IRB Procedures: Noncompliance

1 Purpose

Ensuring that human subject research is conducted ethically [insert hyperlink to Belmont Report] and consistent with federal regulations and University policy for human subject research is a shared responsibility. It is University policy that faculty, students, and staff conducting or overseeing human subject research must report any potential instances of noncompliance. Research subjects and individuals not directly involved in conducting or overseeing human subject research are also encouraged to report suspected noncompliance. This document describes the procedures to be followed in addressing allegations of noncompliance and when reporting findings of serious or continuing noncompliance, as required by 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)(2).

2 Definitions

Noncompliance – Failure (intentional or unintentional) to comply with applicable federal human subject research regulations, University policy for human subject research, or requirements of or determinations by the IRB. Noncompliance can results from the actions of or omissions by individuals responsible for the conduct of human subject research. Noncompliance may be: non-serious or minor; serious; or continuing (see below).

Non-serious or Minor Noncompliance – Noncompliance that does not increase the risk to the research patient, compromise participants' rights or welfare, or affect the integrity of the research/data or the human subject protection program.

> Examples of non-serious or minor noncompliance include but are not limited to: failure to obtain IRB certification that research activity is exempt before conducting research that properly qualifies for exemption under federal human subject research regulations; lapse in continuing review by the IRB; implementation of minor changes to or deviations from an approval protocol without IRB approval of the protocol modification.

Serious Noncompliance – Noncompliance that has the potential to increase risk to research participants, compromise participants' rights or welfare, or affect the integrity of the research/data or the human subjects protection program.

> Examples of serious noncompliance include but are not limited to: conducting or continuing non-exempt human subject research without IRB approval; failure to obtain adequate and effective informed consent from research participants; failure to report or review serious adverse events or unanticipated problems; failure to obtain IRB approval for substantive changes to an approved research protocol prior to their implementation; inclusion of vulnerable populations in research without IRB approval.

Continuing Noncompliance – Noncompliance that has been previously reported, or a pattern of ongoing activities that indicate a lack of understanding of or disinclination to comply with human subject protection requirements, which may, in the absence of intervention by the IRB, affect research participants or the validity of the research and may suggest the potential for future noncompliance.

> Examples of continuing noncompliance include but are not limited to: repeated failures to provide or review progress reports resulting in lapses of IRB approval, inadequate continuing review of ongoing research, or repeated failures to respond to or resolve previous allegations or findings of noncompliance.

Allegation of Noncompliance – an unconfirmed report of noncompliance

Finding of Noncompliance – a determination that an instance of noncompliance has occurred.

3 Procedures for the Initial Inquiry into an Investigation of Noncompliance Allegations

All allegations of noncompliance, whether these reports arise internally (e.g., from University faculty, staff, students, ORA staff, IRB members, etc.) or externally (e.g., research participants, other institutions cooperating in human subject research, federal agencies, etc.) shall be forwarded to the University Research Assurances Manager in the Office of Research Assurances. Allegations of noncompliance will remain confidential, to the extent permitted by Idaho law and consistent with the need to conduct an adequate investigation of the allegations. Allegations may also be reported anonymously using the University Hotline. The University will take measures protect from adverse actions or retaliation any person who, in good faith, makes allegations of noncompliance under this policy. (See FSH 3290 and 3810).

Inquiries and, if necessary, further investigation, will be undertaken in response to allegations of noncompliance will be completed in a thorough but expeditious manner, consistent with the circumstances and seriousness of the alleged noncompliance. The Office of Research shall provide the resources and support necessary for the Office of Research Assurances and the IRB to meet its responsibilities with respect to noncompliance review.

3.1 Initial Inquiry into Allegations

Initial inquiries into allegations of noncompliance will be undertaken by the Chair of the IRB, or the Research Assurances Manager acting on behalf of the Chair. The Chair or Manager will contact the complainant to confirm and develop an understanding of the circumstances of the potential instance of noncompliance, unless the complainant has provided sufficient information to proceed without further contact and when the allegation in question is not made anonymously. The Principle Investigator and Co-Investigator(s), or Student Investigator, will be informed of the allegation, will be asked to provide a response to the allegation, and will be required to provide any information deemed necessary by the Chair or Manager to evaluate the allegation and investigator response. The investigator must provide a written response to the inquiry and any requested information with fourteen (14) days after notification of the allegation. When considered necessary, the Chair of the IRB may temporarily suspend portions or all human subject research activity while the initial inquiry proceeds. (See 3.4, below, and Suspension and Termination of Approved Human Subject Research) [INSERT HYPERLINK WHEN POLICY IS DEVELOPED]. Initial inquiries will be completed within thirty (30) days after receipt of the allegation of noncompliance.

