SJU Saint Joseph's University

IRB Standard Operating Policy and Procedures Number:	5
Title:	Noncompliance
Effective Date:	January 1, 2023
Responsible Office:	Office of Research Services/IRB

Purpose

Federal regulations (45CFR46.103(a)and(b)(5) & 21CFR56.108(b)) require written procedures for ensuring prompt reporting of "any unanticipated problems involving risks to subjects or others; any serious or continuing non-compliance with 45 CFR Part 46 or the requirements or determinations of the IRB; and any suspension or termination of IRB approval" to appropriate institutional officials, supporting department or agency head (or designee), and OHRP. This policy sets forth the definition and examples of noncompliance; the procedures for reporting an allegation of noncompliance to the IRB; and the procedures for the IRB's management of such allegations and of confirmed noncompliance.

Scope and Applicability

SJU's Institutional Review Board (IRB) Standard Operating Policies & Procedures (SOPPs) apply to all research activities involving human subjects conducted by SJU faculty, staff, or students or by anyone conducting research in which the participation of SJU meets the definition of "engagement" as indicated by the Office of Human Research Protections (OHRP)*. These policies rely on and reference the Department of Health and Human Services (DHHS) Regulations pertaining to the Protection of Human Subjects in Research (hereinafter referred to as 45 CFR § 46). The guidance document on "engagement" may be found here.

Definitions

Noncompliance

Failure to comply with federal regulations; the policies or procedures of the IRB; or institutional policies governing human research. Examples of noncompliance include, but are not limited to: (1) conducting human participant research without IRB approval (e.g., before approval; after expiration of approval and in the absence of a continuation application submitted to the IRB; during a suspension of IRB approval; after termination of IRB approval); (2) disregarding or otherwise violating IRB-approved informed consent procedures (e.g., failing to obtain consent/assent, using unapproved or outdated consent, assent, and information sheets, missing signatures, failing to document consent process); (3) deviating from the protocol approved by the IRB; (4) modifying an approved protocol without IRB consent; (5) failing to report or tardily reporting unanticipated problems; (6) failing to maintain adequate records; (7) failing to train research team members in the proper procedures; and (8) failing to follow the mandated changes that secured IRB approval to ensure the safety of research participants. Noncompliance may constitute or may result in unanticipated problems. When there is possibly an unanticipated problem, it must be addressed in accordance with SJU SOPP 4.

Serious Noncompliance

Noncompliance involving one or more of the following: (1) bringing harm to research participants; (2) exposing research participants to a significant risk of substantive harm; (3) compromising the privacy and confidentiality of research participants; (4) causing damage to scientific integrity of the research data that has been collected; (5) engaging in willful or knowing noncompliance; (6) otherwise impacting ethical principles of beneficence, justice and respect adversely.

Continuing Noncompliance

A repeated pattern or un-rectified instance of noncompliance by an individual investigator or research staff member either on a single protocol or multiple protocols.

Policy Statement

This policy applies to research that has been found to meet Exemption criteria as well as research approved at the Expedited and Full Board levels. Principal Investigators (PI's) are responsible for ensuring that research is conducted as set forth in the in the Exempt or IRB-approved protocol. During the course of a research study, a PI may encounter an unexpected event and/or make changes to a protocol. Regardless of whether a change to a protocol has been made, PI's are expected to report unanticipated problems/serious adverse events to the IRB. Failure to do so is considered serious non-compliance.

Reports of non-compliance may come from any individual with knowledge of possible non-compliance, whether internal or external to the University. In response to a report or complaint received by the Research Compliance Coordinator (RCC) by someone other than a PI, in relation to SJU IRB-approved research, the RCC will contact the PI within 24 hours of the report and request that the PI complete and submit a Reportable Event Form through IRBNet. In the case of an anonymous complaint, the complainant will be advised, if possible, that their report will be investigated, but that the scope of the investigation may be affected/limited by their choice to remain anonymous. Reports of non-compliance will be investigated by the RCC, in consultation with the IRB Chair, and the report will be added to the agenda of the next available IRB meeting for review.

Federal regulations stipulate that the IRB "...shall have the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with serious harm to subjects." These regulations further stipulate that "any suspension or termination...shall be reported promptly to the investigator, appropriate institutional officials, and [the sponsoring federal agency, if applicable]."

