

THE NORTH SHORE MEDICAL CENTER Institutional Review Board (IRB) POLICIES AND PROCEDURES	IRB Policy Number: 008.1
Title: <i>IRB General Review Procedures</i>	Page: 1 of 7
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I. PURPOSE

This policy defines the general review procedures of the North Shore Medical Center Institutional Review Board (NSMC IRB).

II. SCOPE

This policy applies to all applications regarding research involving human subjects submitted to the NSMC IRB. The determination of whether a proposed activity constitutes research involving human subjects is described in NSMC IRB Policy 027.

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. Submission and Determination of Type of IRB Review

- 1.1 Principal Investigators (PI) relying on the NSMC IRB for review of human-subjects research are required to complete application forms and submit all necessary information and documents for review to the NSMC IRB.
- 1.2 All review submissions (including initial review applications, applications for continuing review or study closure, change in research, reports of unanticipated problems, or other study events or correspondence) are received, date stamped and entered into the Partners Research Express (ReX) IRB database by the NSMC IRB Administrator (or designee). For new applications, an IRB protocol number is automatically assigned in ReX and used to reference the study in all future communications regarding the study.
- 1.3 The IRB Administrator reviews the submission for completeness (e.g., necessary documents complete and attached) using appropriate checklist(s). The IRB Administrator communicates with the PI or designee regarding any missing or additional required materials.
- 1.4 The IRB Administrator makes the preliminary determination of the type of review required for the submission; specifically Exempt, Expedited or Convened Board review. The IRB Chairperson makes the final determination during the review process. When a PI requests a review (other than convened board) for which the submission does not qualify, revised and/or additional application materials may be requested.

2. Review Process

2.1 Exempt

- 2.1.1 The IRB Administrator provides a copy of all of the required forms and documents submitted by the PI for review to the IRB Chairperson for review together with the exemption checklist and signature form.
- 2.1.2 The IRB Chairperson reviews initial submissions for exemption status in accordance with 45 CFR 46.101(b)(1-6) for DHHS-regulated research and 21 CFR 56.104(c)(d) for FDA-regulated research.

Note: Exemptions 46.101(b)(1-6) do not apply to research involving prisoners, subpart C. Exemption 46.101(b)(2) does not apply to research involving children, subpart D, except for research involving observations of public behavior when the investigator(s) do not participate in the activities being observed. Exemptions 46.101(b)(1-6) do not apply to clinical investigations regulated by the FDA.

2.1.3 If the IRB Chairperson determines that the research is exempt, further IRB review including continuing review is not required, however changes may not be made to the research activity without communication of the changes to the IRB to ensure that the changes are within the parameters for exemption. If the research no longer meets the criteria for exemption, the PI must resubmit the research for review by the IRB at a convened meeting or using the expedited review procedure, whichever is appropriate to the research activities.

2.2 Expedited

2.2.1 The IRB Administrator provides a copy of all of the required forms and documents submitted by the PI for review to the IRB Chairperson for review together with the expedited review checklist and signature form. Expedited reviews are conducted by the NSMC IRB Chairperson or by one or more experienced reviewers designated by the IRB Chairperson from among the members of the IRB.

2.2.2 The expedited review procedure may be used for initial applications, revisions and renewals when the research activities (1) present no more than minimal risk to human subjects, and (2) involve only procedures listed in one or more of the categories authorized by 45 CFR 46.110 and 21 CFR 56.110 [categories listed in 63 FR 60364-60367, November 9, 1998].

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

2.2.2.2 For research proposed to be eligible for expedited review under category #9, the convened IRB is required to concur that the study is minimal risk and eligible to undergo expedited review in the future.

Note: 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 the risk related to invasion of privacy and breach of confidentiality is no greater than minimal. In addition, the expedited review procedures may not be used for classified research involving human subjects. Classified research is research that has a security classification established by an authorized agency of the federal government.

2.2.3 In reviewing the submission under the expedited review procedure, the IRB Chairperson or designee may exercise all of the authorities of the IRB except that the reviewer may not disapprove the research. Research may be disapproved only after review at a convened board meeting.

2.2.4 If the research qualifies for expedited review, the IRB Chairperson or designee documents his/her determination of risk on the expedited review checklist. The IRB Chairperson or designee is responsible for determining that all of the requirements set forth in 45 CFR 46.111 and, when applicable, 21 CFR 56.111 are satisfied.

