ADVERSE EVENT AND/OR UNANTICIPATED PROBLEM

SOP #:	**411**	**VERSION #:**	**1**	**EFFECTIVE DATE:**	**5/1/09**	**SUPERSEDES DOCUMENT:**	**/ /**
THIS POLICY PERTAINS TO:			**ALL RESEARCH CONDUCTED UNDER THE JURISDICTION OF THE IRB**				
RESPONSIBILITY FOR EXECUTING POLICY:			**ASSOCIATE VICE PRESIDENT FOR RESEARCH AND ECONOMIC DEVELOPMENT, IRB CHAIRPERSON, IRB MEMBERS, INVESTIGATORS**				
LAST REVIEWED ON:		**/ /**		**RESULTS:**	**REVISED**		
APPROVAL AUTHORITY:			**Associate Vice President for Research and Economic Development**				
APPROVED BY:						**DATE:**	**/ /**

1. POLICY

The purpose of this policy is to establish the reporting requirement and identify problems that an Investigator must report to the IRB to ensure prompt reporting of unanticipated problems involving risks to participants or others. This policy also establishes the process to determine which are unanticipated problems involving risks to participants or others.

2. SPECIFIC POLICY

2.1 Definitions

Adverse Event: Any untoward or undesirable experience that may present during the conduct of a research study to the subjects or others, or any undesirable experience associated with the use of a medical product in a patient.

Unanticipated: A problem that was unforeseeable at the time of its occurrence based on the information provided to the IRB. The nature or the severity of the event or the frequency of occurrence is not consistent with information presented in the protocol, the brochure, or the informed consent.

Related: More likely than not caused by the research procedures

Unanticipated problem involving risks to participants or others: A problem, which (1) is unanticipated, and (2) indicates that participants are at increased risk of harm.

Risks: The occurrence of harm or probability that harm might occur. The harm may be physical, psychological, financial, social, economic, or legal.

Others: Individuals who are not research subjects.

Unanticipated adverse device effect: Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare or subjects.

Unexpected event: Any harm, the specificity or severity of which is not consistent with the current investigator brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the protocol. Unexpected as used in this definition, refers to an adverse drug experience that has not been previously observed (e.g. included in the investigator brochure) rather than from the perspective of such experience not being anticipated from the pharmacological properties of the pharmaceutical product.

2.2 Problem Reporting

2.2.1 The Investigator must promptly report any of the following events to the IRB, regardless of whether they occur during the study, after study completion, or after participant withdrawal or completion:

- Any event (including on-site and off-site adverse events, injuries, side effects, deaths, or other problems, regardless of whether the event was serious), which in the opinion of the Principal Investigator (1) was unexpected, and (2) was related to the research procedures;
- Any event that requires prompt reporting according to the sponsor;
- Any accidental or unintentional change to the IRB-approved protocol that involved risks or has the potential to recur;
- Any change to the protocol made without prior IRB review to eliminate apparent immediate hazard to a research participant;
- Any publication in the literature, safety monitoring report, interim result, or other finding that indicates an unexpected change to the risks or potential benefits of the research;
- Any compliant of a participant that indicates an unanticipated risk or which cannot be resolved by the research staff;
- Any independent safety monitoring reports or DSMB reports;
- Breach of privacy/confidentiality/data security/loss of study data/destruction of study data due to noncompliance; or
- Incorrect labeling/dosing of study medication or test article.

2.3 Investigator Reporting

The Investigator needs to report to IRB within 5 consecutive days of receipt of notification of serious adverse event or unanticipated problem as follows;

- Complete the Unanticipated Problem/Adverse Event Form and;
- Any associated documents such as MedWatch form, medical record notations, correspondence from the sponsor, etc. The Investigator is responsible for the documentation, investigation, and follow-up of all serious adverse events and unanticipated problems that occur at the site in which the Investigator is responsible for the conduct of the research.

2.4 Review of the Event or Problem

The IRB Chairperson or designee will initially review all Unanticipated Problem/Adverse Event Forms. If appropriate to the event or problem, the IRB Chairperson will also review the protocol, current informed consent, and any other relevant documents pertaining to the event or problem. After initial review, the IRB Chairperson or designee will make one of the following determinations:

The problem is NOT an unanticipated problem involving risks to participants or others (because the event is either anticipated or does not indicate that participants are at increased risk of harm):

- Take no action, document review, and put on IRB agenda for reporting purposes.

