OBJECTIVE

To describe policies and procedures for the submission and review of unanticipated problems (UP), adverse events (AE), and severe adverse events (SAE) and Investigational New Drug (IND) Safety Report form related to approved research submissions.

GENERAL DESCRIPTION

Regulatory guidance provided in 45 CFR 46.103(b)(5) and 21 CFR 56.108(b) requires the Institutional Review Board (IRB) to have in place written procedures for ensuring prompt reporting to the IRB, appropriate Nova Southeastern University (NSU) institutional officials, and applicable regulatory agencies of any unanticipated problems involving risks to human subjects or others.

It is the responsibility of the IRB to review unanticipated problems or adverse events submitted to the IRB office. Unanticipated problems and adverse events that require a change to the study for the safety and welfare of participants will be reviewed by the convened IRB. All other unanticipated problems and adverse events will be reviewed by the IRB Office, which can refer the matter to the convened IRB at its discretion.

For all federally-funded research, the IRB Office will report to the Office for Human Research Protections and the funding agency, as applicable, any incidents determined to be an adverse event that is an unanticipated problem.

In instances where reporting to the FDA is required, the IRB Office will report to the FDA adverse events in keeping with FDA requirements.

For all other studies, the IRB Office will abide by the requirements of the funding agency or agencies.

Investigators must report participant complaints to the IRB Office if they are unable to resolve the complaint, even if it does not meet the definitions of an unanticipated problem or adverse event.

Definitions

Unanticipated problems for non-FDA (Food and Drug Administration) research are considered to include any incident, experience, or outcome that meets all of the following criteria:

- Unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related outcomes, such as the IRB- approved research

protocol and informed consent document; and (b) the characteristics of the subject population being studied;

- Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

For FDA-governed research, the criteria of an *unanticipated problem* are that the event is:

- Unexpected
- Serious
- Would have implications for the conduct of the study (e.g., requiring a significant and usually safety-related, change in the protocol such as revising inclusion/exclusion criteria or including a new monitoring requirement, informed consent, or investigator's brochure).

Serious adverse events are defined as follows:

- Death
- Congenital Anomaly/Birth Defect
- Hospitalization Required or Prolongation of a Hospitalization Life Threatening Event
- Significant or Persistent Disability/Incapacity

Investigational New Drug (IND) Safety Report concerns a product under study and are submitted by a sponsor of an IND to the FDA and to participating investigators conducting studies involving the IND product. Investigators must review all IND Safety Reports and are only required to submit them to the IRB for review under the following circumstances:

- When the report meets the definition of an unanticipated problem;
- When an IND safety report triggers a sponsor-required change to the research protocol or consent form;
- When the sponsor indicates the safety information must be reviewed by the IRB to determine that either a change in research is required or currently enrolled subjects should be informed of the new information.

RESPONSIBILITY

Execution of SOP: Institutional Review Board (IRB) Office Staff, IRB Members, IRB Chairs, Principal Investigator (PI)/Research Personnel

PROCEDURES

1. The investigator is responsible for submitting the unanticipated problems, adverse event, or serious adverse event to the IRB Office for review. Local serious adverse events must be reported within 24 hours of discovery; all other local adverse events and unanticipated problems must be reported within 5 working days of discovery. IND Safety Reports, which meet the criteria outlined in preceding section, must be submitted along with an attestation that the investigator has reviewed the safety report, to the IRB for review by convened IRB. To be reviewed by the convened IRB the safety report must be received by the last business day of the month prior to the meeting of convened IRB.

2. The Post-Approval Monitor is responsible for conducting the initial review of all reported unanticipated problems, adverse events, serious events, or IND Safety Reports.

3. If the problem/adverse event presents possible immediate danger to subjects participating at NSU, the PAM will promptly report to the IRB Chair a recommendation for addressing the incident. All other problems/adverse events reviewed by the Post-Approval Monitor will be presented to the convened IRB for discussion and included in the meeting minutes. The convened IRB may request further information regarding the problem/adverse event. When applicable, the IRB Director and/or Post-Approval Monitor will discuss the reported problem/event with the Institutional Official.

4. The IRB may request corrective actions or substantive changes including:
    a. Changes to the research protocol. Proposed changes must be approved by the IRB prior to implementation except when necessary to eliminate apparent immediate hazards to subjects;
    b. Modification of the inclusion or exclusion criteria to mitigate the newly identified risks; Implementation of additional procedures for monitoring subjects;
    c. Suspension of enrollment of new subjects;
    d. Suspension of research procedures in currently enrolled subjects;
    e. Modification of informed consent documents to include a description of newly recognized risks; and
    f. Provision of additional information about newly recognized risks to previously enrolled subjects

5. The Principal Investigator will be notified by the IRB Office of any required action or any requests for additional information.

6. The IRB Office, via the Institutional Official, will notify any applicable regulatory agency within one month of the IRB receiving the report of an adverse event that is an unanticipated problem from the investigator.

7. The Principal Investigator, any applicable regulatory agencies, and/or institutional departments will be notified if the IRB suspends or terminates research activities. The Principal Investigator is responsible for notifying sponsors of study suspension or termination.

REFERENCES

45 CFR 46.103(a) and 45 CFR 46.103(b)(5)
21 CFR 56.108(b)(1), (b)(2)
21 CFR 56.115(a)(1)