This PAME process description references [IRB WPP X-3](http://www.research.vcu.edu/irb/wpp/wpp_docs/archive/X-3%202-5-07.doc)

Post approval monitoring by the IRB incorporates any type of protocol review conducted by the IRB after initial review and approval. The Post Approval Monitoring and Education (PAME) intiative augments the scope of post-approval monitoring by the IRB. PAME provides an additional layer of protection for human subjects in research, education for investigators and research staff, identifies areas of strength and needs for improvement in research policy and practice across the entire Human Research Protection Program. The PAME process is tailored to each protocol and the method includes identifying issues, resolving them, and providing educational support. The Research Liaison Specialist (RLS) for Human Research Protections is charged with developing, implementing, and monitoring the PAME program. In addition to post approval site visits, the RLS may conduct educational visits as follow up to IRB and/or investigator requests. The RLS is staff within the Office of Research Compliance and Education, and as such does not function under the direct authority of the IRB.

PAME visits focus on assisting investigators and research staff with implementing an IRB approved study including mechanisms to enhance protocol compliance, reporting, or requirements of Good Clinical Practice and/or Best Practice. On request, the RLS may also assist the PI/staff in preparation for a sponsor or federal agency audit or site visit.

Criteria for a PAME visit

In general, the criteria for a PAME visit can be based on a variety or combination of items, including but not limited to:

1. Greater than minimal risk study;
2. Inclusion of vulnerable subjects;
3. Complexity of the study;
4. No other source of post approval monitoring;
5. Investigator with large number of protocols;
6. Investigator-initiated study;
7. Significant Risk Device Studies;
8. Phase I and/or first use in humans studies;
9. Follow-up of corrective actions resulting from routine audits;
10. Investigator and/or study personnel request;
11. Inconsistencies in the protocol submission;
12. Prior and/or continuing compliance issues;
13. A history of past non-compliance with continuing review;
14. In response to a complaint

There are 2 types of PAME visits: “Not for Cause” visits and “For Cause” visits.

*“Not for Cause” or Random Visits*

The “not for cause” visit is designed to involve the PI and research staff in reviewing the terms of their IRB approval and the status of their protocol. It is an opportunity for the PAME visitors, the PI and staff to discuss the research protocol generally, especially as it impacts human subject protections, to ask questions about the current study or future studies, and to share updates in the IRB process. The emphasis is more on conversation and less on study documentation. Any of the above items may prompt a ‘not for cause’ visit.

*“For Cause” or Requested Visits*

“For Cause” PAME Visits are scheduled at the request of the VCU IRB, the ORSP, VCU administration, or as determined to be warranted by the ORCE. While similar to the "not for cause” visit, these visits may include a more in depth evaluation, consisting of audits of study records at the study site, contact with the research sponsor and/or monitoring organizations, contact with other IRB panels, interviews with research staff and research participants, and/or review of records within the IRB.

Determining when to visit

The time goal for scheduling a “not for cause” visit is 4 months prior to the study’s expiration date. This will allow IRB reviewers to have additional information about study status for the Continuing Review and allow the research team to make changes to their protocol based on PAME findings or based on Best Practices, if desired. If a PAME summary letter is not ready in time for the Continuing Review by the Panel, the RLS will make every effort to provide preliminary notes to the reviewers and Chair prior to the Panel meeting wherein the Continuing Review is scheduled.

In the case of a “for cause” visit referral, the visit will be scheduled as soon as possible.

The visit request

The visit request is usually sent two or more weeks before the suggested visit dates. It is sent to the PI and the study coordinator, if known. The email invitation briefly describes the PAME program. It includes a link to this document for further explanation. The invitation states whether this is a “for cause” or “not for cause” visit. The invitation asks for the current number of subjects, whether the study is still enrolling subjects, and suggests dates for the visit.

The invitation includes a link to the Post Approval Monitoring and Education Self-Evaluation Tool (PAME SET). There is a PAME SET form for biomedical research and another for social-behavioral research. These tools can also be used for training new staff and preparing for sponsor/agency audits. PIs and/or research staff are strongly encouraged to complete the PAME SET form and return it to the RLS a week before the meeting. The visits customarily follow the flow of the PAME SET form. If the visit is “for cause,” there will be specific questions on the problematic area(s).

