

<b>Noncompliance in Human Research Activities</b>	Effective Date	5.8.2000
	Revisions Date	5.2.2022

- 1.0 Purpose:** The purpose of this Standard Operating Practice (SOP) is to define noncompliance in human research activities and identify the procedures associated with identifying and making determinations of serious and/or continuing noncompliance.
- 2.0 Persons Affected:** All individuals who hold responsibilities associated with human research activities or are aware of noncompliance in those activities, including, but not limited to, faculty, staff, students, and employees of ECU and its Affiliates, whether or not associated with a specific human research activity.
- 3.0 SOP:** This SOP seeks to ensure that individuals can appropriately identify noncompliance in human research and that East Carolina University, in accordance with its Federalwide Assurance, and Food and Drug Administration regulations, will report serious and/or continuing noncompliance in non-exempt human research activities.
- 4.0 Definitions:**
- 4.1 Allegation of noncompliance:** An unproven assertion of noncompliance with federal regulations, state or local laws, institutional or UMCIRB policies, rules, or UMCIRB determinations.
- 4.2 Complainant:** A person (or persons) making an allegation of non-compliance.
- 4.3 Noncompliance:** Failure (intentional or unintentional) to comply with federal regulations, state or local laws, institution or UMCIRB policies, rules or UMCIRB determinations regarding research involving humans or ethical principles of the Belmont Report. Noncompliance can result from action or omission and may be non-serious (minor), serious and/or continuing.
- 4.4 Continuing Noncompliance:** situation in which there has been a pattern of repeated instances of failure to follow federal regulations, state or local laws, institution, or UMCIRB policies, rules, or UMCIRB determinations. Continuing noncompliance may include, but is not limited to:
- 4.4.1** A pattern of noncompliance that indicates an unwillingness to comply that may adversely affect the rights and welfare of participants and may place participants at an increased risk of harm.
  - 4.4.2** In the judgment of the convened IRB, actions taken suggests a likelihood that instances of noncompliance will continue unless intervention occurs.
  - 4.4.3** Continuing noncompliance is presumed when it persists after the investigator knew or reasonably should have known about it.
  - 4.4.4** Repeated late submission of reportable events.
  - 4.4.5** Repeated lapses of IRB approval during which human research activities occur.
  - 4.4.6** Repeated failure to follow procedures as approved by the IRB.
  - 4.4.7** Repeated informed consent discrepancies.
  - 4.4.8** Repeated failure to maintain research related records as specified by the UMCIRB and federal regulations.

- 4.5 **Preliminary Inquiry:** Initial fact-finding to determine if there is sufficient evidence to support an allegation or apparent instance of noncompliance. The purpose of the Preliminary Inquiry is to gather information pertaining to the possible noncompliance. Reaching a conclusion about whether or not noncompliance occurred is the responsibility of the UMCIRB.
- 4.6 **Respondent:** A person (or persons) named in an allegation of noncompliance.
- 4.7 **Serious Noncompliance:** Noncompliance which, in the judgment of the convened IRB, significantly increases risk of harm to participants, significantly decreases potential benefits, compromises the integrity or validity of the research and/or willfully violates policy/procedures. Some examples of serious noncompliance include but are not limited to:
  - 4.7.1 Non-exempt human research that requires direct intervention or interaction with humans conducted without IRB approval.
  - 4.7.2 Participants enrolled without consent (when not eligible for waiver of consent).
    - 4.7.2.1 Includes participant enrolled with an invalid/outdated consent that is missing information that might affect the participant’s willingness to take part or continue to take part in the research activities.
  - 4.7.3 Participants enrolled who do not meet the inclusion/exclusion criteria in a protocol that involves greater than minimal risk (unless this change was approved by the study sponsor, if applicable, and IRB).
  - 4.7.4 Substantive change to the research implemented without IRB approval (unless implemented to avoid imminent harm to participants).
  - 4.7.5 Failure to report unanticipated problems involving risks to participants or others.
  - 4.7.6 Inappropriate oversight of the research to ensure safety of participants and/or the integrity of the research data.
  - 4.7.7 Failure to report major protocol deviations.
  - 4.7.8 Failure to maintain research records in an accurate or organized manner including IRB records and documentation of informed consent.
  - 4.7.9 Failure to comply with requirements or determinations of the UMCIRB.
- 4.8 **Sufficient Evidence:** the person making the preliminary inquiry and subsequently the full UMCIRB believes it more likely than not, based on the information presented, that an allegation is true.
- 4.9 **Insufficient Evidence:** at the time of full UMCIRB review, if the information presented on a particular issue is equally balanced, the issue is considered not to have sufficient evidence to support the allegation.

