

## NONCOMPLIANCE IN RESEARCH

1. **PURPOSE:** To ensure that all investigators and research personnel comply with all applicable laws and regulations within the jurisdiction in which the research takes place.

2. **POLICY:** The leadership of the Research Service and/or the Louis Stokes Cleveland Department of Veterans Affairs Medical Center (LSCDVAMC), will act upon any disclosure of unanticipated research problems, complaints or irregularities brought to the attention of the Research and Development (R&D) Committee, the Institutional Review Board (IRB), the Institutional Animal Care and Use Committee (IACUC), or the Research Compliance Officer (RCO) by investigators, coordinators, other employees or patients, or research participants.

3. **DEFINITIONS:**

a. **Research Noncompliance:** Failure to comply with or adhere to rules, regulations, policies, and standards of conduct that govern research.

b. **Continuing Research Noncompliance:** A pattern of noncompliance that suggests a likelihood that instances of noncompliance will continue without intervention. Continuing noncompliance also includes failure to respond to a request to resolve an episode of noncompliance.

c. **Serious Non-Compliance:** Noncompliance that involves greater than minimal risk of harm or discomfort to human or animal subjects or others involved in research.

d. **Research Misconduct:** A fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

e. **Allegation of Noncompliance.** An unproved assertion that noncompliance has occurred.

f. **Finding of Noncompliance.** An allegation of noncompliance that is proven true, or a finding or report of noncompliance that is clearly true. For example, a finding during an audit of an unsigned consent document, or an admission by an investigator that a protocol was willfully not followed would represent reports of noncompliance that would require no further action to determine their truth.

4. **RESPONSIBILITIES:**

a. **Associate Chief of Staff for Research (ACOS/R):** The ACOS/R is responsible for ensuring the implementation of this policy. He/she will provide for widespread dissemination of the policy and will assure that appropriate review procedures are promptly implemented when allegations of noncompliance are reported. The ACOS/R will ensure that proper and timely reporting to relevant agencies is made for any investigation of substantial noncompliance. The ACOS/R also represents the LSCDVAMC when it is determined that present or former research personnel are the subject of complaints or investigations that involve outside institutions.

b. **RCO**: The RCO is responsible for facilitating and ensuring that all researchers adhere to the applicable rules, regulations, policies and standards of conduct that govern research. He/she assists and supports the ACOS/R, R&D Committee, the IRB, and the IACUC throughout the inquiry's investigational stages.

c. **IRB**: The IRB has the authority to suspend or terminate research for serious and/or continued noncompliance with the Common Rule, VHA, DHHS, and FDA regulations, based on its own findings and/or determinations.

d. **IACUC**: The IACUC has the authority to suspend research for serious deviations or continuing noncompliance with PHS Policy as stated in the Guide, and Animal Welfare Act Regulations and Standards (AWAR) regulations.

e. **Principal Investigators (PI)**: Ensure that the appropriate body or committee is notified promptly of any serious or continuing noncompliance with applicable regulatory requirements or committee determinations of which they become aware.

f. **Study Staff**: Study staff at every level are responsible for notifying the appropriate body or committee promptly of any serious or continuing noncompliance with applicable regulatory requirements or determinations of the LSCDVAMC of which they become aware, whether or not they themselves are involved in the research. Study staff may also notify the RCO directly of any compliance concerns they may have.

g. **Non-research Staff**: Whether involved in the research or not, all employees and agents of LSCDVAMC are required to notify the appropriate body or committee if they become aware of any serious or continuing noncompliance with regulatory requirements or with the determinations of the respective subcommittee(s).

