Office of Research Assurance

Human Subject Research Protections Standard Operating Procedures (SOP)

SOP- 850: Noncompliance

Number	Effective Date	Version Number	Previous Versions
850	10/21/2024	v.1	N/A

Purpose

The ethical conduct of research is a shared responsibility among NASA, researchers, research participants, and the NASA IRB. The NASA IRB must ensure the rights and welfare of research participants, which includes addressing allegations of noncompliance with IRB requirements and/or federal regulations.

ORA: SOP 850 establishes criteria, responsibilities, and procedures for reporting, investigating, and addressing allegations and findings of noncompliance.

Scope

This policy applies to all human subjects research under the oversight of the NASA IRB, including research receiving an Exempt determination under 14 CFR 1230.104(d). Collaborative research involving Reliance Acknowledgements (RA) in which NASA cedes oversight to another institution follows the terms established in the RA. Projects receiving NASA funding, but under another IRB's oversight are subject to the policy of the reviewing IRB and the terms established in the funding award.

Definitions

Noncompliance is defined as conducting human subjects research in such a way that disregards or violates (1) applicable laws and federal regulations, (2) NASA policies and procedures governing human subject research, and/or (3) the requirements or determinations of NASA Institutional Review Board (IRB). Noncompliance can be intentional or unintentional, and may be deemed minor, serious, and/or continuing as defined below.

Continuing noncompliance is defined as a persistent failure to adhere to laws, regulations, or policies governing human research. A pattern of repeated failure of adherence to human research standards may be considered continuing noncompliance regardless of whether it results from a lack of knowledge or willful lack of commitment to research requirements. Continuing noncompliance is characterized by frequency rather than magnitude.

Examples of continuing noncompliance include, but are not limited to:

- Repeated failure to obtain IRB approval prior to initiating human subjects research activities;

- Continuing to engage in noncompliant activities after being notified or advised of concerns;
- Recurring late submissions of continuing review applications resulting in repeated lapses in approval;
- Recurring failure to follow clinical trials/applicable clinical trials registering/posting requirements
- Multiple instances of noncompliance;
    - this includes multiple incidents within a single project or multiple incidents by a single investigator across more than one project.
- Failure to respond to incidents of noncompliance or failure to enact required corrective actions.

Serious noncompliance: Any action or omission during the conduct of human subjects research, whether intentional or not, that reflects a failure to follow

(1) the applicable laws, regulations, or policies governing human subject research,

(2) or the requirements or determinations of NASA IRB that does *or may* materially compromise the rights, safety or welfare of human research subjects, even if no actual harm occurred.

Noncompliance that substantively affects scientific integrity or validity of the research may be considered serious, even if it does not result in direct harm to research participants.

Acts or omissions determined by the NASA IRB to be intentional or flagrant violations of laws, regulations, policies governing human research, or IRB requirements may also constitute serious noncompliance.

Examples of **serious noncompliance** include, but are not limited to:

- Initiation of human subjects research without prior to IRB review and approval
- Substantive unapproved deviations from IRB-approved protocols (except when to eliminate apparent immediate hazards to subjects)
- Permitting unqualified or untrained individuals to perform research procedures or to monitor subject safety,
- Failure to obtain informed consent or failure to provide participants with all information necessary to constitute meaningful informed consent unless a waiver has been previously granted by the IRB,
- Enrolling subjects who do not meet the approved eligibility criteria when doing so compromises the safety or well-being of the subjects,
- Implementing unapproved changes to research activities that increase risks to participants or adversely affect their rights, safety, or welfare,
- Failure to report serious adverse events or unanticipated problems involving risks to subjects or others as required by IRB policy,
- Instructing or knowingly allowing subordinates to engage in activities that are contrary to IRB or NASA policies or regulatory requirements,
- Providing false or intentionally misleading information to the IRB,
- Multiple issues suggesting a lack of oversight, inaction, or negligence such that research participants' rights, safety, or welfare could be or are adversely affected

Minor noncompliance is defined as any noncompliance is neither serious nor continuing.

