Vice Chair/CR Primary Reviewer Reference Guide

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Federal Requirements
Guidance on Continuing Review

This guidance represents OHRP's current thinking on this topic and should be viewed as recommendations unless specific regulatory requirements are cited. The use of the word must in OHRP guidance means that something is required under HHS regulations at 45 CFR part 46. The use of the word should in OHRP guidance means that something is recommended or suggested, but not required. An institution may use an alternative approach if the approach satisfies the requirements of the HHS regulations at 45 CFR part 46? OHRP is available to discuss alternative approaches at 240-453-6900 or 866-447-4777.

Date: January 15, 2007

Scope: This document describes the requirements of Department of Health and Human Services (HHS) regulations at 45 CFR 46.109(e) for the continuing review of human subjects research by an Institutional Review Board (IRB) at intervals appropriate to the degree of risk, but not less than once per year. In particular, OHRP offers guidance on the following topics:

1. what constitutes substantive and meaningful continuing review;
2. what are some additional considerations for continuing review of multi-center trials monitored by a Data and Safety Monitoring Board (DSMB), Data Monitoring Committee (DMC), other similar body, or sponsor;
3. when may expedited review procedures be used for continuing review;
4. how is the continuing review date determined;
5. what occurs if there is a lapse in continuing review; and
6. what is the required composition of IRBs specifically designated to conduct continuing review.

Target Audience: IRBs, investigators, research institutions, and sponsors.
REGULATORY REQUIREMENTS

The HHS regulations for the protection of human subjects (45 CFR Part 46) require that, among other things, (1) institutions have written procedures which the IRB will follow for (a) conducting its continuing review of research and for reporting its findings and actions to investigators and the institution, and (b) determining which projects require review more often than annually (45 CFR 46.103(b)(4)); (2) except when an expedited review procedure is used, each IRB reviews proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in the nonscientific areas (45 CFR 46.108(b)); and (3) an IRB conducts continuing review of research at intervals appropriate to the degree of risk, but not less often than once a year (45 CFR 46.109(e)).

WHAT CONSTITUTES SUBSTANTIVE AND MEANINGFUL CONTINUING REVIEW?

Continuing review of research must be substantive and meaningful. In accordance with HHS regulations at 45 CFR 46.110(b) and at 46.115(a)(2), continuing review by the convened IRB, with recorded vote on each study, is required unless the research is otherwise appropriate for expedited review under Section 46.110 (see below). Furthermore, HHS regulations at 45 CFR 46.111 set forth the criteria that must be satisfied in order for the IRB to approve research. These criteria include, among other things, determinations by the IRB regarding risks, potential benefits, informed consent, and safeguards for human subjects. The IRB must ensure that these criteria are satisfied at the time of both initial and continuing review. In particular, when conducting continuing review, the IRB needs to determine whether any new information has emerged either from the research itself or from other sources that could alter the IRB’s previous determinations, particularly with respect to risk to subjects. Of note, information regarding any unanticipated problems involving risks to subjects or others (hereinafter referred to as unanticipated problems) that have occurred since the previous IRB review in most cases will be pertinent to the IRB’s determinations at the time of continuing review.

The procedures for continuing review by the convened IRB may include a primary reviewer system.

In conducting continuing review of research not eligible for expedited review, all IRB members should at least receive and review a protocol summary and a status report on the progress of the research that includes:

- the number of subjects accrued;
- a summary of any unanticipated problems and available information regarding adverse events (in many cases, such a summary could be a simple brief statement that there have been no unanticipated problems and that adverse events have occurred at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and any investigator brochure);
- a summary of any withdrawal of subjects from the research since the last IRB review;
- a summary of any complaints about the research since the last IRB review;
• a summary of any recent literature that may be relevant to the research and any amendments or modifications to the research since the last IRB review;
• any relevant multi-center trial reports;
• any other relevant information, especially information about risks associated with the research; and
• a copy of the current informed consent document and any newly proposed consent document.

At least one member of the IRB (i.e., a primary reviewer) also should receive a copy of the complete protocol including any modifications previously approved by the IRB. Furthermore, upon request, any IRB member also should have access to the complete IRB protocol file and relevant IRB minutes prior to or during the convened IRB meeting.

When reviewing the current informed consent document(s), the IRB should ensure the following:

• The currently approved or proposed consent document is still accurate and complete;
• Any significant new findings that may relate to the subject's willingness to continue participation are provided to the subject in accordance with HHS regulations at 45 CFR 46.116(b)(5).

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

Furthermore, the minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

When reviewing research under an expedited review procedure, the IRB Chair (or designated IRB member(s)) should receive and review all of the above-referenced documentation, including the complete protocol.

WHAT ARE SOME ADDITIONAL CONSIDERATIONS FOR CONTINUING REVIEW OF MULTI-CENTER TRIALS MONITORED BY A DSMB, DMC, OTHER SIMILAR BODY, OR SPONSOR?

As noted above, continuing review of research by the IRB should include consideration of, among other things, unanticipated problems, adverse events, and any recent literature that may be relevant to the research.

OHRP recognizes that local investigators participating in multicenter clinical trials usually are unable to prepare a meaningful summary of adverse events for their IRBs because study-wide information regarding adverse events is not readily available to them. In such circumstances, when the clinical trial is subject to oversight by a monitoring entity (e.g., the research sponsor, a coordinating or statistical center, or a DSMB/DMC), OHRP recommends that at the time of
continuing review local investigators submit to their IRBs a current report from the monitoring entity. OHRP further recommends that such reports include the following:

(1) a statement indicating what information (e.g., study-wide adverse events, interim findings, and any recent literature that may be relevant to the research) was reviewed by the monitoring entity;

(2) the date of the review; and

(3) the monitoring entity’s assessment of the information reviewed.

It may also be appropriate for the IRB at the time of continuing review to confirm that any provisions under the previously approved protocol for monitoring study data to ensure safety of subjects have been implemented and are working as intended (e.g., the IRB could require that the investigator provide a report from the monitoring entity described in the IRB-approved protocol).

WHEN MAY EXPEDITED REVIEW PROCEDURES BE USED FOR CONTINUING REVIEW?

The HHS human subjects regulations at 45 CFR 46.110(b)(1) limit the use of expedited review procedures to specific research categories published in the Federal Register at 63 FR 60364-60367 (see http://www.hhs.gov/ohrp/humansubjects/guidance/63fr60364.htm), and to the review of minor changes in previously approved research during the period (of one year or less) for which approval is authorized. IRBs are permitted to use expedited review for the continuing review of research that involves solely one or more of the activities published at 63 FR 60364-60367.

Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify 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 in accordance with HHS regulations at 45 CFR 46.110, have changed or will change, such that expedited IRB review would no longer be permitted for continuing review.

**Expedited Review Category (8):**

Under Category (8), an expedited review procedure may be used for the continuing review of research previously approved by the convened IRB as follows:

(a) 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**

(b) Where no subjects have been enrolled and no additional risks have been identified; **OR**
(c) Where the remaining research activities are limited to data analysis.

Of note, category (8) identifies three situations in which research that is greater than minimal risk and has been initially reviewed by a convened IRB may undergo subsequent continuing review by the expedited review procedure.

For a multi-center protocol, an expedited review procedure may be used by the IRB at a particular site whenever the conditions of category (8)(a), (b), or (c) are satisfied for that site. However, with respect to category 8(b), while the criterion that "no subjects have been enrolled" is interpreted to mean that no subjects have ever been enrolled at a particular site, the criterion that "no additional risks have been identified" is interpreted to mean that neither the investigator nor the IRB at a particular site has identified any additional risks from any site or other relevant source.

**Expedited Review Category (9):**

Under Category (9), an expedited review procedure may be used for continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories (2) through (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

The determination that "no additional risks have been identified" does not need to be made by the convened IRB.

**HOW IS THE CONTINUING REVIEW DATE DETERMINED?**

HHS regulations at 45 CFR 46.108(b) and 109(e) require, respectively, that (1) except when an expedited review procedure is used, each IRB must review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas; and (2) an IRB must conduct continuing review of research at intervals appropriate to the degree of risk, but not less frequently than once per year. The IRB should decide the frequency of continuing review for each study protocol necessary to ensure the continued protection of the rights and welfare of research subjects.

Several scenarios for determining the date of continuing review apply for protocols reviewed by the IRB at a convened meeting. To determine the date by which continuing review must occur, focus on the date of the convened meeting at which IRB approval occurs. (These examples presume the IRB has determined that it will conduct continuing review no sooner than within 1 year).

Scenario 1: The IRB reviews and approves a protocol without any conditions at a convened meeting on October 1, 2002. Continuing review must occur within 1 year of the date of the meeting, that is, by October 1, 2003.
Scenario 2: The IRB reviews a protocol at a convened meeting on October 1, 2002, and approves the protocol contingent on specific minor conditions the IRB chair or his/her designee can verify. On October 31, 2002, the IRB chair or designee confirms that the required minor changes were made. Continuing review must occur within 1 year of the date of the convened IRB meeting at which the IRB reviewed and approved the protocol, that is, by October 1, 2003.

Scenario 3: The IRB reviews a study at a convened meeting on October 1, 2002, and has serious concerns or lacks significant information that requires IRB review of the study at subsequent convened meetings on October 15 and October 29, 2002. At their October 29, 2002 meeting, the IRB completes its review and approves the study. Continuing review must occur within 1 year of the date of the convened meeting at which the IRB reviewed and approved the protocol, that is, by October 29, 2003.

Expeditied Review

For a study approved under expedited review, continuing review must occur within 1 year of the date the IRB Chair or IRB member(s) designated by the Chair gives final approval to the protocol.

Review of a change in a protocol ordinarily does not alter the date by which continuing review must occur. This is because continuing review is review of the full protocol, not simply a change to it.

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 on or before the date when IRB approval expires. OHRP recognizes the logistical advantages of keeping the IRB approval period constant from year to year throughout the life of each project. When continuing review occurs annually and 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. This would be, for example, October 1, 2003, in the above Scenarios 1 and 2, and October 29, 2003, in Scenario 3, even if the continuing reviews took place up to 30 days prior to these dates.

WHAT OCCURS IF THERE IS A LAPSE IN CONTINUING REVIEW?

The IRB and investigators must plan ahead to meet required continuing review dates. If an investigator has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the continuing review date specified by the IRB, the research must stop, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. Enrollment of new subjects cannot occur after the expiration of IRB approval.

When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. Such expiration of IRB approval does not need to be reported to OHRP as a suspension of IRB approval under HHS regulations.
WHAT IS THE REQUIRED COMPOSITION OF IRBS SPECIFICALLY DESIGNATED TO CONDUCT CONTINUING REVIEW?

OHRP is aware that some institutions have designated one or more IRBs for the sole purpose of conducting continuing review. While OHRP acknowledges that such a practice is permissible under the HHS regulations for the protection of human subjects, OHRP reminds institutions that such IRBs must comply with the IRB membership requirements stipulated by HHS regulations at 45 CFR 46.107. In particular, HHS regulations at 45 CFR 46.107(a) require the following for all IRBs, including IRBs that are solely responsible for continuing review:

The IRB must have at least five members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the institution. The IRB must be sufficiently qualified through the experience and expertise of its members, and the diversity of members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. In addition to possessing the professional competence necessary to review specific research activities, the IRB shall be able to ascertain the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice. The IRB must therefore include persons knowledgeable in these areas. If the IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, consideration shall be given to the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

In addition, it should be noted that the other requirements for IRB membership at 45 CFR 46.107(b)-(f) also apply to IRBs conducting continuing review.

OTHER PERTINENT REGULATIONS

For FDA-regulated research, see 21 CFR 50, and 21 CFR 56.
Continuing Review After Study Approval

Institutional Review Boards (IRBs) are responsible for continuing review of ongoing research to ensure that the rights and welfare of human subjects are protected. The Food and Drug Administration (FDA) regulations regarding continuing review require an IRB to develop and follow written procedures for:

- conducting continuing review of research at intervals appropriate to the degree of risk, but not less than once per year [21 CFR 56.108(a)(1) and 56.109(f)];
- determining which studies need verification from sources other than the investigator that no material changes in the research have occurred since the previous IRB review [21 CFR 56.108(a)(2)];
- ensuring that changes in approved research are promptly reported to, and approved by, the IRB [21 CFR 56.108(a)(3-4)]; and
- suspending or terminating approval of research that is not being conducted in accordance with the IRB’s requirements [21 CFR 56.108(b)(2) and 56.113].

The FDA continuing review regulations outline minimum requirements; they do not provide specific instructions to IRBs on how to set up their own rules for continuing review within the framework of the regulations. Therefore, the regulations allow institutions or IRBs to impose greater and more detailed standards of protection for human subjects than those specified by the regulations and permit each IRB to develop procedures appropriate to its needs. By regulation, the IRB has the authority and the responsibility to take appropriate steps such as terminating or suspending approval of research that is not being conducted in accordance with the IRB's requirements.

1. Criteria for Conducting Continuing Review

FDA regulations set forth the criteria to be satisfied if an IRB is to approve research [21 CFR 56.111]. These criteria are the same for initial review and continuing review and include a determination by the IRB that

- risks to subjects are minimized;
- risks to subjects are reasonable in relation to anticipated benefits;
- selection of subjects is equitable;
- informed consent is adequate and appropriately documented;
- where appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects;
- where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data; and
- appropriate safeguards have been included to protect vulnerable subjects.
2. Process for Conducting Continuing Review

Routine continuing review should include IRB review of a written progress report(s) from the clinical investigator. Progress reports include information such as: the number of subjects entered into the research study; a summary description of subject experiences (benefits, adverse reactions); numbers of withdrawals from the research; reasons for withdrawals; the research results obtained thus far; a current risk-benefit assessment based on study results; and any new information since the IRB's last review. Special attention should be paid to determining whether new information or unanticipated risks were discovered since the previous IRB review. Any significant new findings which may relate to the subjects' willingness to continue participation should be provided to the subjects in accordance with 21 CFR 50.25(b)(5).

The IRB should obtain a copy of the consent document currently in use and determine whether the information contained in it is still accurate and complete, including whether new information that may have been obtained during the course of the study needs to be added. Obtaining the consent document also provides a check on whether the document being used by the clinical investigator has current IRB approval.

The purpose of continuing review is to review the progress of the entire study, not just changes in it. Continuing review of a study may not be conducted through an expedited review procedure, unless 1) the study was eligible for, and initially reviewed by, an expedited review procedure, or 2) the study has changed such that the only activities remaining are eligible for expedited review.

The IRB should determine that the frequency and extent of continuing review for each study is adequate to ensure the continued protection of the rights and welfare of research subjects. The factors considered in setting the frequency of review may include: the nature of the study; the degree of risk involved; and the vulnerability of the study subject population. Note that 21 CFR 56.108(a)(2) requires IRBs to follow written procedures for determining the frequency and extent of continuing review.

The continuation of research after expiration of IRB approval is a violation of the regulations [21 CFR 56.103(a)]. If the IRB has not reviewed and approved a research study by the study's current expiration date, i.e., IRB approval has expired, research activities should stop. No new subjects may be enrolled in the study. However, if the investigator is actively pursuing renewal with the IRB and the IRB believes that an over-riding safety concern or ethical issue is involved, the IRB may permit the study to continue for the brief time required to complete the review process.

When study approval is terminated by the IRB, in addition to stopping all research activities, any subjects currently participating should be notified that the study has been terminated. Procedures for withdrawal of enrolled subjects should consider the rights and welfare of subjects. If follow-up of subjects for safety reasons is permitted/required by the IRB, the subjects should be so informed and any adverse events/outcomes should be reported to the IRB and the sponsor.