## 5. PROCEDURES:

### a. **Human Research.**

#### 1) Review of Allegations of Noncompliance

a) The IRB Chairperson and the ACOS/R will review all allegations of noncompliance. They will review all documents relevant to the allegation including:

- i. The last approved IRB application and protocol;
- ii. The last approval letter from the IRB;
- iii. The last approved consent document;
- iv. The grant, if applicable; and
- v. Any other pertinent information (e.g., questionnaires, DSMB

reports, etc.).

b) The IRB Chairperson and ACOS/R will make a determination as to the validity of the allegation. They may request additional information or an audit of the research in question.

c) If the IRB Chairperson and ACOS/R determine that the reported allegation of noncompliance is not valid, no further action will be taken.

d) If the IRB Chairperson and ACOS/R determine that the reported allegation of noncompliance is valid, the noncompliance will be processed according to the section below "Review of Findings of Noncompliance."

e) If the IRB Chairperson and ACOS/R determine that the reported allegation or findings of noncompliance warrants immediate suspension of the research to ensure protection of the rights and welfare of participants, the IRB Chairperson will temporarily suspend enrollment of new subjects or of continued participation of previously enrolled subjects. Such suspensions will be reported to the next convened IRB meeting for review.

f) In the event that the IRB Chairperson and ACOS/R are unable to reach a consensus concerning the reported allegation or finding of noncompliance, the Chief of Staff Wade Park Campus will be consulted to make a determination of the validity of the allegation.

## 2) Review of Findings of Noncompliance

a) If the IRB Chairperson and ACOS/R determine that the reported finding of noncompliance is not serious, not continuing, and the proposed corrective action plan seems adequate, no further action is required, and the IRB is informed at the next convened meeting.

b) If the IRB Chairperson and ACOS/R determine that the reported findings of noncompliance is serious and/or continuing, the matter will be presented to the IRB at the next convened meeting with a recommendation that a formal inquiry (described below) be conducted.

c) The IRB will review all findings of noncompliance referred to them at a convened meeting. All IRB members will receive all documents relevant to the allegation including:

- i. The last approved IRB application;
- ii. The last approved consent document;
- iii. The last approval letter from the IRB; and
- iv. Any other pertinent information (e.g., questionnaires, DSMB reports, etc.).

d) At this stage, the IRB may:

- i. Find that there is no issue of noncompliance;
- ii. Find that there is noncompliance that is neither serious nor continuing and an adequate corrective action plan is in place;
- iii. Find that there may be serious or continuing noncompliance and direct that a formal inquiry (described below) be held; or
- iv. Request additional information.

## 3) Inquiry Procedures

a) The IRB may make a determination that an inquiry is necessary based on several issues that may include but are not limited to:

- i. Subjects' complaint(s) that their rights were violated;

- ii. Report(s) that the PI is not following the protocol as approved by the IRB;
- iii. Unusual and/or unexplained adverse events in a study;
- iv. Repeated failure of the PI to report required information to the IRB.

b) The IRB Chairperson will appoint an ad hoc committee consisting of IRB members, taking into account IRB member expertise and/or whether there are any conflicts of interest. The ad hoc committee will be given a charge by the IRB, which can include any or all of the following:

- i. Review of protocol(s) in question;
- ii. Review of sponsor audit report, if appropriate;
- iii. Review of any relevant documentation, including consent documents, case report forms, subject's investigational and/or medical files etc., as they relate to the PI's execution of her/his study involving human subjects;
- iv. Interviews of appropriate study staff, if necessary;
- v. Preparation of either a written or oral report of the findings, which is presented to the full IRB at its next convened meeting; and/or
- vi. Recommended actions, if appropriate.

#### 4) Final Review

a) The IRB will review the results of the ad hoc committee inquiry at a convened meeting. If the results of the inquiry substantiate the finding of serious or continuing noncompliance, the IRB's possible actions could include, but are not limited to:

- i. Request a corrective action plan from the PI;
- ii. Verify that participant selection is appropriate and observe the actual informed consent process;
- iii. Request an increase in data and safety monitoring of the research activity;
- iv. Request a directed audit of targeted areas of concern;
- v. Request a status report after each participant receives intervention;
- vi. Modify the continuing review cycle;
- vii. Request additional Investigator and staff education;
- viii. Notify current subjects, if the information about the noncompliance might affect their willingness to continue participation;
- ix. Require modification of the protocol;
- x. Require modification of the information disclosed during the consent process;
- xi. Require current participants to re-consent to participation;
- xii. Suspend the study;
- xiii. Terminate the study.

b) The IRB will notify the PI in writing of its determination and the basis for the determination and affords the PI an opportunity to respond.

c) The IRB will communicate all determinations and outcomes to the R&D Committee in writing.

d) If the IRB determines that the noncompliance was serious or continuing, the results of the final review will be reported to regulatory bodies per federal regulations and local policy.

