

COLUMBIA UNIVERSITY INSTITUTIONAL REVIEW BOARD POLICY

NONCOMPLIANCE IN HUMAN SUBJECTS RESEARCH

I. SCOPE

This is a University-wide Policy for responding to potential noncompliance with (a) federal, state or local laws or regulations or institutional policies governing the protection of human subjects in research or (b) requirements or determinations of the Columbia University Institutional Review Board. This Policy applies to all individuals, including Officers of Instruction, Officers of Research, students and staff, who may be involved in human subjects research conducted under the auspices of either Columbia University (the “University”) or NewYork-Presbyterian Hospital at Columbia (“NYP”) and all human subjects research conducted by such individuals.

This Policy does not relate to research misconduct involving fabrication, falsification or plagiarism of research or research results, which is covered by the Columbia University Policy on Misconduct in Research.

II. EFFECTIVE DATE: July 30, 2013; revised March 1, 2016. This Policy replaces the Columbia University Institutional Review Board Policy: Noncompliance with Human Subject Research, dated January 23, 2006 and revised December 1, 2009, February 26, 2010 and November 15, 2012.

III. BACKGROUND

The University is responsible for protecting the safety and welfare of human subjects participating in research conducted under the auspices of the University. In addition, NYP has designated the University’s Institutional Review Board for the review of human subjects research at NYP. Both institutions share the responsibilities for protecting the safety and welfare of human subjects participating in such research. These responsibilities include establishing a policy for responding to potential noncompliance with applicable laws, regulations or policies and taking appropriate actions with respect to such noncompliance. This Policy is designed to address these issues.

IV. DEFINITIONS

For purposes of this Policy, certain terms are defined as follows:

CDF: Compliance Determination Form for use in documenting the IRB, IEC or EVPR determinations related to COT cases.

Continuing Noncompliance: the occurrence of the same or similar Noncompliance after appropriate corrective and preventive action has been instituted, or the failure to institute corrective and preventive actions, taking into consideration all relevant factors, including, for example, (a) whether the continuing Noncompliance was intentional or (b) whether the

investigator complied with the corrective and preventive action requirements and the continuing Noncompliance was not intentional.

COT: the Compliance Oversight Team of the HRPO.

CUMC: Columbia University Medical Center.

CUMC IRB: the IRB that reviews protocols relating to research conducted by researchers who are affiliated with CUMC or NYP.

CU-MS: the University's Morningside Heights campus.

CU-MS IRB: the IRB that reviews protocols relating to research conducted by researchers who are affiliated with Morningside and the Lamont Doherty Earth Observatory (LDEO).

ED: the Executive Director of the IRB.

EVPR: the Executive Vice President for Research.

FDA: the Food and Drug Administration.

HRPO: the University's Human Research Protection Office.

HRPO Officer: any officer-level member of the HRPO staff, including members of the COT.

ICF: an informed consent form.

IEC: the IRB Executive Committee.

Inquiry: the gathering of preliminary information and fact-finding to assess whether an allegation has substance and if so, whether an Investigation is warranted.

Investigation: following an Inquiry, the further investigation of facts with respect to whether Noncompliance has occurred.

IO: The Institutional Official who is the signatory on the Federalwide Assurance of Compliance for each Columbia campus and NYP. The applicable IOs are as follows: (a) with respect to CU-MS, the Executive Vice President for Research, (b) with respect to CUMC, the Senior Vice Dean, College of Physicians and Surgeons and (c) with respect to NYP, the Senior Vice President and Chief Medical Officer of NYP.

IRB: any of the University's Institutional Review Boards or all of the University's Institutional Review Boards collectively, as the context requires.

IRB Chair: with respect to any allegation of Noncompliance, the Chair of the IRB that reviewed the research to which such allegation relates.

IRB Manager: The HRPO Officer who is responsible for management of a designated IRB.

IRB Noncompliance: Noncompliance by any member of the IRB or IRB staff in his/her capacity as such.

Need to Know Individuals: (a) with respect to any allegation of Research Noncompliance, the PI, the IRB Chair, the Chair of the Respondent's department, the applicable IO, the EVPR, the VPRO, the Office of the General Counsel and, if externally funded, the Associate Vice President for Research Administration, plus with respect to any such allegation at CUMC, the Senior Vice Dean of P&S, the Vice Dean for Academic Affairs of P&S and, if the Noncompliance relates to clinical research, the Executive Director of the Clinical Trials Office and (b) with respect to any allegation of IRB Noncompliance, the members of the IEC, the applicable IO, the EVPR and the VPRO.

