Standard Adverse Event Reporting Guidelines for INTERNAL AEs Occurring at UM

This chart is for studies following IRBMED standard AE reporting and requiring CR. It may be appropriate for some studies to consider a Study Specific AE Reporting Plan. See the gray boxes for information about External AE and UaP reporting.

		RELATED	UNRELATED
UNEXPECTED	Potential Unanticipated Problems (UaPs)[3] Note: Some UaPs are not AEs. Report these events via an ORIO.	**Serious Adverse Event[1] –** resulting in • **Death** • **Life-threatening outcome** Submit AE/ORIO report as *soon as possible*, **but** *within 7 calendar days* of becoming aware of event. Assess SAE to determine if UaP (see below for UaP criteria).	**Serious Adverse Event[1]-** resulting in • **Death** • **Life-threatening outcome** Report in aggregate form via separate AE/ORIO submission *in conjunction with SCR*.
		Serious Adverse Event[2] Submit AE/ORIO report *within 14 calendar days* of becoming aware of event. Assess SAE to determine if UaP (see below for UaP criteria).	**Serious Adverse Event[2]** Report in aggregate form via separate AE/ORIO submission *in conjunction with SCR*.
		Non-Serious Adverse Event Report in aggregate form via AE/ORIO report *in conjunction with completion of the SCR*. Assess AE to determine if UaP (see below for UaP criteria).	**Non-Serious Adverse Event** **-Do not report to IRB-** Study teams should continue to monitor and log events as they occur for sponsor reporting purposes.
EXPECTED		**Serious Adverse Event[1],[2]** Submit AE/ORIO report *within 14 calendar days* of becoming aware of event.	**For ALL Unrelated & Expected Adverse Events** **-Do not report to IRB-** Study teams should continue to monitor and log events as they occur. If any events appear to be occurring at a severity or frequency greater than previously known or expected, report as 'unexpected' per these guidelines *within 14 calendar days* of identifying this trend.
		Non-Serious Adverse Event (Moderate/Grade 2*) **-Do not report to IRB-** Study teams should continue to monitor and log events as they occur. If any events appear to be occurring at a frequency greater than previously known or expected, report as unexpected *within 14 calendar days* of identifying trend.	
		Non-Serious Adverse Event (Mild/Grade 1*) **-Do not report to IRB-** Study teams should continue to monitor and log events as they occur. If any events appear to be occurring at a frequency greater than previously known or expected, report as unexpected *within 14 calendar days* of identifying trend.	

[1]Serious Adverse Event (SAE) as reflected in (32-1.4 in eResearch)
• Death
• A life-threatening adverse drug/device experience or outcome
[2]Serious Adverse Event (SAE) as reflected in (32-1.4 in eResearch)
• Inpatient hospitalization or prolongation of existing hospitalization
• A persistent or significant disability/incapacity or permanent damage
• A congenital anomaly or birth defect
• Other serious important medical events
• Based on medical judgment AND may require medical or surgical intervention to prevent one of the above
EXTERNAL Site Adverse Event Reporting Do not report External Adverse Events to the IRB, unless they have been determined by the external site PI to be a UaP. See Statement of Practice here.

[3]Potential Unanticipated Problems Involving Risks to Subjects or Others (UaP)
1) Is the event **unexpected** in nature, frequency, or severity? 2) Is the event **related** to the research? 3) Is there an **increased risk** of potential harm and/or actual harm than was previously known or recognized? • If yes to **all three,** this is a potential UaP. Include "Potential UaP" in description of event when reporting. • If no to any, *this is **not** a potential UaP*. Report as described above. **University of Michigan UaP Reporting** UaPs that are also SAEs should be reported to the IRB according to the AE reporting guidelines detailed in this document. UaPs that are NOT SAEs (e.g., ORIO, AEs) should be reported to the IRB within 14 calendar days of becoming aware of event.
EXTERNAL Site UaP Reporting: Submit External site UaPs *within 14 calendar days* of becoming aware of event.

- **Definitions: SCR**: Scheduled Continuing Review; **Expected**: Has been addressed in one or more of following: Protocol, Investigator Brochure, Package Insert or equivalent, published literature, IRB application, grant application, Data Safety Monitoring Board/Data Safety Committee reports, other documentation, informed consent document (ICD) or characteristics of the study population. Note, per OHRP guidance, event may be "expected" per the natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event; **Unexpected:** Has not been addressed in one or more of the above examples; **Related:** See below; **Unrelated:** See Below.

- **References**: §21 CFR 312.32 Adverse Event Reporting to IRBs OHRP-Which AEs are UaPs? OHRP—Guidance on Reviewing and Reporting UaPs and AEs *Common Terminology Criteria for Adverse Events (CTCAE) - Oncology studies Grade System

Defining Relationship to Study Drug/Device/Procedure: The IRB recognizes that it can be difficult to determine the relationship of event or events to a specific drug/device/procedure when there are several contributing factors. Events should be rated according to the following parameters:

EVENTS RELATED

Definitely Related

- The event is a known effect of the drug, device, or procedure (e.g., listed in the protocol documents including IB, consent, publications)
- The event follows an obvious sequence of time, from the drug's administration, device's implantation or activation, or procedure, for which the event is directly attributed to the administration, implantation, activation, or procedure.
- The event ceases with discontinuation of the drug, device, or procedure (and reoccurs on restarting).
- The event includes data that was only collected for the study.
- The event included disturbing or upsetting questions that the subject was asked for the purpose of the research.

Probably Related

- The event is lesser known or suspected effect of the drug, device, or procedure (listed in the protocol documents including IB, consent, publications, etc.)
- The event follows a reasonable sequence of time from the drug's administration, device implantation, activation, or procedure, for which the event may be attributed to the administration, implantation, activation, or procedure.
- The event ceases or diminishes with discontinuation of the drug, removal/discontinued activation of the device, or procedure.

Possibly Related

- The event is a lesser known or possible effect of the drug, device, or procedure.
- The event occurred within a sequence of time from the drug's administration, device implantation and/or activation, or procedure, for which the event may be attributed to the administration, implantation, activation, or procedure.
- The event could be explained by the characteristics of the population under study.

EVENTS NOT RELATED

Unlikely Related

- The event is NOT a previously known or suspected effect of the test drug, device, or procedure.
- The event does NOT follow a sequence of time from drug administration, device implantation and/or activation, or procedure, for which the event could be attributed to the administration, implantation, activation, or procedure.
- The event can be readily explained by the characteristics of the population under study.

Unrelated

- The event is NOT known to be an effect of the test drug, device, or procedure.
- The event does NOT follow a sequence of time from drug administration, device implantation and/or activation, or procedure, for which the event could be attributed to the administration, implantation, activation, or procedure.
- The event can be readily and easily explained by the characteristics of the population under study.
- Subject never received study drug, study device, or underwent research study procedure.