Procedures

Addressing Allegations of Noncompliance

The IRB or the Office of Research Services (ORS) may become aware of an allegation of noncompliance or of circumstances indicating noncompliance upon the receipt of a complaint from a participant, researcher, SJU employee, or member of the public; from the interpretation of information received during a continuation, amendment, reportable event review; or from the findings of a random or for-cause audit or other quality control activities. Once it has become aware of an allegation of noncompliance, the RCC in ORS will request that the complainant or PI submit a Reportable Event Form. In the case of an anonymous complaint or a request for confidentiality, the RCC will submit this form. The RCC, in consultation with the IRB Chair, will

make the following initial determinations: (a) whether noncompliance is alleged; and (b) whether the allegation indicates that an immediate action such as suspension is warranted.

The RCC will initiate an investigation of the circumstances alleged in the Reportable Event Form, and may elect to investigate by reading relevant documents and communicating with the affected parties. The following outcomes are possible:

1. If the IRB Chair, in consultation with the RCC, determines that the allegation is not credible or is unsubstantiated, then the inquiry ends. This finding will be documented in a written report in the file in IRBNet and the IRB will be advised of the finding on the agenda of the next available meeting. 3.3.2. If the inquiry yields evidence that noncompliance has occurred, then the IRB Chair, in consultation with the RCC, will submit a corresponding report to the full IRB for discussion at the next available meeting.
2. If it is determined that immediate action by the IRB is warranted (in order to protect the rights and welfare of research participants), then the IRB Chair will exercise their authority to suspend the research temporarily and will instruct the RCC to issue a suspension notice for the protocol until the convened IRB reviews and acts on the protocol. The RCC will place the Reportable Event on the agenda for the next available meeting of the convened IRB for their discussion and resolution. The convened IRB must discuss suspensions of all protocols previously approved by the IRB. The convened IRB has the authority to suspend or terminate research activities, taking into consideration protections for subjects' rights and welfare.

Reporting and IRB Review Procedures

<u>Resolving Noncompliance</u>

If it is determined that the noncompliance is neither serious nor continuing, the IRB Chair and RCC will devise a corrective plan, which generally will involve immediate remediation, including one or more, but not limited to the following actions:

a. PI is required to submit a protocol amendment.
b. PI and/or the PI's staff are required to participate in additional training/education for the protection of human subjects in research.
c. The PI is required to develop and submit for IRB approval a Data and Safety Monitoring Plan.
d. The PI is required to submit periodic status reports.
e. The protocol will require IRB review more frequently than once per year.
f. The PI is required to provide current subjects with additional information if it might affect their decision to continue participation in the research, or provide additional information to previously enrolled subjects.
g. The PI is required to re-consent currently enrolled subjects.
h. The PI is required to notify investigators at other research sites of the noncompliance.

If it is determined that the noncompliance is serious or continuing, the RCC, in consultation with the IRB Chair, will conduct a for-cause audit. The protocol PI may request a meeting with the IRB Chair and RCC regarding a determination of serious or continuing noncompliance. If it is determined that an unanticipated problem has occurred, it will be addressed in accordance

with SOPP 6. A protocol PI may decide voluntarily to suspend or terminate some or all of the research activities that may be under current review or investigation. The protocol PI should inform the RCC of this action so that the RCC can notify the IRB Chair and place the protocol on the agenda for the next available IRB meeting. The audit report will be shared with the protocol PI, the director of ORS, the IRB, and, if appropriate, the Institutional Official and/or Dean and/or Chair of the protocol PI's Department. The protocol PI may submit a response to the audit report in writing and/or may request to speak to the IRB at a convened meeting. The RCC will place the report and any written response from the protocol PI as discussion items on the agenda of the next available IRB meeting. The IRB will make a final determination as to whether the evidence supports a finding of serious or continuing noncompliance and, if so, will determine a corrective plan, including time frame for correction, and may, if necessary, initiate suspension or termination. In reviewing information to make a final determination of serious or continuing noncompliance, the IRB should consider:

1. Whether the audit report and any other available information sufficiently supports a determination of non-compliance
2. Whether the audit report and any other available information supports suspension or termination of research in order to protect human subjects or others
3. Additional actions to protect the rights and welfare of currently enrolled subjects
4. Whether procedures for withdrawal of enrolled subjects account for their rights and welfare
5. Whether subjects should be informed of the noncompliance and/or any of the corrective actions.
6. The IRB may invite the protocol PI to a portion of the meeting to answer questions and to discuss the issue of noncompliance. If the protocol PI (and Faculty Advisor when PI is a student) requests, or is requested, to be present at the IRB meeting, he or she may be accompanied by legal counsel, or another member of their department. The role of these individuals is limited to providing information and support to the protocol PI; they will not participate in the discussion between the protocol PI and the IRB.

