8.4 Review of Noncompliance Involving the PI or Study Personnel

1.0 Purpose

The purpose of this policy is to describe the process for reviewing and reporting incidents of noncompliance by the PI and/or study personnel.

2.0 Policy

It is the policy of the Organization that:

- 2.1. Reports of noncompliance with Federal Regulations, HRPP policies, or the requirements or determinations of the IRB, or the provisions of the IRB approved research study must be promptly reported to the ORA.
- 2.2. The PI is ultimately responsible for the proper conduct of research and for assuring that noncompliance is promptly reported in accordance with this policy, and for implementing any required corrective action plan.
- 2.3. Incidents of noncompliance will be promptly addressed by the ORA/IRB and appropriate action taken in order to ensure protection of the rights and welfare of research subjects.
- 2.4. Findings of serious or continuing noncompliance and suspensions or terminations of IRB approval as a result of noncompliance will be promptly reported to OHRP, FDA and sponsors or funding agency heads in accordance with the requirements of 45 CFR 46.108(a)(4), and 21 CFR 56.108(b), and the Organization's FederalWide assurance, as specified in HRPP policy 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

3.0 Definitions

- 3.1. Noncompliance is defined as any failure to follow federal regulations (including but not limited to 45 CFR 46, including any applicable subparts, or 21 CFR 50, 56), HRPP policies, the requirements or determinations of the IRB or the provisions of the IRB approved research study. Noncompliance may be serious and/or continuing, or neither serious nor continuing. Noncompliance may also be classified as an unanticipated problem involving risk to the subject or others (UP) as defined in HRPP policy 8.3 (IRB Review of Unanticipated Problems Involving Risk to the Subject or Others).
  - 3.1.1. Serious noncompliance is defined as a violation of applicable federal regulations, HRPP policies, or the determinations of the IRB which (a) significantly increases the risk to subjects, or otherwise compromises the rights and welfare of research subjects; or (b) appreciably decreases the potential direct benefit to subjects; or (c) compromises the scientific integrity of the research.
    - 3.1.1.1. In accordance with OHRP guidance, non-exempt human subject research conducted without IRB review and approval or without appropriate informed consent, or significant modifications to IRB-approved research without IRB approval is considered serious non-compliance.
    - 3.1.1.2. The IRB may decide that certain classes or types of non-compliance (for example, protocol violations involving drug dosing errors) represent serious noncompliance.
  - 3.1.2. Continuing noncompliance is defined as (1) repeated incidents of the same or substantially similar noncompliance after the investigator or staff has been notified that the action represents non-compliance or despite appropriate retraining and/or a specific corrective action plan; or (2) repeated incidents of the same or substantially similar noncompliance of such a nature that the investigator should have reasonably been expected to know that such an action was noncompliance..

4.0 Reporting an Noncompliance to the ORA

- 4.1. Reports of possible noncompliance by the PI or study team must be made to the ORA within ten (10) business days of the study team becoming aware of the event, or five (5) business days when the possible noncompliance was associated with harm to subjects or others. Reports of noncompliance made by any other person should be made as soon as feasible.
  - 4.1.1. Persons reporting possible noncompliance may do so anonymously and may use any mechanism they wish to report to the ORA. This includes use of the "Report a Problem or Complaint" tab on the IRB website, or through other electronic reporting systems

sponsored by the Organization.

