

Information Sheet for Researchers Reportable Events

What events must researchers report to BRANY IRB?

1. Unanticipated Problems Involving Risks to Participants or Others

Examples may include:

1. Event (including on-site and off-site adverse event reports, injuries, side effects, breaches of confidentiality, deaths, or other problems) that occurs any time during or after the research study, which in the opinion of the principal investigator:
 - a. Involve harm to one or more subjects or others, or placed one or more subjects or others at increased risk of harm
 - b. Unexpected (An event is “unexpected” when its specificity and severity are not accurately reflected in the informed consent document.)
 - c. Related to the research procedures (An event is “related to the research procedures” if in the opinion of the principal investigator, it was more likely than not to be caused by the research procedures or if it is more likely that not that the event affects the rights and welfare of current participants)
2. Information that indicates a change to the risks or potential benefits of the research, in terms of severity or frequency. For example:
 - a. An interim analysis indicates that participants have a lower rate of response to treatment than initially expected
 - b. Safety monitoring indicates that a particular side effect is more severe, or more frequent than initially expected
 - c. A paper is published from another study that shows that an arm of the research study is of no therapeutic value
3. Change in FDA labeling or withdrawal from marketing of a drug, device, or biologic used in a research protocol.
4. Change to the protocol taken without prior IRB review to an eliminate apparent immediate hazard to a research participant
5. Incarceration of a participant
6. Event that requires prompt reporting to the sponsor
7. Complaint of a participant when the complaint indicates unexpected risks or cannot be resolved by the research team
8. Protocol violation (meaning an accidental or unintentional change to the IRB approved protocol) that placed one or more participants at increased risk, or has the potential to occur again.
9. 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 (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.)

BRANY IRB will accept other reports when the investigator is unsure whether the event should be reported.

2. Serious Adverse Events (SAEs) (also described as “on-site” or “internal” adverse events)

Definitions:

a. *For studies subject to 21CFR312 (Investigational New Drugs)*

An **adverse event** (AE) is defined as any untoward medical occurrence associated with the use of a drug in humans, **whether or not considered drug related**.

Adverse events may be categorized as follows:

- (i) **Adverse reaction** - any adverse event **caused by a drug**.

- (ii) **Suspected adverse reaction** - any adverse event for which there is a **reasonable possibility that the drug caused the adverse event**. For the purposes of IND safety reporting, "reasonable possibility" means there is **evidence to suggest a causal relationship between the drug and the adverse event**. Suspected adverse reaction implies a lesser degree of certainty about causality than adverse reaction.
- (iii) **Unexpected Suspected Adverse Reaction** - A suspected adverse reaction is considered "**unexpected**" if it is not listed in the investigator brochure or is not listed at the specificity or severity that has been observed; or, if an investigator brochure is not required or available, is not consistent with the risk information described in the general investigational plan or elsewhere in the current application, as amended. For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the investigator brochure referred only to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the investigator brochure listed only cerebral vascular accidents. **Unexpected**, as used in this definition, also refers to adverse events that are mentioned in the investigator brochure as occurring with a class of drugs or as anticipated from the pharmacological properties of the drug, but are not specifically mentioned as occurring with the particular drug under investigation.
As sub-categories of "adverse events," adverse reactions and suspected adverse reactions may also be unexpected.
- (iv) **Serious Adverse Events (SAEs)** - An *adverse event* is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes:
 - (i) Death,
 - (ii) A life-threatening adverse event,
 - (iii) Inpatient hospitalization or prolongation of existing hospitalization,
 - (iv) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, or
 - (v) A congenital anomaly/birth defect.

Additionally, *important medical events* that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

b. **For studies subject to 21CFR812 (Investigational Devices)**

Unanticipated Adverse Device Effect (UADE) - 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 (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects

SAE and UADE Reporting Procedures:

This paragraph applies to serious adverse events occurring at BRANY IRB-approved investigational sites. Investigators are required to notify the IRB promptly of any unanticipated problems involving risks to subjects or others that occur in research (45 CFR 46.103(b)(5), 21 CFR 56.108(b) and 21 CFR 312.66).

Investigators are also required to report promptly to the IRB any serious adverse event that is reported to the FDA or the Study sponsor in accordance with FDA requirements. Investigators must report all SAEs to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. Investigators must follow regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB. For reports of deaths, investigators must supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports).

Reporting Study Endpoints

Study endpoints (e.g., mortality or major morbidity) as described in the protocol ordinarily would not be reported as a serious adverse event or unexpected suspected adverse reactions to the IRB. However, if a serious and unexpected adverse event occurs for which ***there is evidence suggesting a causal relationship between the drug/device/study intervention and the event*** (e.g., death from anaphylaxis), the event must be reported to the IRB as serious and unexpected suspected adverse reaction even if it is a component of the study endpoint (e.g., all-cause mortality).