5) Additional Actions

a) A finding of serious or continuing noncompliance may also result in the following sanctions, among others:

i. Suspension or termination of IRB approval of specific research protocols, or of all research involving human subjects in which the PI participates.

ii. Sponsor actions: In making decisions about supporting or approving applications or proposals covered by this policy, the DHHS or Agency head may take into account - in addition to all other eligibility requirements and program criteria - factors such as whether: 1) the applicant has been subject to a termination or suspension as described above, and/or 2) the applicant or the person or persons who would direct or has/have directed the scientific and technical aspects of an activity has/have, in the judgment of the DHHS or Agency head, materially failed to discharge responsibility for the protection of the rights and welfare of human subjects.

iii. Institutional action by OHRP. OHRP may

aa. Withhold approval of all new studies reviewed by the IRB;

bb. Direct that no new subjects be added to any ongoing studies;

cc. Terminate all ongoing studies, except when doing so would endanger the subjects; and/or

dd. Notify relevant state, federal and other interested parties of the violations.

iv. Individual disciplinary action of the PI or other staff involved in a study, up to and including dismissal, pursuant to medical center policies and procedures.

b. **Animal Research**

1) **Investigation of Allegations of Improper Animal Care or Use**

a) The IACUC must promptly review all written or oral internal and external allegations of improper animal care and use at the LSCDVAMC, and investigate the allegation if warranted.

b) The IACUC Chairperson will determine the degree of urgency and seriousness of the situation and initiate a timely inquiry and response. Where there is a slight to no change in risk to animals' health or well being, an inquiry will be promptly conducted and a report submitted for discussion and determination of action at the next convened meeting of the full IACUC. If there is any indication that there is a risk to animals' health or well being, the research will be stopped until a formal investigation has been completed.

c) The Chairperson will document the allegation and outcome and send a memorandum to the investigator and attach a copy to the Animal Component of Research Protocol (ACORP).

## 2) Inquiry

a) After an initial inquiry, which includes a discussion with the PI and/or study staff, the IACUC will determine if the incident was due to:

- i. a lack of education of the PI and/or study team,
- ii. a deficient research management procedure, or
- iii. a willful disregard for animal subject protections.

b) If the inquiry finds that the allegation was inaccurate or without foundation, the allegation of noncompliance will be dismissed without any further action. The IACUC will notify the PI in writing of its findings.

c) If the inquiry finds that the issue of noncompliance was due to a lack of education, then the Supervisor of the Animal Research Facility and/or the Consulting Veterinarians will provide remedial instruction to the PI and study staff. The PI will indicate a plan of how to ensure continued education regarding best practices in research.

d) If the inquiry makes a determination that involves halting further studies, the IACUC will notify the PI immediately. The IACUC Chairperson will discuss the situation with the PI and initiate a full investigation by an ad hoc committee of IACUC.

## 3) Investigation

a) A selected ad hoc subcommittee of the IACUC will perform the investigation.

b) Once the investigation is complete, the IACUC will meet to discuss their findings and recommendations for action.

## 4) Outcome

a) If the situation appears to be isolated, a miscommunication or misunderstanding or of a non-continuing nature, the issue will be resolved between the PI and the IACUC along with any further recommendations from the R&D Committee.

b) If it is found that the situation occurred due to lack of education, or a deficient research management procedure, the IACUC Chairperson will meet with the PI and discuss corrective measures.

c) If the investigation indicates that continuing noncompliance, serious noncompliance or scientific misconduct has occurred, the IACUC is compelled to report the incident to outside authorities through the R&D Committee, ACOS/R, and medical center Director.

d) The IACUC must review and consider the PI's response to any corrective actions or steps to eliminate future occurrences.

e) All determinations and outcomes will be communicated to the R&D Committee in writing.

