7.1 Possible IRB Actions

Approval – the project is approved as submitted, or when requested revisions have been addressed and approved. A signed approval letter from the OHRP staff must be received before any research activity begins.

Board Modification – the protocol and/or consent form require minor revisions, such as wording changes, with replacement language provided. For protocols reviewed at a convened IRB meeting, the needed revisions are agreed upon at the IRB meeting. For protocols reviewed under expedited review, the revisions are designated by the reviewer(s). None of the required modifications can be related to the regulatory criteria for approval. These revisions are presented to the PI for incorporation by simple concurrence. Revisions must be made as designated by the IRB or reviewer(s).

To receive approval for a protocol deferred for non-substantive issues:

- For a full review, the PI's response, the revised protocol, and the previously submitted protocol is given to the IRB Chair, Vice-Chair, or a subcommittee of the IRB for review. The reviewer(s) may approve the project upon receipt and approval of the revisions without further action by the IRB.
- For expedited, the PI's response, the revised protocol, and the previously submitted protocol is given to the same reviewer(s) for re-review or to a subcommittee.

Approval of the protocol application will not be granted, and certification will not be issued until all deficiencies, if any, are corrected to the satisfaction of the IRB or the reviewer(s). The date of approval for expedited protocols is the date the conditions were determined to be met. If the research protocol expires before the conditions are reviewed and approved, all research activities must stop until approval is obtained.

The outcome of the IRB's deliberations is once again communicated to the PI in writing. The IRB's determination concerning the amended submission will be documented in the minutes of the next IRB meeting or the file for expedited review.

NOTE: For full board review, the approval period for the protocol is calculated based on the date of the last convened IRB meeting and not on the final approval date.

Deferred for Substantive Issues- there are significant issues with the protocol and/or consent form. This action is taken if substantial modification or clarification is required, or insufficient information is provided to judge the protocol application adequately (e.g., the risks and benefits cannot be assessed with the information provided). IRB approval of the proposed research must not occur until a review of the material the PI submitted by the convened IRB or the expedited reviewer(s).

To receive approval for a protocol deferred for substantive issues:

- For a full review, the PI's response must be submitted for review at a subsequent, convened meeting of the same IRB. The OHRP provides the IRB with the PI's response, the revised protocol, and the previously submitted protocol. The item is placed on the
agenda for re-review at the next meeting.

- For expedited, the PI’s response, the revised protocol, and the previously submitted protocol is given to the same reviewer(s) for re-review.

Approval of the protocol application will not be granted, and certification will not be issued until all deficiencies, if any, are corrected to the satisfaction of the IRB or the reviewer(s). The outcome of the IRB’s deliberations is communicated to the PI in writing. The IRB’s determination concerning the amended submission will be documented in the minutes of the IRB meeting or the file for expedited review.

NOTE: Failure to submit a response to IRB-stipulated changes or inquires related to deferred protocols within 75 days of the IRB date of determination will result in the administrative closure of the IRB file. The PI will receive notification of the closure of the IRB file, including an explanation for this action. The IRB may grant an extension beyond 75 days if the PI provides sufficient cause.

Disapproved – The IRB determines that the research cannot be conducted at WVU or by employees or agents of WVU, or otherwise under the auspices of WVU.

Approval in Principle - as per federal regulations (45 CFR 46.118), there are two circumstances in which the IRB may grant approval required by a sponsoring agency without having reviewed all of the project procedures and consent documents. One is if project procedures are to be developed during the course of the research, but the sponsoring agency requires human subjects’ approval. The other is if the involvement of human subjects depends on the outcomes of work with animal subjects. The IRB may then approve without having reviewed the as yet undeveloped recruitment, consent, and intervention materials. However, if the proposal is funded, the Principal PI must submit such materials for approval at least 60 days before recruiting human subjects into the project, or into any pilot studies or pre-tests. Approval in principle is granted to satisfy sponsoring agency requirements or to allow PIs to have access to funding to begin aspects of the project that do not involve human subjects.

7.2 Project Suspension, Termination, and PI Hold

7.2.1 Suspension and Termination

IRB approval may be suspended or terminated if research is not being conducted following IRB or regulatory requirements or has been associated with unexpected problems or serious harm to participants. (See Section 8 for a discussion of unexpected problems and Section 10 for a discussion of non-compliance).

