Investigator Reporting Obligations to the Emory IRB[1]

Background

Emory investigators are expected to review and assess protocol deviations and adverse events in order to determine if an event is reportable to the IRB. The IRB requires that investigators keep track of these events by keeping them in tracking logs. You may find examples of logs on the Emory IRB website, under the Forms section. For noncompliance events, we recommend consulting the Education and QA Team for additional guidance. You can find our contact information under the contact section of the Emory IRB website.

Definitions

- **Internal vs. External events:** An internal event represents an event that happened to a subject who was enrolled at an Emory site or at a site in which the Emory IRB was the IRB of record. For example, if a subject enrolled at Emory experienced an event at a different medical facility, the event will still be considered an *internal* event. In addition, if another site relied on the Emory IRB for review (through an IAA), that site will be considered *internal*. Please remember: this could also include international sites.

  NOTE: External events involving an Emory sponsor-investigator (i.e. where Emory investigator holds IND/IDE) **-** If the event occurred at an external site under the oversight of an Emory sponsor-investigator (S-I), the event should be reported as if it had occurred at an *internal* site.

- **Prompt vs. Periodic reporting:** Prompt reporting is reporting done with a reportable event form that should occur within 10 business days of event occurrence, or from when the PI first learned about the event. Periodic reporting is reporting done with a summary at the time of continuing review.

Reporting RNIs in studies reviewed by an External IRB

What and How to Report to the External IRB

When assessing the need to report an RNI, please follow the external and the Emory IRB reporting requirement, whichever is more stringent. All events should be reported to the external IRB as they are your IRB of record. Follow the external IRB's SOP's for how to report (either directly, or via the lead study team or coordinating center).

What and How to Report to the Emory IRB

[1] Based on Emory P&P, Chapter 70 & 71

In addition, you are required to report the following egregious events to the Emory IRB promptly via an RNI submission, as well as report them to the Emory Office of Compliance and the Emory Risk Management offices:

- Wrong side surgery
- Wrong drug, wrong patient
- Fabrication or falsification of data
- HIPAA privacy matter (report any inadvertent data disclosure and we will help determine further actions)

Create an RNI submission from within your external IRB study record in eIRB. Upload a copy of the report(s) made to the external reviewing IRB, and any correspondence you have already received from the reviewing IRB (but do not delay waiting for their determination). What/When to Report Events to the IRB

Unanticipated Problems[2] (both internal and external)

Unanticipated problems (UPs) <u>are promptly reportable</u>. UPs are events (adverse events or not) that are assessed by the PI as unexpected, related to study participation, **<u>and</u>** involving risk for participants or others. A reportable event that fulfills all of these characteristics is considered an unanticipated problem:

- To be unanticipated, the event should be unexpected, not described in the study documents, or if described before, it is now presenting with increased severity, duration, or frequency.
- To be related to study participation, the event should be probably or possibly related to study participation, due to drug/device effect, or as a consequence of a study procedure (even if the procedure is considered standard of care). If an event could be explained by the underlying medical condition, it is not considered related.
- To involve risk for participants or others, the event may affect subjects' risk. Even if the event did not result in harm, if the subject could have been affected by the event (safety, rights, welfare), the event is reportable.

Other unanticipated information that changes the risk-benefit ratio, or that indicates participants or others might be at greater risk of harm than was previously known may also be considered a UP. Examples:

- Any change to the protocol taken without prior IRB approval in order to eliminate apparent immediate hazards to participants
- Any publication in the literature, DSMB report, or interim result that indicated an unexpected change to the potential risks of the study

[2] 45 CFR § 46.103; 21 CFR § 56.108(b)(1); 312.32(a), (c); 312.64 (b) & 812(a)(1); OHRP Guidance, January 17, 2007, "Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events"; FDA Draft Guidance, April 2007, "Guidance for Clinical Investigators, Sponsors, and IRBs: Adverse Event Reporting—Improving Human Subject Protection

Deaths[2]

Internal: Even if an internal death is considered anticipated, it should be reported promptly to the IRB if also considered related to study participation. Deaths assessed as not related should be reported periodically (at continuing review).

External: External deaths are not reportable to the IRB unless also considered a UP, or unless at a site under the oversight of an Emory S-I.

Protocol Deviations[2]

All studies may have minor protocol deviations. These deviations may result from human error, subject non-compliance, or confusing and/or ambiguous details.

Internal: Reportable protocol deviations are deviations that are considered substantive and adversely affecting one of the following:

- Rights or welfare of subjects
- Safety of subjects
- Willingness of subjects to continue with study participation
- Integrity of the research data

If a protocol deviation is not considered substantive and/or affecting any of the above-mentioned areas by the PI, the protocol deviation is minor and doesn't need to be reported to the Emory IRB. If a protocol deviation is assessed as not reportable, it is not reportable at any time, not even at continuing review.

If the protocol deviation/protocol non-compliance concerns study documentation associated with an FDA-regulated study or was a protocol deviation undertaken to prevent immediate hazard to a human subject, then the PI shall report the protocol deviation/protocol non-compliance to the Emory IRB.

Reportable protocol deviations are **promptly** reportable.

In addition, it is important to log protocol deviations to identify possible trends that may indicate a substantive problem. It is the responsibility of the principal investigator to analyze whether this information may indicate unanticipated problems or noncompliance.

External: External protocol deviations are not reportable to the IRB, unless considered a UP, or unless the study is under the oversight of an Emory sponsor-investigator. An example of a possible reportable external UP would be a deviation due to device malfunction, which happened at an external site and may affect subjects at Emory.