5) **Suspension of a Protocol**. The IACUC may suspend an Animal Component of Research Protocol (ACORP) that it previously approved, if it determines that the activity is not being conducted in accordance with the ACORP provided by the PI and approved by the IACUC. It may also suspend any animal procedures not approved by the IACUC. The IACUC may suspend an activity only after review of the matter at a properly-convened IACUC meeting and if the vote for suspension is by a majority of a quorum.

6) The main categories of deficiencies that must be reported to outside authorities and the elements needed in the report are as follows:

a) Any serious or continuing non-compliance with PHS Policy (including any serious deviation or continuing non-compliance with the provisions of the Guide, as required by the PHS Policy) or United States Department of Agriculture USDA and AWAR. The report will include:

- i. When and how the IACUC became aware of the problem.
- ii. When the investigation was performed to determine facts and detail the circumstances that led to the non-compliance.
- iii. The results of that investigation, and
- iv. When the IACUC convened a quorum to suspend the activity.
- v. What corrective actions the IACUC approved to stop the noncompliant activity and prevent future recurrences.

b) Suspension of previously approved protocols or procedures or studies that were never approved. The report will include:

- i. When and how the IACUC became aware of the problem.
- ii. When the investigation was performed to determine the facts and detail circumstances that lead to report of non-compliance.
- iii. The results of the investigation.
- iv. When the IACUC convened a quorum to suspend the activity.
- v. What corrective actions the IACUC approved to prevent recurrences.

c) Failure to correct a significant deficiency, identified during a semi-annual IACUC program or facility self-assessment review. The report will include:

- i. The date when the IACUC identified the deficiency.
- ii. The timetable and plan approved for correction.
- iii. Why the correction(s) could not be completed according to the timetable.
- iv. The revised timetable.
- v. The plan to finish the correction(s).

7) Though it is not considered an IACUC suspension, if VACO Office of Research & Development (ORD) places a veterinary hold on a protocol, it must be

reported to other Federal agencies, if the IACUC and medical center Director find that information in the ACORP represents a reportable deficiency.

8) Deficiencies must be reported in writing within 15 business days through the ACOS/R and the medical center Director to the following agencies and offices:

- a) ORD (by contacting the Chief Veterinary Medical Officer's (CVMO) office).
  - b) Office of Laboratory Animal Welfare, as required by PHS Policy.
  - c) The Animal Care Section at USDA Animal and Plant Health Inspection Service (APHIS), as required by AWAR, if the deficiency involves a species meeting the definition of an animal in the AWAR, or if the deficiency impacts the care or use of such a species.
  - d) Association for the Assessment and Accreditation of Laboratory Animal Care International (AAALAC), as required by their rules of accreditation.
  - e) Case Western Reserve University's IACUC, if the project involves animals purchased with funds awarded to the Case.
  - f) The VA Office of Research Oversight (ORO), as required by its policy.
  - g) Any Federal agency (other than the VA) funding an activity that has been suspended.
- 9) If local efforts to correct deficiencies have proven inadequate, individuals may contact the CVMO directly to discuss concerns, solicit guidance, or seek information without requesting or receiving local permission to do so.

6. **REFERENCE:** 38 CFR Parts 16 and 17.85; 21 CFR Parts 11, 50, 56, 312, 314, 812, and 814; VHA Handbooks 1200.1 "Research & Development Committee, 1200.5 "Requirements for the Protection of Human Subjects in Research"; 1200.7 "Use of Animals in Research", Human Research Protection Standard Operating Procedures; Medical Center Policy 151-001 "Research and Development Committee.

7. **RESCISSION:** Medical Center Policy 151-006 dated September 1, 2004 has been rescinded. The review date of this policy is September 1, 2010.

8. **FOLLOW UP RESPONSIBILITY:** Associate Chief of Staff for Research.

WILLIAM D. MONTAGUE  
Medical Center Director