



Albert Einstein College of Medicine

## Unanticipated Problems Procedure

### I. Purpose

This Procedure describes the requirements relating to reporting of unanticipated problems involving risks to subjects or others. For reporting requirements for noncompliance and other events, refer to the procedures “Research Noncompliance” and “Other Reportable Events.”

### II. Scope

This Procedure applies to all human research under the purview of the Einstein Institutional Review Board (“IRB”), including external sites under Einstein IRB oversight. For studies involving affiliated investigators where Einstein has designated another IRB as the reviewing IRB, investigators must still report to the Einstein IRB in accordance with this procedure.\*

### III. Definitions

**Adverse Event:** Any untoward or unfavorable medical occurrence in a human subject, including abnormal signs (for example, abnormal physical exam or laboratory finding), symptoms, or disease, temporally associated with, but not necessarily considered related to, the subject’s participation in the research study. Not all adverse events meet IRB reporting guidelines.

**Unanticipated Problem (“UP”):** any incident, experience, or outcome that meets all of the following criteria:

- A. 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; and (b) the characteristics of the subject population being studied;
- B. related or possibly related to participation in the research (possibly related meaning there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- C. 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.

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\* Studies reviewed by BRANY are exempt from this procedure. Please refer to BRANY reporting requirements for such studies.

**External Adverse Event:** External adverse events are adverse events experienced by subjects enrolled by investigators at sites that are not affiliated with Einstein and are not under the oversight of the Einstein IRB.

**Internal Adverse Events:** Internal adverse events are adverse events experienced by subjects enrolled by investigators at Einstein or its affiliated institutions. In the context of multisite studies in which the Einstein IRB is the single reviewing IRB, all adverse events are considered internal adverse events.

#### IV. Procedure

1. **Unanticipated problems must be submitted within 5 business days of the identification of the event by research staff.**
  - 1.1. Adverse events are only considered an unanticipated problem if they meet the following three criteria: 1) they are unexpected; 2) they are related or possibly related to participation in the research; and 3) they suggest that the research places subjects or others at a greater risk of harm than was previously known or recognized.
  - 1.2. Unanticipated problems may also include other incidents, experiences, and outcomes that are not adverse events. For example, noncompliance or deviations from the protocol that place participants or others at greater risk than was previously known or recognized would be considered unanticipated problems.

**Internal vs. External Adverse Event Reporting Chart**

		<b>Internal Adverse Events</b>	<b>External Adverse Events</b>
<b>Einstein IRB is the Reviewing IRB</b>	Multiple Equivalent IRBs	Internal adverse events must be submitted to the Einstein IRB if, in the opinion of the principal investigator, they meet the criteria of an unanticipated problem.	Adverse events that occurred at other institutions must be submitted to the Einstein IRB only if they result in an amendment to the protocol or informed consent document. These adverse events are reported to the Einstein IRB as a proposed amendment (using the Amendment Form, not the Reportable Event Form).
	Single IRB with Einstein as the Lead IRB	Internal adverse events must be submitted to the Einstein IRB if, in the opinion of the principal investigator, they meet the criteria of an unanticipated problem.	Adverse events at all sites under oversight of the Einstein IRB are considered internal adverse events and must be submitted to the Einstein IRB if, in the opinion of the principal investigator, they meet the criteria of an unanticipated problem.

<b>Einstein IRB is the Relying IRB</b>		<p>For studies involving affiliated investigators where Einstein has designated another IRB as the reviewing IRB, investigators must still report adverse events to the Einstein IRB if, in the opinion of the principal investigator, they meet the criteria of an unanticipated problem.</p> <p>Affiliated investigators must also comply with the external IRB’s policies and procedures for reporting, including its timelines for submissions.</p>	<p>Adverse events experienced by subjects enrolled by investigators at other institutions when an external IRB has been designated as the single reviewing IRB do not need to be submitted to the Einstein IRB.</p>
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**2. Informing the IRB of unanticipated problems**

**2.1.** The Principal Investigator (“PI”) is responsible for reporting to the IRB any unanticipated problem within 5 business days of becoming aware of the problem.

**3. Evaluating unanticipated problem submissions**

**3.1.** Office of Human Research Affairs (“OHRA”) Staff will refer reportable event submissions to the Executive Chair.

**3.2.** The Executive Chair will evaluate reportable events to determine if they meet the definition of an Unanticipated Problem Involving Risks to Subjects or Others (“UP”).

**3.2.1.** If the Executive Chair determines that the event does not represent an UP, the report will be acknowledged by the Chair.