Suspension of IRB approval is a directive of the convened IRB or IRB Chair to temporarily stop some or all previously approved research activities short of permanently stopping all previously approved research activities. Suspension directives made by the IRB Chair must be reported to a meeting of the convened IRB. Suspended protocols remain open and require continuing review.

Termination of IRB approval is a directive of the convened IRB to stop all activities permanently in a previously approved research protocol. Terminated protocols are considered closed and no longer
require continuing review. The convened IRB must make terminations of protocols approved under expedited review.

The IRB shall notify the PI in writing of such suspensions or terminations and shall include a statement of the reasons for the IRB's actions. The terms and conditions of the suspension must be explicit. The PI shall be provided with an opportunity to respond in person or in writing.

When the IRB or an authorized individual suspends or terminates approval is suspended or terminated, the IRB or individual ordering the suspension or termination will notify current participants of the suspension or terminations. In addition, all research activities will be stopped.

The convened IRB or individual ordering the suspension or termination will consider whether procedures for withdrawal of enrolled participants are necessary to protect their rights and welfare of participants, such as transferring participants to another PI; making arrangements for care or follow-up outside the research; allowing the continuation of some research activities under the supervision of an independent monitor, or requiring or permitting follow-up of participants for safety reasons.

If the follow-up of participants for safety reasons is permitted/required by the convened IRB or individual ordering the suspension or termination, the convened IRB or individual ordering the suspension or termination will require that the participants should be so informed and that any adverse events/outcomes be reported to the IRB and the sponsor.

The PI must continue to provide reports on adverse events and unanticipated problems to the IRB and sponsor (i.e., All events that need to be reported need to continue to be reported during the suspension period).

NOTE: Suspension or termination of protocols approved by the IRB can also be issued by WVU officials acting outside of and unrelated to the HRPP (i.e., not necessarily related to protecting the rights and welfare of participants). Such University actions can be made by the University President, Provost, and Deans. Such University actions may be made for any reason in furtherance of the Institution’s interest provided, however, that the aggrieved PI is entitled to all rights and procedures afforded to him/her under the Grievance Policy. The PI must report any suspension or termination of the conduct of research by organization officials to the IRB. The IRB will then determine if suspension or termination of IRB approval is warranted.

7.2.2 PI Hold

A PI may request an administrative hold on a protocol when the PI wishes to temporarily or permanently stop some or all approved research activities. An administrative hold is initiated by a PI. Administrative holds are not suspensions or terminations.

7.2.2.1 Procedures for PI Hold

1. The PI must notify the IRB in writing that:
a. They are voluntarily placing a project on administrative hold.
b. A description of the research activities that will be stopped.
c. Proposed actions to be taken to protect current participants.
d. Actions that will be taken before IRB approval of proposed changes to eliminate apparent immediate harm.

2. Upon receipt of the written notification from the PI, an IRB Manager places the research on the agenda for review.

3. The IRB Chair and/or Director, in consultation with the PIs, determine whether any additional procedures need to be followed to protect the rights and welfare of current participants as described in "Protection of currently enrolled participants" below.

4. The IRB Chair and/or Director, in consultation with the PIs, determine how and when currently enrolled participants will be notified of the administrative hold.

5. PIs may request a modification of the administrative hold by submitting a request for a modification to previously approved research.

7.2.3 Protection of Currently Enrolled Participants

Before an administrative hold, termination, or suspension, is put into effect, the convened IRB or IRB designee considers whether any additional procedures need to be followed to protect the rights and welfare of current participants. Such procedures might include:

- Transferring participants to another PI
- Making arrangements for clinical care outside the research
- Allowing the continuation of some research activities under the supervision of an independent monitor
- Requiring or permitting follow-up of participants for safety reasons
- Requiring adverse events or outcomes to be reported to the IRB and the sponsor
- Notification of current participants
- Notification of former participants

7.3 Continuing Review of Approved Research

The IRB will conduct a continuing review of ongoing research at intervals that are appropriate to the level of risk for each research protocol, but not less than once per year. A continuing review must occur as long as the research remains active for long-term follow-up of participants, even when the research is permanently closed to the enrollment of new participants, and all participants have completed all research-related interventions. Continuing review of research must occur even when the remaining research activities are limited to the analysis of private identifiable information.
7.3.1 Approval Period

At WVU, determination of the approval period and the need for additional supervision and/or participation is made by the IRB on a protocol-by-protocol basis. For example, for a PI who is performing particularly risky research, or for a PI who has recently had a protocol suspended by the IRB due to regulatory concerns, an on-site review by a subcommittee of the IRB might occur, or approval might be subject to an audit of project performance after a few months of enrollment, or after enrollment of the first several participants.

