



EXPEDITED REVIEW PROCEDURE

08/13/2008

It is the policy of the Duke University Health System IRB (DUHS IRB) that qualified human subject research be reviewed using the expedited procedure in accordance with federal regulations. An expedited procedure refers to review of research involving human subjects by the IRB Chair, Vice Chair or qualified IRB member designee in accordance with 45 CFR 46.110 and 21 CFR 56.110.

Background and Definitions

New and ongoing research activities that present no more than minimal risk to human subjects, and involve only procedures listed in one or more of the following categories, or involve only minor changes in previously approved research during the period (one year or less) for which approval is authorized, may be reviewed by the DUHS IRB through the expedited review procedure authorized by 45 CFR 46.110 and 21 CFR 56.110. In compliance with 45 CFR 46.110(b) and 21 CFR 56.110(b), the review may be carried out by the IRB Chair or by an experienced reviewer designated by the IRB Chair from among the members of the IRB (referred to here as designee). An experienced member is one who has been an IRB member for at least one year. Experienced members who are designated by the Senior Chair, in conjunction with the Executive Director, to conduct expedited reviews include, but are not limited to: Chairs, Vice Chairs, Executive Director, and Director, IRB Education Programs. The Senior Chair in conjunction with the Executive Director annually reviews this list and updates it as needed, and IRB staff select one reviewer from this list for each study to be reviewed using the expedited procedure. This reviewer receives and reviews all material that a convened IRB would receive were it to review the research.

Whether for initial review or continuing review, the reviewer evaluates whether the research undergoing review using the expedited procedure:

- Meets all applicability criteria.
- Represents one or more approvable categories of research.
- Designates which category(ies) of approval will apply to the research.

The reviewer uses one of the following review checklists to determine that the research meets the regulatory criteria for approval:

- Primary Reviewer Checklist - New Protocol
- Primary Reviewer Checklist - Continuing Review
- Primary Reviewer Checklist – Business Item / Amendment

For the review of a modification to previously approved research, the reviewer determines that the modification represents a minor change as defined below.

In reviewing the research, the Chair/designee may exercise all of the authorities of the IRB except that the reviewer may not disapprove the research. For example, the reviewer may approve, require modifications to secure approval, or defer action pending receipt of additional information from the investigator. However, a research activity may be disapproved only after review in accordance with the non-expedited procedures set forth in 45 CFR 46.108(b) and 21 CFR 56.108(c).

Minimal risk means that 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(i) and 21 CFR 56.102(i)]. The DUHS IRB interprets this definition to encompass the procedure practiced by the DUHS IRB of regarding minimal risk as the risk encountered by a healthy person in the course of normal daily living. This DUHS procedure is also consistent with the definition of minimal risk set forth in 45 CFR 46.303(d).

A change is minor if it does not represent a material change in the research, i.e.,

- (a) the change does not adversely alter the overall risk/benefit ratio;
- (b) the change will not potentially adversely affect the willingness of current participants to remain in the study or the willingness of potential participants to enroll in the study;
- (c) the change will not diminish the scientific validity of the study,
- (d) any added revision or procedure involves no more than minimal risk to subjects, and
- (e) any added procedure falls into one of the categories (1)-(7) of research that can be reviewed using the expedited procedure.

Applicability:

Activities for Which the Use of the Expedited Review Procedure Is Permissible

(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. 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) Investigators 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) below pertain to both initial and continuing IRB review.

(A) Initial and Continuing Review

As described in OHRP guidance (63 FR 60364-60367), dated November 9, 1998, the following categories of research may be reviewed by the IRB through the expedited procedure. These categories are also available online at: <http://www.hhs.gov/ohrp/humansubjects/guidance/expedited98.htm>.

(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 increase 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, non-pregnant 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.

(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.)

(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis).

(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.

(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 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.

Research in any of these categories may require review at a convened meeting of the IRB if the circumstances of the proposed research involve more than minimal risk.

(B) Approval of Investigator's Response to a Convened Board's Request for Changes following Initial or Continuing Review

The IRB may use the expedited review procedure to approve an investigator's response to a convened board's request for minor changes following initial or continuing review of an IRB protocol. Examples of changes (a) that are not minor, and (b) that are minor are described below.

(a) When IRB approval of a research project is contingent upon substantive change/amplification/clarification/explanation/justification/simplification, the following procedures apply:

When the IRB asks substantive questions about the protocol/consent form or requests additional information that is directly relevant to the IRB's determination of whether the research meets the regulatory criteria for approval (45 CFR 46.111 or 21 CFR 56.111), then approval of the proposed research must be deferred, pending subsequent review of the investigator's response by the IRB at a convened meeting.

