1.0 Purpose:

1.1 The Hartford Healthcare Quality Improvement (QI) Program was established to promote and maintain ethical research conduct. The primary mission of the QI Program is to evaluate and improve human research protections through education, training and Post Approval Monitoring. The QI Program staff will work with investigators, research staff, and the IRB's to ensure research is compliant with regulations, guidance, institutional policies, and best practices for human research protections.

1.2 The QI Program is responsible for reviewing activities associated with human research protections and for providing related education and monitoring. Activities performed by QI staff include;

1.2.1 Routine Post-Approval Monitoring
1.2.2 Risk-Based Post Approval Monitoring
1.2.3 Investigator Requested Monitoring
1.2.4 Consent Monitoring (See policy 805)
1.2.5 For-Cause Auditing
1.2.6 Assistance with IRB submissions, reporting and recordkeeping
1.2.7 Assistance with preparation for external audits by federal agencies
1.2.8 Educational offerings (classes, handouts, lunch & learn etc.)
1.2.9 Point of contact for research related complaints
1.2.10 Consultation to investigators and research staff

1.3 The QI Program applies to all researchers, research staff, and departments engaged in human subject's research at any Hartford Healthcare Partner Institution. This program also applies to any researcher or study that was approved by the Hartford Healthcare IRB, even if the study is taking place at a non-Hartford Healthcare site.

1.4 Only studies that have received Full Board, Expedited or Exempt review are eligible for Post-Approval Monitoring. Studies that have a determination request approved through HRPP of "Not Research" or "Not Human Subject's Research" are not eligible.

2.0 Definitions:

2.1 **Routine Post-Approval Monitoring:** The focus of this type of review includes an assessment of the roles, responsibilities and training of research staff, suitability of the facility to conduct the research, regulatory and IRB compliance, recruitment, eligibility and consenting process, case review for protocol adherence through source documentation and data collection, adverse events and unanticipated problems, data security and other suitable aspects of the study. Routine monitoring is performed as a service to investigators and feedback is typically paired with education for improved compliance. This feedback is typically not shared with the IRB unless serious and/or non-compliance was identified during the review. Although most routine reviews will be scheduled, un-scheduled "mini-reviews" may also be performed.

2.2 **Risk-Based Post-Approval Monitoring:** This is similar to routine post approval monitoring except the focus of the review is on activities to prevent and mitigate likely risks to investigation quality, risks to human subjects and data integrity. Studies selected for risk-based monitoring are selected because of a specific factor that may

increase the risk such as; stage of the study, turnover of personnel, vulnerability of study population etc.

2.3 **Investigator Requested Monitoring:** This is exactly the same as routine post approval monitoring except that the investigator initiated the request. The investigator may also direct the monitoring towards specific areas where they feel they need help or improvement.

2.4 **For-Cause Auditing:** This type of review may be performed at the request of the IRB, IRB Chair, HRPP Director, or Institutional Official. A for-cause review is generally based on a concern, complaint, or an allegation that was brought to the attention of the IRB, HRPP or Institutional Official and will be used to help inform decisions about the conduct of human subject's research and/or human subject's protection. This review may be either scheduled or unscheduled and may involve a full review of a specific study, a full review of all studies for a specific investigator or a targeted review on a specific concern.

3.0 Who Conducts Monitoring or Auditing Activities:

3.1 Post-Approval Monitoring Activities are generally conducted by QI staff under the guidance of the HRPP Director and Institutional Official.

3.2 In addition to QI staff, IRB Chairs, the HRPP Director, IRB Members and IRB Administrators may be asked to assist with monitoring activities depending on the basis of expertise.

4.0 Procedure: As the procedures for routine and risk-based monitoring are the same, they will be discussed together.

4.1 **Routine and Risk-Based Post-Approval Monitoring:** Any study involving human subjects, including medical and non-medical studies may be selected for routine or risk-based monitoring.