3. Process for Dealing with Reports of Adverse Reactions and Unexpected Events

a. Written Procedures

IRB continuing review responsibilities include reviewing reports of adverse reactions and unexpected events involving risks to subjects or others. The IRB should establish a procedure for receiving and reviewing these reports. The level and promptness of review may depend upon factors such as the seriousness of the event, whether the event is described in the study protocol
and consent and whether the event occurred at a location for which the IRB is the IRB of record. The written procedures may include a brief form to be completed by the principal investigator when an adverse event occurs, asking for his/her opinion as to whether the event was related to the study and other information to aid the IRB in an appropriate and efficient review of the event.

Researchers should be made aware of the IRB's policies and procedures concerning reporting and continuing review requirements. This can be accomplished by notifying the investigator, in the IRB's letter of approval, of the requirement to report changes and unanticipated problems in research activities. The IRB's written procedures pertaining to continuing review and reporting requirements should be distributed to ensure that all individuals involved in research activities understand their obligations.

b. Process

Unanticipated risks are sometimes discovered during the course of research. Information that may impact on the risk/benefit ratio should be promptly reported to, and reviewed by, the IRB to ensure adequate protection of the welfare of the subjects. Based upon such information, the IRB may need to reconsider its approval of the study, require modifications to the study or, revise the continuing review timetable.

IRBs are also responsible for ensuring that reports of unanticipated problems involving risks to human subjects or others are reported to the FDA [21 CFR 56.108(b)(1)]. Usually, this reporting is accomplished through the normal reporting channel, i.e., the investigator to the sponsor to FDA.

4. Process for Reviewing Changes in Ongoing Research During the Approval Period

In accord with 21 CFR 56.110(b), 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 chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB.

When a proposed change in a research study 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 subjects [21 CFR 56.108(a)(4)]. 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 subjects' continued welfare.
Issues to Address when Conducting Expedited Reviews

Definition

The Institutional Review Board (IRB) uses an expedited review process to review studies that meet the expedited categories adopted by the Department of Health and Human Services (DHHS), the Food and Drug Administration (FDA), and the Department of Veteran Affairs (VA) and that involve no greater than “minimal risk.” Expedited review procedures can also be utilized for the review of minor revisions submitted for previously approved research during the period for which approval is authorized. (See Guidance on Expedited Review of Minor Changes in Previously Approved Research.)

The expedited review process can be carried out by the Chair of the IRB or one or more experienced reviewers designated by the Chair from among voting members of the IRB. Federal regulations also dictate that when an IRB uses expedited review procedures, there must be a mechanism in place for advising all of the members of the IRB of the research procedures approved under this review process.

Authority of an Expedited Reviewer

The expedited reviewer is responsible for ensuring that all of the information requested in the Expedited Review application is provided. The expedited reviewer make the final determination as to whether research activities meet the expedited review criteria as outlined in the section of this document titled, Definition of Minimal Risk and Guidance to PI and Reviewers.

The expedited reviewer also determines whether the research meets the federal criteria for approval as outlined in 45 CFR 46.111, 21 CFR 56.111, and 38 CFR 16.111. (See Criteria for IRB approval: Reviewer Checklist.)

The expedited reviewer has the authority to approve a study or request additional information. The expedited reviewer does not have the authority to disapprove a study. (See Expedited Initial Review SOP and Continuation Review SOP)

Informed Consent

Expedited reviewers ensure that the investigator conducts the informed consent process and obtains documentation of informed consent, as specified in 45 CFR 46.116 and 117, 21 CFR 50.25, and 38 CFR 16.116 and 117, unless the IRB waives the requirements in accord with federal regulations. (See Informed Consent SOP and Forms E and F in the IRB application which is on the Office of Research Integrity website)
When children are involved as research subjects, the expedited reviewer is also charged with ensuring that there are adequate provisions for obtaining assent from these children. (See UK IRB Policy on Children in Research.)

**Vulnerable Subject Populations**

Federal regulations do not specify whether any certain populations should be globally excluded from a study for it to be eligible for expedited review. The expedited reviewer gives special consideration to protecting the welfare of vulnerable subjects such as children, prisoners, fetuses/neonates, pregnant women, and decisionally challenged/impaired persons. The expedited reviewer also recognizes that additional populations such as students may qualify as vulnerable populations and need safeguards in place for their protection during study participation. (See Protection of Vulnerable Subjects SOP)

**Definition of Minimal Risk and Guidance to PI and Reviewers**

Expedited procedures can only be used to review a study if the only involvement of human subjects fits one or more of the categories specified in the federal regulations and if all of the procedures present no greater than “minimal risk.”

The IRB reviewer confirms that all of the research activities fit in one or more of the expedited categories. If the research includes activities that do not fit in the categories, the study is not eligible for expedited review even if the research involves “minimal risk.”

The Department of Health and Human Services defines *minimal risk* to mean “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests” [45 CFR 46.102(2)(i)].

Investigators are asked to provide a risk assessment, but it is the IRB reviewer’s responsibility to determine whether the research meets the federal definition.

The IRB reviewer must consider two questions:

- Is the *probability* of the harm or discomfort anticipated in the proposed research greater than that encountered ordinarily in daily life or during the performance of routine physical or psychological examinations or tests?

- Is the *magnitude* of the harm or discomfort greater than that encountered ordinarily in the daily life or during the performance of routine physical or psychological examinations or tests?
If the answer is “yes” to either of these questions, then the research does not meet the definition of minimal risk. The IRB policy on risk assessment is included in the UK Assessing the Research Risk document, which is on the ORI website and in the IRB Survival Handbook.

Federal Expedited Review Applicability and Categories

(A) Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

(B) The categories in this list apply regardless of the age of subjects, except as noted.

(C) The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

(D) The expedited review procedure may not be used for classified research involving human subjects.

(E) IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

(F) Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

Research Categories

1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
   (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
   (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.
2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
   (a) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
   (b) From other adults and children considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3) Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) Hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncanulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5) Research involving materials (data, documents, records, or specimens) that have been collected or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)

6) Collection of data from voice, video, digital, or image recordings made for research purposes.
7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (Note: Some research in this category may be exempt from the HHS regulations for the protection of human subjects 45 CFR 46.101 (b)(2) and (b)(3). This listing refers only to research that is not exempt.)

8) Continuing review of research previously approved by the convened IRB as follows:
   (a) 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
   (b) Where no subjects have been enrolled and no additional risks have been identified; or
   (c) Where the remaining research activities are limited to data analysis.

9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Prepared by Ada Sue Selwitz, MA
University of Kentucky
Revised July 2006

Updated 09/18/06
REQUIREMENTS FOR CONDUCTING
A FULL REVIEW

1. Review must be conducted at a convened meeting.

2. A majority of the members of the IRB must be present at the meeting.

3. At least one member whose primary concerns are in nonscientific areas must be present at the meeting. (In addition, FDA policy requires that a physician be present.)

4. To approve research, the IRB must determine that all of the requirements specified in 45 CFR 46.111 and 21 CFR 56.111 are satisfied.

5. For research to be approved, it must receive approval of a majority of the members present at the meeting.

6. IRB members who have a conflicting interest in a research project cannot participate in the review except to provide information requested by the IRB, and then must be absent themselves for the final discussion and vote.

7. The IRB must notify investigators and the institution in writing of its decision to approve, modify, or disapprove the research.

Handout Prepared by Ada Sue Selwitz, M.A., University of Kentucky
UK SOPs
OBJECTIVE

To describe the policy and procedures for initial full review by the Institutional Review Board (IRB).

GENERAL DESCRIPTION

The IRB conducts initial review for non-exempt research at convened meetings unless the research is eligible for expedited initial review. See the procedures for conducting a convened meeting, the definition of quorum, and the requirements for conducting a full review meeting in the Conduct of IRB Meeting SOP. Investigators must submit studies that do not meet the federally mandated criteria for exempt or expedited initial review for full review. (See Exempt and Expedited Initial Review SOPs.)

RESPONSIBILITY

Execution of SOP: IRB Chairs, IRB Members, Principal Investigator (PI)/Study Personnel, Office of Research Integrity (ORI) Staff, ORI Research Compliance Officer (RCO), ORI Research Privacy Specialist (RPS), Veterans Affairs Medical Center (VAMC) Associate Chief of Staff (ACOS) for Research and Development.

PROCEDURES

Submission and Screening

1. The PI or designee completes an application for IRB review of a research protocol for initial full review and submits it to the ORI.

2. ORI staff schedule the IRB application on the agenda for the next available meeting. Each IRB usually meets once or twice a month. ORI staff schedule protocols for review on a
"first-come, first-serve" basis. ORI staff send the PI a request for the PI or designee to attend the meeting unless the ORI or IRB waives the requirement to attend.

3. ORI staff screen the application to determine whether it is complete (e.g., includes all pertinent forms and signatures). If it is not complete, ORI staff return the application to the investigator or, in cases where only a few minor items are missing, the ORI staff call or write the investigator to request the missing items.

4. ORI staff screen the IRB application to ensure coordination with other university committee reviews as outlined in the applicable standard operating procedures or to ensure compliance with pertinent federal requirements. Examples of screening include, but are not limited to, the items listed below.

- If the investigator checks “cancer” on the General Information Sheet (GIS), (i.e., Form A in the full application) he/she must attach final approval from the Markey Cancer Center (MCC). If the investigator omits this attachment, ORI staff may still schedule the protocol for review but request the investigator to send the final MCC approval. The IRB will not issue approval until the investigator submits the final MCC approval.

- If the investigator checks items on the GIS which indicate Institutional Biosafety Committee (IBC) approval is necessary, the investigator must include IBC provisional approval materials. ORI staff check to ensure that the PI has submitted the materials. ORI staff will not schedule the application for review and will return the application to the PI if these materials are missing. ORI staff may check with the Institutional Biosafety Officer for advice. The Institutional Biosafety Officer has the authority to make the final decision as to whether the project requires IBC approval.

- Using the information on the GIS, ORI staff screen to determine whether the PI addressed off-site issues following procedures outlined in the Off-site Research SOP.

- If the investigator checks items on the GIS which indicate the research involves prisoners, ORI staff send the protocol to a prisoner representative for review.

- ORI staff screen the application to see whether the study involves the Veterans Affairs Medical Center (VAMC). If the study involves the VAMC, the PI’s study title must begin with “UK/VA:” followed by the remaining title of the study.

- The ORI determines whether the U.S. Department of Education has funded the research and/or whether the proposed research involves surveying children in the public schools. If so, ORI staff inform the IRB of “No Child Left Behind” requirements.

- If the investigator indicates in the GIS, i.e., Form A, that the research involves an investigational new drug (IND) or investigational device exemption (IDE), ORI staff confirm the validity of the IND or IDE number by ensuring that a copy (containing the number) of the detailed protocol from the sponsor and/or the investigator brochure are part of the protocol materials.
• ORI staff screen the GIS to determine whether the investigator also is serving as the sponsor in accord with FDA regulations. If so, ORI staff notifies the IRB medical chair or designee. The IRB Chair or designee is responsible for providing training on FDA sponsor responsibilities if the study obtains IRB approval.

• ORI staff screen the GIS to determine whether research involves vulnerable subjects and/or sensitive types of research/procedures (e.g., HIV screening). If so, ORI staff add a notation on the agenda for the meeting referring IRB members to the pertinent Protocol Specific Training (PST) materials which are included in the IRB Survival Handbook.

5. ORI staff screen the protocol to determine whether additional expertise is necessary to conduct the review. If so, ORI staff may ask an ad hoc or cultural consultant who has appropriate expertise in the discipline or with non-English speaking populations or locations to participate in the review. ORI maintains a list of potential cultural consultants qualified by cultural and/or linguistic knowledge or training to assist the IRB, as appropriate, and may contact IRB members, UK faculty, or department chairs for advice in identifying consultants.

6. The PI may also recommend cultural consultants provided that they are not directly involved in the study. These consultants may review consent forms, provide verifications of translations, provide guidance on the impact of the research on subjects and the impact of the culture on the research to be conducted.

7. ORI staff ensure that ad hoc or cultural consultants do not have a conflict of interest in accordance with the IRB Member and Consultant Conflict of Interest SOP.

8. ORI staff send the ad hoc or cultural consultants the same information as voting IRB members and a detailed protocol/grant application, if applicable.

9. ORI staff assign a primary reviewer based on the IRB member’s educational background and expertise. VAMC IRB members serve as primary reviewers for VAMC studies if they have the appropriate expertise. If no IRB member has the appropriate expertise, ORI staff ask an ad hoc consultant to serve as primary reviewer.

10. The ORI Research Privacy Specialist (RPS) screens all initial Medical IRB submissions to determine whether a protocol falls under regulations of the Health Insurance and Portability and Accountability Act (HIPAA) Privacy Rule and/or the Family Educational Rights to Privacy Act (FERPA). The Nonmedical IRB staff conduct the same screening for all initial Nonmedical IRB submissions. The Nonmedical IRB staff forward any protocol regulated by the Privacy Rule and/or by FERPA to the RPS, who writes recommendations for each protocol to ensure compliance with the Privacy Rule and/or with FERPA and forwards them to the appropriate IRB. See the HIPAA in Research SOP for additional information regarding HIPAA review procedures.
1. Approximately five to 10 days prior to each convened meeting, ORI staff send packets to voting and selected ex-officio IRB members for review and send PIs requests to attend, unless the requirement is waived by an IRB member or ORI staff. The initial full review applications sent to the IRB members include all applicable sections of the application.
   a. Section 1 - core application with General Information Sheet and research description;
   b. Section 2 - informed consent/assent process and forms, including waiver requests, National Institutes of Health (NIH)-approved sample informed consent document (e.g., cooperative group trial), translated consent document for non-English speaking subjects;
   c. Section 3 - HIPAA forms;
   d. Section 4 - additional materials, including advertisements, proposed data instruments, materials/letters for off-site research, Use of Investigational New Drug (IND) Form, Use of Approved Drugs for Unapproved Use Form, Use of Investigational New Device Form; Use of Radioactive Materials Form;
   e. Section 5 - vulnerable populations, including forms for research involving decisionally impaired individuals, pregnant women, fetuses and/or neonates, prisoners, or children.

2. In addition, the member assigned as the primary reviewer of the study receives the following materials, if applicable:
   - Sponsor's grant application;
   - Contract or device proposal (if the protocol does not involve the administration of drugs);
   - Sponsor's detailed protocol and investigator’s brochure (if the protocol involves the administration of drugs);
   - Financial disclosure form(s),
   - Signature Assurance sheet;
   - Other committee review or final approval materials when applicable;
   - Criteria for IRB Approval Reviewer Checklist;
   - VA Research Reviewer Checklist; and
   - All other application materials.

3. The primary reviewer is responsible for:
   - Comparing the detailed grant application or industry protocol with the IRB application;
   - Informing the full IRB of any discrepancies between the detailed protocol and the summary application materials;
   - Determining whether the project involves a NIH multi-center clinical trial (e.g., cooperative group trial) and, if so, comparing the “Risks” and “Alternatives” section of the NIH-approved sample informed consent document with the UK proposed form to ensure that the NIH and UK sections of the consent are consistent;
   - Reviewing the financial disclosure form and alerting the IRB if a “yes” disclosure is made;
• Reviewing the other committee review/final approvals for consistency in human subjects protection measures;
• Checking the Signature Assurance sheet for appropriate signatures; and
• Conducting an in-depth review.

4. All IRB members review all information in the agenda packet in advance of the meeting (including those protocols for which the IRB member is not the primary reviewer) in enough depth to be familiar with the protocol, to be prepared to discuss the protocol at the meeting, and to be prepared to determine whether the research meets the regulatory criteria for approval.

5. Ad hoc or cultural consultants may provide comments or recommendations in writing to the IRB prior to the meeting or attend the convened meeting to participate in the review. IRB staff maintain documentation of written comments or reports in the protocol file. In cases where the consultant participates in the meeting, the minutes of the meeting document the information provided by the consultant. (See Minutes of IRB Meetings SOP.)