3.1.1 The initial inquiry may result in any of the following actions:

- Dismissal of the allegation, when the allegation is determined to be unsubstantiated
- Required implementation of corrective actions determined necessary to achieve compliance, when the noncompliance is classified as non-serious or minor
- Determination of non-serious or minor noncompliance, with no further action required
- Determination that review by the convened IRB is required, because information gathered during the initial inquiry indicates that the noncompliance is serious and/or continuing.

3.1.2 Conclusion of Initial Inquiry: No Violation or Non-Serious Noncompliance

If the Chair or Manager determines that the allegation of noncompliance cannot be substantiated or finds that the noncompliance was non-serious or minor in nature, the Investigator(s), IRB, and the Institutional Official shall be notified in writing within thirty (30) days after receipt of the allegation of noncompliance. [[Documentation of the outcome of the initial inquiry shall be placed in the protocol(s) associated with the allegation of noncompliance and noted in the Protocol Database.]] If corrective action is required of the Investigator(s) for non-serious noncompliance, this action must be implemented by the Investigator(s) and confirmed by the Chair or Manager before IRB approval(s) can be reinstated. If some or all human research activity was temporarily suspended during the

inquiry, notice of lifting of the suspension and reinstatement of approval(s) will be provide to those entities informed of the suspension, including the Institutional Official, OHRP, and research sponsors.

3.1.3 Conclusion of the Initial Inquiry: Recommendation of Review by the Convened IRB

If the Chair or Manager determine that the allegation(s) require(s) a more extensive or intensive investigation, because of the complexity of the issues involved or the potentially serious and/or continuing nature of the noncompliance, the matter will be referred to the IRB for its determination. The Chair or Manager will provide the IRB with a summary of the initial inquiry and supporting documentation including the allegation(s) of noncompliance, the response of the Investigator(s) to the allegation(s).

The Chair or Manager will notify the complainant and the Investigator(s) of the referral for consideration by the convened IRB and the date of the IRB meeting at which the matter of the alleged noncompliance will be addressed. The Investigator(s) may appear in person at the meeting to respond to the allegation(s) and may be accompanied by a personal advisor or legal counsel, who may not participate in the proceedings. If the investigator intends to appear at the convened meeting, the Chair or Manager must be informed.

If, on review of the initial inquiry materials provided by the Chair or Manager, the IRB determines that further investigation is required prior to the convened meeting, two or more IRB members may be appointed by the Chair to conduct interviews, carry out (with the assistance of ORA staff) an audit of the Investigator(s) research activities, perform literature searches, and consult with experts, as necessary. The results of this investigation, and all other materials to be considered at the convened meeting, will be provided to the IRB seven (7) days before the scheduled meeting. If additional time is require to complete this investigation, the IRB meeting at which the alleged noncompliance was to be considered will be rescheduled and the Investigator(s) notified.

3.2 Convened IRB Consideration of Allegations

At a convened meeting of the IRB, which fulfills the requirements for quorum, the IRB will consider the allegation(s) of noncompliance. The results of the initial inquiry, and any further investigation, will be considered, along with other relevant materials (e.g., research protocol, consent forms, etc.) by the IRB in determining whether the allegations can be substantiated and, if so, whether the noncompliance involved is serious and/or continuing. As part of its evaluation, the IRB will speak with any Investigator(s) who elect(s) to appear at the meeting to respond to the allegations. The IRB will also discuss corrective action(s) that will be required to remedy any noncompliance and/or to avoid future noncompliance. In closed session and by majority vote of members at the convened meeting, the IRB will make its final determination concerning the nature of the noncompliance and any corrective action required.

3.2.1 Corrective Action Required by the Convened IRB

In the event that the IRB determines that the noncompliance is substantiated and warrants corrective action, the IRB will provide the investigator with a corrective action plan that describes the corrective action(s) that must be performed by the Investigator(s) and the deadline(s) for implementation. Corrective action(s) required by the IRB will be based, among a number of factors, on the nature of the noncompliance, the degree to which research participants were placed at risk, the occurrence of previous noncompliance by the same Investigator(s).