After a date is set for the visit, invitations are sent to the IRB Panel chair, reviewers, panel coordinator, and ORCE director. If a Clinical Research Center study, an invitation is sent to the Research Advocate or other CRC staff. If the study involves cancer research, the Administrative Director of Clinical Research for Massey Cancer Center is copied and distributes the invitation letter to the study staff. A week before the visit, copies of review materials are distributed to the accompanying site visitors.

The lead visitor, usually the RLS, will perform a comprehensive review of the IRB file. The lead visitor will pay particular attention to the IRB correspondence with the investigator to ensure that IRB requests have been fulfilled. In addition, the protocol, research plan, consent form, and other documents are reviewed to ensure consistency. Accompanying PAME visitors may review study materials to the extent they choose.

Process for a ‘Not for Cause’ Visit

At the meeting, the PAME process is described again. Visitees are told that the process includes identifying issues, resolving them, and providing educational support. The RLS clarifies that the PAME program is an initiative of the ORCE and not directly affiliated with the IRB.

The Research Specialist Liaison has prepared protocol-specific questions and is the lead on the visit. Visitors are encouraged to ask questions during the visit, time permitting. Findings are verbally summarized at the end of the meeting. The PI (and staff) is informed that a draft summary letter is shared with all visitors and will be sent to PI/staff for comment before the letter is finalized. The summary letter is likely to include recommendations for Best Practice. It is clearly stated at the beginning and throughout the visit that requirements can only come from the IRB. The lead visitor will consult with the ORCE director as needed.

*General Visit Topics*

1. Regulatory Documentation
   1. Compliance with relevant laws, regulations, policies and procedures.
2. IRB Documentation
   1. Compliance of the PI and the research team with the IRB-approved protocol.
3. Subject Selection Criteria, Subject Recruitment Procedures, and the Consent Process
   1. Compliance with the process described in the research plan and/or protocol. Ascertain that the process is consistent with current WPPs, institutional policy, and relevant regulations. Special emphasis on the informed consent process, conformity to inclusion and exclusion criteria, vulnerable subjects, ads, and compensation, if any. Ensure that privacy protections are consistent with those described in the protocol.
4. Conflict of interests
5. Prompt and Non-Prompt Reporting
6. Drug/Device Accountability
7. Recordkeeping/ Data Security
   1. Provisions and practices pertaining to safeguarding confidentiality of data. Compliance with the process described in the research plan and/or protocol.
   2. Ascertain that the process is consistent with current WPPs, institutional policy, and relevant regulations.
8. General Educational Issues, such as plans to increase recruitment.

Should the site visit reveal a finding that is alarming and appears to place research subjects at great risk, the RLS will request that the PI agree to an immediate temporary stoppage of the study while the IRB Chair, IRB reviewer and ORCE Director determine appropriate action. If stopping the study could harm subjects, the investigator is advised to provide a rationale for continuing the study with current subjects. In addition, the investigator is advised to complete a Prompt Report to the IRB describing the problematic scenario found in the site visit. Upon consultation, the IRB Chair or designee may take actions regarding the study, such as suspending enrollment, pending further information.

Process for a ‘For Cause’ Visit

As above, except that one or more of the following areas may be assessed at a greater depth than a “not for cause” visit:

1. Compliance of the PI and the research team with the IRB-approved protocol;
2. Compliance with all relevant laws, regulations, policies and procedures;
3. Respect afforded to research subjects by the PI and the research team as evidenced by the informed consent process, conformity to inclusion and exclusion criteria, special concern for vulnerable subjects, etc.;
4. Observation of the consent process\*;
5. Provisions and practices pertaining to safeguarding confidentiality of data;
6. Compliance with reporting requirements, particularly reporting Unanticipated Problems Involving Risk to Subjects or Others and other terms of VCU IRB approval;
7. Concern for the safety of research subjects;
8. Research participant, family, or staff complaint.

\* The IRB may request monitoring of the consent process at any time as per regulations. Factors that may prompt Consent Observation include any specific complaint or concern raised that may relate to the consent process.