IRB Review

1. A majority of the voting IRB members (or their designated alternates), including at least one member whose primary concerns are in nonscientific areas, must be present in order to conduct a convened meeting. For the Medical IRB, a licensed physician must be present. In addition, a VA representative must be present if the IRB is reviewing protocols involving the VAMC. In order for the IRB to approve the proposed research, the protocol must receive the approval of a simple majority of those members present at the meeting. (See The Conduct of IRB Meetings SOP.)

2. When the IRB reviews research that involves categories of human subjects vulnerable to coercion or undue influence, ORI staff ensure that adequate representation or consultation is present for discussions of research involving vulnerable human subjects. (See Protection of Vulnerable Subjects SOP and Membership of IRB SOP.)

3. All IRB members attending the meeting receive materials listed in the Submission of Applications section above, prior to the convened meeting, have the opportunity to discuss each research protocol during the convened meeting, and participate in the determination of whether the research meets the regulatory criteria for approval.

4. The IRB reviews each initial full review application with the PI or co-investigator present during the convened IRB meeting unless the ORI or IRB waives the requirement. After the PI leaves the meeting, the IRB reviews the application and discusses any controverted issues and their resolution prior to voting.
5. During discussion, the IRB members raise only those issues that the committee determines do not meet the federal criteria for approval as specified in 45 CFR 46.111, 21 CFR 56.111, and 38 CFR 16.111. In addition, the IRB determines whether the risk level assigned by the PI is appropriate. Also, the IRB considers whether the PI’s preliminary assessment of federally mandated specific findings requirements (e.g., request for waiver of informed consent) is acceptable with respect to meeting federal requirements.

6. For research involving a new drug or new device where the PI has not obtained an IND or IDE, the committee determines what action(s) is needed (whether the PI needs to get an IND/IDE or whether PI needs to contact the Food and Drug Administration [FDA] for guidance).

7. In conducting the initial review of the proposed research, the IRB utilizes the Criteria for IRB Approval: Reviewer Checklist. For VA research, the VA reviewer utilizes the VA Research: Reviewer Checklist. The VA reviewer prompts the convened IRB to make determinations as required by VA regulations, using the VA Research: Reviewer Checklist as a guide.

8. A member or consultant with a conflict of interest must leave the room during the vote and only participate in the review by providing information in accordance with the IRB Member and Consultant Conflict of Interest SOP.

**Review Outcome(s)**

1. An IRB member makes a motion, another member seconds the motion, and then the convened IRB votes for or against or abstains from one of the following five actions:

   **APPROVED (Vote for a #1):** IRB approval - A vote for a #1 indicates that the IRB has concluded that the research and consent/assent forms meet the federal criteria for approval. IRB approval verifies that the IRB agrees with the assessment of the protocol and/or specific findings as described by the PI in the application. ORI staff send the investigator an approval letter, according to the guidelines in the ORI Customer Service Standards, accompanied by an informed consent/assent document (if applicable) with the affixed "IRB Approval" validation stamp, which includes valid dates of IRB approval. If the IRB approves a HIPAA Waiver of Authorization Request, ORI staff send a separate approval letter as well. (See Federally Mandated Reporting to External Agencies SOP.)

   **REVISIONS and/or ADDITIONAL INFORMATION REQUIRED (Vote for a #2):** A vote of #2 indicates that the IRB has given the individual chairing the meeting the authority to approve the minor revisions which do not involve substantive issues. The IRB withholds approval pending submission of minor revisions/additional information. ORI staff send the investigator a letter, according to the guidelines in the ORI Customer Service Standards, describing the revisions requested by the IRB.
The PI responds to the IRB’s suggested revisions in writing and sends the response to the ORI, which gives the response to the IRB Chair or member who chaired the meeting for further review. The Chair or designee may forward the responses to the entire IRB for additional review, request additional information, or approve.

**TABLED (Vote for a #3):** A vote of #3 indicates that the IRB withholds approval pending submission of major revisions/additional information. ORI staff send the investigator a letter, according to the guidelines in the ORI Customer Service Standards. The letter lists the reasons for tabling and includes a description of the revisions or clarifications requested. For some studies, the IRB may appoint one or more members of the IRB to discuss the reasons with the investigator. If the vote is for a #3, ORI staff schedule the PI’s response to the requested revisions for review by the full committee; the IRB does not require the PI to attend.

**TABLED (Vote for a #4):** If the vote is for a #4, the IRB follows the same procedure as for a vote of #3, except the PI needs to attend the future IRB meeting at which the IRB reviews his/her response to discuss or answer IRB concerns or questions. ORI staff notify the PI of the request for him/her to attend that future IRB meeting.

**DISAPPROVED (Vote for a #5):** If the vote is for a #5, ORI staff send the investigator a letter describing the reasons for disapproving the protocol. Disapproval of a protocol usually occurs when the IRB determines that the risk of the procedures outweighs any benefit to be gained or if the proposed research does not meet the federal criteria for IRB approval.

2. During the convened meeting, the IRB determines the approval period, as appropriate to the degree of risk but not less frequently than once per year. The IRB will generally set a shorter approval period for high risk protocols or protocols with high risk/low potential benefit ratios.

3. When a protocol receives final approval, the ORI assigns the start of the approval period as the date of the convened IRB meeting. If a protocol has received a vote #2 (minor revisions are requested) and the PI completes the revisions, the approval period starts from the meeting date of the convened IRB at which the protocol was initially reviewed. Should there be serious concerns or a lack of significant information (vote #3 or vote #4) requiring the convened IRB to complete its review and issue approval of the study at a subsequent meeting, the approval period starts with the date of the subsequent convened IRB meeting.

4. Before issuing the IRB approval letter, the ORI staff confirm that all of the applicable Institutional Biosafety Committee, Radiation Safety Committee, Radioactive Drug Research Committee, and Markey Cancer Center approvals are in place. If applicable approvals are not in place, ORI staff notify the investigator in writing, requesting the appropriate information. When the investigator submits the information, ORI staff may put it on an
agenda for review by the IRB, if appropriate. ORI staff only issue the IRB approval letter after obtaining appropriate documentation.

5. Also, before issuing approval, ORI staff ensure that all study personnel have completed the required training. If the PI and study personnel have not completed training, ORI staff notify the PI in writing. The investigator must send the appropriate certifications of training before the IRB can issue approval. An investigator may submit a request for an exception to submission of certifications before the IRB issues approval. The ORI Research Compliance Officer, designated ORI staff person, or the ORI Director may approve exceptions.

6. If the research involves prisoners, ORI staff check to determine whether the PI submitted the protocol for funding to any DHHS agency. If this is the case and the protocol involves prisoners, ORI staff, with input from the PI, prepare and submit a prisoner certification report to the Office for Human Research Protection (OHRP) in accordance with OHRP requirements and the Federally Mandated Reporting to External Agencies SOP.

7. Once the IRB approves a protocol, ORI staff send an approval letter to the PI, which includes the approval period, a reminder to use only the approved consent/assent form, and a reminder that the IRB must approve any changes to the protocol prior to initiation of the changes.

8. Upon request, ORI staff also send the PI a funding agency Certification of Approval form. (See the Federally Mandated Reporting to External Agencies SOP.)

9. At IRB approval, if the PI assumes an FDA sponsor function for a study that involves a drug or device, ORI staff send the PI a list of responsibilities required of investigators assuming a sponsor function and notification that the PI must complete PI-sponsor training presented by the IRB Chair or designee. (See Summary of FDA Requirements for Investigators Who Are Also Considered Sponsors of New Drug and Summary of FDA Requirements for Investigators Who Are Also Considered Sponsors of New Device.)

10. At IRB approval, it is the PI’s responsibility to request an IRB Statement of Compliance if the protocol falls under the International Conference on Harmonisation (ICH) guidance related to Good Clinic Practice (GCP). The ORI maintains a statement of compliance signed by the IRB Chair and provides that statement upon request.

11. If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit them to the IRB via a written document that includes a justification for changing the IRB decision. The IRB reviews the request using the standard procedures.

REFERENCES

21 CFR 50.25
21 CFR 56.111
38 CFR 16.111
45 CFR 46.108
45 CFR 46.111
45 CFR 46.116
45 CFR 46.117
45 CFR 46 Subparts B
45 CFR 46 Subparts C
45 CFR 46 Subparts D & 21 CFR 50 Subpart D
OBJECTIVE

To describe the policies and procedures for conducting continuation review (CR)

GENERAL DESCRIPTION

The Institutional Review Board (IRB) conducts substantive and meaningful continuation review at intervals appropriate to the degree of risk but not less than once per year. The research protocol must satisfy the criteria set forth in 45 CFR 46.111, 21 CFR 56.111, and 38 CFR 16.111 for the IRB to approve the protocol for continuation. The IRB may only use expedited review procedures for continuation review under the following circumstances:

1. The study was initially eligible and continues to be eligible for expedited review procedures; OR
2. The research is permanently closed to the enrollment of new subjects; all subjects have completed all research-related interventions; and the research remains active only for long-term follow-up of subjects; OR
3. Where no subjects have been enrolled at UK and no additional risks have been identified either at UK or at any site if the research involves a multi-site study; OR
4. The only remaining research activities are limited to data analysis; OR
5. The research involves the study of drugs and/or medical devices AND either does not require an Investigational New Drug (IND) (21 CFR Part 312) and/or an Investigational Drug Exemption (IDE) (21 CFR Part 812) and/or the device is approved for marketing and being used in accordance with the approved labeling. The IRB must also have determined and documented at a convened meeting that the research is no greater than minimal risk and no additional risks have been identified.

In accord with federal requirements, the IRB approval period can extend no longer than one year after the start of the approval period. The PI may not continue research after expiration of IRB approval; continuation is a violation of federal requirements specified in 45 CFR 46.103(a), 21 CFR 56.103(a), and 38 CFR 16.103(a). If the IRB approval has expired, the PI must cease all research activities and may not enroll new subjects in the study after the expiration of the IRB approval.
approval. However, if the IRB determines that an overriding safety concern and/or ethical issue is involved or that it is in the best interests of the individual subjects to continue participating in the research activities, the IRB may permit the subjects to continue in the study for the time required to complete the CR process.

**RESPONSIBILITY**

Execution of the SOP: Office of Research Integrity (ORI) Staff, IRB Members, IRB Chair, IRB Vice Chair, ORI Research Privacy Specialist (RPS), Principal Investigator (PI)/Study Personnel; Veterans Affairs Medical Center (VAMC) Associate Chief of Staff (ACOS) for Research and Development

**PROCEDURES**

**CR Requests, Submissions, and Screening**

1. Using the forms and letters generated by the ORI database, ORI staff send CR requests and reminders to the PI before the IRB approval period expires (e.g., approximately twelve weeks, eight weeks, and four weeks prior to expiration). The PI is responsible for responding to those requests in a timely manner.

2. The PI is responsible for completing the application for CR according to the instructions on the form.

3. The PI must submit continuation review reports for studies as long as the research:
   - Remains open to enroll new subjects;
   - Remains active for long-term follow-up (even when the research is permanently closed to enrollment and all subjects have completed all research-related interventions); and/or
   - Requires analysis of data with identifiers.

   See the Study Closure SOP for details on circumstances in which a PI may close a study.

4. Upon receipt of the CR materials, ORI staff screen to determine whether the study is eligible for expedited review.

5. ORI staff also screen the application to ensure compliance with selected federal requirements, such as need for prisoner representative review.

6. If the CR submission includes a new unanticipated problem/adverse event report, ORI staff separate the unanticipated problem/adverse event report from the CR materials and process it under separate cover. ORI staff write a note to accompany the separated problem/adverse event materials indicating that the PI originally submitted them with CR materials. The IRB
Chair reviews the unanticipated problem/adverse event report using standard procedures. (See the Unanticipated/Anticipated Problem/Adverse Event Reporting SOP.)

7. When the ORI receives the CR materials, ORI staff conduct a preliminary screening of the materials submitted and of the IRB’s protocol records to ensure the materials are complete and consistent with IRB requirements.

8. During screening, ORI staff update the ORI database with requested extension dates, number of subjects enrolled, and other information provided by the PI in the CR materials. ORI staff compare answers in the CR materials with the data in the existing IRB file (i.e., physical file or database).

9. ORI staff screen for Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule and/or Family Educational Rights to Privacy Act (FERPA) concerns. If the PI includes a HIPAA form or checks “HIPAA” in the application or if there is a HIPAA or FERPA concern, ORI staff forward the application to the ORI Research Privacy Specialist (RPS) for review. The RPS reviews the application and submits suggestions in writing, which ORI staff forward to the expedited reviewer or the convened IRB for a final determination.

10. ORI staff code the CR in the database, assign a meeting date, and describe the extension/modification requests in the codes/events notes section.

11. ORI staff contact ad hoc and cultural consultants regarding issues for which the IRB does not have the appropriate expertise, using the same procedures as outlined in the Initial Full Review SOP.

12. The ORI may request additional information or materials from the PI if the application is not complete. If the PI does not respond, ORI staff make up to three attempts to contact the PI and/or research staff for additional information/materials, provided there is sufficient time before the end of the approval period.

13. If the ORI does not receive a response from the PI, the ORI sends the CR to the IRB. If the approval period limits the amount of time available to resolve outstanding issues, ORI staff may schedule the protocol for IRB review “as is” to avoid a lapse of approval. ORI staff forward notes detailing the missing or incomplete materials to the IRB.
Medical and Nonmedical Full Continuation Review Procedures

1. The Medical and Nonmedical IRB conduct full CR at regularly scheduled convened meetings.

2. The Vice Chair or designee serves as the primary reviewer for full CR IRB protocols. If the Vice Chair has a conflict of interest (e.g. is study personnel on a protocol for continuation review), is unavailable, or does not have the appropriate expertise to review the CR, ORI staff assign responsibility for the CR to the Chair, another Vice Chair, a voting member of the IRB, or a consultant with the appropriate expertise.

3. Approximately 5-10 days prior to the convened meeting, the primary reviewer receives the following information, but not limited to:
   - A completed CR report form (progress report) for each study, which includes, when applicable, the number of subjects enrolled and withdrawn from the study; summary of unanticipated problems/adverse events involving risks to the subject or others; recent literature; complaints about the research; and any new, significant findings (new findings and implications for subject participation described);
   - A protocol summary and status report on the progress of the research;
   - A copy of the currently approved sponsor protocol for externally funded research (including any prior IRB approved modifications) and/or research description (summary which addresses all elements of criteria for approval); and if applicable:
     - A cover memo if it contains pertinent information to review of protocol;
     - Attachments (e.g., updates/changes, explanations)
     - Summary data safety and monitoring reports;
     - A copy of the consent/assent form for which the investigator is seeking IRB approval (with changes underlined for the primary reviewer);
     - A revised grant application;
     - Copies of signed consent forms for the two most recently enrolled subjects;
     - IRB Continuation Review: Primary Reviewer Checklist;
     - For Veterans Affairs Medical Center (VAMC) studies, the VA Research: Reviewer Checklist;
     - ORI staff recommendations.

See the CR form for a complete list of information and attachments the PI must submit.

4. Approximately 5-10 days prior to the meeting, the IRB members scheduled to attend the meeting receive the following items, but not limited to:
   - The completed CR report form;
   - A cover memo if it contains information pertinent to review of protocol;
   - Attachments (updates/changes, explanations);
• A copy of the consent/assent form for which the investigator is seeking IRB approval;
• A protocol summary and status report of the progress of the research;

5. All IRB members are responsible for reviewing all information in the agenda packet in advance of the meeting (including those protocols for which the IRB member is not the primary reviewer) in enough depth to be familiar with the protocol, to be prepared to discuss the protocol at the meeting, and to be prepared to determine whether the research meets the regulatory criteria for approval.

6. When documentation of informed consent is required, the IRB reviews the informed consent/assent document(s) submitted for re-approval to ensure accuracy and completeness.

7. ORI staff ensure that the complete IRB protocol record is available to all IRB members prior to and, if requested, during the convened meeting. All IRB members have the opportunity to discuss each research protocol during the convened meeting.


