SOP		
Department	**Title**	**Dates**
Research Integrity and Protection	Reportable Events (New Information)	Effective: 1/19/2018
		Approved: 1/15/2018
SOP ID		Last Revised: 11/08/2018
IRB-SOP-204		Expiration: n/a

PURPOSE

This document outlines the information and events that must be reported to the Ascension Wisconsin IRB, as well as the time frame and procedures for the reporting and review.

SCOPE

This procedure applies to research conducted at Ascension Wisconsin or any research reviewed by an Ascension Wisconsin IRB.

DEFINITIONS

Adverse Event (AE) Any unfavorable or unintended event, including abnormal laboratory findings, symptom or disease, or death associated with the research or the use of a medical investigational test article. An AE in research may occur even in the absence of any error or protocol deviation and does not necessarily have to be caused by any identifiable aspect of the research.

Non-Compliance Failure to follow the federal regulations; state and local laws; institutional policies governing human subject research; or the requirements or determinations of the IRB.

- Continuing Non-Compliance A pattern of Non-Compliance:
  - that suggests the likelihood that, without intervention, instances of Non-Compliance will recur, or
  - a repeated unwillingness to comply, or
  - a persistent lack of knowledge of how to comply.

  For example, a single non-compliant action that affects multiple subjects would likely not be considered continuing non-compliance, while repeating the same non-compliant action multiple times would.

- Serious Non-Compliance Non-Compliance such that the failure to comply could:
  - adversely affect the rights, safety, or welfare of a human subject, or
  - place a human subject at increased risk of harm, or
  - cause harm to a human subject, or
  - affect a human subject's willingness to participate in research, or
  - damage or compromise the scientific integrity of research data.

Unanticipated Problem Involving Risks to Subjects or Others ("Unanticipated Problem" or "UPIRSO"): Any event that is:

- unexpected in nature, severity, or frequency; and
- related or possibly related to participation in the research; and
- places subjects or others at a greater risk of harm than was previously known or recognized.

- Unexpected: The harm (or potential harm) is inconsistent with risk information previously reviewed by the IRB in terms of nature, severity or frequency as well as the characteristics of the subject population.

- Possibly related: There is a reasonable probability that the incident, experience or outcome may have been caused by the procedures involved in the research, or that it is associated with the use of any drug, biologic, or medical device that is part of the research.

Suspension of IRB Approval An action of the IRB, IRB designee, Institutional Official, or designee of the Institutional Official to temporarily or permanently withdraw IRB approval of some or all research procedures short of a Termination of IRB Approval. Suspended studies remain open and are subject to continuing review. This action may be reportable to federal agencies.

Termination of IRB Approval An action of the IRB, IRB designee, Institutional Official, or designee of the Institutional Official to permanently withdraw IRB approval of all research procedures. Terminated studies are permanently closed and no longer require continuing review. This action may be reportable to federal agencies.

Prompt Reporting Federal regulations and the Ascension Wisconsin Research Institute require prompt reporting. This means that researchers may sometimes need to report before the situation or issue has been fully resolved. In such cases, researchers are expected to make an initial report within the time frame described below, and then to provide a follow-up report as appropriate.

Here, "prompt" is defined as 7 calendar days of the Investigator becoming aware of the incident.

PROCESS

1. Reporting to the IRB

1.1. Federal regulations and Ascension Wisconsin policy requires researchers to promptly notify Research Integrity and Protection and/or the IRB of the following information and events, for any human subjects research in which Ascension Wisconsin is engaged.

- Unanticipated problem, this includes but is not limited to Serious Adverse event that occurred locally.
- Unanticipated adverse medical device effect.
- Serious non-compliance (or allegation of serious non-compliance).
- Continuing non-compliance (or allegation of continuing non-compliance).
- Emergency deviation from IRB-approved procedures made without prior IRB review to eliminate an apparent immediate hazard to a subject or others.
- Continuation of research procedures after IRB approval has lapsed, because the procedures are of direct benefit to individual subjects or withholding the research intervention (if any) may increase risks to subjects.
- Breach (or risk of breach) of subject confidentiality or privacy.
- Inappropriate access of Protected Health Information (PHI).
- Complaint of a subject that cannot be resolved by the study team.
- Audit, inspection, compliance-related inquiry, or safety-related inquiry from a federal agency
- New information that has implications for the risks of the research. For example:
    - A publication in the literature indicates an increase in the frequency or magnitude of a previously known risk, or uncovers a new risk.
    - An investigator brochure, package insert, or device labeling is revised to indicate an increase in the frequency or magnitude of a previously known risk, or to describe a new risk.
    - A withdrawal, restriction or modification of the marketing approval or FDA labeling of a drug, device, or biologic being used in the research.
- Changes in credentialing, licensing, resources or facilities that will affect the ability to conduct or complete the research as approved by the IRB or the risks of harm to subjects or others.
- Premature suspension or termination of some or all of the research by the sponsor, researcher or institution.
- Safety monitor or Data and Safety Monitoring Board (DSMB) reports with any recommendation or finding (other than continuation as planned).

1.2. Collaborative Research

1.2.1. When the components of the research are distributed across more than one institution or site, the reporting requirements depend upon the IRB review arrangements.

1.2.2. Ascension Wisconsin IRB is the IRB of record for another institution: The researcher follows the Ascension Wisconsin reporting requirements described in this document, for problems involving the other institution or Ascension Wisconsin sites.

