

Section XII: Review of Continuing Projects Involving Human Subjects

12.1 Review of Continuing Human Subject Research Projects

- a. Continuing reviews of research must be substantive and meaningful. According to references (b) and (c) of Enclosure (1), in addition to considering the criteria that was evaluated during the initial review of an approved protocol, certain criteria within a proposed *continuation* of a research protocol must be considered by the Academy's IRB before an approval recommendation can be submitted to the Superintendent for action. These continuation criteria include, but are not limited to, determinations by the Academy's IRB of the risks to participants, potential benefits, informed consent, and safeguards for human subjects in the event the continuation of the project is approved by the Superintendent as recommended via the Academy's IRB process. Additional information that must be reviewed by the Academy's IRB includes information gathered since the research began (under the first approval) such as: the number of participants enrolled in the project, the number of withdrawals or terminations from the project and the reasons for each, any complaints by the participants, any adverse events or unanticipated problems, the results of any recent literature searches that may be relevant to the research, any modifications or amendments to the original research protocol, and any additional information about the risks (potential or real) to the participants associated with the research.
- b. Informed consent forms and any related documentation will also be part of a review by the Academy's IRB of a request to continue a human subject research project.
- c. Per reference (p) of Enclosure (1), the Academy's IRB must ensure that the aforementioned criteria are satisfied during the initial review of a protocol and again during any project continuation review. When conducting a continuation review, the Academy's IRB must determine whether any new information has emerged – either from the research itself or from other sources – that could alter the Academy IRB's previous determinations (particularly with respect to any risks to the human subjects and/or the security of the data about them) and the IRB's approval recommendation, and/or that could influence the Superintendent's decision with respect to continuing the project. In most cases, information regarding any unanticipated problems involving risks to the human subjects in the study or to others (hereafter referred to as *unanticipated problems*) that have occurred since the previous Academy's IRB review will be pertinent to the board's determinations at the time of consideration of a request for a recommendation of "continuation approval" to the Superintendent.
- d. In conducting a review of a request to continue a research project, a protocol summary and a status report on the progress of the research are required. As a minimum, this documentation must include:
- the number and source of the human subject participants;

- a summary of any *unanticipated problems* and available information regarding adverse events. (In many cases, such a summary could be in the form of a brief statement that there have been no *unanticipated problems* and that adverse events have occurred at the expected frequency and level of severity documented in the research protocol, in the informed consent document, and/or in any relevant investigator brochure.)
- a summary of any withdrawal of subjects from the research since the last review of the project by the Academy's IRB and approval by the Superintendent.
- a summary of any complaints about any aspects of the research project since the last review by the Academy's IRB and approval by the Superintendent.
- a summary of any recent literature that may be relevant to the research and any amendments or modifications to the research since the last review by the Academy's IRB and approval by the Superintendent.
- any relevant multi-center trial reports.
- any other relevant information, especially as it relates to risks, associated with the research.

and

- a copy of the current informed consent document(s) and any newly proposed consent document(s).

e. When reviewing the current informed consent document(s), the Academy's IRB must ensure:

- that the currently approved or the proposed consent document(s) is (are) still accurate and complete;
- that any significant new findings that may relate to the subject's willingness to continue participation are provided to the subject in accordance with reference (b) of Enclosure (1).

f. Review of currently approved or newly proposed consent documents must occur during the scheduled continuation review of the research project by the Academy's IRB. Informed consent documents must be reviewed whenever new information becomes available that would require modification of information included on the current informed consent document(s).

g. The minutes of the Academy's IRB meetings must document separate deliberations, actions, and votes on any approval recommendations made to the Superintendent for each protocol undergoing a continuation review by the Academy's IRB.

12.2 Continuation Review using the "Expedited" IRB Process

a. According to reference (b) in Enclosure (1), the use of the "Expedited" IRB review process is strictly limited to two well-defined research categories, as defined in the federal register. The "Expedited" review process may only be used to evaluate minor changes in previously approved research during the period for which the approval was initially granted. (In most cases, the initial approval period was one year.) Guidance on the defined categories of review in the federal register, and how these may apply to a specific human subject research project, can be obtained from the Director of the Academy's HRPP office.

b. In most cases, if the research protocol did not meet the criteria for an "Expedited" IRB review process at the time of its initial evaluation and approval, it will not meet the criteria for an "Expedited" review when the project is being evaluated for continuation.

c. In a few cases and under limited circumstances, the "Expedited" IRB review process may be used for the continuation evaluation even though the process was not applicable for the initial review of the project. The "Expedited" IRB review process may be used for the continuation evaluation of a research project previously approved by the Superintendent if the following apply:

- where: (i) the research is permanently closed to the enrollment of new subjects;
- (ii) all subjects have completed all research-related interventions;
- and (iii) the research remains active only for long-term follow-up of subjects.

OR

- where no subjects have been enrolled and no additional risks have been identified.

OR

- where the remaining research activities are limited to data analysis.

Guidance on how and if these conditions might apply to a human subject research project at USNA can be obtained from the Director of the Academy's HRPP office.

d. It is also possible that research activities that previously qualified for an "Expedited" review in accordance with reference (b) of Enclosure (1) have changed or will change, such that an "Expedited" IRB review process would no longer be permitted for the continuation evaluation.