For each initial or continuing approval, the IRB will indicate an approval period with an approval and expiration date specified. IRB approval is considered to have lapsed at midnight on the expiration date of the approval. For a project approved by the convened IRB, the approval period starts on the date that the IRB conducts its final review of the project; that is, the date that the convened IRB or subcommittee approved the research or the date the convened IRB deferred the research for non-substantive issues. For a project approved under expedited review, the approval period begins on the date the IRB Chair or IRB member(s) designated by the Chair gives final approval to the protocol.

The approval date and approval expiration date are noted on all IRB certifications sent to the PI and must be followed. PIs should allow sufficient time for development and review of renewal submissions.

A review of a modification to a protocol ordinarily does not alter the date by which continuing review must occur. Note: a continuing review is a review of the full protocol, not merely a change to a protocol.

The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur by midnight of the date when IRB approval expires. If the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur.

7.3.2 Continuing Review Process

Notifications will be sent three months, two months, and one month in advance of the expiration date; however, it is the PI’s responsibility to ensure that the continuing review of ongoing research is approved before the expiration date. Per federal regulation, no extension to the date can be granted.

The PI must submit the following for continuing review:

1. The initial review application updated with any changes;
2. The current consent document, if no changes were made, or any newly proposed consent document; and
3. A completed protocol renewal form.

In conducting continuing review of research not eligible for expedited review, all IRB members are provided and review all of the above material. The primary reviewer will review the complete
protocol, including any modifications previously approved by the IRB. At the meeting, the assigned reviewer(s) lead the IRB through the completion of the regulatory criteria for approval in the "Continuing Review" checklists.

HRPP staff attend the convened meetings and have completed protocols available. The IRB staff will retrieve any additional related materials the IRB members request.

In the case of expedited review, the IRB members may request the HRPP staff to provide them with any additional materials required for the review.

Review of currently approved or newly proposed consent documents must occur during the scheduled continuing review of research by the IRB. However, informed consent documents should be reviewed when new information becomes available that would require modification of information in the informed consent document.

7.3.3 Expedited Processes for Continuing Reviews

In conducting a continuing review under expedited review, the reviewers receive all of the above material. The reviewer(s) complete the "Continuing Review" checklists to determine whether the research meets the criteria allowing continuing review using the expedited procedure, and if so, whether the research continues to meet the regulatory criteria for approval.

Generally, if the research did not qualify for expedited review at the time of the initial review, it is not eligible for expedited review at the time of continuing review, except in limited circumstances described by expedited review categories (8) and (9) at 63 FR 60364- 60367. It is also possible that research activities that previously qualified for expedited review following 45 CFR 46.110 have changed or will change, such that expedited IRB review would no longer be permitted for continuing review.

7.3.4 Lapse in IRB Approval

The regulations permit no grace period or approval extension after approval expiration. The HHS OHRP and AAHRPP require the re-approval of protocols by the expiration date.

Research that continues after the approval period has expired is research conducted without IRB approval. If the continuing review does not occur within the timeframe set by the IRB, all research activities must stop. This includes recruitment (e.g., media advertisements must be pulled), enrollment, consent, interventions, interactions, and data collection unless the IRB finds that it is in the best interests of individual participants to continue participating in the research interventions or interactions. If such information is not included in the protocol application, then the PI should contact the IRB with this information.

The IRB sends notifications in time for the protocol renewal to be submitted at least four (4) weeks before the expiration date. It is suggested that PIs submit earlier than four (4) weeks if there are changes or other concerns. This time will allow the IRB sufficient time for processing and reapproving the protocol. The protocol will expire if not reapproved by the expiration date.

NOTE: Expiration will occur even if the PI has provided the continuing information before the
expiration date. Therefore, PIs must allow sufficient time for IRB review before the expiration date.

If the PI wishes to continue the research after closure for administrative reasons, the project will need to be submitted as a new protocol for the initial review with a new protocol number. In that case, the PI should note that there was a previous protocol giving the number of the closed protocol and pertinent data from the initial protocol.