The IRB Chairperson or Administrator may request discussion about an exempt or expedited study at a convened board meeting for educational purposes or, even if the research qualifies for exempt or expedited review, the research may be referred to convened board review.

The IRB Administrator informs all IRB members of the actions taken by the IRB Chairperson at the subsequent convened IRB meeting via distribution of a report that includes those submissions determined to be exempt or approved under expedited review procedures (initial and continuing reviews and changes in approved research during the period of IRB approval).

2.3 Convened Board

- 2.3.1 For submissions determined to require review by the convened IRB (i.e., not eligible for exemption or expedited review or referred by the IRB Chairperson or Administrator), the IRB Administrator adds the item to the agenda for the next available IRB meeting.
- 2.3.1.1 The convened IRB meeting dates and times are determined by the end of each year for the following year. Members are informed of the meeting schedule prior to the end of the year and the meeting dates are posted on the NSMC IRB website.
- 2.3.2 The NSMC IRB uses a primary reviewer system for initial applications, continuing review applications, and amendments requiring convened board review.
- a) The IRB Administrator, in conjunction with the IRB Chairperson when necessary, identifies a primary reviewer for each submission taking into consideration the scientific discipline, the study population, and study procedures described in the protocol and the experience and expertise of the members attending the specific meeting.
- b) The primary reviewer is typically a physician-scientist or other scientist with experience in working with the population being studied and/or expertise in the type of research under consideration, although this is not an absolute requirement, depending upon the type of study.
- c) Primary reviewers receive additional documentation for review (refer to specific NSMC IRB policies for initial, continuing or amendment reviews for details) and are responsible for an in-depth review of all of the materials provided to them relevant to the research.
- d) The IRB Chairperson serves as a back-up reviewer and receives the same materials as the primary reviewer to ensure the review can be conducted at the convened meeting.
- 2.3.3 Approximately one week prior to the meeting, a meeting agenda and copies of forms and documents submitted for IRB review for each item on the agenda are distributed to members planning to attend the meeting. In addition, members are provided with reviewer worksheets (including the regulatory criteria for approval 45 CFR 46.111 and 21 CFR 56.111, as applicable), points to consider for guidance when reviewing the research and requirements for informed consent, where applicable.
- 2.3.4 Members who are not assigned as primary reviewers are expected to review all of the materials provided to them relevant to the research in sufficient depth to vote on the research at the convened meeting.
- 2.3.5 Reviewers may contact the PI (via email or phone) prior to the meeting if they have questions about the study, particularly if they have significant concerns about the study or believe additional information is needed for the IRB to be able to assess the risks and anticipated benefits, if any, to subjects and the importance of the knowledge that may be expected to result from the research.
- 2.3.6 The IRB Chairperson and assigned primary reviewers lead the discussion of each item on the meeting agenda. At the end of the discussion, an IRB member makes a motion proposing a determination for the protocol. A vote on the motion is taken (for, against, or abstain) and recorded in the minutes. All motions are decided by majority vote of the members present for the review.

3. Determinations

3.1 The IRB Chairperson or designee for expedited reviews, or the IRB committee during convened meetings, makes one of the following determinations as a result of the review of research:

- Approval: The submission is approved as submitted without any required modifications. Approval is effective on the day the study is approved by the convened IRB and the approval period is based on the date of the convened meeting at which the IRB approved the submission. When the expedited review procedure is used approval is effective on the day the study is approved by the IRB Chairperson and the approval period is based on the date the IRB Chairperson approved the submission.
 - Approval period: Unless a shorter approval period is required by the IRB, the longest approval period that will be granted is for one year (365 days). For example, if approval is granted on January 1, 2008, the approval period will be from January 1, 2008 through midnight on December 31, 2008 and expired on January 1, 2009.
- Contingent Approval: Specific modification(s) of a protocol or accompanying document(s) are required (to secure approval) under either expedited or convened review procedures. Contingent approval is granted if the activity meets the criteria for approval (defined in 45 CFR 46.111 or 21 CFR 56.111) and the modifications required by the convened IRB are such that they only require minor modifications that would be considered Minimal Risk in nature. However, regardless of the level of risk, contingent approval may be granted when the IRB can provide specific direction to the PI regarding the requested revision and the response would only require simple concurrence by the PI and verification by a single IRB member that the change was made.

