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OFFICE OF HUMAN SUBJECTS RESEARCH PROTECTIONS

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**SOP Title: ALLEGATIONS OF NON-COMPLIANCE WITH REQUIREMENTS OF THE
NIH HUMAN RESEARCH PROTECTION PROGRAM (HRPP)**

**Distribution: Scientific Directors; Clinical Directors; Clinical Investigators, IRB
Chairs, IRB Administrators, Protocol Navigators**

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SOP 16A ALLEGATIONS OF NON-COMPLIANCE WITH REQUIREMENTS OF THE NIH HUMAN RESEARCH PROTECTION PROGRAM (HRPP)

16A.1 PURPOSE

This policy provides definitions, procedures, sample corrective actions, and reporting requirements related to possible non-compliance with requirements of the NIH Human Research Protection Program (HRPP) policies, and applicable regulatory requirements for the protection of human subjects.

16A.2 POLICY

It is the policy of the NIH's HRPP to investigate allegations of non-compliance in a methodical and fair manner and, if necessary, to take corrective action commensurate with the nature and degree of non-compliance. The type of allegation determines the process, as set forth in this SOP. NIH strongly encourages persons to report, through proper channels, all observed or apparent incidents of non-compliance. These incidents may concern active or closed protocols. NIH IRBs are the primary entities responsible for evaluating and making determinations of protocol non-compliance. Other NIH officials and offices, such as the Deputy Director for Intramural Research (DDIR) and the Office of Human Subjects Research Protections (OHSRP), may also participate in these activities, depending on the nature of the issue.

16A.3 DEFINITIONS

Allegation of non-compliance: A disclosure of possible non-compliance through any means of communication (e.g., by written or oral statement) to an NIH official. This may include complaints from research participants, researchers, staff, reports from audits, and discoveries made during review of other human subjects issues, such as protocol deviations.

Complainant: A person who in good faith makes an allegation of non-compliance.

Investigation into non-compliance: The examination and formal determination of whether non-compliance occurred. If the allegation involves a researcher, the IRB conducts the investigation. If the allegation involves an NIH IRB or official, the DDIR appoints the investigating official(s). The conclusion of an investigation may result in actions by an IRB and/or IC or NIH officials (see 16A.6.1.C).

Non-compliance: The failure to comply with applicable NIH HRPP policies, IRB requirements, or regulatory requirements for the protection of human research subjects. This may include, but is not limited to, the following:

- A. Failure to obtain IRB approval for research involving human subjects.
- B. Inadequate or non-existent procedures for informed consent.
- C. Inadequate supervision of research involving experimental drugs, devices, or procedures.
- D. Failure to follow an IRB-approved protocol.
- E. Failure to obtain prospective IRB approval for changes to a protocol.
- F. Failure to report unanticipated problems and protocol deviations (see SOP 16, “Reporting Requirements for Unanticipated Problems, Adverse Events, and Protocol Deviations”).
- G. Failure to obtain continuing IRB review and approval.

Non-compliance may be further characterized as:

- A. **Serious non-compliance:** Non-compliance that:
 - 1. Increases risks, or causes harm, to participants,
 - 2. Decreases potential benefits to participants, or
 - 3. Compromises the integrity of the NIH HRPP
- B. **Continuing non-compliance:** Non-compliance that is recurring. An example may be a pattern of non-compliance that suggests a likelihood that, absent an intervention, non-compliance will continue. Continuing non-compliance could also include a failure to respond to IRB requests to resolve previous allegations of non-compliance.
- C. **Minor (non-serious) non-compliance:** Non-compliance that is neither serious nor continuing.

Respondent: The PI or the person(s) or the entity, if any, against whom an allegation of non-compliance is made.

Review of non-compliance: The preliminary review of an allegation of non-compliance involves a set of questions that determine the appropriate process for resolution of the allegations.

16.A.4 RAISING AND DOCUMENTING ALLEGATIONS OF NON-COMPLIANCE

16A.4.1 WHO MAY RAISE ALLEGATIONS OF NON-COMPLIANCE

- A. Possible non-compliance may be discovered through continuing reviews, reports of unanticipated problems and protocol deviations (see NIH Problem Report Form attached to SOP 16, “Reporting Requirements for Unanticipated Problems, Adverse Events, and Protocol Deviations”) or from individuals who raise allegations of non-compliance.
- B. Any individual or organization may raise an allegation of non-compliance.
- C. Allegations of non-compliance made in good faith will not reflect negatively on the reporting individual, nor lead to reprisal against that individual.

16A.4.2 METHOD AND CONTENT FOR REPORTING ALLEGATIONS OF NON-COMPLIANCE

Allegations of non-compliance may be submitted verbally or in writing (via mail or email) to the appropriate IRB, OHSRP, the DDIR or other IC official. Allegations of non-compliance should include a description of the possible non-compliance, including the protocol title, number, date, time, personnel involved and complainant’s name and contact information, if available.

