



NON-COMPLIANCE WITH THE REQUIREMENTS OF THE HUMAN RESEARCH PROTECTION PROGRAM

3/25/2021

In order to comply with 45 CFR 46.108(a)(4)(i) and 21 CFR 56.108(b)(2), DUHS will promptly report to the Office of Human Research Protection (OHRP) and US Food and Drug Administration (FDA) all applicable events adversely affecting the rights, welfare, and/or safety of human research participants. The required reporting events include any serious or continuing non-compliance with federal policy or determinations made by the IRB.

Definitions

(1) Allegation of non-compliance is an assertion or report of non-compliance.

(2) Documentation is any document, tangible item, or testimony offered or obtained during a non-compliance review that tends to prove or disprove the existence of an alleged fact.

(3) Non-compliance is the failure to follow federal, state, or local regulations governing human subject research, institutional policies related to human subject research, an IRB-approved research protocol, or the requirements or determinations of the IRB. This may pertain to the principal investigator, research staff, or any member or component of the Human Research Protection Program (HRPP).

(a) Serious Non-compliance:

Means actions or omissions by any members of the HRPP that are known or should be known to create an increase in risks to subjects, adversely affects the rights, welfare and safety of the research subjects, or adversely affects the scientific integrity of the study. Willful violation of policies and/or federal regulations may also constitute serious non-compliance.

(b) Continuing Non-compliance:

Means a pattern of repeated actions or omissions by any member of the HRPP that are known or should be known to create an increase risk to subjects, adversely affect the rights, welfare and safety of research subjects, or adversely affect the scientific integrity of the study.

(4) Preponderance of Documentation

Means proof of information that, when compared to the information opposing it, leads to the conclusion that the fact at issue is more probably true than not.

Examples of non-compliance

The actions of anyone or any organization within the HRPP may result in non-compliance. Examples of non-compliance include, but are not limited to:

- Conducting human subject research without first obtaining IRB and institutional approval or an IRB declaration of exemption
- Deviating from or violating the provisions of an IRB-approved protocol
- Failing to secure IRB approval of a protocol due for periodic continuing review prior to its expiration date
- Permitting a protocol's IRB approval to lapse without stopping all research-related activities and submitting a Closing Progress Report to the IRB, or in the event of an overriding safety concern or ethical issue such that it would be in the individual subject's best interest to continue study participation, not arranging with the IRB to continue those activities
- Deviating from written Duke University Health System policies and procedures governing research with human subjects
- Failure of any organization with a defined responsibility for oversight of any part of the HRPP to fulfill its obligations

Requirements for reporting allegations of non-compliance

Investigators, research staff and any other member of the HRPP are required to report any potential, observed, suspected, or apparent non-compliance to the IRB. This refers to all non-compliance, whether or not it may be serious or continuing non-compliance. All institutional members, research participants and others are encouraged to report any potential, observed, suspected, or apparent non-compliance. Reports of non-compliance may also arise from: (i) calls to the Integrity Line, the confidential institutional hotline for reporting compliance concerns; or (ii) as a result of internal or external audits; or (iii) through direct communication to the IRB. Regardless of how reports arise, all allegations of non-compliance related to research with human participants must be referred to the IRB.

Reports of non-compliance must contain enough information to determine whether the report is sufficiently credible and specific so that potential documentation of non-compliance may be identified and acted upon.

Handling allegations of non-compliance

Any **allegation** of non-compliance will be referred to the Executive Director of the IRB or designee. In most instances, the Executive Director or designee will submit a written inquiry to the related Principal Investigator (PI) for the research study in question. However, in cases where the identity of the complainant must be protected, the Executive Director may submit a written request to the Duke University Office of Audit, Risk and Compliance to conduct a directed audit in response to the allegation. Once either the response from the PI or the audit report has been received, the Executive Director, in conjunction with the Lead IRB Chair, may conclude that the allegations have a basis in fact. In such cases, the process under "Handling non-compliance" will be followed. Otherwise, no further action is taken under this policy and the PI is informed that the IRB considers the issue to be resolved. The matter may be referred to other institutional entities for evaluation and management as applicable.

Handling non-compliance

If the Executive Director of the IRB or designee determines the non-compliance is neither serious nor continuing, the process under “**Non-compliance that is determined to be neither serious nor continuing**” is followed.

If the Executive Director of the IRB or designee assesses the non-compliance to potentially be serious and/or continuing, the process under “**Non-compliance that is determined to potentially be serious or continuing**” is followed.

Non-compliance that is determined to be neither serious nor continuing

If the non-compliance is considered to be neither serious nor continuing non-compliance, the Executive Director of the IRB or designee will determine whether any corrective actions are needed, and if so communicate those to the involved individual(s) and ensure all corrective actions are completed. The Executive Director or designee will work with the involved individuals to implement the corrective action plan and will monitor the completion of all required corrective actions. If the Executive Director or designee are unable to work with the involved individuals to implement the corrective action plan, the matter will be considered to be continuing non-compliance and the procedures in “**Non-compliance that is determined to potentially be serious or continuing**” will be followed.