When an approval has expired, IRB review and re-approval must occur before re-initiation of the research. If the approval has lapsed more than 30 days, and the PI has not provided the required continuing review information, the PI must submit a new application for review and approval. If the approval has lapsed 30 days or less, and the PI provides the required continuing review information, the existing protocol may be reviewed for consideration of continued IRB approval.

If a research protocol receives contingent approval at the time of the continuing review and the approval expires before the PI responds to the contingencies, the PI may not enroll new participants or access medical records after the approval expiration date. Once the PI responds, the existing protocol will be reviewed for continuation. If the PI does not respond for an extended period, the IRB may vote to administratively close the project. Decisions must be made in a manner that ensures that closure will not harm any participants previously enrolled who may require ongoing treatment as part of the research project.

7.4 Modifying an Approved Protocol

PIs may wish to modify or amend their approved applications. PIs must obtain IRB approval before making changes to an approved protocol. This requirement applies even when the changes are planned for the period in which IRB approval was granted unless the change is necessary to eliminate an immediate hazard to the participant (in which case the IRB must be notified immediately by contacting the WVU OHRP Director).

Changes in approved research that are initiated without IRB approval to eliminate apparent immediate hazards to the participant are reviewed by the convened IRB to determine whether each change was consistent with ensuring the participants' continued welfare.

Modifications may be approved if they are within the scope of what the IRB authorized initially. For example, if a researcher wishes to add a population to an existing project, but not alter the project procedures or purpose, a modification request is usually appropriate.

Likewise, modifying a procedure without changing the project's purpose or project population may also be appropriate. If, however, the researcher wishes to add a population and significant revisions to the project procedures, he or she will need to submit a new application for IRB approval.

PIs must submit documentation to inform the IRB about the changes in the status of the project, including, but necessarily limited to:

- Completed "Protocol Amendment" form
- Revised PI's brochure or sponsor protocol (if applicable)
- Revised approved consent/parental permission/assent documents (if applicable) or other documentation that would be provided to participants
- Documentation that will be provided to participants related to their willingness to continue participation in the project
- Revised or additional recruitment materials
- Any other relevant documents provided by the PI

OHRP staff will determine whether the proposed changes may be approved through an expedited review process if the changes are minor, or whether the modification warrants full board review. The reviewer(s) using the expedited procedure has the ultimate responsibility to determine that the proposed changes may be approved through the expedited review procedure and, if not, must refer to the protocol for full board review. If an amendment for VA research addresses an issue related to biosafety or radiation safety, the appropriate committee or subcommittee first approves the amendment, when applicable.

7.4.1 Expedited Review of Protocol Modifications

An IRB may use expedited review procedures to review minor changes in ongoing previously-approved research during the period for which approval is authorized. An expedited review may be carried out by the IRB Chair and/or designee(s) among the IRB members.

The reviewer(s) complete the "Reviewer" checklists to determine whether the modifications meet the criteria allowing review of the amendment using the expedited procedure, and if so, whether the research with the proposed changes continues to meet the regulatory criteria for approval.

The reviewer will consider whether the modifications might relate to participants' willingness to continue to take part in the research and, if so, determine if the information should be provided to participants.

7.4.2 Full Board Review of Protocol Modifications

When a proposed change in a research project is not minor (e.g., procedures involving increased risk or discomfort are to be added), then the IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research participants. In such a case, the IRB should be promptly informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the participants' continued welfare.

All IRB members have access to review all documents provided by the PI(s). The primary reviewer presents an overview of the modifications and leads the IRB through the completion of the regulatory criteria for approval at the meeting. The IRB will determine whether the proposed changes continue to meet the regulatory criteria for approval.
When the IRB reviews modifications to previously approved research, the IRB considers whether information about those modifications might relate to participants' willingness to continue to take part in the research and, if so, whether to provide that information to participants.

7.5 Closure of Protocols

7.5.1 Closure of Approved Protocols

The completion of a research project, whether premature or not, is a change in activity and must be reported to the IRB. Although participants will no longer be "at-risk" under the project, a final report to the IRB allows it to close its files as well as providing information that may be used by the IRB in the evaluation and approval of related studies. PIs may submit closure applications to the IRB on a closure report.