Post-visit Activity

After the site visit there may be clarifying communication by phone or email between the PAME lead visitor and the PI or study staff. A post-visit summary letter is developed to capture the main points of the PAME visit and convey the following, as applicable:

1. Consistency with the approved protocol, or findings that are inconsistent with the approved protocol;
2. Recommendations based on Best Practices/GCP and IRB WPPs. Recommendations are intended to be suggestions only (such suggestions can be voluntarily implemented for the current study, other studies, or in planning future studies);
3. Recommendations for support needed to ensure the staff’s ability to meet VCU research standards and Federal guidelines.

The RLS will consult with the ORCE Director and/or IRB Chair about findings that are inconsistent with the approved protocol, as well as suggestions for Best Practice. Identified findings are referenced to VCU IRB Written Policies and Procedures, 45CFR46 and 21CFR50, 56, Good Clinical Practice requirements, and compliance with other relevant policies and regulations, including Conflict of Interests reporting, HIPAA, etc. Post site visit communication, clarifications, or recommendations are reflected in the visit summary letter.

The draft summary letter may undergo modification as it is first reviewed by the ORCE director and accompanying visitors (IRB panel chair, reviewers, panel coordinator, etc.). Every effort will be made to send out the draft letter for their review within one week of the visit with a request for response within 3 working days. A courtesy draft is sent to the investigator and study staff who attended the visit. They have 5 working days to respond. (If the study is with Massey Cancer Center, only the Administrative Director of Clinical Research for the Massey Cancer Center and the investigator(s) receive the courtesy draft of the letter). If no comments are received, the draft is finalized. The courtesy draft is an opportunity for the investigator to review the PAME letter for accuracy and ask questions relative to the findings before the letter is finalized.

*Distribution of final PAME summary letter*

Every effort will be made to send out the final PAME summary letter within 2 weeks of the visit. The PAME summary letter is sent to the PI, study staff, ORCE director, IRB Panel Chair, IRB reviewers, and panel coordinator. (If this is a Massey study, the Administrative Director of Clinical Research for the Massey Cancer Center is copied and will distribute the final letter to study staff. If this is a CRC study, the Research Advocate in the CRC will be copied). The PAME visit letter is to be included with materials distributed to IRB members prior to Continuing Review of the protocol.

*Feedback Loop or Follow up on PAME findings*

Although most protocols do not demonstrate explicit findings that are inconsistent with IRB approval, many post-visit PAME letters will include recommendations or suggestions for Best Practices. As is mentioned several times in the visit, these are suggestions and not requirements. The final PAME summary letter will request that the PI/study staff respond by email to the RLS within 5 working days as to whether, and when, any suggestions will be acted upon. In the response to the RLS, the PI has the option of not acting upon PAME suggestions.

Recent PAME visits are included on the IRB Panel agenda. Depending on available time in the IRB meeting, a verbal summary of PAME visits may be requested by the Chair. If a study submitting Continuing Review underwent a recent PAME visit, the RLS may be asked to provide specific visit information to augment the Continuing Review. The PAME visit findings may generally be used in a variety of ways, such as:

1. If a Full Board study, the Panel discusses and/or makes a determination on the PAME findings. A determination may involve a) no action, b) required changes based on one or more suggestions, c) other action appropriate to the protocol.
2. If an expedited study, the IRB reviewer is requested to make a determination on the visit findings, as above;
3. The IRB uses the findings for general educational purposes. For example, the IRB discusses and gives guidance to investigators on specific issues raised in PAME visits;
4. PAME visit findings in aggregate are presented to the IRB as a mechanism to educate IRB members and improve IRB process and review.

*The role of the RLS in IRB follow-up to PAME findings:.*

Upon the request of the IRB, the RLS may follow through with one or more activities below:

1. Gather more information related to PAME findings and transmit these to the IRB;
2. Relay panel communication to the investigator, as appropriate, prior to receipt of a formal letter from the IRB;
3. Follow up on the submission of IRB required amendments, providing assistance to the investigator as requested;
4. Follow up with investigator and/or research staff in organizing regulatory records and educating about Best Practices.

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