



AMENDMENTS TO PREVIOUSLY APPROVED RESEARCH

4/5/2021

The Duke University Health System Institutional Review Board (DUHS IRB) requires that principal investigators promptly report to the IRB proposed changes in a previously approved research activity. Changes in approved research, including changes to informed consent documents, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject (45 CFR 46.108(a)(3)(iii) and 21 CFR 56.108(a)(3)-(4)). It is the policy of the DUHS IRB to review all requests for amendments to previously approved research to determine if a change in the risk/benefit ratio of the study has occurred.

Definitions

1. **Amendment**: Any change to an IRB-approved study protocol regardless of the level of review it receives initially.
2. **Expeditable Amendment**: A proposed change in research-related activities that does not materially affect an assessment of the risks and benefits of the study and does not substantially change the specific aims or design of the study; a minor change to previously approved research.
3. **Non-Expeditable Amendment**: A proposed change in research-related activities that materially affects an assessment of the risks and benefits of the study or substantially changes the specific aims or design of the study.
4. **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)]. In practice, the DUHS IRB interprets this definition of minimal risk as the risk encountered by a healthy person in the course of normal daily living. This DUHS practice is also consistent with the definition of minimal risk set forth in 45 CFR 46.303(d).
5. **Minor change**: 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 that falls into one of the categories (1)-(7) of research that can be reviewed using the expedited procedure.

Note: An increase in blood draw volume that could otherwise be expedited as category 2 should also be examined against the already approved blood draw volume to confirm that the new total for adults does not exceed 5 ml/kg in any one 24 hour period, and 7 mL/kg in any eight week period and for children does not exceed 3 ml/kg in any 24 hour period, and 7 mL/kg in any eight week period. Increases above these limits must be specifically justified in the research protocol and approved by a convened IRB.

Expeditable Amendments

For research previously approved by a convened IRB, the IRB may use the expedited review procedure to review minor changes in previously approved research. 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”. Please refer to the HRPP policy titled “Expedited Review Procedure”.

Examples of amendments that may be reviewed using the expedited procedure include:

- The addition of research activities that would be considered exempt or eligible for expedited review if considered independent from the main research protocol;
- An increase or decrease in the proposed enrollment of research subjects without prolonging any subject’s period of exposure to study risks that are more than minimal, or without adversely affecting the study design;
- Narrowing the range of the inclusion criteria;
- Broadening the range of the exclusion criteria;
- Alterations in the dosage form (e.g., tablet to capsule or oral liquid) of an administered drug, provided the dose and route of administration remain constant;
- Decreasing the number or volume of biological sample collections, provided that such a change does not affect the collection of information related to safety evaluations;
- An increase in the length of confinement or number of study visits for the purpose of increased safety monitoring;
- A decrease in the length of confinement or number of study visits, provided that such a decrease does not affect the collection of information related to safety evaluations;

- Alterations in human research participant payment or liberalization of the payment schedule with proper justification;
- Changes to improve the clarity of statements or to correct typographical errors, provided that such a change does not alter the content or intent of the statement;
- The addition or deletion of key personnel; this is done with a “KSP change form” rather than a regular amendment. For a change in PI or co-PI, a regular amendment is needed to revise the application and study documents.
- The addition of study sites (which may require a Federal Wide Assurance (FWA) and appropriate IRB approval) or the deletion of study sites.

Non-Expeditable Amendments

For a proposed change in a research study that is not minor, could possibly introduce increased risk to study participants, or might adversely affect the willingness of current participants to remain in the study, the IRB must review and approve changes at a convened meeting before changes can be implemented. Examples of amendments not eligible for review using the expedited procedure may include but are not limited to:

- The addition to the informed consent document of a description of serious unexpected adverse events or other risks;
- Broadening the range of inclusion criteria;
- Narrowing the range of exclusion criteria;
- Alterations in the dosage or the route of administration of a drug;
- Extending the duration of exposure to the test material or intervention;
- The deletion of laboratory tests, monitoring procedures, or study visits directed at the collection of information for safety evaluations; or
- Changes, which, in the opinion of the IRB Chair/designee, do not meet the criteria or intent of a minor modification.

Re-consent/Notification of Participants

The IRB may decide that the changes to the research activities require a change in the informed consent documents and therefore warrant re-consenting of currently enrolled participants or notification of participants who have completed research interventions.

Change to Research-Related Injury Language

When a proposed change in a study involves a revision to the research-related injury language (RRIL) in the consent form(s), such change requires review by the Office of Research Contracts (ORC) to ensure consistency with the relevant language in the study’s legal contract. The study team would submit an amendment with the revised consent form(s) tracked. In addition, they would upload the email from ORC that includes the currently agreed-upon RRIL.

Exempt Research

Any proposed or anticipated changes in a study that was previously declared exempt from IRB review must be submitted to the IRB for approval prior to initiation of the change. The proposed amendment will then be evaluated for appropriate IRB review.

Investigator Responsibilities

Investigators must submit the exact text of an amendment or other revision to the protocol and any proposed changes to the consent documents or other study documents to the IRB. If changes are being made to consent form(s) or any other study documents, investigators must submit a "Track Changes" version of each affected document. Investigators should attach a list of changes and the relevant page number(s) where changes have been made to the sponsor's protocol, investigator brochure, questionnaires, and/or other documents.

The Investigator may make a modification to research activities **to avoid an immediate hazard to the participant**, and may do so without prior IRB approval, but must report this via iRIS within 10 business days as a Protocol Deviation/Violation.

Using iRIS to Submit an Amendment

All amendments must be created and submitted using the IRB electronic system iRIS. A study must be approved before it can be amended. A previous amendment must be approved before another can be created or submitted.

IRB Responsibilities

Amendments, as they are received by the IRB Office, will be triaged by the board specialists based on whether they are considered expeditable or non-expeditable. At any time, the board specialist may consult with the IRB Chair or Executive Director, or designee (the 'reviewer') for assistance in determining the type of review that is required to process the amendment. The reviewer may conduct expedited review of amendments that meet the definition of a minor change to previously approved research.

When a proposed change in a research study represents a non-expeditable amendment, the convened IRB must review and approve changes. A primary reviewer will be assigned and the amendment will be placed on the next available Meeting agenda. Each board member has access to the iRIS meeting agenda and full study documents prior to the meeting, as called for by the policy on Conduct of a Convened Meeting of the DUHS Institutional Review Board, with reference to amendments (business items).

In deciding whether to approve the research, the convened board uses the Primary Reviewer Checklist for Amendments and must decide as a board that the regulatory criteria for approval are met.

The convened board must determine whether re-consenting of currently enrolled participants is necessary and whether participants who have completed research involvement who might be affected should be re-contacted and provided with additional information. This determination should be based on new information regarding a change in the risk-benefit assessment that might possibly affect the participant's decision to continue with the research activities. The IRB must approve any proposed changes to the consent form language.

The IRB has a range of possible actions it may take for an amendment:

- Approve
- Modifications required
- Defer for more information
- Disapprove

Following the IRB meeting, the IRB Writer and Board Specialist will prepare a modification or approval notice, as applicable, denoting the IRB's findings. This will be forwarded to the Chair or his/her designee for signature, then forwarded to the Principal Investigator, via iRIS.

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