



UNIVERSITY OF
SOUTH ALABAMA

IRB SOP 602
Protocol Deviation/Violation/Exception Reporting

Purpose

The purpose of this Standard Operating Procedure (SOP) is to provide guidance in the reporting requirements and responsibilities of the Investigator and the University of South Alabama Institutional Review Board (USA IRB) regarding protocol deviations, violations, or exceptions.

Scope

This SOP applies to all research projects submitted for review by the USA IRB.

Definitions

Continuing non-compliance: A pattern of repeated actions/omissions taken by an investigator or key research personnel that indicates a lack of ability and/or willingness to comply with federal regulations or USA IRB policies/guidelines.

Protocol Deviation: Any change, divergence, or departure from the approved study design or procedures of a research protocol that is under the investigator's control and that has not been approved by the IRB, and *does not affect* the participant's safety, rights, or welfare and/or the completeness, accuracy and integrity of the study data. This term, though sometimes used interchangeably with the term "violation," is (i) most often used when the variance is intended for the safety of one or more research participants or is an unintended change that is not considered as serious as a violation, (ii) is considered *minor* or administrative, and (iii) may involve no more than minimal risk to participants or others.

Non-compliance: Failure to comply with applicable Federal Regulations or USA IRB policies/guidelines

Serious non-compliance: An action or omission taken by an investigator or key research personnel that any other reasonable investigator would have foreseen as compromising the rights and/or welfare of the subject. Examples include, but not limited to:

- Failure to adhere to federal regulations governing use of human subjects in research;
 - failure to obtain IRB approval prior to initiation of research activities
 - failure to notify the IRB of changes in approved procedures
 - failure to obtain and/or document informed consent
 - IRB approval expires due to failure to renew
 - Failure to notify the IRB of changes in the scope/intent of the study
- Failure to adhere to institutional policies where subject's welfare has been adversely affected.

Protocol Violation: Any deviation that *may affect* the subject's rights, safety, or welfare, and/or the completeness, accuracy and integrity of the study data. This term though sometimes used interchangeably with "deviation" is often considered a *major*, more serious, variance from an approved protocol than a deviation.

Protocol Exception- An exception to the currently approved protocol is a planned temporary variance that has received IRB approval prior to its initiation, e.g., enrollment of subject who does not meet eligibility criteria or accommodation of a subject who moves out of the area for the remainder of his/her participation in the research.

Policy

1.0 Protocol Deviations, Violations, and Exceptions

Federal regulations require the IRB to review and approve proposed changes to research studies before initiation of these changes, except when changes are "necessary to eliminate apparent immediate hazards to the subject" [45 CFR 46.103(b)(4)(iii)]. Most proposed changes are reviewed through submission of amendments. Any changes that are made to eliminate apparent immediate hazards to a subject should be reported as soon as possible after they occur as a protocol deviation or violation.

Procedures

Investigators are required to report protocol deviations, violations, and exceptions to the IRB.

The Principal Investigator (PI) must report Protocol Violations, Deviations, and Exceptions to the IRB as outlined below.

1.0 Protocol Violations

1.1 Reporting Procedures

Protocol Violations may be considered serious noncompliance and are to be reported to the IRB within *5 business days* on the Protocol Deviation/Violation Reporting Form. The investigator must develop a corrective action plan to present to the IRB for review and approval. This corrective action plan will outline what steps the investigator has taken or will take to resolve the event and to prevent such events from occurring in the future.

Examples of violations include, but are not limited to the following:

- Intentional deviation from the protocol or regulations in a non-emergency setting
- any unintended or intended deviation from the IRB approved protocol that involves potential risks or has the potential to recur;
- enrollment of subjects not meeting the inclusion/exclusion criteria of an IRB approved protocol;
- failure to withdraw a subject meeting withdrawal criteria;
- inadvertent loss of samples or data;
- failure to obtain informed consent prior to initiation of study-related procedures;
- improper consent procedure;
- failure to follow federal and/or local regulations and policies;
- working under an expired professional license/certification, debarred or disqualified status;
- frequent minor deviations;
- any medication error involving dosing, administration and/or preparation of the study drugs;
- any lapse in study approval where there is a continuation of research activities (i.e. recruitment, enrollment, procedures, data analysis);
- failure to report unanticipated problems to the IRB and/or the sponsor; or
- any event that requires prompt reporting according to the protocol or the study sponsor.
- any emergent deviation from the IRB protocol made without prior IRB review to eliminate apparent immediate hazard to a research subject;
- implementation of *unapproved* recruitment procedures or materials;
- use of an incorrect informed consent version;

1.2 Review by the IRB Committee

Protocol violations are administratively reviewed by the Office of Research Compliance or IRB Office staff, by adding reviewer comments to the submitted package in IRBNet, selecting a recommendation and checking the box confirming the review has been completed. This manner confirms the date of review. Information including violation description, corrective action, risk to the subject, and other pertinent information is listed on the agenda for Full Board review.

Violations will be forwarded to the IRB Chair for review if the violation presents significant risk to the subject(s) or if the event is medically complex. The Chair's determination will be included on the agenda for the next Full Board meeting.