The actions taken to correct noncompliance vary and depend on the nature and seriousness of the noncompliance. The IRB may take any of the following actions:

a. No action
b. Request protocol and/or consent form/process modification
c. Require that all subjects be re-consented
d. Require previous subjects to be informed of any changes to the protocol and/or consent procedures
e. Require observation of consent procedures
f. Require more frequent review of the conduct of the research
g. Require additional training for the research team
h. Require follow-up audit(s) of the research
i. Suspend the research

j. Terminate the research

k. Referral to other institutional entities (e.g. Institutional Official, Dean, General Counsel)

l. Any other action deemed appropriate by the IRB to protect the rights and welfare of research participants

The protocol PI must implement the corrective plan within the required timeframe. The RCC will monitor the protocol PI's implementation of the corrective plan. A failure to implement the corrective plan on time will be reported by the RCC to the IRB Chair for further action, including initiation of procedures for suspension or termination of IRB approval of the research protocol. The convened IRB has the authority to suspend or terminate research activities, taking into consideration protections for participants' rights and welfare.

Upon full implementation of the corrective plan, the IRB Chair (or their designee) will draft a final noncompliance report for review by the IRB at the next available meeting. If the IRB finds that the corrective action plan has been appropriately implemented, the IRB Chair (or their designee) will report the outcome of the review of the reported event to the Director of Research Services (ORS) in order to facilitate necessary institutional reporting procedures (See 5.1 through 5.3).

While the IRB has the authority to take appropriate action concerning a research protocol, neither the IRB nor ORS has the authority to take disciplinary action against any individual relating to a finding of confirmed noncompliance. Instead, disciplinary action shall be the responsibility of the institution.

Informed by any audit reports, corrective plans, and final noncompliance reports, the RCC will develop and administer required and optional educational programs, as specified in corrective plans for the protocol PI and for the research community generally.

<u>Institutional Reporting Procedures</u>

The Director of Research Services (ORS) will ensure compliance with federally mandated reporting requirements concerning unanticipated problems, noncompliance, and suspensions and terminations involving human subject research protocols previously approved by the IRB.

Final Reports

A final report should include the following information: (1) the name of the protocol PI; (2) the IRB's OHRP registration number, SJU's FWA number; (3) protocol title; (4) sponsor of the study; (5) any applicable grant numbers; (6) the dates(s) and nature of the event(s); (7) details concerning how the event was discovered; (8) the IRB's response to the event; (9) the protocol PI's response to the event; (10) investigatory/audit findings; (11) IRB's actions and rationale and any response by the protocol PI; (12) details of the corrective plan; (13) any pertinent details concerning the protocol PI's implementation of the corrective plan; (14) subjects' response to corrective measures; (15) IRB plan for monitoring the outcome of the event; (16) certification of destruction of data resulting from un-approved research activities, if applicable; (17) outcomes of withdrawal and follow-up of subjects, if applicable; and (18) any general educational activities inspired by the incident. Initial Reports: While this information is being compiled for the final report and the corrective plan is being implemented, the IRB and the Director of ORS may elect to have ORS submit an initial report to OHRP and/or FDA in order to ensure prompt reporting. An initial report should include as much of this information as is available.

ORS will draft initial and final reports, and the Director of ORS will be responsible for signing and finalizing them. After initial and final reports are signed, ORS will distribute them to appropriate institutional officials, Department and/or Agency heads, and/or OHRP.

Regulation and Guidance

Federal Regulations

- 45 CFR 46.109; 21 CFR 56.109: IRB Review of Research, mandating IRB review and approval of human participant research.
- 45 CFR 46.103(b)(5)(i), mandating compliance with "...written procedures to ensure prompt reporting to the IRB, appropriate institutional officials, and the Department or Agency head of...any serious or continuing noncompliance with [45 CFR 46(A)] or the requirements or determinations of the IRB... ."
- 21 CFR 56.108(b)(2), mandating compliance with "...written procedures to ensure prompt reporting to the IRB, appropriate institutional officials, and the Food and Drug Administration of...any serious or continuing noncompliance with [21 CFR 56(C)] or the requirements or determinations of the IRB..."

Ethical Codes

- The Nuremberg Code (1948)
- The Belmont Report (1974)
- Declaration of Helsinki (last revised in 2000)

Referenced IRB SOPPs

- SOPP 4: Initial and Continuing Review by the IRB