**5.0 Responsibilities:**

- 5.1 Human Research Protections (HRP) Director (or designee) will:
  - 5.1.1 Ensure compliance with this SOP and provide training opportunities and resources.
  - 5.1.2 Revise this SOP accordingly as new information becomes available.
  - 5.1.3 Raise any applicable issues outside of the UMCIRB jurisdiction and communicate those issues to the appropriate individuals.
  - 5.1.4 Notify the appropriate UMCIRB Chairperson (Biomedical and/or Social & Behavioral), and the appropriate Institutional Official(s) immediately upon determination of an instance of alleged noncompliance.
  - 5.1.5 Provide consultation to the UMCIRB Chairperson and/or the Institutional Official

whether there is sufficient cause to suspend UMCIRB approval immediately to protect human participants.

- 5.1.6** Notify the Respondent of the allegation, unless, in the determination of the Administrative Director, UMCIRB and/or the UMCIRB Chairperson, the investigation would be jeopardized by doing so or the respondent was the person that identified and reported the potential noncompliance.
- 5.1.7** Notify the appropriate UMCIRB (Biomedical and/or Social & Behavioral) of receipt of the allegation or discovery of noncompliance at the next convened IRB meeting.
  - 5.1.7.1** Information is to be presented in a manner that best protects the identity of the Respondent and complainant to the limits possible.
- 5.1.8** Conduct a Preliminary Inquiry to support or refute the potential noncompliance, in utilizing the following resources:
  - 5.1.8.1** Any ECU Division or Departmental information or other available resources necessary to complete the investigation.
  - 5.1.8.2** Reviewing the UMCIRB application material, as applicable.
  - 5.1.8.3** Interviewing individuals who can provide relevant information, including but not limited to the Complainant, Respondent, past or present research participants, and any other relevant individuals identified during the course of the Preliminary Inquiry.
  - 5.1.8.4** Reviewing case report forms, medical records, research records and any other documentation relating to the alleged noncompliance.
  - 5.1.8.5** Interviewing auxiliary services, pharmacy, laboratory, nursing staff, or any other personnel associated with the alleged noncompliance.
  - 5.1.8.6** Interviewing facility administrators.
- 5.1.9** Summarize findings in a Preliminary Inquiry Report (if not documented within an IRB Reportable Event submission) including:
  - 5.1.9.1** Summary of the potential noncompliance.
  - 5.1.9.2** Summary of the Evidence.
- 5.1.10** Provide the appropriate UMCIRB Chair (Biomedical and/or Social & Behavioral) and the appropriate Institutional Official(s) with a copy of the Preliminary Inquiry Report or Reportable Event submission information.
- 5.1.11** Ensure all relevant documents are distributed to the UMCIRB to allow sufficient time for review.
- 5.1.12** If they are not already aware, notify the Respondent in writing of all UMCIRB reviews and deliberations concerning the allegation, including a copy of the Preliminary Inquiry Report (if applicable), and any subsequent action(s) taken by the IRB, copying the Complainant(s) (if applicable) and appropriate institutional administrators/officials, federal agencies, sponsors and Affiliate sites.
- 5.1.13** Maintain the official record of the matter in accordance with the state and federal requirements and institutional policies for records retention, whichever period is longer.
- 5.1.14** Should any serious or continuing noncompliance involve another facility with its own federalwide assurance, the HRP Director will offer that facility the ability to report the event jointly with ECU UMCIRB to applicable agencies. The HRP

Director will prepare the report and send it to the appropriate individual at the other facility for comments prior to finalizing.

- 5.1.15 Should the noncompliance involve another facility with its own federalwide assurance who chooses to send a separate report, the facility will be included in the distribution list.
- 5.1.16 Compose and send reports to promptly notify the Office for Human Research Protection (OHRP), and other applicable agencies (see Distribution List below) and sponsors, of serious or continuing noncompliance.
- 5.2 UMCIRB office staff will:
  - 5.2.1 Assist in compiling preliminary information regarding noncompliance.
  - 5.2.2 Record all deliberations and determinations made by the UMCIRB regarding allegations of noncompliance in the UMCIRB minutes.
- 5.3 Chairperson or designee: will review the potential noncompliance submitted and has the authority to:
  - 5.3.1 Request additional information.
  - 5.3.2 Request a corrective action plan before taking further action or making a final decision.
  - 5.3.3 Request a copy of any correspondence sent to or received from a sponsor, FDA, CRO, or other agency regarding this event.
  - 5.3.4 Request full IRB review of the potential noncompliance (required for serious or continuing noncompliance determinations.)
    - 5.3.4.1 All members attending the IRB meeting will be presented with pertinent information and will have access to all approved study material.
  - 5.3.5 Take any action necessary to protect human participants including the notification of appropriate ECU or Affiliate Institution Officials if immediate action is required to protect participants.
  - 5.3.6 Suspend enrollment or implementation of the study until the convened UMCIRB has had an opportunity to review the potential noncompliance.
- 5.4 UMCIRB is responsible for:
  - 5.4.1 Evaluating Preliminary Inquiries or Reportable Event submissions for determination of noncompliance.
  - 5.4.2 Determining when substantiated noncompliance is serious and/or continuing.
  - 5.4.3 The IRB may consider the following when determining serious noncompliance:
    - 5.4.3.1 Did the noncompliance affect the safety, rights or welfare of the participant?
    - 5.4.3.2 If the study is a clinical trial, which phase is it and does the PI hold the IND/IDE and have additional sponsor responsibilities?
    - 5.4.3.3 Might the noncompliance impair the willingness of subjects to continue participation?
    - 5.4.3.4 Did the noncompliance significantly increase the risk to subjects?
      - 5.4.3.4.1 When the noncompliance deals with PHI data only: review nature and extent of PHI involved (types and likelihood of re-identification), any unauthorized people who used the data, whether data was actually acquired or viewed, and extent to which risk has been mitigated

