, prior to submission to the IRB of record:

- Protocol Development Support
- Reviewing protocol (investigator initiated)
- Connecting with Kristin Busse for IND/IDE review and assistance (investigator initiated)
- Education for new investigators
- Review of feasibility and assistance in assessing this
- Study start up meeting/ initiation meetings
- Ancillary Services Intake Forms (pTRU, Imaging, etc.)
- Clinical Research Addenda

Education

As part of ongoing quality improvement, the HRPP office staff, occasionally in collaboration with other departments, will provide regular education/training opportunities for investigators and research teams conducting research at Children's Wisconsin.

In addition to regular educational offerings on topics related to conducting research at Children's Wisconsin and the protection of human subjects, training may be initiated based on any of the following, or in other circumstances that in the opinion of the HRPP office warrant additional education. Education may be general or may be targeted to a specific concern.

- To address issues of non-compliance noted during post approval monitoring
- To address issues of non-compliance noted during review of reportable events submitted by research teams
- To address issues/gaps in knowledge noted during local context review by HRPP staff or other interactions with research personnel
- At the request of Principal Investigators or other research staff, department or administrative staff
- To assist in study/feasibility planning for newer investigators and research staff
- To assist in orienting and onboarding new research staff

- To inform researchers conducting research at Children's Wisconsin of any CW policy or process changes, regulatory changes, general news or information that may affect research

Children's Wisconsin HRPP office will employ a variety of venues, platforms, and approaches to providing education and information including by not limited to:

- Small group education sessions hosted for researchers
- Office hours with the HRPP staff
- CRI education presentations for researchers
- Regular newsletters
- 1:1 Consultations with researchers
- Utilization of the CITI program training platform
- Web pages on both the External Children's Wisconsin website and the Connect intranet website
- Targeted presentations to departments or research groups

CITI training platform

There are minimum core requirements for CITI course completion for all individuals listed as key personnel for a research projects. See Guidance *CITI Training Requirements*.

In addition, as part of quality improvement, the HRPP office may assign additional, supplemental courses available in CITI as a requirement. This may be required :

- To address non-compliance as part of a CAPA after review of a reportable event
- To address special circumstances in which additional knowledge may be appropriate. For example:
    - When an investigator is new to conducting research at CW
    - When an investigator is planning to do a "special" project such as a HUD, novel therapies, etc.
- To address gaps in knowledge identified through, for example:
    - Post approval monitoring
    - Reportable events
    - Results of sponsor monitoring, DSMB reports, etc.
    - Results of researcher self-auditing

This is part of institutional requirements, and if required for a particular submission, the final IRB approval will be held until this requirement is completed. When MCW Pediatric IRB will be reviewing the submissions, the CITI training requirement will be communicated to the MCW Coordinator managing the submission for MCW IRB review.

If the study is being/had been deferred to an external IRB other than MCW, the "green light letter" issued by the CW HRPP office will be held until the required CITI training is complete.

Routine Assessment of all submitted Reportable Events

The HRPP staff will review all reportable events submitted for projects involving Children's Wisconsin. This will be done at weekly meetings with the Research Integrity Manager (or designee) and a subset of HRPP staff.

This review will assess for:

- Safety issues
- Impact of the event on subjects rights/willingness to continue participation
- New information and the effect on the study (subject safety, willingness to continue to participate)
- Trends in non-compliance that may require further education, outreach, or other with the research community
- Appropriateness of the proposed CAPA
- Need for further review/possible action by the institution (IO, compliance, HRPP, etc)
- Coordinate with Director of Clinical Research Operations for changes needed for CAPA

Risk Based Quality Monitoring

All human subject research being conducted at Children's Wisconsin, with Children's Wisconsin patients, using Children's Wisconsin data or otherwise engaging Children's Wisconsin in human subject research, will be subject to quality monitoring by the CW HRPP office.

Quality Monitoring

Research projects approved at a fully convened IRB meeting, or by expedited review, that are being conducted in CW space, with CW data or with CW patients, are eligible for Quality Monitoring. Once research has undergone local context review and been approved by an Institutional Review Board, it may be selected for quality monitoring by the CW HRPP office. The purpose of these reviews is to monitor for compliance (regulatory as well as local context), and also to provide feedback and guidance to investigators to improve the quality of how research is conducted at Children's Wisconsin.

- This monitoring will allow the CW HRRP office to provide feedback to investigators and study teams regarding how well the research is being conducted in accordance with:
    - The approved protocol
    - Federal regulations and local laws
    - Children's Wisconsin policies, SOPs, guidance documents and local context considerations
    - General good clinical practice
- This monitoring also provides an opportunity for investigators and study teams to ask questions, bring up concerns about the research, and provide additional learning opportunities for investigators and research staff

- The feedback from this monitoring can be used by investigators to prepare for monitoring by other entities such as sponsors or the FDA as well as plan for modifications or continuation of the research
- This monitoring will help provide information from another source to the IRB of record about the conduct of the research which can be considered in the continued oversight by the IRB of record
- This monitoring will allow the CW HRPP office to fulfill its mission to protect the rights, welfare and privacy of individuals participating in IRB approved research conducted at CW by helping to ensure compliance with a variety of standards (regulatory, ethical, local context, scientific quality)
- This monitoring will help improve the quality of human subject research conducted at CW through the above.
- Evaluation of aggregate information collected from this monitoring can direct where education efforts should be targeted, etc.

Review Selection Criteria

The selection of research on which to conduct monitoring is based on a number of factors, as described below.

