Allegations of Noncompliance

The purpose of this policy is to identify the standards and responsibilities for handling reports of noncompliance related to research involving human subjects, and the actions taken when the IRB makes a finding of serious or continuing noncompliance. If at any time during an investigation there are concerns regarding scientific misconduct, such concerns will be referred to the Human Protections Administrator (who also serves as the Institutional Research Integrity Officer). Allegations of research misconduct are potentially related but a separate issue that is covered by Woman's Research Misconduct Policy.

This policy applies to all members of the research staff, investigators conducting research at Woman's, members of the medical staff, employees of Woman's, and IRB members.

Definitions

Allegation of Noncompliance: An assertion of noncompliance that has yet to be proved or supported by evidence.

Continuing Noncompliance: A pattern of noncompliance with repeated failure to adhere to the federal research regulations or institutional policies that may affect the rights or welfare of participants. The pattern of noncompliance is assessed by the number of incidents occurring during the course of implementation of a protocol, or across multiple protocols, conducted at Woman's, and if the same noncompliant action was repeated or many different noncompliant events occurred, especially after a remediation procedure such as training has been provided to the researcher or research staff.

Finding of Noncompliance: Noncompliance that is proven or supported by substantial evidence.

Noncompliance: A violation of any federal, state, or local regulation that governs human research, any institutional policy on human subjects research, or any deviation from the protocol approved by the IRB or stipulations imposed by the IRB as a condition of approval. Noncompliance that may affect subject safety, increase risks to subjects, affect the integrity of the data, violate the rights and welfare of subjects, or affect the subject's willingness to participate in research.

Serious Noncompliance: Noncompliance which, in the judgment of the convened IRB, significantly increases risk to participants, significantly decreases potential benefits, or compromises the integrity of the Human Research Protection Program (HRPP).

Procedures

All employees and agents of Woman's and institutions relying on Woman's IRB share the responsibility for reporting incidences of noncompliance with the regulations or the requirements or determinations of the IRB. Allegations of noncompliance in human subjects research may come from many sources including, but not limited to, the following:

- Investigators or study team members
- R&D/IRB members, study monitors, auditors, or sponsors
- Research participants or family members
- Individuals not directly involved in research
- Staff of the Woman's Hospital Research Center

Reporting allegations of noncompliance

Reports of allegations of non-compliance may be made to any of the following individuals:

- Human Protections Administrator
- IRB Chair or any IRB member
- Research and Development Committee Chair
- Organizational Official (Vice President of Research)
- Any staff member at the Woman's Hospital Research Center: 225-231-5275; resesearch@womans.org

All reports of allegations of noncompliance must be documented by its recipient and forwarded to the IRB Chair (or designee). The report must contain sufficient information to perform an investigation of the allegations. Any conflicts of interest that may interfere with the IRB Chair's or subsequent committee's review of the allegation should be assessed and documented. Anyone with a conflict of interest will be excluded from the review of the allegation.

NOTE: Allegations of noncompliance against IRB members or the IRB Chair will be forwarded to the Organizational Official.

Identity protection

The identity of the individual making an allegation of noncompliance will be protected to the extent possible when this individual makes a report in good faith. This protection holds even if the concerns or allegations are found, upon investigation, to be without merit.

Initial Review of Allegations of Noncompliance

The IRB Chair (or designee) and Human Protections Administrator (HPA) are responsible for the initial review of allegations of noncompliance. The IRB Chair/designee informs the Principal Investigator (PI) of the allegation and the initial review and gathers additional facts (e.g. from an

audit of the study records), when necessary, to better ascertain the nature and scope of the allegation of noncompliance.

The PI must provide the following materials to the IRB Chair or designee and the HPA:

• A report about the investigator's research activities under examination and the associated protocol deviation submission, if one was filed;

• Current versions of applicable study documents (e.g. protocol, consent form(s) investigator's brochure, recruitment materials, data collection forms, etc.) and previous versions of these documents, if necessary; and

• Any other materials relevant to the potential noncompliance, including but not limited to correspondence with the sponsor, other investigators, subjects, regulatory agencies or third parties; monitoring or audit reports; protocol deviations; safety reports; complaints from research subjects; or subject-specific information.

The IRB Chair or designee makes the initial determination of whether review by the convened IRB is required and if there is support for a finding of noncompliance.

No findings of noncompliance

When the IRB Chair/designee determines 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. The written report of findings and determinations of the Chair/designee will be sent to the PI and, when relevant, the affected investigator(s).