2.0 Protocol Deviation

2.1 Reporting Procedures

A Deviation is considered a *minor* or administrative divergence from approved design and procedures when the deviation *does not* affect the subject's rights, safety, or welfare, and/or the completeness, accuracy and integrity of the study data. Deviations should be reported to the IRB using the Protocol Deviation/Violation Reporting Form within *15 business days* of becoming aware of the event.

Examples of deviations include, but are not limited to the following:

- implementation of minor changes to previously *approved* recruitment procedures or materials;
- Missing original signed and dated consent form or missing pages from executed consent form;
- Inappropriate documentation of consent, including:
 - Missing signatures
 - Individual obtaining consent not listed on IRB approved application;
- Not reporting SAEs within the required window
- Subject visit/procedure falls outside of the window of time indicated by the protocol, or is not done per protocol, and there is no increased potential for risk to the subject or any damage to the integrity or completeness of the data.

2.2 Review by the IRB Committee

Protocol deviations are initially administratively reviewed by the Office of Research Compliance or IRB Office staff by adding reviewer comments to the submitted package in IRBNet, selecting a recommendation and checking the box confirming the review has been completed. This manner confirms the date of review. Information including

violation description, corrective action, risk to the subject, and other pertinent information is listed on the agenda for Full Board review.

3.0 Protocol Exception

3.1 Reporting Procedures

A protocol exception is a temporary protocol deviation that is approved by the sponsor or funding agency, (and, if applicable, the FDA) and the IRB, prior to its implementation. Protocol exceptions are generally for a single subject.

Protocol exceptions must be submitted to the USA IRB and granted approval prior to its implementation, except where necessary to eliminate apparent immediate hazards to the Human Subjects. Protocol exceptions should be requested using the Protocol Exception Request Form.

The IRB is only concerned with reviewing exceptions that potentially effect a subject's rights, safety, or welfare. Out of window deviations, when known in advance, do not need to be reported to the IRB prior to implementation. These types of deviations can be treated as a standard protocol deviation.

Examples of exceptions include, but are not limited to the following:

- waiver of one or more inclusion/exclusion criteria
- failure to withdraw a subject meeting withdrawal criteria;
- any medication error involving dosing, administration and/or preparation of the study drugs;
- changes to study procedures

3.2 Review by the IRB Committee

Protocol exceptions should be submitted prior to implementation. Exceptions will be reviewed by the IRB Chair and a decision will be rendered within *two* days. The Chair's decision will be placed on the agenda for the next scheduled Full Board meeting .

4.0 Determination by the IRB Committee (Serious or Continuing)

Non-compliance reviewers will review documents and determine whether:

- There is no issue of serious and/or continuing non-compliance
- There is serious and/or continuing non-compliance
- More information is needed and determination is deferred pending receipt of additional information

- There is a sufficient corrective action plan
- There is or is not a trend of similar non-compliance

If the investigator offers a timely and satisfactory explanation for the concern and a plan to eliminate future incidents of such noncompliance and the IRB accepts, the IRB may elect to terminate the noncompliance investigation process and report that the noncompliance issues were met with no further action.

If the corrective action plan calls for any changes to the previously approved research and the changes involves more than minor modifications, the modification must be reviewed by the convened IRB. Minor changes will be reviewed by expedited review.

If the Investigator does not provide adequate information or corrective action plan, the IRB may ask the investigator to meet with the chair or attend an IRB meeting to discuss the issue(s).

DHHS regulations at 45 CFR 46.103(a) and (b)(5) require unanticipated problems involving risks to subjects, serious or continuing noncompliance, or suspension/termination of IRB approval conducted under an approved assurance be reported to OHRP.

4.1 Actions That May Be Taken During or After the Investigation of Non-Compliance

- No action
- Suspension: suspend enrollment and/or all research procedures for the specific research study in question
- Termination of the research
- Require a response from the investigator with a plan of corrective action
- Initiate audits of all or some part of the investigator's active protocols
- Modification of the research protocol
- Modification of the information disclosed during the consent process
- Additional information provided to past participants
- Modification of the annual review schedule
- Acquire additional information pending final outcome
- Requirements that current participants re-consent to participate (if applicable)
- Monitoring of the research and/or consent process

4.2 Continuity of Care of Research Participants when study is suspended

After the IRB has decided to suspend/terminate a research project, the IRB may make recommendations to investigators regarding ongoing care and treatment of human subjects who had been participating in research. The IRB shall take into consideration, the risk to the subjects from withdrawal of any investigational drug or device or social or behavioral interventions can be continued by another qualified physician or social/behavioral scientists and need further supervision of the participant(s).

4.3 Final Outcome

If a finding of research noncompliance has been made, the IRB, IRB chair, or designee shall decide which corrective action(s) should be taken.

Corrective actions may include any of the following:

- suspension or termination of the investigator's research protocol(s);
- required training with respect to human subjects research and the regulatory requirements for the conduct of such research;
- imposition of changes in such research protocol(s) to further protect Human Subjects;
- a monitoring plan
- imposition of restrictions as a condition for the continuation of research by the investigator

Regulated Documents

45 CFR 46.103, 109

21 CFR 56.108, 109

University Related Documents

Protocol Deviation/Violation Reporting Form (located in IRBNet forms and templates)

Protocol Exception Request Form (located in IRBNet forms and templates)

History:

Effective Date:

Revisions: October, 2018

Responsible Office:

Office of Research Compliance and Assurance