Serious adverse events that are related, but not UPs

Internal: Internal serious adverse events that were assessed as related but not unanticipated are reportable at continuing review.

External: External adverse events that are considered related, but not unanticipated are **not** reportable to the IRB, unless the study is under the oversight of an Emory sponsor-investigator.

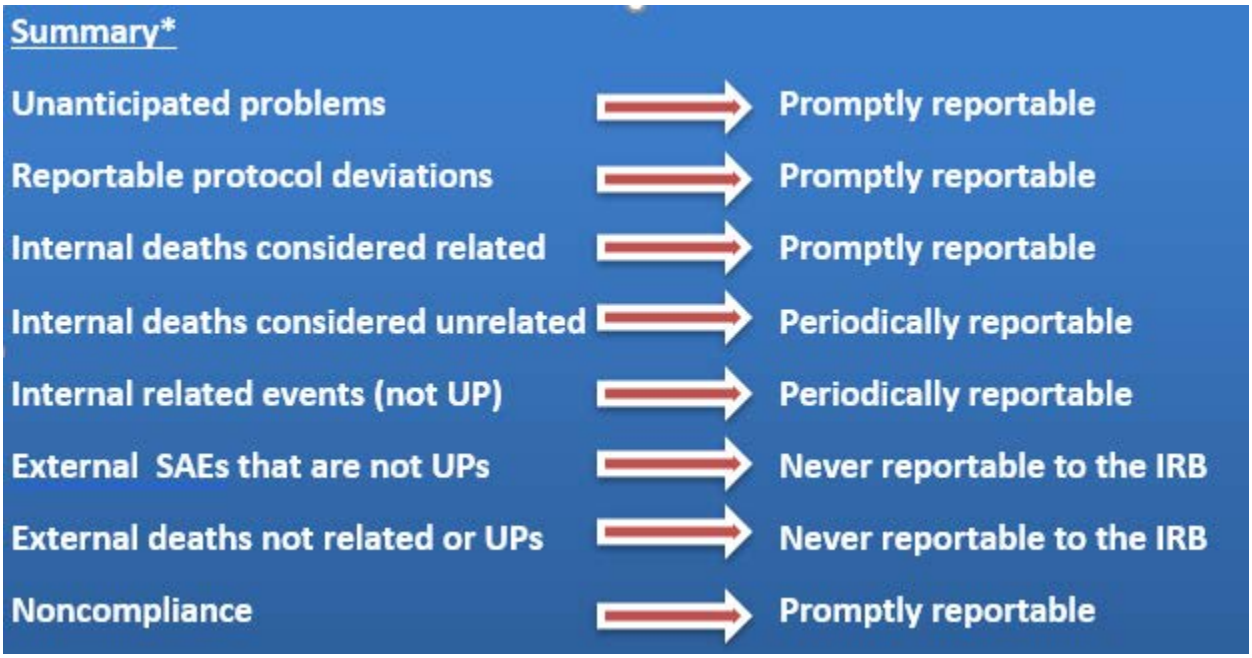
Noncompliance (both internal and external)

Noncompliance is defined as the failure to comply with laws, regulations or Emory IRB Policies and Procedures or failure to follow the requirements or determinations of the IRB. We recommend contacting the Emory IRB Education and QA Team for advice and guidance on these matters, since there is often confusion about what constitutes noncompliance. All noncompliance is promptly reportable to the IRB.

Noncompliance involving documentation required by the federal regulations is reportable to the IRB. For example, if a Form FDA 1572 is not completed or completed incorrectly, even if this is assessed as not adversely affecting rights, welfare or safety of subjects, willingness to participate or data integirty , this noncompliance with regulations should be reported to the IRB.

Sponsor Reporting Obligations

Follow your sponsor reporting requirements, as they may differ from the Emory IRB policies and procedures. If your protocol or contract requires the reporting of issues to the IRB, and the events do not meet the IRB reporting criteria, you should follow your sponsor requirements.



**Remember that external events under the oversight of an Emory S-I should be assessed as internal events.*

How to Report to the IRB

Promptly reportable events should be reported using an eIRB reportable new information (RNI) form.

If the event is reportable periodically, it should be reported at continuing review. The summary at continuing review should include information about the previously reported event/s (e.g. UPs), and related adverse events as explained before. See an example on our website. The information should be uploaded with the continuing review application, and not as a separate RNI.

If the team is working on the continuing review submission and discovers that an event should have been reported promptly, the event should be reported separately with an RNI form.

If an event is promptly reportable, it should be reported using the RNI form under the study. You may find the form under the study main page:

Additional resources:

- Timeframes for Reporting Adverse Events, Protocol Deviations, and UPs (ver.10-21-16) - At-A-Glance one-page chart.
- Assessment Form for Events (Internal/External) (ver. 7-18-14)
- Assessment Form for Non-Emory Sites Under Emory Sponsor Oversight (ver. 4-28-15)
- Assessment Form for Protocol Deviations (ver. 4-28-17)
- Root Cause Analysis Worksheet (ver. 11-23-10)
- Summary at CR Workbook (ver. 1-30-20)

- Investigator Quality Improvement Assessment.
- OHRP Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events
- FDA: Guidance for Clinical Investigators, Sponsors, and IRBs Adverse Event Reporting to IRBs — Improving Human Subject Protection

Other Guidance:

- Guidance for Submitting Multiple Events at One Time (ver. 11-14-14)
- Guidance on How IRB Makes Determinations of Serious or Continuing Noncompliance and UPs (ver. 7-6-15)

If you have other questions, please contact the IRB Education and QA Team.