5.0 ORA Responsibilities

- 5.1. Upon receipt of a report of possible noncompliance the following will occur:
  - 5.1.1. The ORA will conduct the initial investigation. Additional information will be obtained from the reporter, ORA or HRPP records, and/or from other sources as appropriate.
  - 5.1.2. If the initial investigation discloses that no noncompliance occurred, the IRB Analyst responsible will notify the reporter, and no further action need be taken.
  - 5.1.3. If the initial investigation confirms that noncompliance occurred, the IRB Analyst responsible, in consultation with the Executive Chair or designee, will determine:
    - 5.1.3.1. Whether the noncompliance may represent serious or continuing noncompliance
    - 5.1.3.2. Whether additional actions need to be taken immediately to protect the rights and welfare of human subjects, in accordance with HRPP policy 8.6 (Study Hold, Suspension, and Termination).
    - 5.1.3.3. Whether additional investigation is necessary, by the ORA, or by other parties including but not limited to the Institutional Compliance Officer (UNMC, UNO CHMC or BMC as appropriate), General Counsel, other IRB Analysts, other IRB members and internal consultants.
  - 5.1.4. If the report of noncompliance comes from someone other than the investigator the ORA will notify the PI (and other involved individuals) of the investigation, and the investigator will be provided an opportunity to provide any relevant information and/or records that should be considered.
  - 5.1.5. During the investigation, the investigator (or other relevant party) will have a reasonable opportunity to provide additional information.
  - 5.1.6. The IRB, Institutional Official (IO) and Institutional Compliance Officer will be informed of any ongoing investigations as soon as is appropriate to do so.
- 5.2. After completion of the investigation by the ORA and review by the Executive Chair or designee, the following will occur:
  - 5.2.1. A report determined to be possibly serious or continuing noncompliance, will be referred to the convened IRB, along with the results of the investigation.
  - 5.2.2. A report determined to be neither serious, nor continuing will be sent to the convened IRB as a notification item.
- 5.3. Lists of protocol violations noted by a sponsor, CRO or Audit committee after a review of CRFs and other materials may be submitted to the ORA at the time of discovery, and will be reviewed by the ORA in consultation with the Executive Chair or designee. Incidents determined to be possibly serious or continuing noncompliance, will be referred to the convened IRB for action, and incidents determined to be neither serious nor continuing will be sent to the convened IRB as a notification item, as described above.

6.0 IRB Responsibilities

- 6.1. Noncompliance which may represent serious or continuing noncompliance will be referred for review by the convened IRB. The convened IRB will determine:
  - 6.1.1. Whether the incident represents serious and/or continuing noncompliance.
  - 6.1.2. Whether the incident is an unanticipated problem involving risk.
  - 6.1.3. Whether the corrective action plan is adequate.
  - 6.1.4. Whether the research continues to satisfy the approval criteria at 45 CFR 46.111 or 21 CFR 56.111.
  - 6.1.5. Whether subject accrual should be allowed to continue.
  - 6.1.6. Whether currently enrolled subjects should be notified of information related to the incident.
  - 6.1.7. Whether previously enrolled subjects who have completed participation in the study should be notified of information related to the incident.
- 6.2. After making the determinations above, the IRB may take action including, but not limited to:
  - 6.2.1. Requiring modification of protocol or consent forms, require notification and/or re-consent of enrolled subjects, institute monitoring of the research and/or the consent process, require more frequent continuing review.
  - 6.2.2. Auditing the research, or any of the investigator's other active or completed studies.
  - 6.2.3. Requiring additional investigator or study staff education and training.
  - 6.2.4. Suspending or terminating the research.
  - 6.2.5. Making recommendations to the IO regarding restrictions on, or termination of, other protocols submitted by the investigator, or regarding other sanctions against the investigator or staff including withdrawal or modification of pending or published manuscripts and/or destruction of research data or biological materials.
- 6.3. After completion of the review by the convened IRB the investigator (or other relevant party) will be informed of the results of the review, and of any determinations and requirements by the IRB.

7.0 Reporting Noncompliance to Organizational Officials, OHRP, FDA and Department or Agency Heads

All required reports will be submitted in accordance with HRPP policy 8.7 (Reporting Incidents to Institutional Officials and Federal Agencies).

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Revised: 3/8/2023 – Deleted reference to "minor" non-compliance and substituted "neither serious nor continuing"; minor revisions in wording of definition of non-compliance, serious non-compliance, and continuing non-compliance; changes "alleged non-compliance" to "possible non-compliance"; simplified section on reporting non-compliance to ORA; deleted list of types of people who may report non-compliance and of possible ways to report non-compliance; simplified section on ORA responsibilities; clarified method of reporting non-compliance discovered at time of CRO or other audit; stylistic changes{Approved Rusty McCulloh (Institutional Official), Bruce Gordon (Assistant Vice Chancellor for Regulatory Affairs, Executive Chair)}

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