1.2.3. Ascension Wisconsin is deferring IRB review to another non- Ascension Wisconsin IRB: The researcher follows the reporting requirements of the IRB reviewing the research (i.e., the IRB of record) for all sites, including the Ascension Wisconsin site(s).

1.2.3.1. The research must report to the Ascension Wisconsin IRB if the IRB of record makes a determination of Serious Non-Compliance; Continuing Non-Compliance; Suspension of IRB Approval; Termination of IRB Approval; or Unanticipated Problem Involving Risks to Subjects or Others.

1.2.3.2. If Ascension Wisconsin will continue to provide HIPAA Privacy Board Oversight, breaches of confidentiality, inappropriate access of PHI must be reported to the Ascension Wisconsin IRB reporting requirements described in this document.

1.3. External AEs in multicenter trials

1.3.1. Internal adverse events are AEs experienced by subjects enrolled by the researcher at that institution, whereas external adverse events are AEs experienced by subjects enrolled by researchers at other institutions engaged in the trial.

1.3.2. Researchers may routinely receive a large volume of reports of external AEs experienced by subjects enrolled in multicenter clinical trials. These individual reports often lack sufficient information to allow researchers or the local IRB to make meaningful judgments about whether the AE is unexpected or is related or possibly related to the research.

1.3.3. External AEs should only be reported to Ascension Wisconsin IRB if they meet the definition of an Unanticipated Problem.

1.4. The PI must submit reportable events using the appropriate form in Mentor.

1.5. See IRB Guidance: Reportable Events: Non-Compliance, Safety Information and Unanticipated Problems for more information and examples of items that do and do not need to be reported.

2. IRB Review

2.1. Research Integrity and Protection (RI&P) staff conduct a pre-review of all reportable items.

2.2. Staff screens the initial submission and work with the Investigator or study team to gather additional information, clarifications or development of a suitable action plan, as needed.

2.3. Staff complete a IRB pre-review checklist in Mentor and send to the an IRB Chair or Designated Reviewer for review.

2.4. If the Staff feel that the rights and welfare of subjects might be adversely affected before the convened IRB can review the information, they contact the IRB Chair or IRB Manager to consider a Suspension of IRB Approval following the "SOP: Suspension or Termination (SOP-206)."

2.5. The Chair or Designated reviewer may 1) Acknowledge the report; 2) Request further information; 3) Require full IRB review.

2.5.1. If acknowledged, staff processes the determination and adds the review to the report to inform the IRB of items reviewed outside of the convened meeting.

2.5.2. If review by the Convened IRB is required, staff assigns the review to the agenda of the next convened IRB meeting.

2.6. IRB determination concerning appropriate remedies. In reviewing and addressing any serious or unexpected events or a potential unanticipated problem that involves risks to others, the IRB may impose any remedy, or take any action, authorized by law or regulation, including:

- Initiate immediate corrective action, if necessary.
- Delegate a subcommittee or individual to perform further investigation
- Require that individuals who have already consented to participation be notified.

- Require modification of any other aspect of the conduct of the research including recruitment, informed consent, research and clinical procedures, monitoring and safety assurance, and continuing review.
- Alter the frequency of continuing review.
- Require that enrolled subjects be provided with an amended informed consent form, and that the process of providing for informed consent be repeated with revised information. This will be required whenever the information may relate to the participants willingness to continue participating.
- Determine the incident involves serious or continuing noncompliance (see Noncompliance Policy).
- Determine the protocol should be terminated or suspended (see Termination and Suspension Policy).
- Require the investigator to inform other research participants or individuals who may be affected by the event or problem.
- Notification of investigators at other sites
- Observation of the consent process
- Refer concerns or findings to other parts of the organization that administer other policies, laws, and regulations.

2.7. The investigator will receive notification through Mentor as to whether the report was acknowledged, whether additional information, modifications, or action is required, and whether reporting is required.

3. IRB Non-Compliance

Allegations of Serious or Continuing Non-Compliance on the part of IRB staff or IRB members will be referred to the Organizational Official for further action.

4. Reporting to External Agencies

4.1. The organization will promptly notify the federal department, agency and/or Sponsor of suspension, termination, serious or continuing non-compliance and/or unanticipated problem involving subjects or others, as required by federal regulations or other agreement, when applicable.

4.1.1. The Director of Research Integrity and Protection manages this reporting process, with input from the Institutional Official and other stakeholders, such as Corporate Responsibility and Legal, as needed.

4.2. For Department of Defense (DOD) research promptly report all decisions to the Department of Defense (DOD). The Department of Defense (DOD) must concur with the IRB before the subject can continue to participate while a prisoner

REFERENCES

- 21 CFR §56.108(b)
- 45 CFR §46.103(b)(5), 45 CFR §46.108(a)

RELATED MATERIAL

- SOP: Suspensions or Terminations of IRB Approval (SOP-604)
- IRB Guidance: Reportable Events: Non-Compliance, Safety Information and Unanticipated Problems
- OHRP Guidance on Reviewing and Reporting Unanticipated Problems and Adverse Events: http://www.hhs.gov/ohrp/policy/AdvEvntGuid.html
- FDA Guidance: http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM126572.pdf

REVISION HISTORY:

Version #	Date Revised	Reason for/Brief Description of Change	Revised By
01	12/7/2017	New- Initial Integration Update	J. Blundon

02	2/12/18	Update 4.1 for correction regarding reporting requirements; minor grammatical corrections.	J. Blundon
03	11/8/2018	4.1.1. Clarification of who is responsible for reporting to external agencies.	J. Blundon-Kirchen