Noncompliance: any failure to comply with (a) federal, state or local laws or regulations or institutional policies governing the protection of human subjects in research or (b) the requirements or determinations of the IRB.

Non-reportable Noncompliance: any Noncompliance other than Serious Noncompliance, Continuing Noncompliance or Nonsignificant Noncompliance.

Nonsignificant Noncompliance: any Noncompliance that is determined by the IRB staff, an IRB Chair or an IRB to be of such minimal risk that an allegation of Noncompliance is not required to be submitted to the COT.

OHRP: the Office for Human Research Protections in the U.S. Department of Health and Human Services.

Outcome: following an Investigation, the determination as to whether Noncompliance has occurred and what corrective and preventive actions, if any, are required.

P&S: Columbia University College of Physicians and Surgeons.

PI: the principal investigator of the research study to which an allegation relates.

Research Noncompliance: Noncompliance by any person other than a member of the IRB or the IRB staff in his/her capacity as such.

Respondent: the person, including a PI, who is the subject of an allegation of Noncompliance.

Serious Noncompliance: any Noncompliance in a non-exempt study that materially increases the risks or materially compromises the rights and welfare of subjects or the integrity of the research data.

Serious Noncompliance may include, but is not limited to, the following examples:

- Any misadministration of an investigational drug (i.e., the drug, whether or not it is FDA-approved, that is the focus of a clinical investigation);
- Failure to obtain prospective IRB approval of a research study;
- Failure to obtain informed consent from subjects;
- Enrollment of a subject who does not meet all eligibility criteria without obtaining prospective IRB and, if applicable, sponsor approval to be enrolled;
- Obtaining informed consent using an invalid or outdated ICF that does not contain all of the information that might affect an individual's willingness to participate in the research study;

- Failure to perform follow up procedures required in the research protocol when the lack of follow up places the subjects at increased risk of harm;
- Failure to report a serious unanticipated problem to the IRB, as defined by the CU IRB Policy on Reporting to the IRB of Unanticipated Problems Involving Risks;
- Failure to obtain prospective IRB approval of a substantive change in the conduct of the research except when the implementation of such change is required to avoid imminent harm to subjects.

VPRO: the Vice President for Research Operations.

V. RESEARCH NONCOMPLIANCE

A. INITIAL DETERMINATION

1. Concerns about possible Noncompliance can be raised by a HRPO staff member, one or more members of the IRB, a subject or any other person. Any concern not raised by a HRPO Officer should be forwarded to a HRPO Officer for an initial determination.
2. The HRPO Officer to whom the concern is raised may make an initial determination as to whether the concern constitutes Nonsignificant Noncompliance.
3. If the HRPO Officer determines that a concern constitutes Nonsignificant Noncompliance, he/she shall enter the requisite information into the HRPO Nonsignificant Noncompliance Database.

B. ALLEGATION

1. Any concern about possible Noncompliance that is determined not to be Nonsignificant Noncompliance shall be considered to be an allegation and shall be forwarded to the COT for review, unless the circumstances described in Section V.B.2. below apply.
2. If an allegation arises during a HRPO Officer's review of a protocol, and the Officer believes that he/she has all of the information needed to make a determination as to whether a finding of Noncompliance should be made, he/she shall submit the equivalent of a Preliminary COT Report to an IRB Manager, the IRB Chair and, if determined by the IRB Manager or IRB Chair to be necessary, the ED, for review. The IRB Chair or the convened IRB will make the determinations described in the CDF, and the respective IRB Manager will provide a notification of the case and outcome to the COT for tracking and/or reporting purposes. To ensure that all necessary information has been obtained and to review the proposed corrective and preventive action plan for completeness, the COT will be consulted prior to a final determination by the IRB when the level of Noncompliance appears to be Serious.

C. INQUIRY

1. The Inquiry with respect to any alleged Noncompliance shall be conducted by the COT.
2. The Inquiry shall be completed promptly and, at its conclusion, the COT Director shall determine whether there is sufficient evidence to undertake an Investigation.

3. If an Investigation is not warranted, the COT Director shall submit a note to file, enter such determination into the HRPO COT Master database and, if appropriate, notify the person who raised the initial concern, and the person who filed the allegation, (if different), of such determination.