Noncompliance in Exempt research: Human subjects research determined by the NASA IRB to meet the criteria for exempt review under 14 CFR 1230.104 is subject to fewer regulatory requirements than non-exempt research. While NASA IRB policy (ORA SOP:420) allows for implementation of limited changes to an exempted protocol without prior IRB review, noncompliance can still occur in exempt research.

In general, noncompliance in exempt research involves the following:

- Initiating human subjects research activities prior to receiving a written determination of exemption from the NASA IRB.
- Deviations from an exempted protocol that alter the exempt status of the study or are contrary to IRB guidance Modifications to Exempt Research (ORA: SOP-420).

Noncompliance in exempt research is reviewed following the procedures outlined in this document, with flexibilities afforded to exempt research taken into consideration.

In general, **intentional deviations** from the approved protocol constitute noncompliance, unless enacted to eliminate apparent immediate hazards or risks to research subjects. **Unintentional or unavoidable deviations** that are outside of the reasonable control of the researcher(s) do not constitute noncompliance. See SOP 860.

Policy

(1) PI and research teams must obtain NASA IRB approval before conducting human subjects research.

(2) PI and research teams must conduct human subjects research in accordance with the protocol and materials as approved by the NASA Institutional Review Board (IRB), all applicable NASA policies governing human research, applicable laws, and federal regulatory requirements.

(3) All changes/modifications to non-exempt human subjects research must receive NASA IRB approval prior to implementation of the change, except when necessary to eliminate apparent immediate hazards to participant(s), or to protect the life or physical well-being of the participant(s).

   a. If changes are necessary to mitigate or avoid immediate harm, and/or in the event of emergency, the PI may implement changes but must report them to the NASA IRB (and sponsor when applicable) within 5 working days.

(4) Instances of noncompliance, including deviations from the approved protocol/materials made in the interest of participants, must be reported promptly to the NASA IRB following established procedures[1] as outlined in this document.

   a. Instances involving actual or imminent harm to research participants or others must be reported to the IRB immediately.

(5) External reporting. The Office of Research Assurance (ORA) ensures prompt reporting[2] to the Office of Human Research Protections (OHRP) within the Department of Health and Human Services (HHS) and, when applicable, other federal agencies of any IRB determined instances of:

   a. Unanticipated Problems Involving Risks to Subjects or Others (UPIRSO)

[1] 14 CFR 1230.108(a)(3)(iii) and 21 CFR 56.108(a)(3)-(4)
[2] 14 CFR 1230.108(a)(4) and 21 CFR 56.108(b)

b. Serious or continuing noncompliance

c. Suspension or termination of IRB approval

(6) Unless reported directly by the PI, reports of noncompliance are handled as allegations until validated or found invalid and dismissed.

Procedures

Reporting to the NASA IRB

All complaints, deviations (even those made in the interest of an individual subject), potential noncompliance, new information suggesting changes to study risks/benefits, and problems are assessed by the Office of Research Assurance (ORA) Director, ORA Compliance Officer, and/or IRB Chair or designee to ensure continued protection of research participants from avoidable harms.

Reporting complaints, deviations, noncompliance, and problems to the IRB

1. Anyone may submit allegations of noncompliance to the NASA IRB by any means (verbal, in writing, anonymous phone calls to the hotline at 281-244-1800), including NASA IRB staff or IRB members. The NASA IRB maintains confidentiality regarding the identity of the person or persons submitting the allegation to the extent possible.
2. Principal Investigators (PI) are compelled, as a term of IRB approval to *promptly* report instances of noncompliance to the IRB. Research staff who become aware of potential noncompliance should notify the PI as soon as possible to facilitate PI self-reporting.
3. **Reporting Methods.** Different methods are available to notify the IRB regarding potential noncompliance, deviations, problems, or other information.
    a. **Report of New Information (RNI)** in the eIRB.
        i. PI or others with access to the NASA eIRB system may submit an RNI within the eIRB.
        ii. An RNI may be initiated directly from the study workspace (subsequently linked to the main study) or as a generic RNI from the dashboard (may be later linked to relevant study records).
    b. **Contact the OCHMO Office of Research Assurance**
        i. OCHMO Office of Research Assurance email HQ-OORA@mail.NASA.gov
        ii. ANONYMOUS concerns may be submitted through the Office of Research Assurance via telephone at 281-244-1800
    c. Concerned individuals may also reach out directly to IRB staff directly for guidance.