9. When the IRB reviews research that involves categories vulnerable to coercion or undue influence, ORI staff ensure that adequate representation or consultation is present for discussions of research involving vulnerable human subjects. (See Protection of Vulnerable Subjects SOP and Membership of IRB SOP)

10. The IRB/ORI staff conduct the convened meeting in accord with the Conduct of IRB Meetings SOP. Members who have a conflict of interest follow procedures outlined in both the Conduct of IRB Meetings and IRB Member and Consultant Conflict of Interest SOP.

11. ORI staff serve as intermediaries between the PI and the IRB primary reviewer. However, the primary reviewer may contact the PI directly for clarification. The reviewer documents in the CR materials the issues discussed with the PI.

12. Primary reviewers provide recommendations to the IRB at the convened meeting on issues which they determine do not meet the federal criteria for approval, are controverted, need additional information, or concern compliance with the mandatory University of Kentucky human research training requirements.

13. If the primary reviewer is unable to attend the meeting, ORI staff provide his/her comments or recommendations in writing for presentation to the IRB at the convened meeting.

13. The IRB considers CRs scheduled for full review individually for approval. At the meeting, the IRB reviews the CR report and any controverted issues and their resolution prior to voting. During discussion, the IRB members only raise those controverted issues that the IRB
14. The IRB ensures that the PI provides any significant new findings that might relate to the subject’s willingness to continue participation to the subject in accordance with regulations.

15. The convened IRB makes the final determination on the outcome of the review. The primary reviewer or designated IRB member documents the IRB’s determinations on the IRB Continuation Review: Primary Reviewer Checklist.

**Medical and Nonmedical Expedited Continuation Review**

1. The Vice Chair or designee serves as the expedited reviewer for expedited CR protocols. If the expedited reviewer has a conflict of interest (e.g., is study personnel on a protocol for continuation review), is unavailable, or does not have the appropriate expertise to review the CR, ORI staff assign responsibility for the CR to the Chair, another Vice Chair, or a voting member of the IRB.

2. ORI staff send the expedited reviewer the following information, including, but not limited to:
   - A completed CR report form for each study, which includes, when applicable, the number of subjects enrolled and withdrawn from the study, summary of unanticipated problems/adverse events involving risks to the subject or others, recent literature, complaints about the research, and any new, significant findings (new findings and implications for subject participation described);
   - A protocol summary and status report on the progress of the research ONLY for protocols which remain open for data analysis or financial transaction only (in which case the PI does not have to submit the current approved protocol or research description);
   - A copy of the currently approved sponsor protocol (including any prior IRB-approved modifications) and/or research description (summary which addresses all elements of criteria for approval);

and if applicable:
   - A cover memo if it contains pertinent information needed to review of protocol;
   - attachments (e.g., updates/changes, explanations);
   - A copy of the consent/assent form for which the investigator is seeking IRB approval (with changes underlined for the primary reviewer);
   - A revised grant application;
   - Copies of signed consent/assent forms for the two most recently enrolled subjects;
   - IRB Continuation Review: Primary Reviewer Checklist;
   - For VA studies, the VA Research: Reviewer Checklist;
ORI staff recommendations.

3. All expedited reviewers are responsible for reviewing all information in the expedited review packet in enough depth to be familiar with the protocol, to determine whether the research is eligible for expedited review, and to determine whether the research meets the regulatory criteria for approval.

4. The expedited reviewer is responsible for making the final determination that the protocol meets the criteria for expedited review as outlined above. If the expedited reviewer determines full review is necessary, (s)he documents this requirement in the Reviewer’s Recommendations section on the “IRB Continuation Review: Primary Reviewer Checklist”. Upon receipt of the reviewer’s recommendation, ORI staff implement full continuation review procedures.

5. The expedited reviewer applies the same criteria for approval as outlined above for full review (i.e., applies 45 CFR 45.111, 21 CFR 56.111, and 38 CFR 16.111), and completes the “IRB Continuation Review Primary Reviewer Checklist” as documentation of his/her determination. The expedited reviewer raises controverted issues he/she determines do not meet federal criteria and/ or may request additional information.

6. When documentation of informed consent/assent is required, the expedited reviewer reviews the informed consent/assent document(s) submitted for re-approval to ensure accuracy and completeness.

7. ORI staff serve as intermediaries between the PI and the IRB expedited reviewer. However, the expedited reviewer may contact the PI directly for clarification. The reviewer documents in the CR materials the issues discussed with the PI.

8. The expedited reviewer documents in the CR materials any determination pertaining to specific findings, as mandated by federal regulations that were not previously addressed by the IRB. (Expedited reviewer approval of the CR materials documents that the reviewer agrees with the PI’s assessment of the specific findings).

9. The expedited reviewer ensures that the PI provides any significant new findings that might relate to the subject’s willingness to continue participation in accordance with regulations. The reviewer uses the IRB Continuation Review: Primary Reviewer Checklist as a prompt.

10. If the approval might lapse before completion of the CR, the expedited reviewer can make a determination to allow subjects currently participating to continue in accord with procedures described in the section below on lapses of approval.

11. ORI staff list expedited CRs on the IRB agenda to advise the IRB of the expedited CRs.
VA Research: Additional Issues for Expedited and Full CR

1. If the IRB has not previously made a determination, the VA IRB representative and/or the VA Associate Chief of Staff (ACOS), using the VA Research: Reviewer Checklist as a guide, prompt the convened IRB or the expedited reviewer through ORI staff to make determinations as required by VA regulations.

Review Outcome(s)

1. For full CR, an IRB member makes a motion, the motion is seconded, and then the IRB members vote for, against, or abstain from one of the following five actions:

   - APPROVED (Vote for a #1): IRB approval - A vote of #1 indicates that the IRB concluded that the research and, if applicable, consent forms meet the federal criteria for approval. The IRB’s approval vote verifies that the IRB members agree with the information/materials submitted for continuation of the protocol and/or specific findings described in the CR report by the PI. ORI staff send the investigator an approval letter according to the guidelines in the ORI Customer Service Standard, if applicable, accompanied by an informed consent/assent document with the affixed "IRB Approval" validation stamp, which includes valid dates of IRB approval.

   - REVISIONS and/or ADDITIONAL INFORMATION REQUIRED (Vote for a #2): A vote of #2 indicates that the IRB has given the individual chairing the meeting, or the primary reviewer, the authority to approve the minor revisions which do not involve substantive issues. The IRB approves the protocol pending submission of minor revisions/additional information. In accordance with ORI Customer Service Standards, ORI staff send a letter to the PI describing the revisions requested by the IRB.

The PI responds to the IRB’s suggested revisions in writing and sends the response to the ORI. Those responses are given to the individual who was designated at the IRB meeting to review the requested revisions. That individual may forward the responses to the entire IRB for additional review, request additional information, or approve.

   - TABLED - Vote for a #3: A vote of #3 indicates the IRB withholds approval pending submission of major revisions/additional information. ORI staff send the PI a letter according to the guidelines in the Customer Service Standard. The letter lists the reasons for tabling and includes a description of the revisions or clarifications requested. For some studies, the IRB may appoint one or more members of the IRB to discuss the reasons with the investigator. If the vote is for a #3, ORI staff schedule the PI’s response
to the requested revisions for review by the full committee. The PI is not required to attend.

- **TABLED – Vote for a #4**: A vote of #4 follows the same procedure as a vote of #3 except the PI needs to attend the future IRB meeting at which the IRB reviews his/her response to discuss or answer IRB concerns or questions. ORI staff notify the PI of the request for him/her to attend that future IRB meeting.

- **DISAPPROVED (Vote for a #5)**: A vote of #5 indicates the IRB disapproves the protocol. ORI staff send the investigator a letter according to the guidelines in the ORI Customer Service Standard, describing the reasons for disapproving the protocol. This outcome usually occurs when the IRB determines that the risk of the procedures outweighs any benefit to be gained or if the federal criteria have not been met.

2. For expedited CR, the expedited reviewer may make the following determinations: 1) approved; 2) revisions and/or additional information required; 3) review by the full committee required. The expedited reviewer exercises all the authority of the IRB except he/she may not disapprove the CR. Only the convened IRB may disapprove the CR.

3. During the convened meeting, the IRB determines the approval period as appropriate to the degree of risk but not less frequently than once per year. The IRB will generally set a shorter approval period (for CR to occur more often than annually) for high risk protocols or protocols with a high risk/low potential benefit ratio. No approval period extends beyond one year. When a protocol receives final approval, ORI staff document the approval period in the approval letter to the investigator. For full CR, ORI staff include the approval period in the meeting minutes.

4. For full CR, the date of the start of the approval period is the date of the convened meeting. When the outcome of the IRB vote is a “2” (approved pending submission of minor revisions), the ORI staff issue approval after the IRB Chair or the individual chairing the meeting reviews and approves the PI’s response. The approval period begins on the date on which the protocol was reviewed by the convened IRB. For expedited CR, the date of the start of the approval period is the date the expedited reviewer approves the study.

5. Upon request, ORI staff also send the PI a funding agency Certification of Approval form. (See the Federally Mandated Reporting to External Agencies SOP)

6. The ORI maintains a “Statement of Compliance,” signed by the IRB Chair and provides that statement to PIs upon request if the protocol falls under the International Conference on Harmonisation (ICH) guidance related to Good Clinical Practice (GCP).
7. If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit his/her concerns to the IRB in writing with a justification for altering the IRB decision. The IRB reviews the request using the standard IRB review procedures.

Lapse of Approval

1. If a PI fails to return the CR report form or the IRB has not completed review by the end of the approval period, ORI staff notify the PI in writing that the approval will lapse or has lapsed. ORI staff inform the PI that research must cease and no new subject enrollment may occur after the date of lapse. ORI staff also inform the PI that he/she should, if appropriate, notify subjects that the study approval has lapsed and that, if applicable, it is his/her responsibility to notify the funding agency of the expiration of the IRB approval.

2. The PI may ask the IRB for permission to allow subjects currently participating to continue due to overriding safety concerns, ethical issues, or because it is in the best interest of the individual subjects. The IRB makes the final determination, if appropriate. The ORI or IRB notifies the PI in writing of that determination. (For VA studies, see Lapse of Approval in VA Studies below.)

3. In the case of a study in which the PI is actively pursuing renewal, but he/she could not respond to the IRB request for changes before the end of the approval period, with the result that a lapse of approval has occurred, ORI staff send the resubmitted materials to the same IRB that requested the changes. The IRB may subsequently approve the study for continuation.

4. If a protocol approval has expired due to failure of the PI to submit a continuation review report or to respond to the IRB’s request for revisions and the PI subsequently submits the CR materials/revisions after the end of the approval, the ORI requests from the PI a written summary of events that occurred in the interim. If the PI submitted the materials/revisions less than three months from the end of the approval period, ORI staff forward the PI’s summary and the CR materials/revisions to the IRB. The IRB reviews the materials/revisions following procedures outlined in the Continuation Review SOP.

5. If a protocol approval has expired due to failure of the PI to submit a CR report or respond to the IRB’s request for revisions and the PI subsequently submits the CR materials/revisions more than three months after the end of the approval, the IRB requires a new initial review application. ORI staff assign the protocol to an initial review committee and request a written summary of events that occurred in the interim from the PI. ORI staff forward a copy of the summary to the IRB with the initial review application. ORI staff link the new application to the previous protocol number and keep any previous CR materials with the new submission.

6. When continuing review and approval of a research study do not occur prior to the end of the approval period, the IRB does not report the expiration as a suspension of approval under
Food and Drug Administration, Department of Health and Human Services, or VA regulations.

Lapse of Approval in VA Studies

1. If approval of a UK/VA study lapses during the CR process, already enrolled subjects may only continue research activities when the IRB or IRB Chair, in consultation with the VAMC ACOS for Research and Development, finds that it is in the best interest of individual subjects to continue participation.

2. For VAMC research for which approval has lapsed, the IRB notifies the PI to immediately submit to the IRB Chair a list of subjects for whom stopping research activities would cause harm.

3. If applicable, IRB policy requires the PI to notify the funding agency of the lapse of IRB approval.

4. During the time period in which consultation is occurring within the VA, the IRB may determine that subjects may continue at UK.

REFERENCES

21 CFR 56.108(a)(1)&(2)
21 CFR 56.109(f)
21 CFR 56.110
21 CFR 56.111
21 CFR 56.115(a)(3)&(7)
38 CFR 16.103(b)(4)
38 CFR 16.108(b)
38 CFR 16.109(e)
38 CFR 16.110
38 CFR 16.111
38 CFR 16.115(a)(3)&(7)
45 CFR 46.103(b)(4)
45 CFR 46.108(b)
45 CFR 46.109(e)
45 CFR 46.110
45 CFR 46.111
45 CFR 46.115(a)(3)&(7)
**OBJECTIVE**

To describe the policies and procedures for conducting expedited initial review.

**GENERAL DESCRIPTION**

The Institutional Review Board (IRB) uses an expedited review process to review studies that meet the categories adopted by the Department of Health and Human Services (DHHS), the Food and Drug Administration (FDA), or the Department of Veteran Affairs (VA) and that involve no greater than “minimal risk”. The federally mandated categories and the definition of “minimal risk” are attached. Expedited review procedures allow the IRB to review and approve studies that meet the criteria in the attached document without convening a meeting of the full IRB. The IRB Chair, one or more experienced reviewers from among the Medical IRB voting membership (regular and alternate members), or the Nonmedical Expedited Review Subcommittee conducts expedited initial review.

The expedited reviewers only approve research that meets the federal criteria for approval as specified in 45 CFR 46.111, 21 CFR 56.111, and 38 CFR 16.111. Also, expedited reviewers ensure that the informed consent process and documentation as specified in 45 CFR 46.166 and 117, 21 CFR 50.25, and 38 CFR 16.116 and 117 are carried out unless the IRB can waive the requirements in accord with federal regulations. (See Informed Consent SOP.)

The expedited reviewers exercise all of the authority of the IRB except that the reviewers may not disapprove the research. The IRB only disapproves a research activity in accord with non-expedited procedures set forth in the DHHS, FDA, and VA regulations.

The IRB agenda for convened meetings advises the IRB of research studies approved using expedited review procedures. Any member can request to review the entire IRB file for an expedited study.
RESPONSIBILITY

Execution of SOP: IRB Chair, IRB Members, Office of Research Integrity (ORI) Staff, Research Privacy Specialist (RPS), ORI Research Compliance Officer (RCO), Veterans Affairs Medical Center (VAMC) Associate Chief of Staff (ACOS) for Research and Development, Principal Investigator (PI)/Study Personnel.

PROCEDURES

Assigning Reviewers

1. Each year, after finalizing the list of IRB members, ORI staff select and recommend experienced members from each IRB committee to serve as expedited reviewers for monthly rotating terms. Members must have served on an IRB for three months to qualify as an experienced member.

2. ORI staff make initial Medical IRB reviewer and Nonmedical IRB subcommittee assignments based on the member’s familiarity with IRB issues, experience, and expertise, and forward the proposed assignments to the respective IRB Chair for his/her review and approval. ORI staff forward the approved list of expedited reviewers to the IRB members.

3. The expedited reviewer notifies ORI staff if he/she is not available to conduct expedited review during the assigned time period or has a conflict of interest as outlined in the IRB Member and Consultant Conflict of Interest SOP.

Submission and Screening

1. The PI makes a preliminary determination that a protocol is eligible for expedited review based on the criteria in the attached document. The IRB makes the final determination regarding whether a protocol is eligible for expedited review.

2. The PI submits a completed expedited review application to the ORI. Instructions for preparing the application are available in the IRB Survival Handbook and on the ORI website. The investigator may call the ORI with questions.

3. Upon receipt of the application, ORI staff screen it for completeness and accuracy and make a preliminary determination as to whether the application meets the criteria for expedited review. If the application does not meet the criteria for expedited review, ORI staff advise the PI to resubmit the study for full or exempt review.
4. ORI staff follow the screening procedures outlined in the Initial Full Review SOP (e.g., screening for coordination with other university review committees; for vulnerable subjects or federally mandated specific findings; for waiver of informed consent or documentation requests; for completion of mandatory training requirements; for need of additional expertise or prisoner representative review). See the Initial Full Review SOP for a detailed description of ORI staff procedures.