4.1.1 **Study Selection:** Studies may be selected for monitoring either randomly from a list of all open protocols or for a specific reason, such as but not limited to;

- Level of IRB review (Full Board, Expedited or Exempt)
- Level or type of risk to the subject population
- Involvement of vulnerable populations
- Studies conducted by researchers or research staff that are new to research
- High or low enrollment
- Investigator held IND's or IDE's
- A specific disease or department (i.e. Oncology, Psychiatry)
- A specific type of funding (i.e. Federal)
- Potential conflict of interest

4.1.1.1 If a study is selected but it is discovered that the study has already received monitoring within 1 year or the study is scheduled to be terminated with the IRB prior to the monitoring

visit, this will be brought to he attention of the HRPP Director. The Director may request that a different study be selected in its place.

4.1.2 **Notification of Selection:**

4.1.2.1 **Scheduled:** The majority of monitoring visits will be scheduled. The Principal Investigator (PI) and primary study contact will be notified electronically or in writing that a particular study has been selected for monitoring. The QI staff will arrange a mutually agreed upon appointment for on-site review, which will typically take place within 2-4 weeks of notification.

4.1.2.1.1 Investigators and research staff will be asked to complete a self-assessment checklist prior to the monitoring visit. The purpose of this checklist is to help give investigators an idea of what will be reviewed during the monitoring visit. The other purpose is to give them opportunity to identify any problems and make corrections prior to the visit.

4.1.2.1.1.1 The self-assessment is also a useful tool outside of the monitoring visit. Researchers are encouraged to use this tool periodically to help identify potential noncompliance issues so that they may take appropriate action before the items become serious and/or reportable problems.

4.1.2.1.2 Investigators cannot refuse post-approval monitoring but if they have a particular conflict such as an FDA audit or other special circumstance they can arrange to have the review conducted at a later date. They should notify the QI staff as soon as possible of any potential conflicts.

4.1.2.1.3 If an investigator refuses to arrange a time for the post approval monitoring visit, the IRB will be notified and an un-scheduled visit will be mandated.

4.1.2.1.4 If the QI staff is not permitted into the research facility or is not permitted access to the research data or materials to be monitored, the IRB and Institutional Official will be notified. A determination will be made on a case by case basis.

4.1.2.1.4.1 In such cases, the IRB may make a determination to suspend the research study or suspend the investigator's research privileges until a Post-Approval Monitoring review can be conducted.

4.1.2.2 **Unscheduled:** The PI will not be notified in advance of unscheduled visits. Even though this visit is unscheduled, it is still considered a monitoring visit and not a "for-cause audit". These will typically be a "mini-review" focused on one piece of the post-approval monitoring visit such as; consent process and documentation, AE submissions, data confidentiality and file security etc.

4.1.3 **Expectations during the Post-Approval Monitoring Visit:**

4.1.3.1 The review will typically take 1-3 days depending on the complexity of the study and number of charts to be reviewed. The length of time may vary, quick spot checks may only last a few hours while more complex studies may warrant more than 3 days.

4.1.3.2 Study teams should provide the QI staff with a table or desk and suitable lighting with which to work.

4.1.3.3 Study teams should provide the QI staff with access to all research records, data, study drugs/devices, and applicable study related logs. If any records are stored electronically please make sure the QI staff has access to them.

4.1.3.4 Study teams should provide the QI staff with a tour of the facility and all areas where the research is conducted or research data is stored.

4.1.3.5 The PI and/or research staff member is not expected to be present for the entire review. However, the QI staff will ask to meet with the PI and/or research staff before and at the end of the review. The PI and/or research staff may also be asked to be available (or to check in periodically) to answer any questions that may arise during the review.

4.1.3.6 At the conclusion of the monitoring visit the QI staff will ask to meet with the PI and/or research staff to briefly review any significant findings and recommendations. The QI staff will work with the investigator to help correct any problems noted and will provide recommendations for process improvements to increase compliance, when necessary.

4.1.4 **Communication of findings after the review:**

4.1.4.1 After the monitoring visit the QI staff will write a report outlining the findings of the on-site review. If any corrective actions were discovered that need to be addressed by the PI, these will be included in the final report.

