

THE NORTH SHORE MEDICAL CENTER Institutional Review Board (IRB) POLICIES AND PROCEDURES	IRB Policy Number: 024.1
Title: <i>Amendments to Approved Research</i>	Page: 1 of 4
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I. PURPOSE

The purpose of this policy is to define the procedures the North Shore Medical Center Institutional Review Board (NSMC IRB) follow to ensure prompt reporting to the NSMC IRB of proposed changes in approved non-exempt human-subjects research and clinical investigations and for ensuring that changes are not initiated without NSMC IRB review and approval, except where necessary to eliminate apparent immediate hazards to the subject. [45 CFR 46.103(4)(iii) and 21 CFR 56.108(3)(4)]

II. SCOPE

Non-exempt human-subjects research and clinical investigations approved by the NSMC IRB are subject to this policy.

III. DEFINITIONS

Department of Health and Human Services (DHHS) definitions:

Research: A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. [45 CFR 46.102(d)]

Human Subject: A living individual about whom an investigator (whether professional or student) conducting research obtains (1) Data through intervention or interaction with the individual, or (2) Identifiable private information.

Intervention includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

Interaction includes communication or interpersonal contact between investigator and subject.

Private information includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects. [45 CFR 46.102(f)(1)(2)]

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), 21 CFR 50.3(k)

Food and Drug Administration (FDA) definitions:

Clinical Investigation: Any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this chapter, regarding nonclinical studies. The terms *research*, *clinical research*, *clinical study*, *study*, and *clinical investigation* are deemed to be synonymous [21 CFR 50.3(c) and 21 CFR 56.102(c)]

Human Subject: An individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. [21 CFR 50.3(g) and 21 CFR 56.102(g)]

IV. PROCEDURE

1. Required Application Materials

1.1 Principal Investigators (PI) conducting human-subjects research approved by the NSMC IRB are required to submit proposed changes in approved research for review and approval prior to initiation of the change, except where necessary to eliminate apparent immediate hazards to the subject.

1.1.1 In addition to submission of a completed Partners Human Research Committee (PHRC) *Amendment Form*, PI's must submit the exact text of a modification or other revision to the protocol and any proposed changes to the consent document to the NSMC IRB, where applicable. When there are numerous changes to the research protocol, a summary of the changes should also be submitted.

1.1.2 Modifications to the consent document must take into account both prospective research subjects and, if applicable, research subjects already enrolled in the study. The latter may be addressed by re-consenting the subject using the modified consent document.

2. Submission Processing and General Review Procedures

2.1 Refer to IRB Policy 008 IRB *General Review Procedures* for details regarding processing of submissions, general review procedures, primary reviewers, determinations and communications.

3. Classification of Minor vs. Major Change

3.1 As per 45 CFR 46.110 (b) and 21 CFR 56.110(b), an IRB may use the expedited review procedure to review either or both of the following:

- (1) Some or all of the research appearing on the list and found by the reviewer(s) to involve no more than minimal risk
- (2) **Minor changes in previously approved research during the period (of one year or less) for which approval is authorized.**

The proposed change is considered minor when the research meets all of the following criteria:

- The proposed change does not significantly alter the risk to benefit assessment the IRB relied upon to approve the protocol;
- The proposed change does not significantly affect the safety of subjects;
- The proposed change does not involve the addition of invasive procedures (procedures not otherwise eligible for expedited review, e.g. collection of blood samples in limited amounts);
- The proposed change does not involve the addition of procedures, interactions or interventions that add significant medical, social or psychological risks;
- The proposed change does not involve addition of a vulnerable population in research not otherwise eligible for expedited review; and
- The proposed change does not significantly alter the scientific question or the scientific quality of the study.

Examples of **minor** modifications **may** include, but are not limited to, the following:

- a) The addition of research activities that would be considered exempt or expedited if considered independent from the main research protocol;
- b) Minimal increases or decreases in the number of participants;
- c) Narrowing the range of the inclusion criteria, in order to decrease risk;
- d) Broadening the range of the exclusion criteria, in order to decrease risk;
- e) 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;
- f) 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;
- g) A decrease in the number of study visits, provided that such a decrease does not affect the collection of information related to safety evaluations;
- h) Alterations in human research participant payment or liberalization of the payment schedule with proper justification;
- i) 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;
- j) The addition or deletion of qualified Investigators or research personnel;
- k) The addition of study sites (which may require a Federal Wide Assurance (FWA) and appropriate IRB approval) or the deletion of study sites;

- 3.2 When a proposed change in a research study is not minor, then the IRB must review and approve changes at a convened meeting before the changes can be implemented.

Examples of **major** modifications **may** include, but are not limited to, the following:

- a) Broadening the range of inclusion criteria;
- b) Narrowing the range of exclusion criteria;
- c) Alterations in the dosage or route of administration of an administered drug;
- d) Extending substantially the duration of exposure to the test material or intervention;
- e) The deletion of laboratory tests, monitoring procedures, or study visits directed at the collection of information for safety evaluations;
- f) The addition of serious unexpected adverse events or other significant risks to the informed consent document; or
- g) Changes, which, in the opinion of the IRB Chairperson or Administrator, do not meet the criteria or intent of a minor modification.

4. Changes Made Without IRB Approval to Eliminate Apparent Immediate Hazards

- 4.1 Changes made without prior IRB approval to eliminate apparent immediate hazards to subjects must be reported to the IRB within 24 hours. Changes made to eliminate apparent immediate hazards to the subjects will be reviewed by the IRB according to the procedures described in IRB Policy 020 *Unanticipated Problems and Adverse Event Reporting Policy*.

5. Distribution of Materials

- 5.1 For review of proposed changes to approved research at convened IRB meetings, all members attending the meeting shall receive at a minimum, a copy of the required forms, summary of changes, revised informed consent form (if any) and revised advertisements/recruitment materials (if any) submitted by the investigator. The primary reviewer will receive the above plus a copy of the detailed protocol. These documents are available to all members upon request.
- 5.2 For review of proposed changes to approved research via expedited review, the IRB Chairperson or designee will receive all documents for review.

6. Criteria for Review and Approval and other IRB Considerations

- 6.1 The criteria for approval of proposed changes to previously approved research is the same as those for initial review described in IRB Policy 015 *Initial Review of Research*.
- 6.2 Revision approvals do not change the approval or expiration date of the project. The approval letter simply approves the modification or revision to the project and allows Investigators to begin using the modified or new documents, procedures, etc. The responsible PI must receive a letter from the IRB approving the proposed revisions before the changes are implemented except as allowed per section 4.1.
- 6.3 The NSMC IRB communicates the requirement for prior approval of any changes in written approval notification letters (i.e., investigators informed that they must submit changes in approved research to the IRB for approval prior to initiation), written review notification letters (i.e., investigators informed that proposed changes cannot be initiated until approved) and in the continuing review application form (i.e., investigators reminded that all changes in approved research must be submitted to the IRB for approval prior to initiation).

V. RELATED POLICIES, REGULATIONS, AND REFERENCES

IRB 008 IRB General Review Procedures
IRB 015 Initial Review of Research
IRB 020 Unanticipated Problems and Adverse Event Reporting Policy
Form *PHRC Amendment Form*

DHHS Regulations 45 CFR Part 46
FDA Regulations 21 CFR Parts 50, 56