DEFINITIONS

Modification means proposed changes in the conduct of the study that may affect the protection of human subjects. A minor modification is a modification that involves no more than minimal risk and which all added procedures fall into categories one through seven of the categories of research allowing review using the expedited procedure. (See PRO150 Procedure for Continuing Review of Research by the Expedited Procedure.) Minor modifications proposed for previously approved research may be reviewed in an expedited procedure by the IRB in accordance with 45 CFR 46.110 and 21 CFR 56.110. When a proposed change in a research study is not minor, the IRB must review and approve changes at a convened meeting before the change can be implemented. The only exception is when a change is necessary to eliminate apparent immediate hazards to the research subjects. Problems or new information that may affect the risk-benefit assessment must be promptly reported to, and reviewed by, the IRB to ensure adequate protection of human subjects per POL006 UAB Policy to Ensure Prompt Reporting of Unanticipated Problems Involving Risks to Subjects or Others to the IRB and PRO106 Procedure To Ensure Prompt Reporting Of Unanticipated Problems Involving Risks to Subjects or Others.

PROCEDURE

Investigator’s Responsibilities

The Investigator:

- Refrains from initiating modifications (changes to the research) without IRB review and approval of those modifications in approved research during a period for which IRB approval has been given, except when necessary to eliminate apparent immediate hazards to the subjects;
- Submits a completed FOR224 Project Revision/Amendment Form to the OIRB for approval of proposed modifications (changes) in the approved research and any proposed plans to re-consent previously enrolled subjects;
- Submits with Project Revision/Amendment Form one copy of all modified documents related to the modification (e.g., informed consent document(s), recruitment material, or advertisements, and PORF if DoD sponsored study);
- Submits applicable special populations supplemental forms pertaining to vulnerable subjects (i.e. FOR220 “Pregnant Women, Fetuses, and Neonates”; FOR221 “Prisoners”; FOR222 “Children”) when a modification affects participants from vulnerable populations;
• Reports modifications (changes) taken prior to IRB approval to eliminate an apparent immediate hazard to subjects by completing the Project Revision/Amendment Form and submitting it within 5 working days of initiating the change.

OIRB Responsibilities

The Clerical Staff:

• Routes all project revision/amendment materials with accompanying file to a senior staff member;

• Distributes amendment materials to IRB in accordance with (see PRO145 Procedure for Timing of Document Distribution for IRB Meetings);

• Distributes minor protocol amendments approved via expedited procedures with the convened IRB meeting agenda; copies and mails signed and dated approval form when approved, and stamped informed consent document if applicable, to Principal Investigator;

• Prepares a list of protocol amendments approved through the expedited procedure for convened IRB confirmation.

• Files materials in protocol file.

The Senior Staff:

• For all modifications:
  o Reviews all project revision/amendment materials for completeness;
  o Requests additional information from research team, as needed;
  o Reviews modification for effect on data safety monitoring plan;
  o Marks minor modifications in amendment and all modified document(s) for review by the IRB Chair;
  o Forwards project revision/amendment materials to either the IRB Chair (or designee) for review and either approval or referral to the convened IRB.

• For modifications referred to the convened IRB:
  o Refers submissions for entry into IRB database;
  o Reviews modifications prior to meeting;
  o Takes notes on IRB actions for each protocol during convened meeting along with technical writer;
  o Drafts, reviews, and signs letters on behalf of the IRB to the principal investigator.

The Administrative Staff:

• For modifications referred to the convened IRB:
  o Drafts letter of IRB action to principal investigator for review by senior staff and/or Chair;
Assures entry of protocols scheduled for IRB review into information system database;
Enters final actions into the information system database;
Once final approval is issued, enters date issued into information system database and mails approval form and stamped approved informed consent document(s);
Includes information in the draft minutes of the IRB meeting for review by the senior staff documenting the regulatory criteria are met in accordance with 45 CFR §§46.103, 46.109, 46.111, and 46.116; with 21 CFR §§56.103, 56.109, 56.111, and 56.116, and any other funding agency, as applicable;

IRB Responsibilities

The Chair (or designee) or experienced IRB member designated by the IRB and appointed by the Chair:

- Reviews the proposal and verifies that the modifications to the research represent minor modifications.
- Reviews all modified documents;
- Uses GUI329 Criteria for Approval Tool to determine whether the research meets the criteria at 45 CFR 46.111, and Subpart D if applicable, and 21 CFR 56.111 if applicable, and 21 CFR 56 Subpart D if applicable.
- Reviews and determines if the requirements of PRO125, if applicable, are satisfied; in addition to 46 CFR 46 Subparts B and D, if applicable, and 21 CFR 56 Subpart D, if applicable for minor modifications related to vulnerable populations.
- Approves the research study or approves research following modifications to receive approval, if the above criteria are satisfied and returns to Senior Staff to review approval status.
- Refers the protocols that cannot be reviewed by the above procedure to Senior Staff to schedule for convened IRB review.
- Reviews and may approve proposed modifications that are:
  - Minor modifications—modifications that involve no more than minimal risk and in which all added procedures fall into categories one through seven of the categories of research allowing review using the expedited procedure;
  - Reduce the risks/discomforts to the subject;
  - Study staff changes (e.g., subinvestigators or research nurses);
  - Advertisements of previously approved research.
- Signs and dates minor modifications;
- Sends to administrative staff for copying and distribution to a convened IRB meeting;
• Refers all modifications not approved under criteria above to the next available convened IRB meeting.

Each Primary IRB reviewer:

• Receives and reviews in depth all of the following assigned materials for project revision/amendment for presentation at convened IRB meeting:
  o Project Revision/Amendment Form;
  o Revised informed consent document(s), if applicable;
  o Revised sponsor’s protocol;
  o Revised Investigator’s Brochure or package insert, if applicable;
  o Recruitment materials, advertisements, or questionnaires, if applicable;
  o Change in protocol status.

Each IRB member assigned to the convened IRB meeting:

• Receives and reviews the minor modifications approved under expedited procedure in enough depth to discuss at the meeting;
• Receives and reviews materials for project revision/amendment in enough depth to discuss the information at the convened meeting.

The IRB:

• Ratifies all minor modifications approved by the Chair (or designee) or experienced IRB member;
• Takes action on all project revision/amendment materials referred by the Chair and documents the regulatory criteria are met in accordance with 45 CFR §§46.103, 46.109, 46.111, and 46.116; with 21 CFR §§56.103, 56.109, 56.111, and 56.116, and any other funding agency, as applicable;
• Review and makes a determination whether the requirements of PRO125, if applicable are satisfied; in addition to 45 CFR 46 Subparts B, C, and D, if applicable, and 21 CFR 56 Subpart D, if applicable when the research involves vulnerable populations;
• Decides whether the modifications require the investigators to provide information relating to protocol changes that may affect a participant’s willingness to continue to take part in the research;
• Reviews and makes a determination on modifications for change in the data safety monitoring plan;
• Takes action and assigns one of the following classifications to the modification:
  o Approved—No modifications required. Research activity meets 45 CFR 46.111 or 21 CFR 56.111;
• Provides written communication to the principal investigator of IRB action within 10 working days. If a protocol is deferred or disapproved for any reason, the committee includes reasons for the action and an invitation to respond to the IRB in writing or in person. Any suspension or termination of IRB approval or sponsor-imposed suspension will be processed according to POL038 UAB Policy on Suspension or Termination of IRB-Approved Research and Administrative Hold and PRO140 Procedure for Suspension or Termination of IRB-Approved Research and Administrative Hold.