D. INVESTIGATION

1. If the COT Director determines that an Investigation is warranted, he/she shall direct the COT to proceed with the Investigation. The Investigation will cover only the specific allegation unless the findings indicate that the Allegation should be expanded. If any facts are at issue, the COT may contact the Respondent or any other appropriate persons for verification of such facts.
2. The COT shall complete the Investigation promptly and, at its conclusion shall send the findings to the Respondent and to the respective IRB Manager, for verification of facts. The COT shall request a response within a specified interval; however, the Investigation will proceed whether or not a response to the COT's findings is received.
3. The COT shall prepare and submit an initial written report (the "Preliminary COT Report") to the applicable IRB Manager who will route the Report to the IRB Chair, and, if determined by the IRB Chair to be necessary, the ED for review.
 - a. The reviewing IRB may request guidance from the ED and/or the IEC, e.g., with respect to complex situations that span multiple protocols, appropriate corrective and preventive actions or institutional concerns.
 - b. If the case involves multiple protocols for which there are multiple reviewing IRBs, or a Respondent who is a member of the reviewing IRB, the Preliminary COT Report will instead be routed to the IEC.
 - c. If an HRPO Officer has concerns related to the integrity or objectivity of any aspect of the Investigation, he/she should discuss such concerns with the ED, the VPRO or the EVPR.
4. The Preliminary COT Report shall include the recommendation of the COT as to whether a finding of Noncompliance should be made and, if so, the initial recommendation of the COT as to which corrective and preventive action(s) should be taken.
5. The IRB Chair or, at the request of the IRB Chair, the convened IRB, may accept, reject or modify the conclusions and recommendations in the Preliminary COT Report. The IRB Chair or convened IRB shall make the determination as to whether Noncompliance has occurred and if so, whether such Noncompliance constitutes Non-reportable, Serious or Continuing Noncompliance, what corrective and preventive actions are necessary and other determinations as appropriate. Determinations will be documented on the CDF or in the Rascal Notes or IRB meeting minutes.
6. Corrective and preventive action(s) may include, but are not limited to, any of the following:
 - a. imposition of changes in the research protocol(s) to further protect human subjects;
 - b. required training with respect to human subjects research and the regulatory requirements for the conduct of such research;

- c. imposition of restrictions as a condition for the continuation of research by the Respondent;
 - d. notification to the subjects;
 - e. destruction of data collected during the period of Noncompliance;
 - f. disallowance of the publication of data collected during the period of Noncompliance;
 - g. oversight monitoring by the COT;
 - h. suspension or termination of the Respondent's research protocol(s); or
 - i. any other appropriate action.
8. If the Preliminary COT Report is not accepted by the IRB Chair or the IRB, the COT will undertake the necessary actions to meet the IRB Chair or IRB's requests, and when completed, shall generate a revised Preliminary COT Report for consideration by the IRB Chair or IRB.
 9. When the Preliminary COT Report is accepted by the IRB Chair or the IRB, a Final COT Report will be prepared by the COT. This Report will reflect the final determinations of the IRB, and recommendations or requirements, if any, for the Respondent. If a determination of Noncompliance has been made, the Report will subsequently be forwarded to the Need to Know Individuals. If Noncompliance is not found, the Report will be provided to the Respondent only.

E. THE OUTCOME PHASE

1. If the Respondent disagrees with the Final COT Report and any finding of Noncompliance, he/she may so notify the IRB Manager, the COT Director, the IRB Chair and the ED, with copies to the Chair of the Respondent's Department and the applicable IO, citing the reasons for such disagreement within 30 days of receipt of the Final COT report. The IRB Chair or the applicable IRB will make a final decision as to the finding of Noncompliance and the corrective and preventive action plan and shall so notify the Need to Know Individuals. Such decision shall be final in all respects and the PI shall have no further right to disagree.
2. If the PI agrees with the Final COT Report and the finding of Noncompliance, or following the final decision of the IRB Chair or the IRB, the COT Director, in the case of Minor Noncompliance, or the IRB Chair or the IRB, in the case of Serious or Continuing Noncompliance, will determine if the corrective and preventive action plan has been implemented. If it is so determined, the case will be closed. Notice of closure shall be sent to the Need to Know Individuals.

