

THE NORTH SHORE MEDICAL CENTER Institutional Review Board (IRB) POLICIES AND PROCEDURES	IRB Policy Number: 026.0
Title: <i>Investigations of Non-Compliance</i>	Page: 1 of 6
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I. PURPOSE

The purpose of this policy is to define the duty and responsibility of individuals to report to the North Shore Medical Center Institutional Review Board (NSMC IRB) observed or apparent noncompliance with federal, state and local laws and regulations or the requirements or determinations of the NSMC IRB and the procedures the NSMC IRB follows when reviewing reports of observed or apparent noncompliance.

This policy is established to comply in part with the regulatory requirement in 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)(2) requiring IRBs to have written procedures which the IRB will follow for ensuring prompt reporting to the IRB, appropriate institutional officials, Office for Human Research Protections, and, when applicable, the Food and Drug Administration (FDA), any serious or continuing noncompliance with the regulations or the requirements or determinations of the IRB.

II. SCOPE

Any incident of noncompliance with human subject protection requirements must be reported to the NSMC IRB immediately. Allegations of noncompliance may be reported to the IRB office, IRB chair, or IRB members by anyone, including investigators, research staff, research subjects, students, faculty, staff, administrators, external parties, etc. Alternatively, noncompliance may be reported via the PHS/NSMC Compliance Help Line (800) 856-1983. This is available 24 hours a day, 7 days a week. Callers can report anonymously or identify themselves and a non-retaliation policy is in place for anyone who uses the Line.

The IRB investigates allegations and instances of noncompliance, determine immediate actions to protect subjects, report serious or continuing noncompliance to appropriate authorities (including government agencies), require modifications to, suspension or termination of research activities and takes other actions as needed to protect human subjects or comply with institutional policies and procedures.

This policy applies to all activities of the NSMC IRB and all activities regarding research involving human subjects reviewed by the NSMC IRB.

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)]

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)]

Noncompliance: Any failure to comply with any applicable federal, state, or local laws and regulations or the requirements or determinations of the NSMC IRB, which include NSMC IRB and institutional policies related to human subject protection.

Minor Noncompliance: Any non-compliance that is not serious or continuing noncompliance. For example, minor noncompliance might include the following violations: (1) missing an original signed and dated research consent form; (2) missing pages of executed research consent forms; (3) inappropriate documentation of informed consent, e.g., missing one or more signatures or date; (4) obtaining informed consent using an invalid/outdated research consent form that contains all of the information required by the NSMC IRB; (5) failure to submit continuing review forms/documents prior to expiration of IRB approval; (6) unplanned deviation from the approved protocol where the deviation does not impact the rights and welfare of subjects or the integrity of the research.

Serious Noncompliance: Any noncompliance that negatively impacts the rights and welfare of subjects or compromises the integrity of the study data. For example, serious noncompliance might include, but is not limited to, the following violations: (1) failure to obtain prospective IRB approval; (2) failure to obtain informed consent of subject(s); (3) enrollment of subject(s) who do not meet all eligibility criteria; (4) obtaining informed consent using an invalid/outdated research consent form that is missing information that might affect the individual's willingness to participate or continue to participate in the research; (5) failure to perform follow-up as outlined in the protocol where the lack of follow-up places the subject at increased risk of harm; (6) failure to report a serious unanticipated problem involving risks to subjects or others, including adverse events; and (7) compromising subject privacy or confidentiality.

Continuing Noncompliance: Any noncompliance that occurs repeatedly after appropriate remedial education or corrective action has been instituted taking into consideration all relevant factors, including, for example: (1) whether the continuing noncompliance was intentional, or (2) whether the investigator collaborated in remedial activity and the continuing noncompliance was not intentional.