**3.2.1.1.** OHRA Staff will add the acknowledged report as item on the minutes to notify the IRB committee.

**3.2.1.2.** OHRA Staff will inform the investigator in writing of the acknowledgement.

**3.2.2.** If the determination is that the event represents an UP, the report is forwarded to the full IRB committee for review.

**3.2.3.** If the Executive Chair is unable to make a determination, the report is forwarded to the full IRB committee for review.

**4. IRB review of Unanticipated Problems**

**4.1.** Prior to IRB review, OHRA Staff provides the following documents to IRB members as applicable: the report describing the event; the most recently approved consent form, protocol, application; and any other relevant study documents.

**4.2.** The IRB will review the reported event to determine if it represents an UP.

**4.3.** If the IRB determines that the event does not represent an UP, the report may be acknowledged by the full committee.

- 4.4. If the IRB committee determines that the event does constitute an UP, the IRB considers the following added protections:
  - 4.4.1. Modification of the research protocol;
  - 4.4.2. Modification of the information disclosed during the consent process;
  - 4.4.3. An increase in monitoring of the research activity via a data safety monitor or board;
  - 4.4.4. Monitoring the research or consent process;
  - 4.4.5. A directed audit of targeted areas of concern;
  - 4.4.6. Modification of the continuing review cycle;
  - 4.4.7. Additional Investigator and staff education focused on human research protections from OHRA Staff or other available sources;
  - 4.4.8. Notification of current subjects, if the information about the non-compliance might affect their willingness to continue participation;
  - 4.4.9. Suspension of all or part of the study;
  - 4.4.10. Termination of the study;
  - 4.4.11. Other actions as appropriate.
- 4.5. UP determinations will be reported to appropriate Institutional Officials, sponsors, the FDA, and the OHRP, as appropriate.<sup>1</sup>

## **V. Effective Date**

Effective as of: 22 August 2019

Implementation Period: Six months from the effective date.

## **VI. Procedure Management and Responsibilities**

Einstein's Office of Human Research Affairs is the Responsible Office under this Procedure. The Executive Dean is the Responsible Executive for this Procedure. The OHRA Director is the Responsible Officer for the Management of this Procedure.

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<sup>1</sup> See the Procedure "Reporting to Institutional Officials, Sponsors, and Federal Agencies."

## Appendix A

### Examples of events that likely constitute unanticipated problems:

- Audit, inspection, or inquiry by a federal agency or other auditing entity (e.g., internal to the institution) that resulted in a finding that indicates subjects were placed at increased risk of harm.
- Suspension of an investigator's privileges to conduct research by the researcher's institution or suspension of a physician researcher's medical license.
- Occurrence of a safety issue, which results in premature study closure.
- Identification of a new risk (e.g., one not described in the protocol, consent documents, package inserts, investigational drug brochure, or device information).
- Identification of an increased risk, including a known risk that is occurring more frequently or with greater severity than previously expected.
- Occurrence of an event within the study that indicates an increased risk of harm and requires a change to the protocol or consent document.
- Malfunction of a device used as part of the research that increases risks or resulted in harm to subject(s).
- Withdrawal, restriction, or modification for safety reasons of a marketed approval of a drug, device, or biologic that is used in a research protocol.
- Protocol deviation that harmed a subject or placed subject at risk of harm, including:
  - Missed study tests or study visit(s) that could affect subject safety.
  - Enrollment of a subject who did not meet all eligibility criteria.
  - Failure to follow safety-monitoring plan.
  - Prescribing, dispensing, or administration error that results in a subject receiving an incorrect drug or dose.
- Protocol deviation to eliminate an immediate hazard to a subject which is made without prior IRB approval.
- Breach of confidentiality, where one or more research records containing private identifiable information about a subject was disclosed to persons not authorized to have access to the information.
- A stolen laptop or thumb drive with private identifiable information, if the device is not encrypted or password protected.
- Unresolved research-related complaints concerning the safety or welfare of the participant.
- Unexpected pregnancy on a study that could expose a fetus to harm.
- Incorrect imaging scan performed for research purposes that results in increased exposure of subject(s) to radiation or radiopharmaceuticals that would not have otherwise occurred.
- Errors in research-related laboratory reports that increased risks to participants.
- Instances in which subject(s) experienced physical abuse as a result of others becoming aware of their participation in the research.
- Unexpected violence by participants in a group counseling session.

## Appendix B

### Reportable Adverse Events Decision Chart