4.1.4.1.1 The QI staff will make every effort to complete the report within 5 business days.

4.1.4.1.2 If an IRB Chair/Member participated in the on-site review, the QI staff may give them the opportunity to review and edit the report prior to sending it to the PI.

4.1.4.2 In addition to the monitoring report, the QI staff will also prepare an Attributes Legend that not only details the provider accuracy rate for the overall monitoring visit but also the accuracy rate for specific categories (i.e., Regulatory & Training, Informed Consent Content & Process etc.).

4.1.4.2.1 Attribute Ratings:

4.1.4.2.1.1 If a specific attribute was fully complete, the investigator will receive 1 point.

4.1.4.2.1.2 If a specific attribute was partially complete or only minor errors were found, the investigator will receive 0.5 points.

4.1.4.2.1.3 If a specific attribute was not complete or major errors were found, the investigator will receive 0 points.

4.1.4.2.2 If certain attributes were not reviewed during the visit or if they did not apply to the study, the attribute will be marked as N/A. These attributes marked as N/A will not be considered when totaling the Provider accuracy rate.

4.1.4.3 Once the report is complete a draft copy of the report and the Attributes Legend will be sent electronically to the HRPP Director.

4.1.4.4 Once the draft report is approved, the final version along with the Attributes Legend will be sent to the PI, HRPP Director and Institutional Official (IO).

4.1.4.5 If the report contains any corrective actions, the QI staff will add a requested response date to the report. The date will be determined on a case by case basis but in most cases will typically provide the PI with 2-3 weeks to submit their response.

4.1.5 **Responding to Post-Approval Monitoring report and corrective actions:**

4.1.5.1 The PI is <u>only</u> required to submit a response to the report <u>if</u> it included corrective actions. If no corrective actions were listed then no further action from the PI is needed.

4.1.5.2 The PI is expected to submit a written response to all corrective actions by the date proposed on the draft report. Please include the following in the response;

4.1.5.2.1 A complete response to each corrective action item.

*Incomplete responses such as, "We are working on it" are not acceptable.

4.1.5.2.2 If a corrective action item requests more than a clarification (i.e. specific log to be made, correction to be made or SOP to be provided, etc…) a copy of the item must be included with the response.

*A response indicating the correction was made without providing proof of the correction will not be considered sufficient.

4.1.5.3 The response may be prepared by the research staff but the report must be approved by the PI. The PI may either physically sign the report or if the report is sent electronically, the PI should e-mail or be cc'd on the e-mail response submitted to the QI staff indicating they have reviewed and approved the submission of the report.

4.1.5.4 If the PI is unable to respond to the corrective actions by the proposed date they may request an extension from the QI staff. Extensions will be granted on a case by case basis.

4.1.5.5 If a PI fails to respond to corrective actions they will be contacted by the QI staff to determine why they haven't responded, and to come to a mutually agreeable arrangement of when they will respond by. If no mutually agreeable arrangement is made or if the PI continues to fail to respond, the QI staff will notify the HRPP Director. If sufficient concerns arise from the lack of response, the QI staff may also notify the IRB and/or Institutional Official.

*A failure to respond may constitute serious non-compliance.

4.1.6 **Reporting of Post-Approval Monitoring visits and PI responses:**

4.1.6.1 The final report and the PI's response will be saved electronically in a shared database that only the QI staff, HRPP Director and Institutional Official has access to. In addition; a hard copy of the monitoring notes and report responses may also be saved in the QI staff's locked office.

4.1.6.2 Any corrective action items from post-approval monitoring visits that required reporting to the IRB will be entered into the Non-Compliance Tracking log and reported to the IRB in aggregate.

4.1.6.3 If unanticipated problems and/or serious and/or non-compliance are identified during the review, the QI staff will notify the site and assist them in reporting the event(s) to the IRB. If the site does not report the events in a timely manner, the QI Program is

obligated to report the event(s) to the IRB and Institutional Official and the Research Department as applicable.

4.2 **Investigator Requested Monitoring:** All of the procedures listed under 3.1 apply here. The only difference is in study selection because the investigator requests the Post-Approval Monitoring review.

