Reportable Events Policy

Purpose

During the conduct of research involving human subjects, events may occur that involve risk or injury to the participants; these can be characterized as adverse events and/or unanticipated problems. In addition there may be deviations or errors in the research process. The purpose of this policy statement is to provide guidance with respect to the subset of such events that must be reported to the IRB.

Policy

1. Research studies involving human subjects must include procedures for identifying, monitoring, and reporting adverse events (AE), unanticipated problems (UP), and protocol deviations or errors (PD).

2. For clinical trials and studies with greater than minimal risk, these procedures must be described in the study’s Institutional Review Board-approved data and safety monitoring plan.

3. For all studies, a log of all AE, UP and PD events that come to the attention of the staff responsible for the research must be maintained by the PI.

   * Anticipated non-serious adverse events need not be logged. For studies that are greater than minimal risk, this log must be submitted to the IRB as part of the continuing review of the protocol.

4. The Principal Investigator must review all AE, UP, and PD events to ascertain if:
   a. they meet criteria for submission to the IRB; and
   b. they require modification of the protocol or consent documents.

5. Submission of such reports must be complete and timely.

Definitions

1. Adverse Event:\1:

   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. Adverse Events encompass both physical and/or psychological harms.

   In the context of multicenter clinical trials, Adverse Events can be characterized as either internal adverse events or external adverse events. From the perspective of one particular institution engaged in a multicenter clinical trial, internal adverse events are those adverse events experienced by subjects enrolled by the investigator(s) at that institution, whereas external adverse events are those adverse events experienced by subjects enrolled by investigators at other institutions engaged in the clinical trial. In the context of a single-center clinical trial, all Adverse Events would be considered internal adverse events.

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\1 http://www.hhs.gov/ohrp/policy/advevntguid.html#Q2 II. What are adverse events.
2. **Unanticipated Problem:** Any event, deviation, or problem, that meets **ALL** of the following criteria:
   - *unexpected; AND*
   - *possibly, probably or definitely related to study participation; AND*
   - *serious.*

   a. **Unexpected:** An event can be categorized as unexpected if it occurs in one or more subjects participating in a research protocol; and the nature, severity, or frequency of which is **not** consistent with either:
      - i. The known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in protocol-related documents such as: the IRB-approved research protocol; any applicable investigator brochure: the current IRB-approved informed consent document; or other relevant sources of information, such as product labeling and package inserts; or
      - ii. The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject’s predisposing risk factor profile for the adverse event.

   b. **Serious:** An adverse event or suspected adverse reaction 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 reaction,
      - iii. inpatient hospitalization or prolongation of existing hospitalization,
      - iv. persistent or significant disability/incapacity,
      - v. a congenital anomaly/birth defect,
      - vi. or based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the 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).

3. **Protocol Deviation:** Any change in the processes or procedures of research that were not approved by amendment of an IRB-approved protocol.

4. **Protocol Exception:** A planned, one-time deviation from the IRB-approved protocol (e.g. enrollment of a subject who does not meet inclusion criteria, or one-time dose changes for a single subject).

5. **Systematic Data Collection Error:** Data collection errors that may affect the scientific soundness of the investigational plan.

**Required Reporting**

**Unanticipated Problems** must be reported to the IRB using the Reportable Events Form within **5 business days** of the identification of the event by the research staff. Only the Principal Investigator may sign off on reportable event submissions, although any member of the research team may initiate the report. Exceptions (e.g. when the PI is unavailable for an extended period of time) will be considered by the IRB on a case-by-case basis.
[N.B. Internal Adverse Events that have been anticipated in the risks outlined in the protocol and informed consent document, or that are clearly unrelated to the research protocol, or that are not serious, do not have to be reported individually to the IRB. However they must be recorded in the adverse events log. Anticipated non-serious adverse events need not be reported to the IRB or logged.]

**External Adverse Events** that are serious, unexpected, and related or possibly related to the research must be reviewed by the PI. They should be submitted to the IRB **only** if they result in an amendment to the protocol or informed consent document. These AEs are then reported to the IRB as the basis for the proposed amendment (using the Amendment Form, not the Reportable Event Form).

Other events that must be reported to the IRB include:
- The death of a participant in a “greater-than-minimal-risk” protocol being conducted at a site under the jurisdiction of the Einstein IRB, even if “anticipated”, if it occurs within 30 days of a study-related procedure or the administration of a study drug.
- A Protocol Deviation that may place the participant or others at greater medical, physiological, social risk or economic risk than was previously known or recognized.
- Deviation from the IRB Informed Consent Policy.
- Any deviation from IRB or Institutional Policy or Procedure which has the potential to adversely impact one or more subjects or the overall integrity of data collected.
- Systematic data collection error that has the potential to adversely impact the overall integrity of the data collected.
- Breach of confidentiality.
- Any incident, experience, or outcome that indicates that the participant or others were placed at greater medical, physiological, social risk or economic risk than was previously known or recognized.
- Any action taken to eliminate an apparent immediate hazard to a research subject.
- Incarceration of a research subject.
- Sponsor or regulatory audit that requires corrective action.
- Any reporting the PI is required to report directly to the FDA (e.g. the PI is the sponsor-Investigator, a protocol involving the use of an HUD).
- Complaint from a participant or other individual when the complaint indicates unexpected risks or the complaint cannot be resolved by the research team.
- Disqualification or suspension of the Investigator by the FDA, NIH or other agency.
- Suspension or restriction of an Investigator’s clinical professional license.
- Any reporting that the IRB cites as a condition of approval of the protocol.

**Event Logging**

An internal log(s) of all* AE, UP and PD events that come to the attention of the staff responsible for the research must be maintained. The log(s) will be examined by the IRB during the course of a routine or for-cause audit of the protocol. For studies that are greater than minimal risk, this log must be submitted to the IRB as part of the continuing review of the protocol.

*NOTE: Anticipated non-serious AEs need not be logged.

**Protocol Exception Requests**

Requests for one-time deviation from the approved protocol must be submitted to and approved by the IRB **prior to** implementation. A waiver must be obtained from the sponsor of the study prior to the planned deviation. These requests must be submitted using the Protocol Exception Request Form. Rescheduling of research appointments due to holidays, vacations or accommodation of research subjects do not require the submission of an exception request if the safety of the subject will not be affected. Note: Protocol Exception Requests that are not IRB approved prior to implementation must be
reported to the IRB as reportable events (under the category, “deviation from IRB Policy which has the potential to adversely impact one or more subjects or the overall integrity of data collected”).

**Research Misconduct**

Research Misconduct constitutes a breach of professional integrity and is of serious concern to both Albert Einstein College of Medicine and Montefiore Medical Center. Research misconduct must be reported in accordance with the applicable institution’s research misconduct policy.

For YU/Einstein:
[http://www.einstein.yu.edu/docs/administration/policies/research-misconduct.pdf](http://www.einstein.yu.edu/docs/administration/policies/research-misconduct.pdf)

For Montefiore:

Questions about the reporting of research misconduct may be addressed by confidential communication to the institution’s Research Integrity Officer, as designated in each institution’s Research Misconduct Policy.