The completion of a sponsored protocol will have a reminder in the closure acceptance letter stating the following: "Please be aware that if the sponsor contacts you with any information directly affecting participant safety, you must submit this information to the IRB regardless of the status of the project. A notification should be sent to the WVU OHRP, and the full report should be added to the project.

7.5.2 Administrative Closure of Protocols Not Received by the IRB

Protocol submissions that have not been received by the IRB during that six-month timeframe will be closed administratively in the electronic system. Notifications will be sent to the PI, beginning at three months after creation, and periodically throughout the six-month lifespan of a protocol not received by the IRB. If the PI does not respond to notifications, the protocol will be closed at the end of the six months.

7.6 Informing PIs of IRB Determinations

All IRB actions are communicated to the Principal PI (PI), or designated primary contact person for the protocol, in writing within ten (10) working days via a template letter prepared by the IRB staff and signed by the IRB Chair or designee. Upon approval, a notification will be sent to the PI. The approval letter, informed consent, and other applicable documents will be located in the electronic system for retrieval. The approval period will be watermarked on the informed consent form.

For a deferral or modifications, a notification will be sent to the PI. The modifications letter, containing the requested revisions, will be located in the electronic system for retrieval. For disapprovals, terminations or suspensions, the notification will include the basis for making that decision and should be copied to the Chair of the appropriate department.

The IRB reports findings and actions to the Institution in the form of the meeting minutes, which are distributed by WVU OHRP staff to the WVU Institutional Official and are stored permanently and securely by the OHRP.

7.7 PI Appeal of IRB Decisions

When an IRB protocol presented at a convened meeting is disapproved or deferred, the IRB will notify the PI in writing about the specific deficiencies and the modifications that are necessary for
appropriate IRB approval. The IRB shall include in its written notification a statement of the reasons for its decision. The PI may respond in person or writing. If an PI disagrees with any Board decisions or actions, he or she may request reconsideration by either appearing before the Board or by requesting an Advisory Review Panel. This request must be made to WVU OHRP in writing, within seven calendar days of the PI's receipt of the Board's notification.

7.7.1 Appeal Procedures

The entire appeal process must be completed within 120 calendar days of the PI's receipt of the Board's notification to suspend or terminate the project.

The decision of the Board becomes final under any of the following circumstances:

- The PI chooses not to appeal
- The PI fails to notify WVU OHRP within seven calendar days of receipt of the Board's notification of a decision to appeal.
- The PI or a representative fails to appear before the Board at its next regularly scheduled meeting.
- The PI fails to request the formation of an advisory review panel within seven calendar days after receiving the Board’s decision.
- The PI fails to make documents concerning the project available to the advisory review panel within seven calendar days of being requested to do so.

Final decisions are made after receipt of the Advisory Review Panel recommendation. The Board will notify all appropriate parties.

7.7.2 PI Appears Before the Board

An PI may ask to appear before the Board to request that the Board reconsider a decision; this appearance must be at the next regularly scheduled IRB meeting. The Board may affirm, modify, or reverse its original decision. Within seven calendar days, the Board will notify the PI of its decision. If the PI is still dissatisfied, he or she may now have seven calendar days to request (in writing to WVU OHRP) formation of an Advisory Panel Review.

7.7.3 Advisory Review Panel

The Advisory Review Panel must be formed within 15 calendar days of the PI's request for its formation.

The Advisory Review Panel shall consist of three persons:

1. The IRB chair chooses one member; this person may not be a current member of the Board or the IRB staff.
2. The principal PI chooses one member; this person may not be a member of the PI’s department and may not have had any direct involvement in the activities in question.
3. One member is chosen by the Institutional Official (IO); this person will serve as Chair, may not be a current member of the Board or the IRB staff, may not be a member of the
PI's department, and may not have had any direct involvement in the activities in question.

7.7.3.1 Recommendation Report

Within 30 calendar days of its formation, the panel will complete its investigation and transmit to the IRB chair, a written report of its findings and recommendations. During its investigation, the panel may involve the General Counsel's office. The Board will consider this report at a regular or special meeting held within 30 calendar days of the Chair's receipt of the report.

The Board will provide written notice (within seven calendar days) of its decision to the appropriate PI (s), department chair(s), and members of the advisory panel, and others as deemed appropriate.

7.7.3.2 Determination

The Institutional Review Board's determination on accepting the Advisory Review Panel report recommendation will constitute the final decision regarding the PI's appeal.