Noncompliance that is not serious or continuing

When the facts support a finding of noncompliance that is NOT serious or continuing:

When the IRB Chair/designee determines that the facts support a finding of noncompliance that is not serious or continuing as defined in this policy, the IRB Chair or designee will either allow the research to continue with no further action required or require one or more of the following actions before the research can continue:

(a) Require modifications in the research and/or consent form;

(b) Require that subjects who are still participating in the research be re-consented or notified in writing of the noncompliance;

(c) Require that subjects whose participation has ended be notified in writing of the noncompliance;

(d) Modify the continuing review schedule;

(e) Require review of the study activity by the Office of Research Compliance;

(f) Require training; and/or

(g) Any other action that is deemed appropriate to the noncompliance.

The written report of findings and determinations of the IRB Chair or designee and corrective action, if any, will be sent to the PI and when relevant, the affected investigator(s). Modifications submitted by the investigator in response to the report will be reviewed by the IRB at the next convened meeting.

Findings of serious or continued noncompliance

When the IRB Chair or designee determines that there is possible serious or continuing noncompliance as defined in this policy, or if the matter cannot be investigated adequately without IRB intervention, the matter will be referred to the Organizational Official and the Institutional Review Board. The IRB's determination will be provided to the PI.

Suspension of the Research

The PI may voluntarily place the research on hold in whole or in part while the investigation 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) (SOP 410).

At any point during the investigation the IRB Chair or designee, or the IRB, may suspend in whole or in part or terminate the research. Such suspensions or terminations must be reported to the appropriate regulatory bodies. Refer to the Termination and Suspension of Research policy for more information.

Consideration by the IRB

When an initial assessment by the IRB Chair results in a determination that there is serious or continued noncompliance, all members of the IRB will review the report of noncompliance, the associated study documents that were submitted, including any relevant audit reports, and the IRB Chair or designee's preliminary report of findings and determination of serious or continuing noncompliance. The IRB may consider new or additional information. The IRB may make one of the following determinations listed below as a result of its review:

(a) Acknowledge the report and allow the research to continue with no additional action required;

(b) Defer action pending additional information;

(c) Require modifications in the research (e.g. protocol, consent form);

(d) Modification of information disclosed during the consent process;

(e) Require that subjects who are still participating in the research be re-consented or notified of the noncompliance when such information may relate to their willingness to continue participation;

(f) Require that subjects whose participation has ended be notified of the noncompliance;

(g) Modify the continuing review schedule;

(h) Suspend IRB approval of the research;

(i) Terminate IRB approval of the research;

(j) Require training for the PI or the PI and study team;

(k) Require periodic audits and monitoring of the research and/or consent process by the IRB audit committee and/or HPA; and/or

(l) Any other action the IRB deems appropriate to the noncompliance

The IRB's findings and actions will be communicated in writing to the PI as well as to the Organizational Official, Institutional Official, and other agencies (sponsor, OHRP, FDA) as appropriate.

Reporting timeframes

The maximum time allowed for reporting the IRB's findings and actions of noncompliance to the institution and any other agencies is two weeks. An initial report of this nature may indicate that the report only contains cursory information and that a follow-up report will be submitted.

For OHRP

The regulations at 45 CFR 46.103(a) and (b)(5) do not specify a time frame for reporting, except to say this must be done "promptly." For a more serious incident, this may mean reporting to OHRP within days. For a less serious incident, a few weeks may be sufficient. It may be appropriate to send an initial report and indicate that a follow-up or final report will follow by the earlier of a specific date or when an investigation has been completed or a corrective action plan has been implemented.

For guidance on reporting to OHRP: https://www.hhs.gov/ohrp/compliance-and-reporting/guidance-on-reporting-incident/index.html

For FDA

FDA does not specify a timeframe for reporting noncompliance, other than "promptly." For guidance on reporting to FDA:

https://www.fda.gov/science-research/report-problems-fda/mandatory-irb-reporting-fda-contacts

For AAHRPP

For reporting noncompliance to AAHRPP, the noncompliance findings should be reported as soon as possible, but generally within 48 hours after the institution or any researcher becomes aware of:

- Any negative actions by a government oversight office, including, but not limited to: OHRP Determination Letters, FDA Warning Letters, FDA 483 Inspection Reports with official action indicated, FDA Restrictions placed on the IRB or investigators, and corresponding compliance actions taken under non-US authorities related to human research protections.
- Any litigation, arbitration, or settlements initiated related to human research protections.
- Any press coverage (including, but not limited to radio, TV, newspaper, online publications) of a negative nature regarding Woman's HRPP.