Non-compliance that is assessed to be serious or continuing

If the non-compliance is initially assessed to represent serious or continuing non-compliance, the Executive Director of the IRB or designee will use any of the following mechanisms to investigate the allegation(s):

- (1) communicate directly with the PI and/or relevant study team,
- (2) communicate with the complainant(s), and/or
- (3) contact the Office of Audit, Risk and Compliance, and any other relevant internal departments at Duke.

Once all available documentation has been received, the Executive Director or IRB Lead Chair, will refer the allegation(s) to IRB #9, the DUHS IRB’s dedicated non-compliance board, for formal review. The Vice Dean for Scientific Integrity and the Vice Dean for Clinical Research for the School of Medicine will be apprised of the investigation and review by the convened IRB.

Information provided to the IRB for review of serious or continuing non-compliance

A primary reviewer will be assigned to present non-compliance that is referred to IRB #9 for review and action. The primary reviewer will have access to all evidence gathered during the investigation. All evidence including the final report and response will be provided to all members attending the IRB meeting. In addition, all attending members will have access to the entire study record in the IRB’s software, iRIS, including study documents, audit reports, other submissions, safety events, and correspondence throughout the history of the study. All attending members will be expected to review these materials.

Responses from the affected parties

All individuals involved in the non-compliance will have the opportunity to provide their written response to the convened IRB using the format in Attachment I. All such parties will have at least 7 calendar days to prepare their written responses. Attending members at IRB #9 will have at least 3 business days to review these responses prior to discussion at the convened meeting, unless the convened IRB must meet sooner to act upon possible direct hazard to participants.

Actions of the convened IRB

The convened IRB will confirm by vote whether there is a preponderance of the Documentation to make a recommendation of serious and/or continuing non-compliance for the Institutional Official's (IO's) final determination. The IRB may, at its own discretion, request an in-person presentation from any individuals involved in the non-compliance or the investigation of the non-compliance. In making such a request, the IRB must consider equal representation by opposing parties.

If the IRB does not find the non-compliance to be serious or continuing, the non-compliance along with any recommendations will be referred back to the Executive Director or designee and the process for "Non-compliance that is determined to be neither serious nor continuing" is followed.

If the convened IRB finds that the non-compliance is serious or continuing, it may immediately suspend the research if it finds that doing so is necessary to eliminate apparent immediate hazards to the research subject. The IRB will specify any required corrective actions, which may include:

- Suspension of the research
- Termination of the research
- Notification of current participants (required when such information might relate to participants' willingness to continue to take part in the research)
- Modification of the research protocol
- Modification of the information disclosed during the consent process
- Additional information provided to past participants
- Requirement that current participants re-consent to participation
- Modification of the continuing review schedule
- Monitoring of the research
- Monitoring of the consent
- Obtaining more information pending a final decision
- Referral to other organizational entities such as legal counsel, risk management, human resources, the privacy office or the IO
- Providing additional recommendations to the IO
- Other actions appropriate for the local context

If the convened IRB concludes that a limited number of individuals involved with the study were responsible for the serious or continuing non-compliance, then it may require corrective actions from only those individuals. It may also suspend or terminate research privileges for those individuals.

The Executive Director or designee and appropriate CRU administrators will work with the individuals involved in the non-compliance to implement the corrective action plan and will monitor the completion of all required corrective actions.

Final Authority

The IO has the final authority to confirm the IRB's recommendation of serious and/or continuing non-compliance. The IO may constitute additional investigative groups with members drawn from appropriate divisions across the Health System, School of Medicine and/or School of Nursing to further consider the non-compliance. This group will report its findings to the IO in a timeframe prescribed by the IO.

Reporting

The Principal Investigator of the affected research study will be apprised of the convened IRB's recommendation in the post-meeting modifications letter. This letter will also contain any corrective actions required by the IRB. The IO or designee will report the institution's determination and findings to all appropriate entities within DUHS and to relevant regulatory agencies, as described in the policy titled "Reporting of IRB Findings to Institutional Officials and Federal Regulatory Agencies".

Previous Version Date(s): 6/20/2008, 1/7/2009, 2/10/2011, 4/22/2011, 2/19/2016, 6/23/2020.

Attachment I

**NOTICE FROM THE DUHS IRB
REGARDING AN ALLEGATION OF NON-COMPLIANCE**

The DUHS IRB has received a report of alleged non-compliance related to a research study involving human subjects with which you are associated. As part of its review, the IRB is requesting your response. Please complete the following fields, and return this form to **(list name and email)** in the IRB office no later than **(enter date 1 week from receipt)**. Your responses will be included in the discussion of this alleged non-compliance at the next available meeting of IRB #9 and will be held in strict confidence by all attending IRB members and IRB Chairs/staff.

Name of Respondent: (unless requesting anonymity)

PRO #: (Prepopulated by IRB)

Study Title: (Prepopulated by IRB)

Description of Event/Complaint: (prepopulated by IRB)

IRB Concerns /Respondent Replies (list IRB concerns individually with textboxes for replies)



Please use the textbox below to provide additional information that you believe the IRB should have in order to make a determination regarding this alleged non-compliance. You may also attach separate documents to support your statements.