12.3 Determining the Continuing Review Date

a. Reference (b) of Enclosure (1) requires that, except when an “Expedited” IRB review procedure is used, the Academy’s IRB must review proposed research at convened meetings at which a majority of the members of the Academy’s IRB are present, and at least one member whose primary concerns are in nonscientific areas must be in attendance. Additionally, the Academy’s IRB must conduct continuation evaluations of research protocols at intervals appropriate to the degree of risk to the human subjects participating in the project, but the evaluations cannot be less frequent than once per year. The Academy’s IRB must recommend to the Superintendent the frequency of continuation evaluations for each protocol to verify the continued protection of the rights and welfare of the human subjects and/or the data about the human subjects.

b. Several scenarios for determining the date of continuing review apply for protocols reviewed via the Academy’s IRB process. To determine the date by which continuing review must occur, the date when the Academy’s IRB recommended approval to the Superintendent must be known. (The following examples presume the Academy’s IRB has determined that it will conduct its continuation review on a approved project no sooner than within one year.)

- Scenario 1: The Academy’s IRB (or Chair of the Academy’s IRB, as appropriate and permitted) reviews a protocol and recommends approval to the Superintendent, without any conditions, on 1 October 2007. The continuation review must occur within one year of the date of the approval recommendation. (*i.e.*, no later than 1 October 2008)
- Scenario 2: The Academy’s IRB (or Chair of the Academy’s IRB, as appropriate and permitted) reviews a protocol on 1 October 2007, and recommends an approval to the Superintendent, with the protocol contingent on the PI making specific minor changes that the Academy’s IRB Chair can verify. On 31 October 2007, the Chair of the Academy’s IRB confirms that the required minor changes were made by the principal investigator. The continuation review must occur within one year of the date at which the board (or the IRB Chair) reviewed the protocol and recommended an approval to the Superintendent. (*i.e.*, no later than 1 October 2008) The 31 October date is **not** the start date for the review clock.
- Scenario 3: The Academy’s IRB (or Chair of the Academy’s IRB, as appropriate and permitted) reviews a protocol on 1 October 2007, and has serious concerns about the protocol content or the protocol lacks significant information. These deficiencies require additional reviews of the project protocol at subsequent convened meetings of the Institutional Review Board on 15 October and 29 October 2007. At the 29 October meeting, the Academy’s IRB completes its evaluation and decides to recommend approval of the study to the Superintendent. The continuation review must occur within one year of the date of the convened meeting at which the IRB reviewed and approved the protocol. (*i.e.*, no later than 29 October 2008)

c. Summary: The date the Superintendent approves the project is not the start date for the review clock. The continuation evaluation must occur within one year of the date the recommendation for approval is made at a convened meeting of the Academy's IRB or within one year of the date that the IRB Chair or Vice Chair (as permitted by the issued DoN Assurance) recommends approval to the Superintendent on an "Exempt" or "Expedited" project.

d. Activity of the project, such as participant selection, distribution of informed consent forms, data collection, and/or data analysis may not begin until the Superintendent has approved the project and the principal investigator has been notified in writing by the Academy's HRPP office, of the approval. Activity on the project is not tied to the approval recommendation date.

e. Changes to an approved project are submitted to the Academy's IRB via "amendments". Review of a change in a protocol does not extend the date by which the continuation evaluation must occur; because the continuation evaluation is a review of the complete protocol, not simply an evaluation of changes (amendments) made to it.

1. Making a change to an approved protocol can never extend the approval period of a project. (*i.e.*, A new clock is not started with an amendment.)

2. Making a change to an approved protocol can shorten the approval period of a project.

f. When a continuation evaluation occurs annually and the Academy's IRB performs a continuation evaluation within the 30 day period before the Superintendent's approval period expires, the Academy's IRB may retain the anniversary date as the date by which the continuing review must occur. As applied to the three scenarios above: Scenarios 1 and 2: 1 October 2008 and Scenario 3: 29 October 2008, even if the continuation evaluations took place up to 30 days prior to these dates.

g. The principal investigator is responsible for ensuring that continuation protocol requests are submitted to the Academy's HRPP office in time for an appropriate review by the Academy's IRB and a subsequent approval action by the Superintendent - prior to the expiration date of the current approval. While reminders about protocol approval dates may be sent to principal investigators as a courtesy, it is not the responsibility of the Academy's HRPP office or the Academy's IRB to initiate the request for a project continuation. In all cases, the paperwork and the request for a continuation approval remain the responsibility of the principal investigator for the project.

h. The applicable regulations in law and the procedures in this policies and procedures document make **no provision for any grace period** extending the activity on a research project involving human subjects and/or the data about human subjects beyond the expiration date of the Superintendent's approval. Therefore, the continuation evaluation and the issuance of an updated approval of a research protocol must occur on or before the date when the Superintendent's approval expires.

i. The Academy's IRB, the Academy's HRPP office, the Superintendent, and the project investigators must plan ahead to meet required continuing review dates.

1. By the continuing review date specified by the Academy's IRB on the project: If an investigator fails to provide continuation evaluation information to the Academy's HRPP office and thus to the IRB or the Academy's IRB has received the information but it has not been able to review the research study with sufficient time to obtain the Superintendent's approval, the research must stop.

2. In a very few and special circumstances, with the Academy's IRB recommendation, the Superintendent can grant permission for the study to continue without the new approval being issued because the Academy's IRB, the Director of the HRPP office and the Superintendent have determined that it is in the best interests of the individual human subjects to continue participating in the research interventions or interactions.

3. Under no circumstances may enrollment of new subjects occur after the expiration of the Superintendent's approval. (This restriction also applies to any special circumstance cases, as just described.)

j. When a continuation evaluation of a research protocol does not occur prior to the end of the approval period specified by the Superintendent, regardless of whether the principal investigator has or has not requested a continuation approval, the current approval expires automatically.