Corrective actions required by the convened IRB may include but are not limited to:

- Modification of the research protocol or consent form
- Notification of current and/or past participants
- Re-consent of current research participants, when changes to the research may relate to their willingness to continue in the research
- Required education or mentoring for the Investigator(s) or research staff
- Ongoing monitoring (including audits) of the research or consent process

- Increased frequency of continuing review (i.e., requiring that the research receive continuing review more often that once per year)
- Required additional resources to support the research activities
- Limitation of research activities or use of research data
- Suspension of IRB approval for one or more of the Investigator(s)' studies
- Termination of IRB approval for one or more of the Investigator(s)' studies

The Chair or Manager will review the Investigator(s) response to and implementation of the corrective action plan. If the Investigator(s) responsible for implementation do not complete the required corrective actions within the timeframe specified in the corrective action plan, additional action may be required. The Chair or Manager may suspend IRB approval(s) for ongoing human research studies of the Investigator(s); the Chair or Manager may also recommend termination of IRB approval (s) for ongoing human research studies of the Investigator(s). Upon consideration of the circumstances surrounding the failure of the Investigator(s) to timely perform required corrective action(s), the IRB may formally terminate approval for one or more of the Investigator(s)' studies. Suspension or termination, if not previously reported, will be reported to all required parties (See Suspension and Termination of Approved Human Subject Research) [INSERT HYPERLINK WHEN POLICY IS DEVELOPED].

3.3. Appeals

Consistent with federal human subject regulations, research reviewed and approved by the IRB may receive further institutional review. The University may impose additional, institutional conditions for approval or may disapprove the research approved by the IRB. The University may not, however, approve research that has been disapproved by the IRB. (45 CFR 46.112). Determinations by the convened IRB to suspend, terminate, or require corrective action represent disapproval of research that cannot be countermanded by the University. Investigator(s) may, however, petition for reconsideration of determinations of the convened IRB. Such petitions must be made in writing within 30 days of the determination by the convened IRB and submitted to the Vice President for Research and Economic Development, who serves as the Institutional Official. The Institutional Official will convey the petition to the IRB, which will review the request and notify the Investigator(s) within fourteen days of its decision to affirm its previous determination or to reconsider the determination. The decision of the IRB, whether affirming the previous determination or, upon reconsideration, altering its previous determination, is final; no further appeal is permitted. Investigators may also petition for evaluation by the convened IRB of determinations made by Chair or Manager during the initial inquiry; determinations by the convened IRB in response to such petitions are not subject to further appeal.

[[3.4 Reporting of Serious and/or Continuing Noncompliance, and Suspension or Termination of IRB Approval

Noncompliance that is found by the IRB to be serious and/or continuing shall, within fourteen (14) days of the determination, be reported by the IRB Chair or Manager to the Investigator(s), and the Investigator(s)' Dean and Department Chair. Within thirty (30) days, a determination of serious and/or continuing noncompliance shall be reported to OHRP, FDA (when the noncompliance is related to FDA-regulated research), and any sponsors of the research. Suspension, whether as part the initial inquiry or the convened IRB review, or termination of IRB approval within fourteen (14) days of the determination, be reported by the IRB Chair or Manager to the Investigator(s), and the Investigator(s)' Dean and Department Chair. Within thirty (30) days, a suspension or termination shall be reported to OHRP, FDA (when the noncompliance is related to FDA-regulated research), and any sponsors of the research.]]

3.5 Record Retention for Noncompliance Proceedings

Records related to review and investigation of noncompliance shall be retained by ORA, on behalf of the IRB, for a minimum of three (3) years after completion of the related research or implementation of required corrective actions, whichever is longer. Copies of determination decisions and corrective action

plans, if applicable, shall be filed with the related research protocol(s) and the noncompliance determination shall be entered into the Protocol Database.

3.6 Applicable Regulations and Guidelines

45 CFR 46.103(b)(5)
45 CFR 46.111(b)(5)
45 CFR 46.112
45 CFR 46.113
45 CFR 46.115
21 CFR 50.25(b)(5)
21 CFR 56.108(b)(2)
21 CFR 56.112
21 CFR 56.113
21 CFR 56.115