Risk Based Selection

When we are assessing selection of a project for review, HRPP staff will check if there has been a recent audit or review by MCW, FDA, or any other external entity. If so, HRPP staff will review that external report to help us decide if we have enough from that, or if we feel additional monitoring is needed.

- Investigator initiated clinical trials
    - Greater than minimal risk
    - Those involving an IND/IDE for which the investigator is also the sponsor
- Greater than Minimal Risk projects
    - FDA-regulated research
    - Other Federally-funded projects (i.e., DoD, NIH, etc.)
    - Research conducted through a cooperative group
    - Industry sponsored research

Additional Selection criteria (this could apply to minimal risk research as well as greater than minimal risk research)

- Based on Reportable Events reviewed by the CW HRPP
    - Trends in identified problems
    - Proposed CAPAs - follow up on implementation and effectiveness
- New investigators conducting research at CW
- Investigators identified as having a history of non-compliance
    - Through review of Reportable Events
    - Through staff interaction with them/Local context reviews

- Departments identified as having a history of non-compliance
    - Through review of Reportable Events
    - Through staff interaction with them/Local context reviews
- Identified by staff as research that staff feels needs monitoring to assess and improve quality
    - All staff can add to the list of candidates for monitoring based on their insight, what they see in reviewing for Local context and interacting with investigators and research teams, etc.
    - Via discussion of concerns about a research project at weekly HRPP staff meetings
- Reliance on external IRBs (not MCW)
- Based on receipt of complaint – either by subjects or MCW/CW staff or others
- Based on information/concerns relayed to the HRPP office by MCW/CW staff or others about a particular research project, investigator, study team
- Investigator/study team request for monitoring for feedback

Process for Selecting and Scheduling Quality Monitoring

- Review new approvals by designated HRRP staff
    - When we receive approval letters for new research from the MCW IRB, HRPP staff will vet the study to assess if this should be placed on the monitoring schedule
    - When a new reliance on an external IRB (not MCW) is established, HRPP staff will vet to assess if this should be placed on the monitoring schedule
- Discuss at Reportable Events meetings
    - Are there any projects with REs that were reviewed should be placed on the monitoring schedule
- Discuss at weekly CW HRPP staff meetings
    - Are there are any studies that should be placed on the monitoring schedule
- When a study is identified as a candidate for quality monitoring:
    - Determine if there has already been recent monitoring by any of the following and if that monitoring is sufficient (review report) or if the HRPP office feels we should still do additional monitoring (for example to follow up on addressing anything identified by external monitoring)
        - Review by the MCW HRPP
        - FDA inspection
        - Monitoring by the sponsor
        - Self-monitoring by the investigator
    - If the candidate will proceed with monitoring
        - Send notice to the PI and Study team
        - Coordinate with the PI and study team for a workable time
        - Place on the shared Quality Monitoring Calendar
        - Send confirmation to PI and study team

- Determine which HRPP staff will be doing the monitoring and indicate this on the shared Quality Monitoring Calendar

Quality Monitoring Process

The review will be conducted remotely using Box, CW EPIC, and Zoom as needed.

The HRPP staff conducting the review will utilize checklists to assess and document the conduct of the research. Activities may include:

- discussion with the PI, investigators, and other study team members to discuss the conduct and documentation of the research project
- review of the approved protocol and other study documents and comparison between what was approved and how the study is being conducted
- review of signed consent forms
- review of collected research data
- Review of compliance with submission deadlines (e.g. CPR, if late submissions or lapses)
- review of the regulatory file
- discussion of the review activities and subsequent findings and recommendations

After the review is completed, a written Routine Review Summary is provided to the principal investigator and primary contact, as well as to the IRB of record. This summary may include a requirement to provide the HRPP office with a Corrective and Preventative Action Plan to address any findings or concerns noted during the review.

The Routine Review summary, and if applicable the research teams corrective action plan, is forwarded to the overseeing IRB.

Requesting Quality Monitoring

There may be circumstances in which a PI would like a review and feedback for a project. This may be for their own department's assessment of research, to prepare for external monitoring (sponsor, cooperative group, FDA), or for their own information.

If an investigator would like to schedule a routine review for a particular project, or group of projects, this can be requested by contacting the CW HRRP office at cwhrpp@childrenswi.org

Investigator Self-Monitoring

This is a mechanism that investigators can use at any time to prepare for upcoming audits or inspections by regulatory bodies (FDA, OHRP) or sponsors, as well as ensure the ongoing quality and compliance in the conduct of their own research.

This may also be a mandatory activity requested by the HRRP office in response to concerns that arise through reportable events or other means.

The HRPP website has self-audit checklists study teams can utilize as a guide to perform a self-audit. Questions and requests for assistance can be directed to the CW HRPP office as needed.

Referral to Corporate Compliance

- Anything reported through the Compliance Hotline will be handled by Corporate Compliance
- Identification of concerns regarding possible research misconduct, breaches in HIPAA privacy and confidentiality, data integrity, billing compliance, or other matters generally handled by Corporate Compliance

Assessment of the IRB of Record

The HRPP office will keep track of projects that have undergone Local Context review to follow up after approval. The HRPP will review approved projects to assess whether or not the IRB review adhered to and was consistent with the Local Context requirements.

HRPP Quality

Implement after the other facets of this program have been established

Quality Improvement Activities – Special Projects

Each year the HRPP office will implement a quality improvement initiative/activity. This would be related to HRPP functions and processes and may include work with research teams and PIs, as well as collaboration with other CW and/or MCW departments.

The activity will be selected in collaboration with the Institutional Official, the Research Integrity Manager, HRPP staff, and possibly other departments such as Corporate Compliance.