Examples of board actions requiring review of the investigator's response by the convened board:

- Request for additional information on pre-clinical or clinical experience with the drug/device/biologic. This additional information is directly relevant to the board's determination of whether risks to subjects are reasonable in relation to anticipated benefits.
- Request for justification and rationale for doing research biopsies in healthy volunteers. The response has direct bearing on minimizing risks by using procedures that do not unnecessarily expose subjects to risk.

(b) However, the IRB may stipulate specific revisions requiring only simple concurrence by the investigator, or request additional information that is not relevant to the IRB's determination of whether the revised research meets the regulatory criteria for approval; these revisions are regarded as minor changes.

If the investigator's response is concordant with the stipulations, or the additional information is provided as requested, the IRB Chair/designee may approve the revised protocol on behalf of the convened board using the expedited review procedure. Board action to permit this would be to approve the protocol subject to the required modifications being made.

Examples of board actions permitting review of the investigator's response using the expedited procedure:

- Rather than asking the investigator to describe plans for monitoring the data to ensure the safety of subjects, the board determines what level of monitoring is appropriate and requires the investigator to incorporate the stipulated plan into the protocol.
- Although there might be some ambiguity in the protocol regarding the age range of subjects to be enrolled, the board determines that one or more age ranges would meet the regulatory requirements for approval. The investigator is asked to specify which will be the criterion for eligibility, and if the choice fits within the IRB's predetermined acceptable range, the protocol may be approved using the expedited review procedure.

- Although it is unclear whether results of genetic testing will be returned to subjects, rather than asking the investigator to clarify, the board determines whether results should be returned and the investigator is asked to concur with the board's decision.
- To further minimize the risk to individual participants, the board requires that those with known history of a particular condition, for example known heart disease, be excluded from participation.
- To assist in the future review of a protocol, the IRB asks the investigator to add specific information from the sponsor's protocol to the IRB protocol summary.

(C) Minor Changes in Previously Approved Research

For research previously approved by a convened IRB, the IRB may use the expedited review procedure to review minor changes in previously approved research during the period (one year or less) for which approval is authorized.

Examples of this include:

- Acknowledgement of an adverse event report that is determined not to represent an unanticipated problem involving risks to subjects or others.
- Initially determining (subject to confirmation by a convened IRB) that an adverse consequence of research participation represents an unanticipated problem involving risks to subjects or others.
- Approving a waiver of consent/HIPAA authorization for ascertainment and recruitment of potential subjects.

The IRB may also use the expedited review procedure to review any change to research previously approved using the expedited procedure, as long as the change meets the above definition of "minor".

Actions To Be Taken By The IRB Chair/Designee

The IRB Chair/designee is responsible for determining whether the research is eligible for review using the expedited procedure. The IRB Chair/designee, once determining that the research meets the applicability criteria for review using the expedited procedure, then uses the listing of expedited review categories published in the Federal Register at 63 FR 60364-60367 (noted above) to guide him/her in determining if the research fits within the applicable expedited review categories. If applicable, the IRB Chair/designee also documents that the consent form includes the basic elements of consent +/- HIPAA authorization or documents protocol-specific findings permitting approval of a waiver or alteration of consent +/- HIPAA authorization.

If the proposed research is not eligible for review using the expedited procedure, the IRB Chair/designee requests that the research protocol be scheduled for review at a convened IRB meeting.

The IRB Chair/designee may consult another IRB member(s) or a non-IRB member consultant with special expertise in the scientific area or discipline or special population being studied; however the IRB Chair/designee is responsible for the review and approval of research using the expedited procedure. When a consultant is to be used, the IRB Chair/designee follows the policies and procedures for use of a consultant as described in DUHS IRB Use of Consultants.

When the IRB Chair/designee requires modifications to secure approval or defers action pending receipt of additional information, the investigator is notified in writing of the required modifications or additional information required for review. The investigator is asked to submit a point-by-point response and revised documents to the IRB.

When received, the IRB Chair/designee reviews the investigator's response, including revised documents, and indicates whether the modifications have been made as requested and whether the protocol can receive final approval. The IRB Chair/designee may continue to request additional modifications or information until the protocol is approved or referred for review at a convened meeting of the IRB.

The IRB Chair/designee may use the Expedited Review Checklist to document approval and provide the basis for approving the protocol/protocol-associated document through the expedited review procedure. The IRB Chair/designee may request additional information from the investigator to make this determination.

Notification of IRB Approval Resulting From Use of the Expedited Review Procedure

The investigator is notified of the outcome of a review that uses the expedited procedure. This notification process is consistent with that described elsewhere for initial or continuing review. If ancillary committee review is required, this review is provided to the person performing the review using the expedited procedure, which must occur prior to final approval by the IRB reviewer.

IRB members are informed of all research activities approved using the expedited procedure by way of the report of expedited review activities. This report listing all new and ongoing research activities approved using the expedited procedure is distributed with the agenda and meeting materials for the next convened IRB meeting following preparation of the report.