4.2.1 **How to Request a Post Approval Monitoring Visit:**

4.2.1.1 Investigators interested in requesting a Post Approval Monitoring visit should send a request via e-mail to the QI staff. In the body of the e-mail please clarify the study IRB#, PI name and reason for the review (i.e. in preparation for an FDA inspection).

4.2.1.2 Within 5 business days of receipt of the request, a member of the QI Program staff will contact the investigator to arrange a mutually agreed upon time for the review.

4.2.1.3 If the study already received Post-Approval Monitoring within 1 year of the request, the QI staff may ask to postpone the review, unless the investigator notes a specific concern that needs more immediate attention.

4.2.1.4 Investigator-initiated requests will be scheduled based on the level of need as determined by the QI staff. Therefore, an investigator requesting review prior to an FDA audit or because of concerns of non-compliance, may receive priority over a routine request.

4.3 **For-Cause Auditing:** This type of review is performed when concerns regarding compliance, protocol adherence or subject's safety are brought to the attention of the IRB or Institutional Official. This review is typically targeted only to the area of concern but may expand to a full review if the QI staff deems it warranted.

4.3.1 **Study Selection:** Any study approved by the Hartford Healthcare IRB or conducted on the premises of any Hartford Healthcare facility may be selected for "For-Cause Auditing."

4.3.1.1 Any concerns regarding compliance, protocol adherence or subject safety will be brought to the attention of the HRPP Director. The HRPP Director will consult with the IRB Chair and/or Institutional Official to determine whether the concern needs immediate addressing or if it can wait to be presented at the next IRB meeting.

4.3.1.2 **Concerns needing immediate attention:**

4.3.1.2.1 If a concern is determined to need immediate addressing, the IRB Chair and/or HRPP Director may make a determination to issue a For-Cause Audit.

4.3.1.2.2 If a concern requires immediate attention to protect subject safety, privacy or integrity of the research data, IRB Chair or HRPP Director may also take other appropriate actions to mitigate the concern (i.e. suspending research privileges until an audit can be conducted, notifying IT security, sequestering records etc.)

4.3.1.2.3 If an immediate audit is needed, the QI staff will be notified of the decision and will make every attempt to begin the review within 24-48 hours of notification.

4.3.1.3 **Concerns that can wait for the next convened IRB meeting:**

4.3.1.3.1 If a concern can wait for the next IRB meeting, it will be presented to the full committee for a determination on whether a For-Cause Audit is needed.

4.3.1.3.2 If the committee determines to issue a For-Cause Audit, the QI staff will be notified and will make every attempt to complete the review prior to next scheduled IRB meeting for the panel that issued the audit.

4.3.1.4 The fully convened IRB, IRB Chair, or HRPP Director (in cases that do not require immediate attention) may issue a For-Cause Audit.

4.3.2 **Notification of Selection:**

4.3.2.1 For-Cause Auditing may be scheduled with <u>24 hours notice or without notice</u> if there is concern for the welfare of human subjects.

4.3.2.2 If the Investigator is given notice, they will receive electronic communication from the QI staff notifying them of the IRB's decision to issue a For-Cause Audit.

4.3.2.2.1 The investigators will be informed that the audit is "For-Cause" but they may not be informed about the nature of the cause, until after the review is complete.

4.3.2.2.2 Investigators cannot refuse a For-Cause Audit but if they have a particular conflict (i.e. they are out of town etc.) they will be expected to inform the QI staff. In cases of conflict the PI will be expected to make sure a co-investigator or other member of the study team will be available to assist the QI staff.

4.3.2.3 If no notice is given, the Investigator or their staff will be informed in person that the audit is "For-Cause" but they may not be informed about the nature of the cause, until after the audit is complete.

4.3.2.3.1 If an investigator refuses to allow the QI staff access to the research data and facility the IRB and/or Institutional Official will be notified. A determination will be made on a case by case basis.

4.3.2.3.1.1 In such cases, the IRB may make a determination to suspend the research study or suspend the investigator's research privileges until an audit can be conducted.

