1. PURPOSE

1.1. This SOP defines the Human Research Protection Program (HRPP) Post Approval Monitoring (PAM) Research Education Sessions, Directed or For-Cause Reviews and Quality Assurance functions within the Carilion Clinic HRPO.

2. AUTHORITY AND SCOPE

2.1. The Carilion HRPO Post Approval Monitoring Program (PAM) is under the general direction of the HRPO Director. The HRPO Program includes the following:

2.1.1. Research Education Sessions: Conducted based upon risk category or type of study. Circumstances where Post Approval Monitoring may occur include, but are not limited to:

2.1.1.1. Investigator Initiated Studies (minimal risk and greater than minimal risk);

2.1.1.2. Investigator/Sponsor Investigational New Drug (IND)/Investigational Device Exemption (IDE) studies;

2.1.1.3. Protocols that require periodic audits as indicated by boards or committees within the institution;

2.1.1.4. Studies assessed by the IRB to include a high degree of risk (adverse events, protocol deviations, type of study, or vulnerable populations); or

2.1.1.5. New, or inexperienced investigator(s) or research staff.

2.1.2. Directed or For-Cause Review: Conducted at the request of the Institutional Review Board (IRB), IRB Chair, HRPO Director, Institutional Official or designee or other Leadership Entities as applicable. Circumstances when a For-Cause Review may occur include, but are not limited to:

2.1.2.1. As part of an ongoing corrective action plan;

2.1.2.2. To support a review associated with Reportable New Information or the IRB's assessment of potential non-compliance including failure to follow the approved protocol, or the most recently approved version of the consent form, and/or;

2.1.2.3. When there are concerns regarding whether the rights and welfare of participants enrolled in research are adequately protected.

2.1.2.4. When there are concerns about the validity or integrity of the data collected.

2.1.3. Voluntary Reviews: Conducted upon request of Principal Investigator to support self-assessment and improvement efforts by Investigator and Study Team.

2.1.4. IRB Minutes Review: Conducted periodically to assure compliance and support the operations of the IRB.

2.1.5. Human Research Protections Office Quality Assurance: Conducted periodically to track and improve overall processes and procedures and institutional compliance with human research protection program requirements. This may include Research Participant surveys that can be utilized as part of the PAM, Directed or For-Cause Reviews, or sent out independently.

3. RESPONSIBILITIES

3.1. HRPO staff members are responsible for ensuring these procedures are carried out.

4. PROCEDURE

4.1. Post Approval Monitoring(PAM) Research Education Session (RES):

4.1.1. Selection and Scheduling:

4.1.1.1. The PAM studies are selected as follows:

4.1.1.1.1. Through request by the IRB, IRB Chair, HRPO Director, or Institutional Official or designee, to assess general compliance with regulatory and institutional requirements based upon specified study characteristics.

4.1.1.1.2. Random selection.

4.1.1.2. The Principal Investigator and Study Coordinator will be contacted to:

4.1.1.2.1. Schedule the review in a timely manner; approximately 10 days after the initial communication from the HRPO designee.

4.1.1.2.2. The HRPO designee will provide an overview of the scope, process and required workspace needed for the review; and

4.1.1.2.3. Will provide a copy of the worksheet that will be used as a general guide for review to the Investigator and Study Coordinator.

4.1.2. Review Procedures:

4.1.2.1. In advance of the review visit, the HRPO designee reviews the protocol information on file with the IRB;

4.1.2.2. On the day of the review, the HRPO designee will meet with the Investigator and designated study staff at the open and close of the review, if possible, to discuss, for example, who on the staff is responsible for various procedures, who is involved in the consent process and how informed consent is obtained, as well as other pertinent topics. The investigator will arrange for a private work area for the conduct of the review. At a minimum, designated study staff should make themselves available for documentation retrieval, to answer any questions, or to provide clarification as needed;

4.1.2.3. The investigator will provide the following study files (as applicable) for the review:

4.1.2.3.1. All approved study related regulatory documents;

4.1.2.3.2. Subject screening/enrollment log;

4.1.2.3.3. Case report forms;

4.1.2.3.4. Source documents;

4.1.2.3.5. Informed consents, assents, and HIPAA for all enrolled and screened participants

4.1.2.3.6. Study drug/product accountability logs, as applicable;

4.1.2.3.7. Device accountability logs, as applicable;

4.1.2.3.8. Lab logs. as applicable;

4.1.2.3.9. Other documents/files as requested that supports study administration.

4.1.2.4. Research records are expected to be maintained, by the study team, in a review-ready state at all times. The study team will have an opportunity to locate and provide materials or documentation not present in the files at time of review, but the initial absence of material or documentation will be noted in the findings.

4.1.2.5. The HRPO designee will select which of the research participants will be included in the PAM. If the number of subjects is small, all records may be reviewed. If there are a large number of subjects, a sample that will consist of either five subjects or 10% of the enrolled subjects, whichever number is greater. In the case of a for-cause audit, 100% of the research subjects' records may be reviewed.

4.1.3. Findings

4.1.3.1. Finding types may include, but are not limited to:

4.1.3.1.1. No further action necessary;

4.1.3.1.2. Minor administrative issue(s) with best practice or additional education recommendation for corrective action;

4.1.3.1.3. Finding that meets the definition of 'Reportable New Information' with best practice or other recommendation for corrective action.