Allegations may be made anonymously, e.g., by leaving a telephone message or submitting an unsigned document. Such allegations will be pursued only to the extent that sufficient information is available to perform a review of non-compliance.

The identity of the individual making an allegation of non-compliance will be kept confidential to the extent possible. Disclosure will be limited to those who need

to know, consistent with a thorough, competent, objective and fair proceeding, and except as may otherwise be prescribed by applicable law.

16A.4.3 TIMING OF ALLEGATIONS

Observed or apparent non-compliance should be reported to the IRB or to OHSRP as soon as possible.

16A.4.4 DOCUMENTATION OF ALLEGATIONS

All allegations of non-compliance, written or verbal (including anonymous allegations), will be documented and kept on file in the IRB administrative office or OHSRP, as applicable. The following information will be documented:

- A. Title, number and PI of the protocol.
- B. A description of the possible non-compliance including the date, time, personnel involved, and
- C. The name and contact information of the person reporting the non-compliance, unless the allegation is anonymous. The identity of the individual reporting the allegation will be kept confidential to the extent possible but complete confidentiality cannot always be maintained.

16A.4.5 NOTIFICATION OF ALLEGATIONS

When an allegation involving serious or continued non-compliance is received, the NIH official or office receiving the allegation (e.g., IRB, OHSRP, the DDIR or other IC official) will notify the appropriate IRB and OHSRP, if not already informed, as soon as possible (and no later than 2 working days after receipt). When an allegation involves possible minor non-compliance, the IRB will be notified according to SOP 16. When the allegation involves the IRB (see 16A.9, below), the NIH official or office receiving the allegation will inform the DDIR and OHSRP, if not already informed.

16A.4.6 RESPONSE TO POSSIBLE SERIOUS AND/OR CONTINUING NON-COMPLIANCE

At any point in this process, if any individual or entity considers that serious and/or continuing non-compliance has occurred or is likely to occur, the individual

or entity should notify the IRB and may request that research be suspended (see SOP 11, “Suspensions and Terminations of IRB-approved Research and Administrative Holds”).

16A.5 INDIVIDUALS OR GROUPS THAT EVALUATE ALLEGATIONS OF NON-COMPLIANCE

A. Evaluation when allegations involve serious or continuing non-compliance by researchers

NIH IRBs have the primary responsibility for managing allegations of researcher non-compliance. In most circumstances the IRB conducts the initial review and gathers information (if required); however, in some cases, e.g., allegations that involve the possibility of serious or continuing non-compliance, an *ad hoc* Special Committee, may be needed to assist in the collection of information. In all cases, including those involving a Special Committee, the IRB is the only entity that makes conclusions about allegations of HRPP non-compliance that involve researchers.

B. Evaluation when allegations involve non-compliance by an IRB or NIH official

When an allegation involves non-compliance by an NIH IRB, or NIH official, the DDIR determines who will conduct the review and evaluation, and may appoint a Special Committee for this purpose.

16A.5.1 APPOINTMENT OF A SPECIAL COMMITTEE BY THE DDIR

If in the judgment of the DDIR a Special Committee is needed, the DDIR will select the individuals to serve on the Special Committee and will decide who will Chair the Committee. A Special Committee may consist of a representative from OHSRP, the relevant IRB Chair or a designated representative from the IRB, and/or other NIH employees, depending on the nature of the issue.

A. Factors that may justify creation of a Special Committee:

1. Immediate action is required to protect human subjects.
2. The issue involves more than one IC or NIH IRB.

3. The issue involves an outside institution.
4. The allegation involves non-compliance by an IRB or NIH official
5. Outside entities, such as Congress or the Inspector General, are requesting information from NIH about the non-compliance.

B. Responsibilities of a Special Committee:

1. The Special Committee will evaluate allegations and gather information, following a plan established by the OHSRP and the IRB Chair. This evaluation plan may include internal or independent audits, document reviews, and/or interviewing the PI and any other individuals who have knowledge of the allegation(s).
2. The Special Committee will, as appropriate, prepare a report that includes the name of the respondent(s), a description of the allegations, a list of the evidence examined, and summary or source documents (if pertinent). This work will be completed as soon as possible, generally no later than forty-five (45) days from receipt of the allegation. The evaluation official(s) will provide this report to the appropriate NIH IRB and to the respondent.
3. Records will be maintained of the committee's activities

16A.5.2. CONSULTANTS

If there are issues pertinent to other research review committees, e.g., NIH Biosafety Committee, NIH Radiation Safety Committee, relevant Animal Care and Use Committee, these entities will be contacted to determine if their involvement or consultation is appropriate. Additionally, the individuals or groups looking into allegations of non-compliance may seek advice from expert consultants as necessary (e.g., FDA expertise).