5. ORI staff also screen for Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule and/or Family Educational Rights and Privacy Act (FERPA) concerns. If the PI includes a HIPAA form or checks “HIPAA” in the application or if there are any HIPAA or FERPA concerns, ORI staff forward the application to the ORI Research Privacy Specialist for review. The RPS reviews the application and submits suggestions in writing. ORI staff forward these suggestions to the medical expedited reviewer or the nonmedical expedited subcommittee for a final determination.

6. ORI staff enter the application into the ORI computerized tracking system. The tracking system assigns a number to the application.

7. After completing application screening, ORI staff retain the original application in the ORI and send a copy of the application to the expedited reviewer(s).

8. The IRB Chair, one or more experienced reviewers from among the Medical IRB voting membership (regular and alternate members), or the Nonmedical IRB Expedited Review Subcommittee conducts expedited initial review.

**Nonmedical IRB Expedited Review Process**

1. A Nonmedical IRB Expedited Review Subcommittee comprised of the Chair, Vice Chair, and two IRB expedited reviewers usually conducts expedited reviews at a convened meeting.

2. ORI staff send the materials in the full review agenda packet. The ORI sends the detailed protocol/grant application to one of the subcommittee members following primary review procedures.

3. Typically, only members assigned to serve on the subcommittee attend the expedited review portion of the meeting, but any IRB member who would like to attend may do so. However, he/she may not vote unless he/she has had the opportunity to review the same materials as those sent to the subcommittee. The subcommittee may review and approve protocols as long as one voting IRB member is present (i.e., Chair, Vice Chair, or any of the designated IRB subcommittee members).

4. The subcommittee, with assistance from ORI staff, documents federally mandated specific findings (e.g., Subpart B, C, D, or waiver of informed consent or documentation) and
controverted issues by completing the expedited reviewer signature page and/or by inclusion of discussion in the minutes of the convened meeting. In conducting the initial review of the proposed research, the subcommittee utilizes the Criteria for IRB Approval: Reviewer Checklist.

5. An IRB member who serves on both the Nonmedical IRB and the UK Psychology Department Subject Use and Research Ethics Committee (SURE) may review studies submitted to the Nonmedical IRB that require expedited approval from both the IRB and the SURE. The IRB subcommittee does not review these expedited studies unless the SURE-designated IRB member is not available. (See the Subject Use and Research Ethics Committee/IRB Coordination SOP.)

6. If an investigator needs an expedited review prior to a convened meeting, the Nonmedical IRB Chair, Vice Chair, or any experienced voting member (i.e., regular or alternate) may serve as the expedited reviewer following the same procedures as those used for the Medical IRB expedited review process.

Medical IRB Expedited Review Process

1. For the Medical IRB primary expedited reviewer conducts expedited reviews outside of a convened meeting. If the primary expedited review is not available or has a conflict of interest, the ORI contacts a secondary reviewer to conduct the review.

2. The ORI sends the application materials to the primary expedited reviewer on the Medical IRB. If the reviewer is unable to respond within approximately 10 days, ORI staff send the reviewer up to two reminders. If the expedited reviewer still does not respond, ORI staff forward the protocol to the secondary reviewer.

3. The expedited reviewer contacts the PI for any clarification needed and documents the issues discussed on the expedited reviewer signature page. The expedited reviewer also utilizes the Criteria for IRB Approval: Reviewer Checklist to document that the research meets the federal criteria for IRB approval.

4. For VA studies, ORI staff send the expedited review application materials to the VAMC Associate Chief of Staff. He/she reviews the application to ensure compliance with VA requirements using the VA Research: Reviewer Checklist as a guide.

5. ORI staff document any issues pertaining to special findings (e.g., requests for waiver of informed consent or documentation or Subpart B, C, D findings) through the materials submitted by the PI and the expedited reviewer’s final approval of the application. The reviewer only raises controverted issues that he/she has determined do not meet the federal criteria for approval or UK IRB policies.
Materials Sent to Medical and Nonmedical IRB Reviewers

1. Both the medical and nonmedical expedited reviewers receive the following IRB application materials and IRB forms:
   - Section 1 - core application with General Information Sheet and research description;
   - Section 2 - informed consent/assent process and forms, including waiver requests, NIH sponsored cooperative group trial forms, translated consent document for non-English speaking subjects;
   - Section 3 - HIPAA forms;
   - Section 4 - additional materials, including advertisements, proposal data instruments, materials/letters for off-site research, Use of Investigational New Drug (IND) Form, Use of Approved Drugs for Unapproved Use Form, Use of Radioactive Materials Form;
   - Section 5 - vulnerable populations, including forms for research involving decisionally impaired individuals, pregnant women, fetuses and/or neonates, prisoners, or children;
   - Expedited reviewer signature page;
   - Criteria for IRB Approval: Reviewer Checklist;
   - ORI staff comments/recommendations, if applicable;
   - Expedited review categories form.

2. All expedited reviewers review all information in the expedited review packet in enough depth to be familiar with the protocol, to determine whether the research is eligible for expedited review, and to be prepared to determine whether the research meets the regulatory criteria for approval.

Review Outcomes

1. Both medical and nonmedical expedited reviewers make the final determination as to whether research activities meet the expedited review criteria outlined in the attached document.

2. The reviewers also determine whether the research meets the federal criteria for approval as outlined in 45 CFR 46.111, 21 CFR 56.111, and 38 CFR 16.111.

3. Expedited reviewers also ensure that the investigator will conduct the informed consent process and obtain documentation of informed consent, as specified in 45 CFR 46.116 and 117, 21 CFR 50.25, and 38 CFR 16.116 and 117, unless the IRB waives the requirements in accord with federal regulations. (See Informed Consent SOP)

4. The expedited reviewers only raise those controverted issues or request changes that they have determined do not meet the federal criteria for approval or UK IRB policies.
5. The expedited reviewers make one of the following three determinations in regard to the protocol and consent forms:

- **APPROVED**: IRB approval indicates that the IRB reviewer(s) has concluded that the research and consent forms meet the federal criteria for approval. An IRB approval vote verifies that the IRB agrees with the assessment of the protocol and/or specific findings as described by the PI in the application. ORI staff send the investigator an approval letter according to the guidelines in the ORI Customer Service Standard, accompanied by an informed consent/assent document with the affixed "IRB Approval" validation stamp which includes valid dates of IRB approval. Upon request, ORI staff also send the PI a funding agency Certification of Approval form.

- **REVISIONS and/or ADDITIONAL INFORMATION REQUIRED**: The IRB reviewer(s) withhold approval pending submission of revisions/additional information. ORI staff send the investigator a letter according to the guidelines in the ORI Customer Service Standards, describing the revisions requested by the IRB expedited reviewers. The PI responds to revisions requested by the IRB in writing and sends the response to the ORI. ORI staff forward those responses to the expedited reviewer for further review.

- **FULL REVIEW REQUIRED**: The IRB expedited reviewers may determine that the protocol requires full review by the IRB at a convened meeting.

6. The medical and nonmedical expedited reviewer(s) can determine that the research is eligible for a less stringent mechanism of review (i.e., the project is exempt from requirements for review or the activities do not fall under the purview of the IRB). In these cases, the IRB does not require a new application provided the IRB, with assistance from ORI staff, documents the exempt categories or the rationale for determining that the activities do not meet the federal definitions of research, clinical investigation, or human subject.

7. The ORI procedures for notifying the PI of the review outcome, obtaining follow up correspondence, and issuing approval letters outlined in the Initial Full Review SOP apply for expedited review as well. See Initial Full Review SOP for details.

8. Once the IRB reviewer(s) approves the study, he/she assigns the approval period at intervals appropriate to the degree of risk but not less than once per year. The date the expedited reviewer signs off final approval on the study is the date the approval period starts. ORI staff document the approval period dates in the approval letter to the PI.

9. If the PI has concerns regarding the IRB decision/recommendations for changes in the study, he/she may submit his/her concerns to the IRB reviewer via a written document that includes justification for changing the IRB decision. The PI sends the request to the expedited
reviewer and/or to the IRB Chair or Vice Chair for final resolution. If the investigator is still dissatisfied with the IRB decision, ORI staff send the protocol to the convened IRB for review.

REFERENCES

21 CFR 56.102(i)
21 CFR 56.110
38 CFR 16.110
38 CFR 16.102(i)
45 CFR 46.102(i)
45 CFR 46.110
63 FR 60364-60367; 63 FR60353 – 60356 DHHS-FDA list published in Federal Register November 9, 1998
Federally Mandated Expedited Review Criteria – Effective November 9, 1998 – Definition of Minimal Risk Guidance to PI and Reviewers

Expedited procedures can only be used to review a study if the only involvement of human subjects fits one or more of the categories specified in the federal regulations and if all of the procedures present no greater than “minimal risk.”

The IRB reviewer confirms that all of the research activities fit in one or more of the expedited categories. If the research includes activities that do not fit in the categories, the study is not eligible for expedited review even if the research involves “minimal risk.”

The Department of Health and Human Services defines minimal risk to mean “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests” [45 CFR 46.102(2)(i)].

Investigators are asked to provide a risk assessment, but it is the IRB reviewer’s responsibility to determine whether the research meets the federal definition.

The IRB reviewer must consider two questions:

- Is the probability of the harm or discomfort anticipated in the proposed research greater than that encountered ordinarily in daily life or during the performance of routine physical or psychological examinations or tests? OR

- Is the magnitude of the harm or discomfort greater than that encountered ordinarily in the daily life or during the performance of routine physical or psychological examinations or tests?

If the answer is “yes” to either of these questions, then the research does not meet the definition of minimal risk. The IRB policy on risk assessment is included in the UK Assessing the Research Risk document, which is on the ORI website and in the IRB Survival Handbook.

Federal Expedited Review Applicability and Categories

(A) Research activities that (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the following categories, may be reviewed by the IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. The activities listed should not be deemed to be of minimal risk simply because they are included on this list. Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects.

(B) The categories in this list apply regardless of the age of subjects, except as noted.

(C) The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.
The expedited review procedure may not be used for classified research involving human subjects.

IRBs are reminded that the standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review—expedited or convened—utilized by the IRB.

Categories one (1) through seven (7) pertain to both initial and continuing IRB review.

Research Categories

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
   (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)
   (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:
   (a) From healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or
   (b) From other adults and children considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means.
   Examples: (a) Hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of the membranes prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device for new indications.) Examples: (a) Physical sensors that are applied either to the surface of the body or to a body fluid; (b) monitoring devices for the purpose of clinical diagnosis or management; (c) collection of data obtained by electrocardiography, electroencephalography, or other similar monitoring methods.

5. Collection of biological specimens for research purposes by noninvasive means.
   Examples: (a) Hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of the membranes prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

6. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device for new indications.) Examples: (a) Physical sensors that are applied either to the surface of the body or to a body fluid; (b) monitoring devices for the purpose of clinical diagnosis or management; (c) collection of data obtained by electrocardiography, electroencephalography, or other similar monitoring methods.

7. Collection of biological specimens for research purposes by noninvasive means.
   Examples: (a) Hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of the membranes prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.
the body or at a distance and do not involve input of significant amounts of energy into the
subject or an invasion of the subject’s privacy; (b) weighing or testing sensory acuity; (c)
magnetic resonance imaging; (d) electrocardiography, electroencephalography,
thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound,
diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate
exercise, muscular strength testing, body composition assessment, and flexibility testing
where appropriate given the age, weight, and health of the individual.

5) Research involving materials (data, documents, records, or specimens) that have been
collected or will be collected solely for nonresearch purposes (such as medical treatment or
diagnosis). (Note: Some research in this category may be exempt from the HHS regulations
for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research
that is not exempt.)

6) Collection of data from voice, video, digital, or image recordings made for research purposes.

7) Research on individual or group characteristics or behavior (including, but not limited to,
research on perception, cognition, motivation, identity, language, communication, cultural
beliefs or practices, and social behavior) or research employing survey, interview, oral
history, focus group, program evaluation, human factors evaluation, or quality assurance
methodologies. (Note: Some research in this category may be exempt from the HHS
regulations for the protection of human subjects 45 CFR 46.101 (b)(2) and (b)(3). This listing
refers only to research that is not exempt.)

8) Continuing review of research previously approved by the convened IRB as follows:
   (a) 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
   (b) Where no subjects have been enrolled and no additional risks have been identified; or
   (c) Where the remaining research activities are limited to data analysis.

9) Continuing review of research, not conducted under an investigational new drug application
or investigational device exemption where categories two (2) through eight (8) do not apply
but the IRB has determined and documented at a convened meeting that the research involves
no greater than minimal risk and no additional risks have been identified.
UK Process
**Continuation Review (CR) & Primary Reviewer Checklists Flow**

1. **Continuation Review - Primary Reviewer Checklist** (aka **PR Checklist**)
2. Criteria for IRB Approval: Short Form Checklist (aka **Short Checklist**)
3. Additional Criteria for IRB Approval of VA Research: Reviewer Checklist (aka **VA Checklist**)

*Start*

ORI staff fill-in top of PR Checklist

**For Full CR, Short Checklist shared/displayed at meeting. (not put in study file)**

---

Reviewed

**Criteria for Approval met?**

Yes

Chair/designee documents determinations on PR Checklist and signs.

Chair/designee documents determinations, marks "approve" box on PR Checklist and signs.

Checklist(s) placed in protocol file

IRB approval materials issued

No

VA Protocol

PI response received

PI response, CR materials, and new PR Checklist sent to IRB Chair/designee

Revisions approved

VA Reviewer documents determinations, marks "Yes" box on VA Checklist, signs, and returns to ORI staff.

Signed VA Checklist placed in protocol file

VA Checklist attached to each CR and sent to the VA Associate Chief of Staff (ACOS).

Reviewed

VA Criteria for Approval met?

Yes

No

VA Reviewer documents determinations, marks "No" box on VA Checklist, signs, and returns to ORI staff.

---

For Full CR, Short Checklist shared/displayed at meeting. (not put in study file)
Goals:

- Provide an extensive CR screening process which will enable the IRB member(s) to focus on substantive issues.
- Come to a consensus regarding which screening responsibilities the AA’s will be held accountable for.
- Streamline and centralize communications between PA’s, AA’s, and Reviewers – see Communications Log
- Discover/re-discover coding, prioritization techniques, and manual tracking techniques to prevent approval lapses.
- Full CRs – Reconcile what the committee approves with what our office is issuing to PI (minutes vs. approval letter vs. database). ORI staff can not make decisions about what is approved – need IRB to make determinations.