1. **Suggested content when reporting.** Regardless of reporting method, sufficient information must be provided to allow for an assessment of the issue and to determine the appropriate course of action.
    a. When possible, the report should include the following:
        i. Study Identification: PI name, study title, ID number,
        ii. Description of the problem, situation, or incident, including specific changes to procedures in the approved research plan if applicable
        iii. PI's assessment of why the event occurred.

iv. Assessment of potential impacts (e.g., increased participant risk, reduced research benefits, or compromised research integrity)

2. **Suggested content when reporting.** Regardless of reporting method, sufficient information must be provided to allow for an assessment of the issue and to determine the appropriate course of action.
    a. When possible, the report should include the following:
        i. Study Identification: PI name, study title, ID number,
        ii. Description of the problem, situation, or incident, including specific changes to procedures in the approved research plan if applicable
        iii. PI's assessment of why the event occurred.
        iv. Assessment of potential impacts (e.g., increased participant risk, reduced research benefits, or compromised research integrity)
        v. Description of immediate changes to the protocol that were made in response to the situation, if any.
        vi. Description of corrective actions that were implemented or that are proposed to prevent future similar occurrences.
        vii. Relevant materials or documents

After Receipt of a Report

1. The ORA Compliance officer, and/or the IRB Chair/designee promptly conduct an initial assessment to determine an appropriate follow-up and course of action.
2. The NASA IRB Chair or delegate will be included on all correspondence related to the alleged concern/report.
3. For instances in which the NASA IRB Chair has a real or perceived conflict of interest, he/she/they will name a delegate to conduct an assessment and if warranted, an investigation.
4. The NASA IRB Chair or delegate determines whether other stakeholders need to be notified throughout the assessment/investigation/finding/action process (e.g., Legal, Safety Office, Crew Office).

Assessment of Allegations/Reports

Alleged and identified instances of noncompliance are nuanced and context specific. Accordingly, each instance is assessed and managed on a case-by-case basis.

1. The NASA IRB Chair or delegate, in consultation with the NASA IRB when appropriate, reviews and deems an allegation/report substantiated or unsubstantiated (i.e. finds no supporting facts or documentation). The NASA IRA Chair may consult with the ORA Director, Compliance officer, NASA IRB members, or staff during investigations.
    - For unsubstantiated allegations/reports, the NASA IRB Chair or delegate may decide:
        i. no additional action is needed,
        ii. further investigation/more information is required, or
        iii. to present the allegation to the convened NASA IRB.

- For substantiated allegations/reports, the NASA IRB Chair or delegate may:
    i. work directly with the PI or complainant for minor noncompliance, rule out serious or continuing noncompliance,
    ii. decide further investigation/more information is required, or
    iii. to present the allegation to the convened NASA IRB.
- When allegations may involve adverse events, unanticipated problems, or serious or continuing noncompliance, the NASA IRB Chair presents the allegation/report to the convened NASA IRB. Protocol deviations, adverse events, and unanticipated problems are handled according to ORA: SOP-860.
- When allegations/reports may involve research misconduct the NASA Chief Scientist Office will be notified.
- The NASA IRB Chair will communicate his/her/their decision to the complainant and, when applicable, to the individual against whom the allegation was raised.