IV. PROCEDURE

1. Reporting Observed or Apparent Noncompliance

- 1.1 The reporting party is responsible for reporting observed or apparent noncompliance in good faith, maintaining confidentiality, and cooperating with any internal inquiries. NSMC intends to protect, to the extent possible, the privacy of an individual who in good faith reports noncompliance on the part of another individual. Reports of noncompliance made in good faith will not reflect negatively on the individual reporting such noncompliance and, when applicable, will not affect his/her employment, in accordance with *Partners Non-Retaliation Policy*.
- 1.2 If an individual is unsure whether there are grounds to suspect noncompliance, s/he may call upon the NSMC IRB Chairperson and Administrator to discuss the situation informally.
- 1.3 Observed or apparent noncompliance should be reported to the NSMC IRB Chairperson and Administrator as soon as possible after the noncompliance is observed or discovered. Reports of noncompliance should be made in writing; however, in some cases, reports of noncompliance may be made orally. When a report of noncompliance is received orally, the person receiving the report is responsible for creating a written account of the report.
- 1.4 Reports of noncompliance, whether written or oral, should include a complete description of the noncompliance, of the observed circumstances and, the names of the individuals involved, if known. Whenever possible, the report should contain sufficient details to allow an assessment of noncompliance.

2. Investigating Reports of Noncompliance

- 2.1 The NSMC IRB Chairperson and Administrator shall be responsible for gathering or causing to be gathered (through an audit or otherwise) further facts to better ascertain the nature and scope of noncompliance, if any. The fact gathering process shall include an interview with the affected investigator(s). Failure of the investigator(s) to cooperate with such a request or with any other inquiry or process described in this Policy shall itself be grounds for NSMC IRB action.
- 2.2 Following completion of the initial fact gathering process, the NSMC IRB Chairperson and Administrator shall issue or cause to be issued a preliminary written report of findings of fact and one of the following determinations:
- a) No Noncompliance
When the NSMC IRB Chairperson and Administrator determine that the facts do not support a finding of noncompliance as defined in this Policy, the report of noncompliance will be dismissed and no further action will be taken under this Policy. The written report of findings of fact and determinations shall be sent to the Principal Investigator and, when relevant, the affected investigator(s).
- b) Minor Noncompliance
When the NSMC IRB Chairperson and Administrator determine that the facts support a finding of minor noncompliance as defined in this Policy, the NSMC IRB Chairperson will either approve the research to continue with no further action required or require one or more of the following corrective actions before the research can continue:
- Require minor modifications in the research and/or consent form;
 - Require that subjects who are still participating in the research be re-consented or notified in writing of the noncompliance;
 - Require that subjects whose participation has ended be notified in writing of the noncompliance;
 - Modify the continuing review schedule;

- Require remedial education; and/or
- Any other action the IRB deemed appropriate to the noncompliance.

The written report of findings of fact and determinations and corrective action, if any, shall be sent to the Principal Investigator and, when relevant, the affected investigator(s). No further action will be taken under this Policy.

Modifications submitted by the investigator in response to the report shall be reviewed by the NSMC IRB according to the policy on review of proposed minor changes in approved research using the expedited review procedure (NSMC IRB Policy 024 *Amendments to Approved Research*).

c) Serious or Continuing Noncompliance

When the NSMC IRB Chairperson and Administrator determine that the facts support a finding of serious or continuing noncompliance as defined in this Policy, the matter shall be referred to the NSMC IRB for review as described in Section IV.5. The IRB membership will also be immediately informed of the preliminary findings and that an investigation is ongoing.

The written report of findings of fact and determinations shall be sent to the Principal Investigator and, when relevant, the affected investigator(s) and a preliminary report of serious or continuing noncompliance shall be submitted by the NSMC IRB Chairperson and Administrator to the Office for Human Research Protections (OHRP) and, when applicable, the Food and Drug Administration (FDA), with copies to the institutional official (IO), the NSMC Compliance Officer and, when appropriate, the head of the relevant hospital department or service.