Office of Research Integrity (ORI)
Continuation Review (CR) Screening/Review Responsibilities

The ORI staff person makes preliminary screening of the protocol file, and makes sure all information/materials submitted are appropriate, enabling Primary Reviewer to focus on human subject protection issues. ORI staff person checks the following:

1) All necessary materials included per “Attachments and # of Copies Required” section on CR/FR report form.
   - TWO copies of the completed form (ORI AA make extra copy of any materials if necessary – no need to return to PI for this unless other needs are extensive)
   - TWO copies of any attachments or cover memorandum, if applicable.
   - IRB approved a consent/assent form (entire copy) for the two subjects most recently enrolled (if enrolled within the last year)
   - TWO clean copies of the currently approved consent/assent form (w/o the "IRB Approval" stamp), if open to enrollment
     - If changes requested, include two copies with changes underlined and PI provide explanation of how the changes differ from the currently approved consent form.
   - One copy of the grant proposal (if new or revised grant application that has not previously been submitted to the IRB)
   - One copy of the complete current protocol containing any modifications previously approved by the IRB
     - If changes requested, one copy should contain underlined changes – ideally 2nd copy w/o underlined changes included.
   - One copy of the Investigator Brochure if changed since the last review
   - Two copies of a protocol summary and a status report on the progress of the research for FULL CRs
     - If the research involves extramural funding, the following will be accepted to fulfill this requirement:
       - the most recent Progress Report Summary or project summary submitted to your funding agency; OR,
       - the Project Data Sheet with the abstract attachment if VA Research and Development Committee approved study; OR,
       - if PI is sponsor [(s)he has own IND/IDE] the most recent progress report sent to the FDA
     - If closing the study, summary of the results and statement that it is a final abstract.
   - Question #9 – re: HHS 310 form – for ORI office use.
   - Question #10 – PI response determines whether protocol is eligible for expedited review or whether protocol can be closed. [If eligible for expedited review, copies of CR materials are not attached to the agenda, and PR will be the only IRB member to receive copy for review.]
   - Question #11 Indicates whether PI needs re-approval and/or an extension (or close out). [PI’s response determines coding we put in ORI system.]
   - Question #12a – ORI system populates total # subjects enrolled to date & PI should indicate current total enrolled.
     #12b – This response should equal ORI system total # of subjects enrolled less the new total PI indicates in 12a. Response tells you whether or not copies of signed consent document(s) should be included. If yes, signed consent(s) should be screened to:
       - make sure outdated/inappropriate consent document(s) was/were not used;
       - changes to consent document(s) was/were not made prior to IRB approval; and
       - appropriate signatures were been obtained (based on IRB approved study personnel listings in protocol file)
   Note: “Enrolled” includes all subjects who have signed a consent form or on whom data has been collected (see http://www.research.uky.edu/ori/hotline/Listserv%20Announc/May_2006_2.pdf for details).

Total in #12b should not exceed the approved “estimated number of subjects by completion” listed as part of #12d.
#12c – response tells you:
  i. whether the PI needs to provide a new estimate for # of subject to be enrolled by completion (see 12d); and,
  ii. whether clean copies of informed consent document(s) should be included for re-approval. If consent document(s) included for re-approval, compare clean copy submitted with currently approved consent
document(s) in file to ensure changes have not been inadvertently made or wrong version submitted. May need to communicate with PI if discrepancies noted.

6) Question #13 – “yes” response should trigger screening for current approval for enrollment of prisoners. If prisoners not previously approved for enrollment, initiate procedures for approval of prisoners (see Form V & http://www.research.uky.edu/ori/FormsHELP/SSV.htm)

7) Question #14 – If PI indicates info is not available, screen for explanation.

8) Question #15 - If yes, compare off-site facilities named with those approved at Initial Review or last CR (whichever was most recent). If any differ, initiate procedures for approval of new off-site facilities (see Form N, http://www.research.uky.edu/ori/FormsHELP/S4N.htm, and http://www.research.uky.edu/ori/ORIFORMS/10-ORIs_Off-Site_Research_Guidance.pdf) and also note whether the protocol is federally funded (as indicated in #42).

9) Question #16 – Response(s) identify whether the study is a VA study. If yes, screen to see if currently approved as VA study and whether VA requirements still met. If not a currently approved VA study and PI indicates VA involvement, screen to ensure VA requirements met. E.g., VA consent document included, VA 10-1223 included, study title changed to include “UK/VA:” at the beginning; we send to VA reviewer with VA Reviewer Checklist, etc... For details see: http://www.research.uky.edu/ori/FormsHELP/S4R.htm Also, if yes, screen to ensure PI responded to #36b.

10) Questions #17-#20 – Screen for “Yes” response(s) and ensure explanation(s)/materials included as applicable.
11) Question #21 – Screen for “yes” response(s) and ensure appropriate/updated study personnel materials included.
12) Question #22 – Screen for “no” response. Time factor may determine whether PI notified to try and resolve training issue before forwarding to IRB vs. send to IRB as-is with “Current PI/SP not Retrained” form (see template: J:\Master Internal Documents\Continuation Review\memo templates\CurrentSP Not Re-Trained HSP Questions to Vice Chair.doc)

13) Question #23 – corresponds to CR report form item #6 which should have already indicated whether there are changes to the current protocol.
14) Question #24 & #25 – screen for response which may indicate clarification or additional information needed from PI. If a waiver of documentation has been approved, recommend ORI staff person underline “documentation was waived by the IRB” in the question, and initial next to it to confirm.
15) Question #26 – response may indicate relevant report should be included.
16) Question #27 & #28 – response(s) may indicate additional materials should be included.
17) Question #29 & #30 -- response(s) may indicate additional materials should be included.
18) Question #31-#33 – response(s) may indicate additional materials should be included.
19) Question #34 & #35 – response(s) may indicate additional materials should be included.
20) Questions #36 & #37 – any corrections provided by PI should be entered into ORI system.
21) Question #38a – Screen for any new categories of subjects marked. If new subject category, screen for current approval for that subject population. If not currently approved, initiate process for obtaining IRB approval – may involve additional form (e.g., Form T, U, V, W), translated consent document(s), additional information/material from PI, etc...
22) Question #38b – screen #16 to determine whether PI should provide a response to this question.
23) Question #39 – #42 - are for the PI to review and confirm accuracy. If nothing is marked, then we assume all info is correct. If PI makes changes on any items, screen for current approval, and update ORI system. Addition of certain categories may require the PI to meet additional requirements and/or require further IRB review.
24) Question #43 -- screen for response.
25) Last but not least! Make sure PI signed on line provided on last page of CR/FR report – this indicates to the IRB that the PI attests to the accuracy of all the information provided. Some exceptions have been allowed with prior approval by IRB (e.g., approval due to lapse and PI out of country w/o FAX access – PI identifies in writing (e-mail) who can sign on his/her behalf).

Primary Reviewer (PR) Responsibilities for Review:

1) Double check information provided by PI. (make sure ORI staff person did not miss out on necessary materials)
2) Check CONTENT of abstract, consent document(s), attachment(s). Request additional information or changes as necessary for human subject protections per federal, state, or local IRB policy.
3) If PI requests any modifications, PR should review before approving protocol for continuation.
4) Complete CR Primary Reviewer Checklist and if applicable VA Reviewer Checklist.
5) If PR is requesting information or changes, (s)he should make notes in space provided on CR Primary Reviewer Checklist, and, if Full CR, report at the IRB meeting for which the CRs were reviewed. The ORI staff person will be responsible for following up on the requested materials following standard operating procedures for continuation review.
6) PR may refer to IRB Survival Handbook for guidelines on regulations during review. Original study records are available upon PR’s request.
Communications Log -- Replaces Post-it notes

Coding: See - J:\Master Internal Documents\ORI System\ CR Coding Training.doc

ORI requests for information: Enter CR62

Amendment/Extension: Amendment or extension requests included with the CR submission (should already have a 00 code under the corresponding section in the ORI system), are coded a 10 with full for review type and put on future agenda.

Removal of SP: Coding 00 for removal of SP when requested by PI – not for training issues.

DSMB summary report: If coding – putting under Amendment.

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**Full Versus Expedition Continuation Review**

For both Full and Expedited continuation reviews, Primary Reviewer (PR) receives complete CR packet including, when applicable, but not limited to:

- CR report form, cover memo, attachment(s) (updates/changes, explanation(s), research summary(s)), revised grant application, signed consent forms for two most recently enrolled subjects, copy of consent form for which PI is seeking IRB approval (changes are highlighted for PR). Original study records are available upon PR’s request.

For each study scheduled for full continuation review, the UK Institutional Review Board (IRB) members scheduled to attend the meeting receive, when applicable, but not limited to:

- CR report form, cover memo if it contains pertinent information to review of protocol, attachment(s) (updates/changes, explanation(s), research summary(s)), copy of consent form for which PI is seeking IRB approval.
Dear IRB Reviewer,

For this CR # __________________ The following current Study Personnel (SP) have not completed the mandatory retraining in human subject’s protection:

_____________________________________________________________________

PI/SP need HSP training (valid for 3 years only).
Is there other appropriate SP with the needed expertise for this study including consenting subjects and/or providing necessary human subject’s protection? Yes or No?

Reviewer Comments:

• If Yes, there are other adequate SP listed on the study, ORI staff will remove the above not retrained SP as part of the CR. A notice about the removal of the above SP will be included in the modified approval letter.
• If No, will this CR need to be taken back to a FULL Committee IRB Meeting to decide whether or not to withhold continuation approval? Yes or No?
COMMUNICATIONS LOG

IRB #: ___________________________  PI Last name: ___________________________

- Record chronologically all telephone contacts and e-mail communications with the PI or IRB
- Entry should identify nature of communication (request for clarification & whether clarification rec’d verbally, or request for clarification and documentation pending)
- Sign and date each entry
- Entries subsequent to requests for info/documentation should indicate:
  A. PI responded & materials included with CR sent to reviewer/IRB
  B. PI responded & materials sent separately to reviewer/IRB
  C. Other

Method of Communication Key:  P – Phone       E – E-mail       F – FAX

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<th>Method of Communication</th>
<th>TOPIC/DISCUSSION</th>
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3/20/07  J:\Master Internal Documents\Continuation Review\procedural\CR_communications_Log.doc
Two circumstances when IRB approved active protocols may be closed by the PI and/or the IRB

In April 2006, the University of Kentucky (UK) Institutional Review Board (IRB) adopted two new circumstances permitting IRB approved protocols to be closed by the Principal Investigator (PI) and/or the IRB.

Since that time, the IRB and Office of Sponsored Projects Administration (OSPA) agreed to eliminate the policy which required protocols to remain under IRB approval while a sponsored program account (ledger 4) remained active. Accordingly, the two previously described circumstances under which IRB approved protocols can be closed by the Principal Investigator (PI) and/or the IRB have been revised. They now stand as follows:

If a study is open, and the only activity remaining is analysis of data collected during the study, the study may be closed by the PI if the data is de-identified and there are no subject identifying codes or links to the de-identified data.

A memorandum from the PI must be submitted to the Office of Research Integrity (ORI) in order to close a study when the only activity remaining is analysis of data collected during the study and the data are de-identified (there can not be any subject identifying codes or links to the de-identified data). The memorandum must contain all of the following information:

- a request for inactivation of IRB approval
- confirmation that all subjects have been enrolled
- assurance that data collection is complete
- confirmation that only data analysis, as approved in the protocol, of already collected data remains
- assurance that data are de-identified (provide explanation what this means)
- assurance that there are no subject identifying codes or links to the de-identified data

If a study has been open for a period of three or more years and there have been no subjects enrolled in the study, the IRB requires that the study be closed.

If at continuation review the investigator reports to the IRB that the study has been open for a period of three or more years and there have been no subjects enrolled into the study, the IRB require that the PI submit a withdrawal request memo. A notification of closure letter is sent to the investigator.

The PI must complete and submit a final review report form with the requested materials to the IRB unless:

1. He/she never initiated the study; or,
2. A review (initial or continuation) has been conducted within the last six months and no subjects have been enrolled since the last review.

A copy of this handout may be downloaded from the ORI Educational Materials, Regulations and Policy Guidance web page under the topic "Closure of a Study": http://www.research.uky.edu/ori/human/guidance.htm. For details on additional study closure circumstances, see the IRB/ORI "Study Closure" Standard Operating Procedure (SOP) available on ORI’s SOP web page: http://www.research.uky.edu/ori/human/SOPs & Policies.htm#4

If you have questions regarding this information please contact Helene Lake-Bullock in the Office of Research Integrity (ORI) at Ph: 257- 9428 or hlbullo@uky.edu
Forms
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<th>Continuation Review</th>
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<th>IRB Number</th>
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<td>(APPROVENDDATE)</td>
<td>(PROTOCOLNUM)</td>
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</table>

TO: {FIRSTNAME} {LASTNAME}, {DEGREE}  
{DEPTDESC}  
{ADDRESS}  
PI phone #: {PHONE}  

FROM: Chairperson/Vice Chairperson  
Institutional Review Board (IRB)  

SUBJECT: Continuation Review Request for Protocol Number (PROTOCOLNUM)  

DATE: {MEMODATE}  

In accordance with federal regulations, the IRB conducts periodic continuing review of all currently approved projects. Your protocol entitled {PROTOCOLTITLE} is scheduled for continuation review.  

If this form is not returned in a timely manner IRB approval will expire, effective at the end of your current approval period. Materials should be submitted to THE OFFICE OF RESEARCH INTEGRITY, 305 KINKEAD HALL, 0057 BY {FOLLOWUPDATE}.  

If you have any questions, please contact Karen Larson at 859-257-9819 (Medical IRB #3 & #6), Gail Cadwallader at 859-257-0581 (Medical IRB #1 & #2), Tamara Arrington at 859-257-1639 for nonmedical expedited reviews, or John Ryan at 859-323-2446 for nonmedical full reviews.  

ATTACHMENTS AND # OF COPIES REQUIRED  

1. TWO copies of this completed form.  
2. TWO copies of any attachments or cover memorandum, if applicable.  
3. If subjects have been enrolled within the last year, and the IRB approved a consent/assent form for your study, submit two copies of the entire signed consent/assent forms for the two subjects enrolled.  
4. If open to enrollment, submit TWO clean copies of the currently approved consent form (WITHOUT the "IRB Approval" stamp); [NOTE: If approved, the form(s) will be returned to you with an accompanying approval stamp: Only informed consent/assent documents with a valid "IRB Approval" stamp can be used to enroll subjects.]  
   **If you are making changes to the consent document(s), include two copies with the changes underlined, and provide an explanation of how the changes differ from the currently approved consent form.**  
5. If you have submitted a new or revised grant application for this project that has not previously been submitted to the IRB, submit one copy of the grant proposal.  
6. In conducting continuing review on studies for which IRB approval will remain active, federal policy requires the IRB review a copy of the complete current protocol (modifications previously approved by the IRB should be incorporated into the protocol). Please attach ONE copy of the most current protocol, and include a copy of the Investigator Brochure if it has changed since the last review.  
   **Changes made to protocol/research description ("Form B")?**  
   IF YES, INCLUDE ONE COPY WITH THE CHANGES UNDERLINED.  
7. In conduction continuing review of research that requires FULL REVIEW (not eligible for expedited review), federal policy requires that all IRB members receive and review a protocol summary and a status report on the progress of the research. Submit TWO copies approximately one page in length of a protocol summary and a status report on the progress of the research.  
   If your research involves extramural funding, you may:  
   a) use the most recent Progress Report Summary of project summary submitted to your funding agency to meet this requirement; OR,  
   b) if this is a VA Research and Development Committee approved study, you may submit the Project Data Sheet with the abstract attachment to meet this requirement; OR,  
   c) if you are conducting the study under your own IND/IDE (Investigator Sponsored), attach TWO copies of the most recent progress report sent to the FDA.  
8. In you are closing the study, summarize the results of your study and state that this is a final abstract.  

COMPLETE THE FOLLOWING ITEMS (# 9-33)  

9. **Do you need the Office of Research Integrity (ORI) to complete an HHS Protection of Human Subjects Assurance/Certification/Declaration (310 Form) for you?**  
(If your study is federally funded, your funding agency may request a 310 Form.)
10. Check all that apply:
   a) _____ The study is permanently closed to enrollment of new subjects.
   _____ All subjects have completed all research-related interventions.
   _____ The study remains active for long-term follow-up of subjects.
   b) _____ The only remaining activity for this study is data analysis.
   [NOTE: As long as data analysis is being conducted, your protocol should remain under IRB approval unless certain circumstances are met. For details, see the UK ORI/IRB Study Closure SOP: http://www.research.uky.edu/ori/human/SOPs & Policies.htm#4 Update #11 if necessary.]
   c) _____ IRB approval can be inactivated (all study activities are complete).

11. a) _____ Do you need your IRB approval to continue past the end of your current approval period {APPROVENDDATE}?
   b) The estimated project end date you provided to the IRB is {PROJECTENDDATE}. If you have a new estimated project end date, provide it here: ________________________
   _____ Check here if no change.