16A.6 REVIEW, EVALUATION AND INVESTIGATION OF ALLEGATIONS OF NON-COMPLIANCE BY RESEARCHERS

16A.6.1 THE PROCESS FOR DECISION-MAKING

A. **Review of non-compliance and creation of an information-gathering plan:**

When an NIH official (IRB, DDIR or OHSRP) obtains an allegation of non-compliance, the first step is a preliminary review involving the following three questions:

1. Is the allegation credible?
2. Does the allegation fit within the scope of the NIH HRPP program?
(OHSRP may advise if there are any questions about the purview of the IRB and/or scope of the NIH HRPP.)
3. Does the allegation involve possible serious or continuing non-compliance?

The review will take place within seven working days of receipt of the allegation.

If the reviewing official(s) answer “yes” to all of the questions above, the reviewing official should notify other officials so that the appropriate NIH IRB, OHSRP and the DDIR are all aware of these allegations. OHSRP and the IRB Chair should agree on an evaluation plan to obtain additional information about the allegations. If the answer to questions 1 or 2 is “no,” the matter should be dismissed or referred to a more appropriate entity for consideration, e.g., allegations concerning scientific misconduct in the Intramural Program should be referred in accord with NIH Intramural Research Program Policies & Procedures for Research Misconduct. If the answer to both questions 1 and 2 is “yes,” but the answer to 3 is “no,” the IRB should proceed with the matter as an issue involving non-compliance that is neither serious nor continuing (see SOP 16, “Reporting Requirements for Unanticipated Problems, Adverse Events, and Protocol Deviations”).

- ### B. **Information-gathering stage:**
- The purpose of the information-gathering stage is to assess the nature of the allegations and to collect relevant available evidence concerning allegations of possible serious or continuing non-compliance. In some cases, depending on the information-gathering plan made by OHSRP and the IRB chair, allegations of serious or continuing non-compliance may involve the creation of a Special Committee. At the conclusion of this stage, additional information may be summarized in an

evaluation report. This evaluation report does not make conclusions or result in a determination of non-compliance.

- C. **IRB determinations:** The fact-finding is completed by the IRB. An IRB meeting will be scheduled so that the respondent and IRB members have sufficient time (generally not more than 30 days) to review the allegation(s) and the evaluation report (if any). If the respondent wishes to provide written materials, they must be provided to the IRB at least three working days before the meeting. The IRB will document its decisions in its minutes. The IRB may need to schedule additional IRB meetings in addition to its regularly scheduled meeting(s) to address the allegations in a timely manner.

If the IRB adds allegations to those already communicated to the respondent, or obtains additional information than that which is provided in the evaluation report (if any), the respondent must be provided with a copy of these new allegations and/or reports (to the extent permitted by law) and the respondent must be given an opportunity to respond.

The IRB will review the allegation(s), the evaluation report (if any) and supporting documentation (if any), and decide whether additional evidence is needed, and give the respondent an opportunity to respond to the allegations. The respondent may bring counsel (as a guest, not to represent the respondent) to an IRB meeting. A confidentiality requirement may be imposed if required by law or NIH policy (e.g., for discussion of Privacy Act-protected data.)

1. The IRB will make a determination of whether the evidence represents a minor, serious and/or continuing non-compliance (if any), and what, if any, additional IRB action is required. At a convened meeting, the IRB will vote and document its determinations and actions in the meeting minutes. The IRB will communicate its decisions to the respondent and other appropriate NIH officials, e.g. as described below.

16A.6.2 IRB ACTIONS

After a determination of noncompliance is made, possible actions include:

- A. Action on a finding of minor non-compliance: The IRB may allow the research to continue with no further action required or may require modifications that constitute a minor change in the research. If changes to

the research protocol are required, the PI will submit an amendment to the IRB. Minor changes to previously approved research may be eligible for review under expedited review procedures consistent with the requirements of SOP 7A, "Requirements for Expedited Review of Research by NIH IRBs".

