



WESTERN INSTITUTIONAL REVIEW BOARD®
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WIRB Reporting System for Unanticipated Problems that are Adverse Events

Federal Regulation 21 CFR 56.108(b)(1) and 45 CFR 46.103(b)(5) require the IRB to “follow written procedures for ensuring prompt reporting to the IRB...any unanticipated problems involving risks to human subjects or others...”

An unanticipated problem is defined as 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 documents, such as the IRB-approved research protocol and informed consent document, or the Investigator Brochure; 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 drugs, devices or procedures involved in the research); and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

All reports to the IRB of unanticipated problems should explain clearly why the event is "unanticipated" and clearly explain why the event represents a “problem involving risks to human subjects or others.”

WIRB expects reports to the IRB of unanticipated problems to include a corrective action plan to address the issue, or written justification for why none is provided.

Please note that unnecessarily reporting problems that do not meet the criteria outlined above may impair the Board’s ability to review and respond in a timely manner to actual situations where subject rights, welfare or safety are threatened.

Adverse events are any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research.

FDA guidance documents recognize that:

1. “individual adverse event reports generally require an evaluation of their relevance and significance to the study, including an evaluation of other adverse events, before they can be considered to be an unanticipated problem,” and
2. “All reports to the IRB of unanticipated problems should explain clearly why the event described represents a ‘problem’ for the study and why it is ‘unanticipated.’”

FDA believes that reports that lack such evaluation should not be provided to the IRB.

The reporting requirements for WIRB may differ from the reporting requirements for the sponsor. Report to WIRB only adverse events that in the opinion of the investigator may **represent unanticipated problems involving risks to the other subjects in the research.**

A. For adverse events that are determined to be unanticipated problems occurring at your site:

Use the Report Form for Unanticipated Problems that are Adverse Events to report an unanticipated adverse event that occurred at your site.

Investigators are required to report adverse events that fit the following criteria *within 10 working days* of the time the investigator becomes aware of them:

- Event is **Unexpected** (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document, or the Investigator Brochure; 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 subjects or others at a greater risk of harm** (including physical, psychological, economic, or social harm) than was previously known or recognized.

If the adverse event is clearly not related to the study drug, device, procedures, or washout process, it would not represent a risk to other subjects in the research or a “problem” for the study and, therefore, does not have to be reported to WIRB.

B. For adverse events that are determined to be unanticipated problems that did not occur at your site (non-site adverse reports such as IND safety reports, SUSAR reports, and so forth):

WIRB will accept non-site adverse event reports submitted by investigators and from sponsors on behalf of investigators, if, in accord with 21 CFR 312.32,

- the event described is both serious and unexpected,
- the report identifies all previous safety reports concerning similar adverse experiences,
- the report analyzes the significance of the current adverse experience in light of the previous reports, **and**
- the report outlines a corrective action plan (such as a consent form change or protocol change).

WIRB will not accept non-site adverse events that do not identify all previous safety reports concerning similar adverse experiences, analyze the significance of the current adverse experience in light of the previous reports and outline a proposed correction action plan. These submitted reports will generally be returned to the submitter with a description of the WIRB reporting requirements and guidance encouraging the submitter to resubmit with the required analysis.

If you have arranged for the sponsor to report the unanticipated problem directly to WIRB, we do not expect you to provide us with a duplicate copy of the report received from the sponsor.

If the sponsor, CRO or SMO does not submit non-site adverse events that are determined to be unanticipated problems to WIRB on behalf of your site, you are required to submit them, **along with the required explanation outlined above**, within 10 days of the date you receive them.

WIRB recognizes that for multicenter studies, the sponsor is in a better position to process and analyze adverse event information for the entire study, and to assess whether an occurrence is both "unanticipated" and a "problem" for the study. Accordingly, you may rely on the sponsor's assessment and provide to WIRB a report of the unanticipated problem prepared by the sponsor.



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**Report Form for Unanticipated Problems that are Adverse Events
(due within 10 days of identifying an unanticipated problem that is an adverse event)**

Principal Investigator Name: _____
WIRB Protocol No.: _____
Sponsor Protocol No.: _____
Sponsor: _____
Study Drug/Device: _____
Date of this Report: _____
Date of Occurrence: _____
Subject ID: _____
(If applicable)

1. AE Description / Treatment / Outcome (including relevant dates):

2. Pertinent subject history:

3. Why do you consider the event “unanticipated”?

Report Form for Unanticipated Problems that are Adverse Events (continued)

**4. Why do you consider the event a “problem involving risks to human subjects or others”?
(In other words, how does this event suggest that subjects or others are at greater risk of harm than was previously known?)**

5. What changes do you propose to the consent form and/or the protocol in order to protect the rights, welfare and safety of the research subjects?

If none are proposed, provide the rationale for why changes are not needed.

Printed or Typed Name of Person Completing This Form

Company/Title

Phone number

Fax number

E-mail