12. a) ORI’s electronic records indicate the total # of subjects enrolled since activation of the study is: {SUBJECTCOUNTTODATE}.
   b) _____ The # of enrolled subjects that have not been previously reported to the IRB.
   _____ New total # of subjects enrolled since activation of the study.
   c) _____ Is your study closed to enrollment of new subjects?
   d) Our records show the IRB approved estimate for # of subjects by completion is: {SUBJECTCOUNT} _____ Please update this estimate if necessary.

13. _____ During the course of your research, have any prisoners been enrolled, OR subjects been enrolled that became involuntarily confined/detained in a penal institution, that have not been previously reported to the IRB?
   If YES, and you have received funding from the Department of Health and Human Services (HHS), a Certification Letter should have been submitted to the Office for Human Research Protections (OHRP); prisoners and individuals who have become involuntarily confined/detained in a penal institution can not continue participation in the research until OHRP issues approval. If the Certification has not been submitted, contact the Office of Research Integrity (ORI) at 257-3038.

14. Subject Demographic Information
   Please complete this section based on subjects who have enrolled in the study.
   _____ Check here if the information is not available, and clarify why:

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<td>Other or unknown-------------------------</td>
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15. _____ Is the research being conducted at any site other than UK Campus, UKMC, VAMC, or Markey Cancer Center?
   If YES, please provide a detailed list of all off-site facilities, specifying active and nonactive sites, at which research procedures have been or will be initiated. If adding a new off-site facility, complete and submit “Form N”.

16. a) _____ Is the study open at the VA Medical Center?
   b) _____ Is the study currently enrolling human subjects from the VA?
   c) _____ Are there any VA human subjects in follow-up?
   [Note: If "Yes" to a, b, or c, your study is considered a "VA study". If this is not a VA study, please answer "N/A" for any VA questions that follow.]
For items 17 - 19, report events which have not been described on any prior renewal/continuation review applications. If you have no events to report, please answer questions 17 - 19 with "no".

17. _____ Have any subjects withdrawn from the research?
   **If yes, attach a detailed explanation.
   _____ If this is a VA study, provide the cumulative number of subjects withdrawn since inception of the project.

18. _____ Have there been any complaints about the research?
   **If yes, attach a detailed explanation.

19. Please answer the following:
   
   a) _____ Has any recent relevant literature developed during the course of the research?
   b) _____ Have any interim findings developed during the course of the research?
   If yes to either question, discuss their implications for subject participation on additional sheets.

20. _____ Since the last IRB Continuation Review, have subjects experienced any benefits? If yes, please describe below or on attached sheets:
    ______________________________________________________________________________________
    ______________________________________________________________________________________

21. If there have been any changes in study personnel (SP) that have not been previously reported to the IRB, please attach two copies of a current list of all study personnel, denoting the changes, and include the following information for each person: Name, Social Security Number, Rank/Degree and, Responsibility in Project (including whether the person is authorized to obtain informed consent).

   _____ CHANGES MADE TO SP LIST?
   _____ UPDATED SP LIST ENCLOSED?
   
   (Use Study Personnel List Template, or page(s) from the General Information Sheet (GIS) found in original IRB application.)

22. _____ Have the new personnel completed the mandatory IRB training? [see the policy on Mandatory Education for New Study Personnel and Mandatory Education Renewal (required every three years): http://www.research.uky.edu/ori/human/Human_Research_Mandatory_Education.htm]

23. If substantive changes need to be made to the original protocol, on a separate sheet briefly describe the changes and explain why they are essential.

   NOTE: No changes in the research procedures should have occurred without previous IRB review. Approval from the IRB must be obtained before implementing any changes.

For your information, our electronic records, which began in August 1999, reflect the following total number of amendments submitted to the IRB: {MODCOUNT}

24. Unless the requirement for documentation was waived by the IRB, a copy of the approved informed consent/assent form should have been signed by each of the subjects in the study.

   _____ Has this requirement been met?

25. Specify where the records containing the signed consent/assent forms are/will be located (bldg. & room #):
    ______________________________________________________________________________________
    ______________________________________________________________________________________

26. _____ Since the last IRB Continuation Review, have there been any relevant multi-site trial reports?
   **If YES, and the reports have not already been submitted to the IRB, please attach.

27. _____ Is this study monitored by a Data Safety and Monitoring Board (DSMB) or is there a Data Safety and Monitoring Plan?
   **If no, proceed to Question 29.

28. Attach 2 copies of any summary Data Safety Monitoring report that has been issued during the last 12 months.
   _____ Yes, attached
   _____ No reports issued

29. _____ Were there any problems/adverse events during the last 12 months (internal and/or external; anticipated or unanticipated; serious/life-threatening or not serious/life-threatening; or, related or not related)?
   **If yes, complete #30.

   [Note: It is the IRB's expectation that all problems and/or adverse events requiring reporting are submitted in the appropriate time frame. Your response to this Continuation Review is considered assurance that all reportable problems/adverse events have been submitted for IRB review according to the Prompt]
30. Provide a written summary of all problems/adverse events that occurred since the study was initiated (whether anticipated or unanticipated; serious/life-threatening or not serious/life-threatening; or, related or not related) and the PI assessment whether the problems/events warrant changes for the protocol, consent process, or risk/benefit ratio. The summary should include both a qualitative and quantitative assessment of the severity of the events and the outcome of the events. (Attach summary)

31. _____ Does your protocol fall under the purview of the Food & Drug Administration (FDA)?
   **If yes, please respond to items 32 and 33.

32. _____ Has your research protocol been audited by a FDA representative since the last IRB review?

33. _____ If YES, was a FDA 483 issued?
   **If yes, please include a copy with this form.

34. a) All investigators conducting research at the University of Kentucky are required to complete a Disclosure of Financial Interest Form.

   _____ Have there been any changes to your/your study personnel's personal financial situation that would require updating your Disclosure of Financial Interest (DFI) form?
   **If "Yes", complete a Disclosure of Financial Interest Form (see IRB application Section 6: "Form X" for externally funded research, or "Form Y" for non-sponsored research).

   b) _____ Have you, or any of your study personnel answered yes to ANY of the four questions on that form? If yes, include two copies of the completed form.

35. _____ If the project is funded by extramural funding, has the sponsor offered any of the research team enrollment incentives or other personal benefit bonuses? (these benefits could take the form of cash/check, travel reimbursements, gift checks, etc.)
   _____ Not Sponsored
   Please note: It is University of Kentucky policy that personal benefit bonuses are not allowed. If these conditions change during the course of the study, please notify the IRB.

---

REVIEW THE ITEMS BELOW.
PLEASE MAKE APPROPRIATE CORRECTIONS ON THIS FORM.

36. PI's Social Security #: (SOCIAL SECURITY NUMBER) Degree and Rank: (DEGREE)
   PI's Telephone #: (PHONE #)  PI's Dept: (DEPARTMENT)

37. Age Level of Subject: (SUBJECT AGE (YOUNGEST)) to (SUBJECT AGE (OLDEST))

38. b) If this is a VA study, provide the number of subjects enrolled from each category of subject marked in 38a (e.g., Name of subject category: #).

39. Our records indicate that you are using the General Clinical Research Center (GCRC): (YES or NO)

40. Our records indicate the following attributes apply to your research: (Mark any additional attributes with an "X", as applicable.)
   [ ] HIV / AIDS Research; [ ] HIV Screening; [ ] Aging Research; [ ] Cancer Research;
   [ ] Genetic Research; [ ] Collection of Bio Specimens for Banking; [ ] Emergency Use (Single Patient);
   [ ] Psychology Dept. / SURE Committee; [ ] Utilization of UK General Clinical Research Ctr.;
   [ ] Multicenter Clinical Trial(exclude NIH Coop Group); [ ] Acute Care Waiver of Informed Consent;
   [ ] Gene Therapy; [ ] Collection of Biological Specimens; [ ] NIH Coop Groups (i.e. SWOG, RTOG);
   [ ] Academic Degree / Required Research; [ ] Drug Research; [ ] Other Research Categories;
   [ ] HIPAA; [ ] HIPAA Waiver; [ ] Alcohol Research; [ ] Certificate of Confidentiality;
   [ ] Clinical Research Office (UK); [ ] Data Safety & Monitoring Board; [ ] Deception; [ ] Gene Transfer;
   [ ] International Research; [ ] Internet; [ ] Medical Device; [ ] Placebo Controlled Trial;
   [ ] Recombinant DNA; [ ] Pluripotent Stem Cell Research; [ ] Transplants; [ ] Vaccine Trials;
   [ ] Waiver of Informed Consent; [ ] Waiver of Requirement for Documentation of Informed Consent;
   [ ] Collection of Bio Specimens for Banking(VA);

41. Our records indicate that the items marked with an "X" apply to your research:
   [ ] Approved Drug for Unapproved Use; [ ] FDA Approved Device(s); [ ] FDA Approved Drug for Approved Use;
   [ ] Investigational New Device; [ ] Investigational New Drugs; [ ] New Drug for Cancer;
[ ] None of the above drug/devices; [ ] Other Drug/Device;

42. Our records indicate the following as the funding source for your research: (Make whatever changes are necessary to correctly reflect the funding status of your research):

[ ] Federal Agencies other than HHS/NIH; [ ] State; [ ] Internal Grant Program;
[ ] Other Institutions of Higher Education; [ ] (HHS) Department of Health & Human Services;
[ ] Industry (other than Pharmaceutical Companies); [ ] Pharmaceutical Company;
[ ] Private Foundation / Association; [ ] Other Federal Agencies; [ ] Detailed Protocol/Grant Application;
[ ] General Clinic Research Center; [ ] (NIH) National Institutes of Health;
[ ] (CDC) Center For Disease Control; [ ] (SAMHSA) Administration;
[ ] (HRSA) Health Resources and Services Administration; [ ] Veteran’s Affairs (VA);
[ ] National Science Foundation;

UKRF Grant/Contract #_________________

43. Select and use appropriate statement below:

For Extramurally Sponsored Studies or FDA Regulated Studies

_____ I have reviewed all the investigational data from this study, including a compilation of all internal and external adverse event/unanticipated problems along with information from the sponsor including, if applicable, updated investigator brochures and data and safety monitoring board reports and conclude that the human subject risk/benefit relationship is not altered and that it is not necessary to modify the protocol or the informed consent process.

OR

_____ I have reviewed all the investigational data from this study, including a compilation of all internal and externally generated adverse event/unanticipated problems along with information from the sponsor including, if applicable, updated investigator brochures and data and safety monitoring board reports and conclude that the risk/benefit relationship has been altered. We have previously or are in the process of submitting requests, with this report, for modification of the research protocol and informed consent process.

43a. For Studies Without Extramural Funding

_____ I have reviewed all the investigational data from this study, including a compilation of all internal and external adverse event/unanticipated problems and conclude that the human subject risk/benefit relationship is not altered and that it is not necessary to modify the protocol or the informed consent process.

OR

_____ I have reviewed all the investigational data from this study, including a compilation of all internal and externally generated adverse event/unanticipated problems conclude that the risk/benefit relationship has been altered. We have previously or are in the process of submitting requests, with this report, for modification of the research protocol and informed consent process.

Principal Investigator Signature:_____________________________________________________

Date:_____________________________________________________

Please retain a copy of this completed application in your study records.

Oct-2007
<table>
<thead>
<tr>
<th><strong>Reviewer’s Recommendations</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Approve</td>
</tr>
<tr>
<td>□ Approve pending minor revisions/additional information (you review)</td>
</tr>
<tr>
<td>□ Withhold approval for major revisions/additional information (committee reviews at meeting)</td>
</tr>
<tr>
<td>□ PI does not need to attend meeting</td>
</tr>
<tr>
<td>□ PI needs to attend meeting</td>
</tr>
<tr>
<td>□ Withhold approval for other (circle one: full review expedited review)</td>
</tr>
<tr>
<td>□ Change Review type to (circle one: full review expedited review)</td>
</tr>
</tbody>
</table>

**Recommended Interval for Continuation Review:**  □ 12 months  □ 6 months  □ Other ____________________

(Reviewer’s Signature) ____________________  (Date) ____________

---

University of Kentucky Institutional Review Board  7/24/07
**IRB Continuation Review**  
**CRITERIA FOR IRB APPROVAL**

1.  
   - Risks are reasonable in relation to anticipated benefits, and the importance of the knowledge.
   - Procedures are consistent with sound research design/no unnecessary exposure to risk.
   - Procedures used are already being performed for diagnostic/treatment purposes.
   - Likelihood of harm and magnitude of harm addressed (in research proposal).
   - The research is likely to achieve its proposed aims.
   - The importance of the knowledge expected to result is clear.

2.  
   - Subject selection is equitable (in relation to:)
   - Objectives of the research;
   - The setting in which the research is to take place;
   - The special problems of research involving special populations;
   - Recruitment methods
   - Inclusion/exclusion criteria

* If N/A for any of #3 below, “Form E” (a request for waiver/alteration of the informed consent process) must be completed by the PI and the criteria met.

3.  
   - Adequate provisions are in place for seeking informed consent.
     - N/A*
   - Subject/subject’s LAR are allowed sufficient opportunity to consider whether to participate.
     - N/A*
   - The possibility of coercion or undue influence is minimized.
     - N/A*
   - The language is understandable to the subject/subject’s LAR.
     - N/A*
   - No exculpatory language waiving or appearing to waive any of the subject’s legal rights.
     - N/A*
   - No exculpatory language releasing PI/sponsor/institution/agents from liability for negligence.
     - N/A*

** If N/A for #4 below, “Form F” (a request for waiver/alteration of documentation of informed consent) must be completed by the PI and the criteria met.

4.  
   - The provisions for documenting informed consent/assent are appropriate.
     - N/A**

5.  
   - Adequate provisions are in place for protecting the privacy of subjects.

6.  
   - Adequate provisions are in place for maintaining confidentiality of the data.

7.  
   - Research staff/investigators have the appropriate expertise.

8.  
   - The research setting supports adequate safeguards.

9.  
   - Additional safeguards for vulnerable populations are included.
     - N/A

10.  
    - For greater than minimal risk, clinical research, or NIH funded/FDA regulated clinical trial, adequate provisions are in place for monitoring the data collected.
     - N/A

11.  
    - If a multicenter study & lead PI/UK is coord. inst., communication among sites is adequate.
     - N/A

12.  
    - Proposed payment and/or cost to subjects is appropriate.
     - N/A

13.  
    - If PI/research staff conflict of interest (COI), the COI in relation to human research protections is appropriately minimized or managed (e.g., limit who obtains informed consent; add disclosure(s) in informed consent process, etc...).
     - N/A

14.  
    - Review and approval by other committees/units has been conducted.
     - N/A

15.  
    - Approval from external institutions has been obtained from an authorized official.
     - N/A

16.  
    - A signature assurance sheet appropriately signed is on file.
     - N/A

University of Kentucky Institutional Review Board  
6/15/07
IRB Continuation Review
Primary Reviewer Checklist

<table>
<thead>
<tr>
<th>Reviewer:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Principal Investigator:</td>
<td>IRB #:</td>
</tr>
</tbody>
</table>

Some of the following may or may not apply to the research. You only need to provide comments/recommendations for items deemed to involve controverted issues.

[MINOR concerns include, but are not limited to: typographical errors, grammar, pagination, headers/footers, template language, signatures; MAJOR concerns include, but are not limited to: risk/benefit ratio, ethical concerns, cognitive ability, failure to obtain consent, waiver of consent, etc.]