OR

The problem is considered an unanticipated problem involving risks to participants or others (because the problem is (1) unanticipated and (2) indicates that participants are at increased risk of harm):

- The IRB Chairperson may determine that immediate action is needed to ensure the participants safety; the IRB Chairperson may request that the Investigator suspend some or all of the research pending review of the event at the next convened IRB meeting. Suspensions ordered by the IRB Chairperson will follow IRB procedures outlined in SOP 410 Suspension and Termination.
- The IRB Chairperson or designee will present the problem to the IRB at the next convened meeting. The IRB members will be provided a copy of the event form and all appropriate documentation including current protocol and informed consent. The IRB will deliberate and vote to determine whether the event represents an unanticipated problem involving risks to subject or others based on whether the event was (1) unanticipated and (2) indicated that participants are at increased risk of harm. If the event is determined to be an unanticipated problem involving risks to participants or others, the IRB will deliberate and vote to approve on the following actions, including, but not limited to:
    - No action;
    - Modification of the research protocol;
    - Modification of the information disclosed during the consent process;
    - Additional information provided to past participants;
    - Notification of current participants (required when such information may relate to participants' willingness to continue to take part in the research);
    - Requirement that current participants re-consent to participation;
    - Modification of the continuing review schedule;
    - Monitoring of the research;
    - Monitoring of the consent;
    - Suspension of the research;
    - Termination of the research;
    - Request for more information pending final decision;
    - Refer to other organizational entities (e.g. legal council, institutional official); or
    - Other actions as appropriate.

The determination and vote will be reported in the minutes and the Investigator will be notified.

2.5 Notification

No action required: If the problem is determined to not be an unanticipated problem involving risks to participants or others, the Investigator will be sent a letter indicating that the IRB has received the report and that no action will be required.

Full Committee Review: The Investigator will be notified within 5 consecutive days of the IRB meeting of the committee's determination and action(s). If the problem is determined to be an unanticipated problem involving risks to participants or others, the problem will be reported to the appropriate individuals and agencies per SOP 409. A copy of this report will also be disseminated to the IRB members at the next convened IRB meeting.

3. RESPONSIBILITY

The Associate Vice President for Research and Economic Development is responsible for notifying, if appropriate, individuals and agencies of the unanticipated problem involving risks to participants or others per SOP 409 Reporting Requirement for Unanticipated Problem, Serious and Continuing Non-Compliance or Suspension or Termination of IRB Approval.

The IRB Chairperson or designee will review all Unanticipated Problem/Adverse Event Forms and if the problem might represent an unanticipated problem involving risks to participants or others, present the problem to the Full IRB at a convened meeting.

IRB members are responsible for determining if the problem represents an unanticipated problem involving risks to subject or others.

IRB Secretary is responsible for sending out letters to Investigators and appropriate individuals and agencies.

4. APPLICABLE REGULATIONS AND GUIDELINES

45 CFR 46.103(b)(5)(i)
21 CFR 56.108(b)(1)
21 CFR 312.32
21 CFR 812.3(s)
OHRP DRAFT Guidance on Reporting and Reviewing Adverse Events and Unanticipated Problems Involving Risks to Subjects or Others

5. ATTACHMENTS

RR 411-A Adverse Event/Unanticipated Problems Involving Risk to Participants and Others

6. PROCEDURES EMPLOYED TO IMPLEMENT THIS POLICY

Who	Task
IRB Chairperson or designee	Initial review of Unanticipated Problem/Adverse Event Form. Determine if the problem is an unanticipated problem involving risks to participants or others; If the event might be an unanticipated problem involving risks to participants or others, present the facts to the IRB at a convened IRB meeting
IRB Members	Review the facts and make determination, establish an action plan and timeline for the Investigator.
IRB Secretary	After IRB meeting, notify the Investigator within 5 consecutive days of IRB determination.
Associate Vice President for Research and Economic Development	Notify within 30 days all appropriate individuals and agencies. Provide a copy of the report to the IRB members at the next convened meeting.