4.1.3.1.4. Major finding, indicating potential harm or imminent risk of harm to participants' safety and well-being. These findings will be reported immediately by the staff member conducting the review to the HRPO Director and IRB Chair, and when necessary to the Institutional Official or designee.

4.1.3.1.5. Potential misconduct will also be reported to the Office of Integrity and Compliance

4.1.3.1.6. If a random or for-cause audit reveals the possibility of serious or continuing non-compliance with federal regulations or determination of the IRB, the procedures outlined in Standard Operating Guideline 6.4 will be followed.

4.1.4. Documentation and Distribution of Findings

4.1.4.1. Observations, findings, and any concerns will be documented.

4.1.4.2. At the conclusion of the review, the HRPO designee will verbally debrief the investigator and/or designated study team members regarding findings, applicable recommendations, and next steps.

4.1.4.3. A written report of findings and recommendations will be generated and shared with the principal investigator, HRPO and IRB Chairperson within 10 days of the review.

4.1.4.4. The investigator is asked to review the written report and provide a response and corrective action, when necessary, within 10 days of receipt of the HRPO recommendations.

4.1.4.5. In the event the Investigator disagrees with the findings of fact or wishes to provide clarification, the Investigator may provide the rebuttal and/or clarifications, in writing. The provided information and any corrective action plan will be submitted to the HRPO.

4.1.4.6. The investigator is also asked to submit each incident of Reportable New Information found through the review that has not already been reported to the IRB.

4.1.4.7. Follow-up reviews may be scheduled to confirm ongoing adherence to corrective action recommendation and continued compliance.

4.1.5. Directed or For Cause Review

4.1.5.1. Selection and Scheduling

4.1.5.1.1. The IRB Chair, HRPO Director, Institutional Official or designee ("Requestor"), and/or other Leadership Entities as applicable may request a directed or for-cause review. No pre-notification is required by the HRPO, however, when able notification may be provided to the investigator either on the day of the audit or in advance of the audit.

4.1.5.1.2. The Requestor will notify the HRPO of the investigator whose study will be subject to a directed or for-cause review. An official notification will be sent to the

investigator with a copy to their department head. This notice will include the scope, timing, scheduling process and next steps.

4.1.5.1.3. Unless directed to contact the Investigator sooner, the HRPO designee will contact the Investigator by the next business day following receipt of the review request and will work with the Investigator and study team to schedule the review within the timeline established by the requestor.

4.1.5.1.4. If scheduling and/or completion of review will not be possible within the established timeframe due to circumstances beyond the Investigator's control, the HRPO designee will notify the Requestor and request additional guidance.

4.1.5.1.5. As research records are expected to always be maintained in an audit-ready state, time needed for record preparation is not an acceptable reason to request delay.

4.1.5.2. Review Procedures

4.1.5.2.1. Review procedures will follow those outlined in 4.1.2, above.

4.1.5.3. Documentation and Distribution of Findings

4.1.5.3.1. The report and associated findings are shared with the Requestor, HRPO Director, IRB Chair and the IO as needed. The findings are also provided to the Investigator and their Department Head.

4.1.5.3.2. if the audit findings are not addressed in a timely manner, or not resolved to IRB satisfaction, the IRB can suspend or terminate the study in accordance with 45 CFR—Public Welfare (Department of Health and Human Services) {CFR §46.113} and CFR Part 56—Institutional Review Boards {CFR §56.113}.

4.1.5.3.3. Copies of audits, IRB surveys, and copies of monitoring reports will be kept in the Human Research Protections Office secure shared drive.

4.1.6. Voluntary Review

4.1.6.1. The Principal Investigator, or study team member with Principal Investigator's support, may conduct a self-assessment or ask for a voluntary review/assistive review by an HRPO designee.

4.1.7. IRB Minutes Reviews

4.1.7.1. The HRPO designee reviews the IRB minutes for compliance.

4.1.7.2. The HRPO designee prepares a report of findings, if any, and forwards to the IRB Chair and HRPO Director.

4.1.7.3. The HRPO Director or designee develops a corrective action plan if necessary or provides clarification to findings and communicates the findings and any corrective action plan as appropriate.

4.1.8. Human Research Protection Program Quality Improvement

4.1.8.1. The HRPO designee will provide a report of general trends and findings from the audits and reviews to the Institutional Official, HRPO Director, IRB Chair and others as necessary.

4.1.8.2. The staff will review the findings and develop corrective and educational action plans as necessary.

4.1.8.3. The HRPO designee will monitor the impact of the corrective and education plans on findings and will report outcomes to the applicable individuals.

4.1.8.4. Research participants can elect to be contacted for a follow-up survey regarding their experience as a research participant. They indicate this choice when engaging in the consent process. Participants may be contacted as a result of an audit or independent of an audit. When independent of an audit, studies will be chosen at random, and participants will be contacted using the contact information that they provided to the study team. The HRPO designee will follow up with research participants who have indicated that they agree to be contacted for the follow-up survey.

5. MATERIAL

6. APPROVAL AND REVISIONS

6.1. 07 APR 21: HRPO Director, Carley Emerson, originally created and approved

6.2. 8/14/23: Human Research Protections Office Director, Meredith Talmadge, updated to reflect procedures outlined in 6.6 Conduct of Research: IRB Compliance Activities (Audits, Surveys) and 6.7 Conduct of Research-Post approval Educational Activities

7. REFERENCES

7.1. OHRP 45 CFR 46.103(b)(5); 45CFR46.109(e);

7.2. FDA 21CFR56.108(b); 21CFR56.109(f),