- B. Action on a finding of serious and/or continuing non-compliance: The IRB will take prompt and appropriate action to assure the safety and welfare of human research subjects and the integrity of the research. These actions may include, but are not limited to, the following:
1. Require modifications in the protocol and/or consent document(s), or require consent monitoring.
 2. Require that subjects who are still participating in the research be notified of the non-compliance and/or re-consented.
 3. Require, if appropriate, that subjects whose participation has ended be notified of the non-compliance.
 4. Modify the continuing review schedule.
 5. Suspend the research (see SOP 11, "Suspensions and Terminations of IRB Approval and Administrative Holds").
 6. Terminate the research (see SOP 11, "Suspensions and Terminations of IRB Approval and Administrative Holds").
 7. Require monitoring of the research by a QI/QA team (see SOP 23, "Quality Management System for the HRPP") and/or the IRB.
 8. Require educational measures for researchers/research staff.
 9. Any other remedial or corrective action the IRB deems appropriate.
- C. Non-HRPP issues: The examination of allegation(s) may uncover problems that are not under the HRPP purview of OHSRP or the IRB. For example, poor record keeping or inadequate supervision of clinical procedures not related to the human subjects research might not be a matter of HRPP compliance. The IRB/OHSRP may not make determinations about these

issues, but may refer their concerns to other appropriate entities such as the IC or Clinical Center, to address appropriately, consistent with applicable NIH Policies.

16A.7 IRB AND OHSRP REPORTING TO NIH OFFICIALS AND OTHER ENTITIES

- A. At any point during the proceeding, if a convened IRB or OHSRP determines that facts suggest serious and/or continuing noncompliance, the appropriate NIH officials will be notified (e.g., the DDIR, the appropriate Clinical Director, and/or other IC officials).
- B. Determinations of serious and/or continuing non-compliance will be reported to OHSRP and the DDIR.
- C. Reporting to OHRP and the FDA will be handled according to SOP 24 “NIH Reporting to OHRP and the FDA Regarding Unanticipated Problems, Serious or Continuing Non-Compliance or Terminations or Suspensions”. The IRB will not initiate any public disclosure of the findings.
- D. If there is evidence of a possible violation of the NIH policy on misconduct in scientific research, the matter will be forwarded to the NIH Agency Intramural Research Integrity Officer (AIRIO) for further investigation.

16A.8 REQUEST FOR IRB RECONSIDERATION

Researchers may request reconsideration of a determination of non-compliance in the following circumstances:

- A. New information exists that was not available during the investigation.
- B. Material failure by the OHSRP, the IRB or other investigative group to follow the noncompliance policy and procedures set forth in this SOP.
- C. The corrective action(s) is perceived to exceed the severity of the non-compliance.

16A.8.1 PROCESS FOR IRB RECONSIDERATION

An appeal for reconsideration of the decision of the IRB will be handled in accordance with SOP 7B, "Requirements for the Conduct of Research Review at a Convened NIH IRB", section 7B12 "Reconsideration of the IRB's Decisions." and SOP 11, "Suspensions and Terminations of IRB-approved Research and Administrative Holds", as applicable.

16A.8.2 ADDITIONAL INSTITUTIONAL ACTIONS

The DDIR or IC may institute additional actions as needed.

16A.9 REVIEW, EVALUATION AND INVESTIGATION OF ALLEGATIONS OF NON-COMPLIANCE BY AN IRB OR NIH OFFICIAL

16A.9.1 THE PROCESS FOR MANAGING ALLEGATIONS OF NON-COMPLIANCE BY AN IRB OR NIH OFFICIAL

Allegations of an IRB or NIH official's non-compliance will undergo the following process.

Review of the allegation(s): The DDIR or OHSRP, at the DDIR's discretion, will perform a preliminary review to determine whether the allegation(s) is within the scope of this SOP, whether it has merit (i.e., there are supporting evidence, documents or statements), and whether it represents possible minor, serious or continuing non-compliance. If it does, the DDIR will determine whether OHSRP or a Special Committee will evaluate the allegation.

Evaluation of the allegation(s): The evaluation official(s) (Special Committee or OHSRP) will prepare a plan to obtain additional information about the allegation(s). This evaluation plan may include, for example, audits or interviewing individuals who have knowledge of the allegation(s).

The evaluation official(s) will gather relevant evidence pursuant to the evaluation plan, prepare a report that includes the name of the respondent(s), a description of the allegations, a list of the evidence examined, and summary of or copies of source documents (if pertinent). This work will be completed in as soon as possible, generally no later than forty-five (45) days from receipt of the allegation. This report will be provided to the DDIR and to the respondent(s). If the evaluation official(s) add allegations to those provided to the respondent(s) or requests additional information, the respondent(s) must be provided with a copy

of these new allegations and/or reports and given sufficient time to review and respond.

The evaluation official(s) will meet to review the allegations and evidence, decide whether additional evidence is needed, and give the respondent(s) an opportunity to respond to the allegations. The respondent(s) may bring counsel (as a guest, not to represent the respondent(s)). The committee may invite others to attend the meeting.

The evaluation official(s) will then make a determination of whether the evidence represents serious, minor or continuing non-compliance, or whether the allegation is unjustified and no action is required.

The evaluation official(s) will document its determination(s) in writing and make recommendations to the DDIR regarding possible corrective action. The DDIR will institute corrective actions as needed.