F. NOT FOR CAUSE AUDITS

1. If possible Noncompliance is identified during a COT not for cause audit, the COT may make the initial determination as to the type of Noncompliance in accordance with Section A above.
2. If the Noncompliance is determined not to be Nonsignificant Noncompliance, the COT shall follow the same steps set forth in Sections D and E above with respect to

investigating, reporting and taking corrective and preventive action with respect to such Noncompliance.

VI. IRB NONCOMPLIANCE

A. INITIAL DETERMINATION, ALLEGATION AND INQUIRY

The steps described in Sections V.A, V.B and V.C above shall be followed with respect to any concern about possible IRB Noncompliance.

B. INVESTIGATION

1. If the COT Director determines that an Investigation is warranted, he/she shall direct the COT auditor(s) to proceed with such Investigation. The Investigation will cover only the specific allegation unless findings indicate that the Allegation should be expanded. If any facts are at issue, the COT may contact the Respondent or any other appropriate persons for verification of such facts.
2. The COT shall complete the Investigation promptly and, at its conclusion, shall submit a Preliminary COT Report to the IEC for review. If the possible Noncompliance involves a member of the IEC, the Preliminary COT Report should be submitted to the EVPR. The Preliminary COT Report shall include the COT's recommendation as to whether a finding of Noncompliance should be made and, if so, the COT's initial recommendation as to which corrective and preventive action(s) should be taken.
3. The IEC or the EVPR, as the case may be, may accept, reject or modify the conclusions and recommendations of the COT in the Preliminary COT Report and shall make the determination as to whether Noncompliance has occurred and if so, whether such Noncompliance constitutes Non-reportable, Serious or Continuing Noncompliance and what corrective and preventive actions are necessary. The Preliminary COT Report will then be finalized.
4. Corrective and preventive action(s) may include, but are not limited to, any of the following:
 - a. required training with respect to human subjects research and the regulatory requirements relating to such research;
 - b. if the Respondent is a HRPO staff member, suspension or termination of employment;
 - c. if the Respondent is a member of the IRB, suspension or termination of his/her appointment to the IRB; or
 - d. any other appropriate action.
- e. If the Preliminary COT Report is not accepted, the COT shall undertake the necessary actions to meet the IEC's or the EVPR's requests, and when completed, shall generate a revised Preliminary COT Report for consideration by the IEC or the EVPR.
- f. When the Preliminary Report is accepted, a Final COT Report will be prepared by the COT. This Report will reflect the final determinations of the IEC or the EVPR, and recommendations or requirements, if any, for the Respondent. If a determination of

Noncompliance has been made, the report will subsequently be forwarded to the Need to Know Individuals. If Noncompliance is not found, the Report will be provided to the Respondent only.

C. THE OUTCOME PHASE

1. If the Respondent disagrees with the Final COT Report and the finding of Noncompliance, he/she may so notify IEC or the EVPR, as applicable, citing the reasons for such disagreement. The IEC or the EVPR will make a final decision as to the finding of Noncompliance and the corrective and preventive action plan and may, at his/her discretion, notify the Need to Know Individuals. Such decision shall be final in all respects and the Respondent shall have no further right to disagree.
2. If the Respondent agrees with the Final COT Report and the finding of Noncompliance, or following the final decision of the IEC or the EVPR, the IEC or the EVPR will determine if the corrective and preventive action plan has been implemented. If it is so determined, the case will be closed. Notice of closure may, at the discretion of the IEC or the EVPR, be sent to the Need to Know Individuals.

VII. NOTIFICATION TO REGULATORY AGENCIES OR SPONSORS:

The ED shall report a finding of Serious or Continuing Noncompliance to the appropriate regulatory agency and sponsor as required by applicable law or regulations, or the sponsor's grant or contract. The ED will work with the Office of Research Administration to facilitate sponsor notification when it is required.

All Serious or Continuing Noncompliance will minimally be reported to OHRP, Director of Compliance Oversight. If the research involves an investigational drug, the case will also be reported to FDA, Division of Scientific Investigations, Office of Compliance. If the research involves an investigational device, the Serious or Continuing Noncompliance will also be reported to the FDA/Center for Devices and Radiological Health (CDRH), Director, Division of Bioresearch Monitoring.

Allegations that fall outside of the mandatory reporting requirements shall be reported to the regulatory agency, the sponsor, or any other relevant person(s) involved in the research project at the discretion of the ED or the EVPR.