All **serious adverse events** and **unexpected suspected adverse reactions** that occur during a study, or in a post-study period of reasonable duration (30 days, or longer if in the judgment of the PI reporting is appropriate after 30 days), must be reported via the **Reportable Event Form**, with supporting documentation as soon as possible, but in no event later than 5 business days of the researcher becoming aware of the event.

In keeping with 21CFR812.150(a)(1), an investigator shall submit to the sponsor and to the reviewing IRB a report of any **unanticipated adverse device effect** occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect, via the **Reportable Event Form**.

Reports to the IRB must contain a sufficient amount of information to permit the reviewer to judge whether the event raises new questions about risks to participants. All reports will be preliminarily reviewed by a member of the IRB administrative staff and will be subsequently reviewed by the IRB Chairperson, or designee.

All events should be followed up to resolution. Any new findings pertaining to a previously reported event must be submitted as a follow-up report. Such submission should indicate whether it is an Initial or Follow-up report.

3. **Protocol Deviations and Protocol Exceptions:**

Definitions and Reporting Procedures:

Protocol Deviation: Any temporary alteration/modification to the IRB-approved protocol. The protocol may include the detailed protocol, protocol summary, consent form, recruitment materials, questionnaires, and any other information relating to the research study. Deviations can be major or minor.

Major Protocol Deviation: A deviation that affects subject safety, rights, welfare, or data integrity.

Examples of major protocol deviations include (but are not limited to):

- Failure to obtain informed consent (i.e., no documentation of informed consent, consent obtained after study procedures were initiated)
- Enrolling subject who does not meet inclusion/exclusion criteria
- Use of study procedures not approved by the IRB
- Failure to report serious adverse events to the IRB and/or sponsor (per applicable requirements)
- Failure of subject to show up for a study appointment that results in missing treatment
- Failure to perform a required study procedure or lab test that could affect subject safety or integrity of study data (e.g., procedure or lab test results needed to determine eligibility for the research)
- Error in dispensing or dosing of drug/study medication, whether committed by subject or study team
- Error involving use of device
- Study visit conducted outside of required timeframe, only if it affects subject safety
- Failure to follow safety monitoring plan
- Enrollment of subjects after IRB-approval of study expired

Major protocol deviations must be reported to the IRB within ten (10) working days of discovery using the Reportable Event Form.

Examples of minor protocol deviations include (but are not limited to):

- Missing original signed and dated consent form (only photocopy available)

- Inappropriate documentation of informed consent, including:
 - Copy not given to the person signing the consent form
 - Someone other than the subjects dated the consent form
 - Expired consent used, but the version letter is identical to the currently approved consent form.
- Deviations from the approved study procedure that do not affect subject safety or data integrity
- Study procedure conducted out of sequence
- Omitting an approved portion of the protocol
- Failure to perform a required lab test
- Missing lab results
- Study visit conducted outside of required timeframe
- Failure of subject to return study medication

Minor protocol deviations should be reported in aggregate to the IRB at continuing review or with notification of study closure, using the **Minor Deviation Log**

Protocol Exception: A deviation that has been submitted to the IRB for review, and has been approved by the IRB prior to initiation.

If the investigator wishes to deviate from the IRB-approved protocol, he or she must submit such a request using the **Reportable Event Form** to the IRB for review and approval prior to initiation of such deviation.

Which form do I use to report the above to BRANY IRB?

The Reportable Event Form

The **Reportable Event Form** is available as an xForm, or electronic submission form, through BRANY IRB's IRBManager web portal ([link to IRBManager Login](#)).

Reports to BRANY IRB must contain a sufficient amount of information to permit the reviewer to judge whether the event raises new questions about risks to participants. Additional relevant documents should be included, as necessary.

Report Contents

- A detailed description of the incident
- Indication as to whether the reported event placed any subject at risk
- Indication as to whether the reported event affected the integrity of the study data
- A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the reported event, when applicable
- Information regarding changes implemented by the study team to ensure that such a reported event will not occur in the future, when applicable.

The Minor Deviation Log

The **Minor Deviation Log** is available for download on BRANY IRB's Web site: www.branyirb.com, and is available as a generated document in *IRBManager* (BRANY IRB's electronic protocol tracking system). It should be submitted with your continuing review xForm (#11) or your notification of study closure xForm (#04).

Who do I call if I have a question?

Any questions or feedback may be directed to Raffaella Hart, IRB Director at rhart@brany.com or by calling 516-470-6909.

Version 11.06.2013