DUKE UNIVERSITY HEALTH SYSTEM
Human Research Protection Program

EXPEDITED REVIEW

12/19/2023

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 an IRB Chair, Executive Director, 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 categories listed below, or involve only minor changes in previously approved research during the period for which approval is authorized, may be reviewed by the DUHS IRB through the expedited review procedure authorized by 45 CFR46.110 and 21 CFR 56.110.

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 Lead Chair, in conjunction with the Executive Director, to conduct expedited reviews include, but are not limited to: Chairs, Executive Director, and IRB Administrative Reviewers.

Items for expedited review will be assigned to reviewers by the Administrative Manager or other designated IRB staff member. If, for reason of competing priorities, a self-identified conflict of interest, or reluctance due to more limited expertise than another designated expedited reviewer, the assigned reviewer requests the review responsibility be reassigned, they will indicate the need for the reassignment, and an IRB staff member will reassign the review responsibility.

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 expeditable categories of research.
- Designates which category(ies) of approval will apply to the research.

If an expedited reviewer determines that research appearing on the list of expedited categories of research is more than minimal risk, thus needing a review by the convened board, the reviewer documents their rationale for that decision in iRIS.

The reviewer may use one of the following review checklists as a guide 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 Continuing Review by the expedited procedure, the reviewer will consider (among other documents), the continuing review progress report, which includes a summary since the last IRB review of any complaints about the research, amendments or modifications in the research, and any interim findings that may have come out in the past year.

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. The reviewer may approve, require modifications to secure approval, or defer action pending receipt of additional information from the investigator. 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(j) and 21 CFR 56.102(i)]. The DUHS IRB interprets this definition minimal risk to mean the risk encountered by a healthy person in the course of normal daily living. This DUHS interpretation 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 involving no more than minimal risk to participants,
e) any added procedure that 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 categories listed below, 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 the 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 at the OHRP web site: https://www.hhs.gov/ohrp/regulations-and-policy/guidance/categories-of-research-expedited-review-procedure-1998/index.html

(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.

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 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 non-research 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 of categories 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.

(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.

In addition, the following categories not listed in the OHRP guidance (63 FR 60364-60367) may also be eligible for expedited review:

- Administrative Review of a protocol for which Duke is not the IRB of record, including any changes to consent documents submitted/amended for use at Duke.
- A study of a humanitarian use device for which a convened board has determined that continuing review may occur using the expedited procedure per 21 CFR 56.110

- Review of a blanket protocol to provide approval of the grant. No research will be conducted under the blanket protocol. All projects involving human subjects under the grant will be submitted to IRB individually.

- Coordinating Center or Statistical Center protocol, for which Duke activities are mostly administrative and no greater than minimal risk. Studies for which federal funding is routed through Duke may not undergo expedited review if the overall study activities are greater than minimal risk. See also HHS Guidance on Engagement of Institutions in Human Participant Research.

(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.

Changes regarded as minor:

- Specific revisions stipulated by the IRB requiring only simple concurrence by the investigator

- Requests for additional information that is not relevant to the IRB's determination of whether the research meets the regulatory criteria for approval

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. This action is permitted when the IRB requires modifications (stipulated in the meeting) to secure approval**.**

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

- If the submission does not include an adequate plan for monitoring the data to ensure the safety of participants, 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 participants 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 participants, 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.

Changes that are NOT minor and that may not be expedited by the Chair:

- 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.

- When the investigator refuses to make modifications stipulated by the convened board, the Chair cannot approve the protocol. The modifications proposed by the investigator, and their justification for not making the IRB's changes, must be reviewed by the convened IRB for approval for disapproval.

Other 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 participants 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 participants to risk.

(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. The definition of a minor change is listed above.

Examples of a minor change 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 participants.

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 then determines the applicable category of expedited review. If applicable, the IRB Chair/designee also documents that the consent form includes the basic elements of consent +/- HIPAA authorization, agrees with the investigator who documents protocol-specific findings permitting approval of a waiver or alteration of consent +/- HIPAA authorization, or requires changes to the request for 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 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 it is referred for review at a convened meeting of the IRB. This may occur if the investigator requests such a review, or if the IRB Chair/designee concludes that their further dialogue with the investigator about the requested protocol changes would be unlikely to resolve their disagreement.

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 available to the expedited reviewer in iRIS and must occur prior to final approval by the IRB.

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 posted monthly in iRIS, on the IRB #7 meeting agenda, and is available for all members to view.

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