3. Referral to Other Institutional Officials

- 3.1 At any point during the initial fact gathering process or later, when the NSMC IRB Chairperson and Administrator determines that the facts raise issues apart from or in addition to noncompliance with applicable federal, state, and local laws and regulations or the requirements or determinations of the NSMC IRB, the NSMC IRB Chairperson and Administrator shall notify or refer the matter or relevant aspects of the matter to other institutional officials for review or other remedial or correction action.

4. Temporary Suspension (Hold) or Termination of Research

- 4.1 Voluntary Hold Placed on Research by the Investigator

The Principal Investigator (PI) may voluntarily place the research on hold in whole or in part while the investigation into reports of noncompliance is being conducted. Such temporary holds are not subject to the reporting requirements in 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)(2).

- 4.2 Temporary Suspension or Termination of Research by the IRB

At any point during the initial fact gathering process or later, the NSMC IRB Chairperson may temporarily suspend in whole or in part or terminate the research. Such suspensions or terminations will be conducted according to NSMC IRB Policy 009 *Suspension or Termination of IRB Approval of Research*.

5. Review of Serious or Continuing Noncompliance at a Convened NSMC IRB Meeting

- 5.1 The NSMC IRB Chairperson and members shall receive a copy of the initial report of noncompliance, written reports of findings of fact and determinations and recommendations and, any audit or other report generated as part of the initial fact gathering process. The entire

protocol file and/or minutes of meetings at which the protocol was discussed previously shall be made available to members, upon request. The NSMC IRB Chairperson and Administrator shall be responsible for presenting the report of serious or continuing noncompliance to the IRB.

- 5.2 By majority vote of a quorum of the membership present at the convened meeting, the NSMC IRB will make a determination as to the noncompliance and take one or more of the following actions with respect to the research:
- Approve the research to continue with no further action required;
 - Defer action pending additional information;
 - Require modifications in the research and/or consent form;
 - Require that subjects who are still participating in the research be re-consented or notified in writing of the noncompliance;
 - Require that subjects whose participation has ended be notified in writing of the noncompliance;
 - Modify the continuing review schedule;
 - Suspend the research;
 - Terminate the research;
 - Require periodic audits by the NSMC Compliance office; or
 - Any other action the NSMC IRB deems appropriate to the noncompliance.
- 5.3 By majority vote of a quorum of the membership present at the convened meeting, the NSMC IRB may also take one or more of the following actions with respect to the affected investigator(s), if applicable:
- Require remedial education;
 - Require oversight by a senior investigator;
 - Restrict the conduct of research; and/or
 - Restrict research privileges.

6. Reporting Serious or Continuing Noncompliance and, When Applicable, Suspension or Termination of the Research

- 6.1 Within fifteen (15) days of the IRB meeting, the NSMC IRB Chairperson and Administrator shall be responsible for submitting a final report of the serious or continuing noncompliance and, when applicable, suspension or termination of the research to the Office for Human Research Protections (OHRP) and, when applicable, the Food and Drug Administration (FDA), with copies to the Principal Investigator, Institutional Official, IRB membership, NSMC Compliance Officer, NSMC Legal Counsel, and, when appropriate, the head of the relevant hospital department or service.

7. Communications with Investigators

- 7.1 The findings and actions of the NSMC IRB shall be communicated in writing to the Principal Investigator and, when relevant, to the affected investigator(s).
- 7.2 An investigator who believes that the IRB has erred in the finding of noncompliance 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. The request should clearly indicate the facts or the interpretation in dispute, providing supporting evidence where applicable.

8. Recordkeeping

- 8.1 The NSMC IRB Administrator or designee is responsible for preparing a description of the noncompliance and recording the findings and actions of the NSMC IRB in the Minutes.

8.2 The records of the fact gathering process and review by the NSMCIRB and associated findings of fact and determinations and recommendations shall be maintained in the IRB Office with the protocol file.

V. RELATED POLICIES, REGULATIONS, AND REFERENCES

IRB 009 Suspension or Termination of IRB Approval of Research.
IRB 024 Amendments to Approved Research

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