4.3.3 **Expectations during the Audit:**

4.3.3.1 The duration of the audit is dependent on the complexity of the study and number of charts to be reviewed.

4.3.3.2 Provide the QI staff with a table or desk and suitable lighting with which to work.

4.3.3.3 Provide the QI staff with access to all research records, data, study drugs/devices and applicable study related logs. If any records are stored electronically please make sure the QI staff has access to them.

4.3.3.4 Provide the QI staff with a tour of the facility and all areas where the research is conducted or research data is stored.

4.3.3.5 The PI and/or research staff member is not expected to be present for the entire review. However the QI staff may ask to meet with the PI and/or research staff before and at the end of the review. The PI and/or research staff may also be asked to be available (or to check in periodically) to answer any questions that may arise during the review.

4.3.3.6 At the conclusion of the audit the QI staff will submit a report of any findings to the IRB for review. Upon review of the report, the IRB will then disseminate any corrective actions to the investigator..

4.3.4 **Communication of findings after the audit:**

4.3.4.1 If the audit involved concerns that need immediate addressing, such as those involving subject safety, the QI staff will give a brief verbal summary of the findings to the HRPP Director, IRB Chair, and/or Institutional Official immediately upon discovery.

4.3.4.2 After the monitoring visit the QI staff will write a report outlining the findings of the audit, for review by the IRB. If any corrective actions are indicated they will be included in the report.

4.3.4.2.1 The QI staff will make every effort to complete the report within 5 business days.

4.3.4.3 Once the report is complete a draft copy will be sent electronically to the HRPP Director, the IRB Chair and/or the Institutional Official for review.

4.3.4.3.1 At this point the IRB Chair may make a determination to suspend the research study or suspend the investigator's research privileges (if they were not suspended already) until the report is reviewed by the IRB.

4.3.4.4 If corrective actions have been proposed by the QI staff, the IRB will need to determine whether they agree with the corrective actions of if they want to make changes to them.

4.3.4.5 All corrective actions accepted by the IRB will then be submitted to the investigator.

4.3.5 **Responding to Audit report corrective actions:**

4.3.5.1 The PI is only required to submit a response to the IRB if corrective actions were requested. If no corrective actions were requested, then no further action from the PI is needed.

4.3.5.2 The PI is expected to submit a written response to all corrective actions by the date proposed by the IRB. Please include the following in the response;

4.3.5.2.1 A complete response to each corrective action item. *Incomplete responses such as, "We are working on it" are not acceptable.

4.3.5.2.2 If a corrective action item requests more than a clarification (i.e. specific log to be made, correction to be made or SOP to be provided, etc…) please provide a copy of the item with the response.

*A response indicating the correction was made without providing proof of the correction will not be considered sufficient.

4.3.5.3 If the PI is unable to respond to the corrective actions by the proposed date they must inform the QI staff /or HRPP Director

and request an extension from the IRB Chair. Extensions will be granted on a case by case basis.

4.3.5.4 If a PI fails to respond to corrective actions by the proposed date, they will be contacted by the QI and/or IRB staff to determine why they haven't responded, and to come to a mutually agreeable arrangement of when they will respond by. If no mutually agreeable arrangement is made or if the PI continues to fail to respond, the QI and/or IRB staff will notify the IRB and Institutional Official.

*A failure to respond may constitute serious non-compliance.

4.3.6 **Reporting of PI responses to corrective actions:**

4.3.6.1 The final report and the PI's response will be distributed to the IRB Chair, HRPP Director and Institutional Official. A copy of the report will be reviewed by the fully convened IRB.

5.0 Documentation:

5.1 Research Administration will maintain all records related to the implementation of this policy, electronic communications, and notifications to investigators, funding or regulatory agencies, etc.

5.2 Records will be archived for a period of at least three years following the termination or completion of the research activities.

6.0 References:

6.1 Guidance for Industry, Oversight of Clinical Investigations –A Risk-Based Approach to Monitoring, August 2013. https://www.fda.gov/media/116754/download

7.0 Revision History:

Rev #	Initials	Effective Date	Description of Change(s)
00	PMJ	3/18/14	New issue
01	PMJ	2/17/20	Review and Revision

Element 1.5.A.