The IRB Chairperson or another IRB member has the authority to review the changes submitted via expedited review unless the IRB requires or the IRB Chairperson decides that the material or information must be reviewed by the convened IRB. Board requested changes may be taken to the convened IRB if all changes are not met. Upon satisfactory review, approval is released as of the date that the requested information or materials are approved. However, the expiration date of IRB approval is based on the date of the convened meeting at which the IRB approved the research with modifications. When the expedited review procedure is used, approval is effective on the date the study is approved by the IRB Chairperson and the approval period is based on the date the IRB Chairperson approved the protocol.

- Deferral: Significant questions regarding the proposal are raised or the information provided is determined to be inadequate to assess risk/benefit ratio under either expedited or convened review procedures. The submission may be reconsidered after additional substantive information and/or modifications are received from the PI.
- Disapproval: The IRB determines the proposal fails to meet one or more criteria for approval of research. The study, as designed, cannot be approved and the IRB can think of no modifications or additional information that will likely result in an approval. Disapproval cannot be granted through the expedited review mechanism and shall be given only by majority vote at a convened meeting of the IRB.

4. Communications

All written communications are sent by the IRB Administrative staff and may be signed by either the IRB Chairperson or by the IRB Administrator (when documentation of IRB Chairperson signature exists on reviewer worksheets or for documented convened board decisions).

4.1 Letters of Approval

- 4.1.1 When an exemption application or other submission under either expedited or convened board review procedures is approved, written notification in the form of an approval letter is sent to the PI usually within one week of the determination.
- 4.1.2 The approval letter includes at a minimum the IRB protocol number, any required conditions of approval, date of approval, date approval expires, and in the case of exempt or expedited research the relevant category(ies) for determination. The approval letter is accompanied by IRB-stamped approved documents (e.g., consent/assent documents, subject information sheets, advertising/subject recruitment materials).

4.2 Request for Revisions/Modifications (Contingent Approval or Deferral)

- 4.2.1 When modifications to secure approval are required or action is deferred pending additional information under either the expedited or convened board review procedures, written notification of the IRB's action, together with the reason(s) for the decision and the specific modifications or clarifications, are provided in writing to the PI usually within one week of the determination.
- 4.2.2 The PI is asked to submit a point-by-point response and revised documents to the IRB within 60 days of the review date. Unless the PI requests an extension or there are extenuating circumstances, the research is withdrawn from further review at the end of the 60-day period if no response is received. If no response is received after 90 days, a written notice of study closure for lack of response will be sent to the PI and placed in IRB study file.
- 4.2.3 The PI's responses may be reviewed by the IRB Chairperson via expedited review only when the PI has agreed to and made the requested changes or the protocol is eligible for review using the expedited procedure. Otherwise, the modifications are reviewed at the next convened IRB meeting. Additional modifications or information may continue to be requested until the research is approved.

4.3 Letters of Disapproval

- 4.3.1 When the IRB disapproves the research, the PI is notified in writing of the action and the basis for the disapproval; however, a detailed critique of the protocol is not provided.
- 4.3.2 The decision of the NSMC IRB to disapprove the research cannot be overruled by any other institutional body or individual(s); however, an investigator may appeal the decision of the IRB (refer to Section IV.5 below).

4.4 Reporting to the Institutional Official

- 4.4.1 The IRB Administrator provides the Senior Vice President for Medical Affairs/Chief Medical Officer, who also serves as the Institutional Official for NSMC's Federalwide Assurance, with documentation of IRB findings and actions via distribution of IRB meeting minutes and relevant correspondence with PI's.

5. **Appeal of IRB Action**

- 5.1 An investigator may appeal an IRB decision to disapprove a study or appeal IRB-required revisions to submitted documents. The investigator may appeal the decision of the IRB either in person at a convened meeting or in writing to the IRB Chairperson and reviewed by the convened IRB.

V. RELATED POLICIES, REGULATIONS, AND REFERENCES

IRB 004 IRB Composition and Roster
IRB 014 Record Requirements
IRB 015 Initial Review of Research
IRB 022 Continuing Review of Approved Research
IRB 024 Amendments to Approved Research

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