Investigation of Allegations/Reports

1. When the NASA IRB Chair or delegate determines further inquiry is necessary, NASA IRB staff will notify the complainant. When allegations/reports involve co-investigators and/or other research staff, the NASA IRB staff may also contact those individuals. The Principal Investigator (PI) and above parties may be notified via telephone and/or email with documentation of the notification.
2. The NASA IRB Chair or delegate may appoint IRB members or staff to gather information pertaining to the allegation/report, including but not limited to the IRB protocol and procedures, research data (published and unpublished data), informed consent forms, inclusion/exclusion criteria, or any other pertinent information. The investigation may also include interviews with the complainant or respondent, individuals who received the complaint, and or any other individuals related to the allegation/report. The NASA IRB Chair, IRB members, or staff may request additional information from the complainant as needed.
3. When an allegation/report involves serious or continuing concerns, the NASA IRB Chair or delegate, in consultation with the convened board or others, will determine whether further inquiry is necessary. Nature of the allegation is determined by frequency, duration, and or seriousness of the violation(s).
4. When allegations/reports are deemed substantiated and participants are at immediate risk, the IRB Chair considers study suspension (See SOP 470).
5. The respondent may submit a written rebuttal to an allegation/report to ORA. The ORA Director or Deputy Director may request additional information from the respondent as needed.
6. The Compliance Officer conducting the investigation prepare a summary report for the convened IRB and ORA Director. The report should include a summary of allegations/concerns, interview/document investigation summaries, and copies of correspondence, and recommendations if appropriate.

Review of Serious and/or Continuing Noncompliance

1. The NASA IRB Chair, delegate, and staff advise the NASA IRB regarding applicable regulations, laws, ethical considerations, assists with documentation of the review, answers questions, maintains records as required by law, and liaises with Federal agencies as required.
2. At a convened meeting at which quorum is present, the NASA IRB reviews the materials concerning the allegation of serious and/or continuing noncompliance. The NASA IRB

determines whether additional information is needed. The respondent may be given the opportunity to attend the meeting prior to final action.

Outcomes

1. The NASA IRB Chair, delegate, or convened IRB makes the determination whether the allegation/concern is substantiated, and if so, whether the allegation is deemed serious and/or continuing noncompliance based on the materials following the investigation.
2. The NASA IRB Chair or delegate, in consultation with convened IRB when appropriate, will determine a finding. Findings include:
    a. Dismissal
    b. Adverse event/UPIRSO
    c. Minor noncompliance
    d. Serious noncompliance, and/or
    e. Continuing noncompliance
3. Actions may include, but are not limited to:
    a. Approve continuation of research activities with no changes;
    b. A warning letter
    c. Request formal education (topic based);
    d. Request changes (minor or major) to the research procedures and/or documents;
    e. Modify the continuing review schedule;
    f. Require continuing review;
    g. Require monitoring or research and informed consent processes
    h. Suspend or terminate IRB approval
    i. Disapprove continuation
    j. Require inspections of other active protocols of the same researcher(s)
    k. Require the researcher contact participants with additional information
    l. Require reconsent of enrolled participants
    m. Require the researchers inform publishers/editors for manuscripts related to the project
    n. Require a corrective action plan
    o. Restricting the ability to serve as PI on human subjects protocols (e.g., requiring a co-PI, barring future eligibility as PI, etc.)
4. The NASA IRB staff informs the following individuals of the allegation/concern, review process, findings of review, and outcome:
    a. Respondent/researcher
    b. Complainant
    c. Institutional Official
    d. Sponsor, if appropriate
    e. HHS Office of Human Research Protections (OHRP) per the requirements set forth in 14 CFR 1230.103(b)(5)
    f. Food and Drug Administration for FDA-regulated research in accordance with 21 CFR 56.108(b) and 21 CFR 56.113.
    g. Other administrative personnel as appropriate
5. The respondent may submit concerns in writing to ORA within 30 days of the issuance of the finding. Concerns are limited to 1. review of the procedures employed to reach the decision, 2. introduction of new information that could potentially change the finding/decision, and 3. grievances against actions posted as a result of the finding.

6. The NASA IRB chair or delegate, in consultation with the NASA IRB when appropriate, resolves concerns raised by the respondent through direct communication. Concerns may be referred to the Institutional Official for additional action as needed.

References

University of New Mexico, Office of the Institutional Review board, SOP 402 – Research Noncompliance

14CFR1230

21CFR50, 56

Version	Version notes	Originator	Approved by	Date
1		J. Ensley Gorshe/J. Kisenwether	M. Covington	21Oct2024