<table>
<thead>
<tr>
<th>Area to Address</th>
<th>Page</th>
<th>Specific Requests/Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consent Document(s)/Process</td>
<td></td>
<td>For Minor concerns regarding the consent document submitted for approval, you may write the corrections on your copy of the consent document(s) and return it to the ORI staff person. For other minor or major concerns about the consent document(s)/process, please describe in the space to the right.</td>
</tr>
<tr>
<td>Study Personnel Changes:</td>
<td></td>
<td>□ Human subject protections training for each new (or existing) study personnel (SP) has not been completed. □ Other (e.g., expertise not appropriate). Please describe:</td>
</tr>
<tr>
<td>Unanticipated problem(s)/Adverse Event(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subject Withdrawals</td>
<td></td>
<td></td>
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<tr>
<td>Deviations/Exceptions/Violations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other (e.g., unanswered question, form missing):</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
VA Research: Reviewer Checklist

<table>
<thead>
<tr>
<th>Reviewer:</th>
<th>IRB #:</th>
<th>PI:</th>
<th>Date Mailed:</th>
</tr>
</thead>
</table>

Title of Project: __________________________

Deadline for submitting final recommendation to ____________, Kinkead Hall 0057: ________________

**Instructions:** Review the criteria below which applies to the proposed research. IRB approval should only be issued if all criteria are met. Check the appropriate boxes within the “Reviewer Determination” section to document your determination, and sign and date on the line provided.

### Reviewer Determination

<table>
<thead>
<tr>
<th>N/A</th>
<th>I. Payment to Subjects – REQUIRED DETERMINATION</th>
</tr>
</thead>
</table>
| ☐ N/A | If the research **proposes payment** to subjects, *select A or B*:

**A.** ☐ Payment is prohibited because the research is integrated with the subject’s medical care and the research makes no special demands on the subject beyond those of standard medical care. N/A ☐

**B.** ☐ Payment is permitted because *(select one)*:
- ☐ The proposed study is not directly intended to enhance the diagnosis or treatment of the medical condition for which the subject is being treated, and the standard of practice in affiliated non-VA institutions is to pay subjects in this situation.
- ☐ The proposal is a multi-institutional study, and subjects at a collaborating non-VA institution are to be paid for the same participation in the same study at the same rate proposed.
- ☐ The proposal offers a comparable situation in which, in the opinion of the IRB, payment of subjects is appropriate.
- ☐ Transportation expenses incurred by the subject, that would not be incurred in the normal course of receiving treatment, would not be reimbursed by any other mechanism.
| N/A |

<table>
<thead>
<tr>
<th>N/A</th>
<th>II. Flagging Medical Records – REQUIRED DETERMINATION</th>
</tr>
</thead>
</table>
| ☐ N/A (e.g., no identifiers) | Does the subject’s medical record (electronic or paper) need to be flagged to protect his/her safety by indicating their participation in the study (date entered study, date study participation terminated) and the source of more information on the study? If “NO”:

The IRB is waiving the requirement to flag the subject’s medical record because *(select one)*:
- ☐ subject’s participation in the study involves only one encounter, involves only the use of a questionnaire or the use of previously collected biological specimens;
  - OR
- ☐ identification of the patient as a subject in a particular study (if the study is not greater than minimal risk) would place the subject at greater than minimal risk
| N/A |

<table>
<thead>
<tr>
<th>☐ III. REQUIRED DETERMINATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>☐ The research proposal meets all of the applicable criteria in the list that follows. The research proposal does not meet all of the applicable criteria in the list that follows (you may make requests, comments, and/or explanations in the space that follows, or circle the criterion not met).</td>
</tr>
</tbody>
</table>

**Comments:**

Reviewer Signature: __________________________ Date: __________________________
<table>
<thead>
<tr>
<th>N/A</th>
<th>Payment to Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>o The description of payment is adequate (includes timing; method of payment; and the informed consent details the payment process and whether the amount will be reported to the IRS and may be counted as income). N/A</td>
</tr>
<tr>
<td>2.</td>
<td>o The investigator has substantiated in the research proposal that payments are reasonable and commensurate with the expected contributions of the subject and they do not constitute undue pressure/influence to participate or enroll in the research study. N/A</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N/A</th>
<th>Data and Safety Monitoring [required for greater than minimal risk studies, clinical research, NIH funded/FDA-regulated clinical trials]</th>
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</thead>
<tbody>
<tr>
<td>3.</td>
<td>o The research plan: N/A</td>
</tr>
<tr>
<td></td>
<td>• describes adequate provisions for monitoring data collected to ensure the safety of subjects; N/A</td>
</tr>
<tr>
<td></td>
<td>• includes a plan for reporting findings to the IRB; N/A</td>
</tr>
<tr>
<td></td>
<td>• includes procedures for reporting to other appropriate agencies; N/A</td>
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<tr>
<td></td>
<td>• includes establishing a Data Safety Monitoring Board (DSMB); N/A</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N/A</th>
<th>Continuation Review [The following items represent the additional criteria to be met for IRB approval of VA research.]</th>
</tr>
</thead>
<tbody>
<tr>
<td>4.</td>
<td>o At continuation review, the following items were reviewed: N/A</td>
</tr>
<tr>
<td></td>
<td>• Brief summary of research methodology and procedures N/A</td>
</tr>
<tr>
<td></td>
<td>• Cumulative # of subjects withdrawn since inception of project and reason N/A</td>
</tr>
<tr>
<td></td>
<td>• Number considered vulnerable populations N/A</td>
</tr>
<tr>
<td></td>
<td>• An assurance that all serious adverse events and unanticipated problems involving risk to subjects or others are reported N/A</td>
</tr>
</tbody>
</table>

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<tr>
<th>Informed Consent</th>
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<tbody>
<tr>
<td>5.</td>
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<td>6.</td>
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<td>7.</td>
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</table>
conducted under the supervision of one or more VA employees, subjects are eligible for treatment unless injuries are due to noncompliance by a research subject with study procedures. VA will provide medical care in those circumstances where VA has some responsibility for the need for medical care. If this study meets these criteria, the following statement should be included in this section: “If you are eligible for Veterans Affairs medical benefits, the VA may provide medical care if you get hurt or get sick as a result of taking part in this study. The necessary care must be provided in a VA medical facility unless an exception is granted. In cases of exceptions, the VAMC Director may contract for such care. Exceptions include: situations where a VA facility is not capable of furnishing economical care, situations where a VA facility is not capable of furnishing the care or services required and situations involving a non-veteran research subject. The VA does not provide medical treatment for a research-related injury in cases where injuries result from noncompliance by a research subject with study procedures.

A co-payment from you may be required for medical care and services provided by the VA.”

If this study proposes recruitment of non-veterans, the consent form should contain a statement outlining what medical care will be provided in case of a research-related injury pertaining to non-veterans enrolled in a VA approved study.

<table>
<thead>
<tr>
<th>WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS, CONCERNS, OR COMPLAINTS?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Section:</td>
</tr>
<tr>
<td>➔ Includes investigator contact info</td>
</tr>
<tr>
<td>➔ Includes ORI contact info for questions about rights as a volunteer in the research (&quot;Office of Research Integrity at the University of Kentucky at 859-257-9428 or toll free at 1-866-400-9428&quot;).</td>
</tr>
<tr>
<td>➔ Includes contact info for the Associate Chief of Staff for Research &amp; Development (ACOS/R&amp;D) or the Administrative Officer for Research &amp; Development (AO/R&amp;D) [859-281-4927] as an additional office to call if the subject has concerns or questions about his/her rights and welfare.</td>
</tr>
</tbody>
</table>

| WHAT ELSE DO YOU NEED TO KNOW? Section: |
| Include statement (required for veteran subjects): |
| "If you are a veteran taking part in a research study at the VAMC, a copy of your signed/dated consent form will be placed in your medical record". |

| WHAT ELSE DO YOU NEED TO KNOW? |
| If the researcher believes that bodily fluids, substances or tissues of a research subject could lead to the development of a commercially valuable product statement included: |
| "I authorize the use of my bodily fluids, substances or tissues for research purposes. The sample(s) (blood, tissue or fluids) that I am giving might be used in studies that lead to new products for research, diagnosis or treatment. These products may have some commercial value. By signing this consent form, I give up all rights to any commercial application related to information or samples that I have given during my participation in this research project". |

| In addition to the standard signature (and date) lines (per UK’s model consent form), the Signatures section includes a line for the signature and date of a witness whose role is to witness the subject’s or the subject’s legally-authorized representative’s signature. |

8. The investigator has provided formal delegation of the responsibility for obtaining informed consent and the delegate has appropriate training (e.g., CITI) as well as any appropriate study-specific training. [If no, the IRB may not issue approval for the delegate to obtain informed consent.]  

9. For recruitment of decisionally impaired subjects, "Form T" is completed and included in the IRB application and the following criteria are satisfactorily addressed (see “Form T” Section 3 and select questions under “Form T” Section 2):  

N/A

Vulnerable Populations (that may be considered as research subjects in an approved VA research study)  
[Note: The UK IRB does not approve recruitment of children or pregnant women from the VAMC; VA policy will not allow enrollment of prisoners unless a waiver from the requirement is granted.]  

N/A
### VA Research: Reviewer Checklist

<table>
<thead>
<tr>
<th>Reviewer:</th>
<th>IRB #:</th>
<th>PI:</th>
<th>Date Mailed:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Title of Project:</strong></td>
<td></td>
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</tbody>
</table>

- [Per PI’s response to Section 2, #1] Individuals with impaired decision-making capacity are suitable for this research and there is compelling justification for their inclusion. [Note: When competent subjects can be used, VA subjects determined to be incompetent may not be recruited.]

- [Per PI’s response to Section 3, #1] Procedures for communicating that participation is voluntary are adequate.

- [Per PI’s response to Section 3, #2] Adequate procedures are in place to ensure that subject’s representatives are well informed regarding their roles and obligations to protect the subject.

- [Per PI’s response to Section 3, #4] If the research presents some probability of harm, there is at least a greater probability of direct benefit.

<table>
<thead>
<tr>
<th>Non-Veteran Recruitment</th>
<th>N/A □</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>[applies to studies being conducted exclusively at the VA (e.g., does not include a UK study)]</strong></td>
<td></td>
</tr>
<tr>
<td>10. □ If non-veterans are to be considered for recruitment, it has been determined that there are insufficient veterans available to complete the study.</td>
<td>N/A □</td>
</tr>
<tr>
<td>11. □ If this study proposes recruitment of non-veterans, a statement is included in the consent form outlining what medical care will be provided in case of a research-related injury pertaining to non-veterans enrolled in a VA approved study.</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tissue/Specimen Banking</th>
<th>N/A □</th>
</tr>
</thead>
<tbody>
<tr>
<td>12. □ The research involves the banking of human biological specimens and the proposal indicates the specimens will be maintained at either a VA-sponsored or VA (ORD) approved tissue bank.</td>
<td></td>
</tr>
</tbody>
</table>

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6/13/07  
J:\Master Outreach Documents\Survival Handbook\F - IRB applications-Forms\Reviewer Documents\Checklists\270000-Criteria_for_Approval_VA_CHECLLIST_revised.doc
**Modalities Reviewer Signature Page**

**ORI USE ONLY**

<table>
<thead>
<tr>
<th>IRB Reviewer:</th>
<th>IRB #:</th>
<th>PI:</th>
</tr>
</thead>
</table>

- [ ] Single reviewer (change is "minor")
- [ ] Full Review Scheduled

**Title of Project:**

*See “Guidance on Expedited Review of Minor Changes in Previously Approved Research” for what constitutes a minor change.*


---

Please mark the applicable box(es) under each section:

**Section I.** (refer to Criteria for IRB Approval checklist on the back of this page, if necessary)

- [ ] A. The criteria for IRB approval are met.
- [ ] B. The criteria for IRB approval are *not* met.

**Section II.**

Any previously approved research categories requiring documented determinations:

- [ ] A. are not affected by this modification request;
- [ ] B. are affected by this modification request *(requested revisions specified in the comments section apply).*

Examples:

- eligibility for expedited review (Form A-1);
- waiver of informed consent (Form E);
- waiver of documentation of informed consent (Form F);
- decisionally impaired/challenged (Form T);
- pregnant women (Form U);
- fetuses &/or neonates (Form U);
- prisoners (Form V);
- children (Form W);

---

**Section III.**

IRB Determination:

- (1) Approved (I.A and II.A above apply)
- (2) Approval Pending Minor Revisions – non-substantive materials requested. Subsequent expedited review of PI response (see “Comments/Requested Revisions” below).
- (3) Approval Deferred – substantive clarifications or modifications regarding the protocol or informed consent document(s) required. Subsequent review at convened meeting. PI not required to attend.
- (4) Approval Deferred – substantive clarification or modification regarding the protocol or informed consent document(s) required. Subsequent review at convened meeting. PI attendance required.
- (5) Disapproved – Determination made at a convened meeting.

**Comments/Requested Revisions**

Please specify which forms are needed, if any, to appropriately document required determinations (e.g., Form E for waiver of informed consent). Attach additional pages, if necessary:

---

**IRB Reviewer Signature**

**Date**

6/13/07

J:\Master Outreach Documents\Survival Handbook\F - IRB applications-Forms\Reviewer Documents\Signature Pages\Modification_Reviewer_Sign_page.doc
CRITERIA FOR IRB APPROVAL
University of Kentucky Institutional Review Board

1. Risks are reasonable in relation to anticipated benefits, and the importance of the knowledge.
   - Procedures are consistent with sound research design/no unnecessary exposure to risk.
   - Procedures used are already being performed for diagnostic/treatment purposes.
   - Likelihood of harm and magnitude of harm addressed (in research proposal).
   - The research is likely to achieve its proposed aims.
   - The importance of the knowledge expected to result is clear.

2. Subject selection is equitable (in relation to:)
   - Objectives of the research;
   - The setting in which the research is to take place;
   - The special problems of research involving special populations;
   - Recruitment methods
   - Inclusion/exclusion criteria

3. Adequate provisions are in place for seeking informed consent. N/A*
   - Subject/subject’s LAR are allowed sufficient opportunity to consider whether to participate. N/A*
   - The possibility of coercion or undue influence is minimized. N/A*
   - The language is understandable to the subject/subject’s LAR. N/A*
   - No exculpatory language waiving or appearing to waive any of the subject’s legal rights. N/A*
   - No exculpatory language releasing PI/sponsor/institution/agents from liability for negligence. N/A*

4. The provisions for documenting informed consent/assent are appropriate. N/A**

5. Adequate provisions are in place for protecting the privacy of subjects.

6. Adequate provisions are in place for maintaining confidentiality of the data.

7. Research staff/ investigators have the appropriate expertise.

8. The research setting supports adequate safeguards.

9. Additional safeguards for vulnerable populations are included. N/A

10. For greater than minimal risk, clinical research, or NIH funded/FDA regulated clinical trial, adequate provisions are in place for monitoring the data collected. N/A

11. If a multicenter study & lead PI/UK is coord. inst., communication among sites is adequate. N/A

12. Proposed payment and/or cost to subjects is appropriate. N/A

13. If PI/research staff conflict of interest (COI), the COI in relation to human research protections is appropriately minimized or managed (e.g., limit who obtains informed consent; add disclosure(s) in informed consent process, etc...). N/A

14. Review and approval by other committees/units has been conducted. N/A

15. Approval from external institutions has been obtained from an authorized official. N/A

Note: You are evaluating this protocol because you have a close working knowledge, understanding and appreciation of prison conditions from the perspective of the prisoner, and/or the appropriate background and experience to serve as a prisoner representative.

Given the context of this review [Initial Review, Continuation Review, Modification Review, or Unanticipated Problem/Adverse Event Review], you are being asked to:

• assess the appropriateness of the research for the prisoner population;
• assess the appropriateness of the proposed method of obtaining informed consent;
• assess whether the research represents the category of research permissible under 46.306(a)(2) [as specified by the PI in Section 1 of “Form V”, if applicable];
• assess whether the research meets the conditions for approval outlined in 45.305 [as specified by the PI in Section 2 of “Form V”, if applicable].
• identify other issues relating to the nature of the research that may be of concern (e.g., appropriate space for procedures, appropriate facilities for managing adverse events, “Form V”, if applicable).

Comments/Requested Revisions (Attach additional sheets, if necessary):

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Prisoner Representative Signature

DATE

6/21/07

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