5.4.3.5 Is the noncompliance, if made known to the public, very likely to damage community trust in the research institution?

5.4.4 The IRB may consider the following when determining continuing noncompliance:

5.4.4.1 When the investigator should have known of the noncompliance.

5.4.4.2 When the investigator did know of the noncompliance.

5.4.4.3 Whether the study team failed to comply with a directive from the UMCIRB to resolve previous, similar noncompliance.

5.4.5 The IRB may:

5.4.5.1 Request a corrective action plan or more information before taking further action or making a final decision.

5.4.5.2 Require specific revisions to the currently approved protocol and/or consent.

5.4.5.3 Place restrictions on the Principal Investigator, coordinator or any research personnel that may have been responsible for the noncompliance.

5.4.5.4 Suspend or terminate the study or any portion of that study which may increase risks to participants or others.

5.4.5.5 Require notification to past or current participants when such information may relate to participants' willingness to continue to take part in the research.

5.4.5.6 Modify the continuing review schedule.

5.4.5.7 Monitor the research or consent process.

5.4.5.8 Refer to other appropriate entity.

5.4.5.9 Require additional training.

5.4.5.10 Initiate audits of all or some part of the Respondent's active protocols.

5.4.5.11 Suspend or disqualify the Respondent from engaging in human research activities at the University.

5.4.5.12 Determine that the data was not collected following ethical standards outlined in the Common Rule and the Belmont Report, therefore, it cannot be used.

5.4.5.13 Make recommendation to the HRP Director or designee for notification to OHRP, FDA, and/or other federal agencies as appropriate for serious or continuing noncompliance.

5.4.5.14 Request other actions as the UMCIRB determines to be appropriate.

5.5 Other individuals, including investigators and research personnel, involved with human research activities: are responsible for reporting potential noncompliance, including, but not limited to, allegations of serious or continuing noncompliance, to the UMCIRB.

6.0 Distribution List: List of agencies or institutional entities which, if providing financial support or have oversight responsibilities, would be notified in the determination of serious or continuing noncompliance:

6.1 Agency for International Development (22 CFR 225)

6.2 Central Intelligence Agency (Executive order)

6.3 Consumer Products Safety Commission (16 CFR 1028)

6.4 Department of Agriculture (7 CFR 1c)

6.5 Department of Commerce (15 CFR 27)

6.6 Department of Defense (32 CFR 219)

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- 6.7 Department of Education (34 CFR 97)
- 6.8 Department of Energy (10 CFR 745)
- 6.9 Department of Health and Human Services (45 CFR 46)
- 6.10 Department of Homeland Security (6 U.S.C. section 112)
- 6.11 Department of Housing and Urban Development (24 CFR 60)
- 6.12 Department of Justice (28 CFR 46)
- 6.13 Department of Transportation (49 CFR 11)
- 6.14 Department of Veterans' Affairs (38 CFR 16), Office of Research Oversight
- 6.15 Environmental Protection Agency (40 CFR 26)
- 6.16 National Aeronautics and Space Administration (14 CFR 1230)
- 6.17 National Science Foundation (45 CFR 690)
- 6.18 Social Security Administration (42 U.S.C. section 901)
- 6.19 Food and Drug Administration (21 CFR 56)
- 6.20 Division, Department, or Unit Chairperson and Dean
- 6.21 Administrators at Affiliate site(s)
- 6.22 Any Compliance Officers, Risk Management, or State Agencies that may have a need to be informed
- 6.23 Biomedical and/or Social & Behavioral IRB members and ex-officios

**Revision History:**

Date	Change	Reference Section(s)
6.25.2013	Updated to stand-alone document.	All
7.31.2014	Updated new office name; clarified that potential noncompliance maybe reported by the individual that performed or was responsible for the study procedures and removal of notification to ORCA as that office has been dissolved.	
5.31.2018	Clarified responsibilities and updated Distribution list.	5.1, 6.0
1.15.2020	Updated office name; clarified responsibilities	All sections; 5.1
5.2.2022	Added effective date and updated footer.	

**References:**

FDA. Code of Federal Regulations:

<http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50> and <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56>

DHHS, OHRP. Code of Federal Regulations:

<http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.html>