

# U-M IBC Adverse Event Reporting Requirements for Human Gene Transfer Clinical Trials

This document describes reporting requirements for AEs that occur at U-M on human gene transfer (HGT) clinical trials. This is considered a [Study Specific AE Reporting Plan](#) which must be followed in addition to any such plan from the study sponsor or other regulatory body.

IBC = Institutional Biosafety Committee    NIH OBA = NIH Office of Biotechnology Activities

Reporting to the U-M IBC on human gene transfer clinical trials occurs through the AE/ORIO function of the IRB application.

SECTION 1: Report timing

SECTION 2: How to report

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## SECTION 1: REPORT TIMING for Local AEs on Human Gene Transfer Clinical Trials

	RELATED	UNRELATED
U N E X P E C T E D	<p><b>Serious Adverse Event</b> – resulting in:</p> <ul style="list-style-type: none"> <li>• Death</li> <li>• Life-threatening outcome</li> </ul> <p>Submit AE/ORIO report as <i>soon as possible</i>, but <b>within 7 calendar days</b> of becoming aware of event for IBC and IRB review. <b>NOTE: Reporting to NIH OBA is required within the same timeframe.</b></p> <p>Assess SAE to determine if it meets Unanticipated Problem (UaP) criteria (see Definitions on page 2).</p>	<p><b>Serious Adverse Event</b> – resulting in:</p> <ul style="list-style-type: none"> <li>• Death</li> <li>• Life-threatening outcome</li> </ul> <p>Submit AE/ORIO report <b>within 7 calendar days</b> of becoming aware of event for IBC review.</p>
	<p><b>Serious Adverse Event</b> – resulting in:</p> <ul style="list-style-type: none"> <li>• Inpatient hospitalization or prolongation of existing hospitalization</li> <li>• A persistent or significant disability/incapacity or permanent damage</li> <li>• A congenital anomaly or birth defect</li> <li>• Other serious medical events that based on appropriate medical judgment may require medical or surgical intervention to prevent one of the above outcomes.</li> </ul> <p>Submit AE/ORIO report <b>within 14 calendar days</b> of becoming aware of event for IBC and IRB review. <b>NOTE: Reporting to NIH OBA is required within the same timeframe.</b></p> <p>Assess SAE to determine if it meets Unanticipated Problem (UaP) criteria (see Definitions on page 2).</p>	<p><b>Serious Adverse Event</b> – resulting in:</p> <ul style="list-style-type: none"> <li>• Inpatient hospitalization or prolongation of existing hospitalization</li> <li>• A persistent or significant disability/incapacity or permanent damage</li> <li>• A congenital anomaly or birth defect</li> <li>• Other serious medical events that based on appropriate medical judgment may require medical or surgical intervention to prevent one of the above outcomes.</li> </ul> <p>Submit AE/ORIO report <b>within 14 calendar days</b> of becoming aware of event for IBC review.</p>
	<p><b>Non-Serious Adverse Event</b></p> <p>Submit AE/ORIO report <b>within 14 calendar days</b> of becoming aware of event for IBC review. <b>NOTE: Reporting to NIH OBA is required within the same timeframe.</b></p> <p>Assess AE to determine if it meets Unanticipated Problem (UaP) criteria (see Definitions on page 2).</p>	<p><b>Non-Serious Adverse Event</b></p> <p>Submit AE/ORIO report <b>within 14 calendar days</b> of becoming aware of event for IBC review.</p>
E X P E C T E D	<p><b>Serious Adverse Event</b> – Submit AE/ORIO report <b>within 14 calendar days</b> of becoming aware of event for IBC review.</p>	<p><b>Unrelated &amp; Expected Adverse Events</b> Do not report, however, 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' <b>within 14 calendar days</b> of identifying trend.</p>
	<p><b>Non-Serious Adverse Event (Moderate/Grade 2* or Mild/Grade 1*)</b> Do not report, however, 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' <b>within 14 calendar days</b> of identifying trend.</p>	

### REPORTING ALSO REQUIRED by the IBC and NIH OBA for the following occurrences:

- A change in determination about an adverse event from not related to related; or
- Any serious adverse event that occurs after the end of a clinical trial and is determined to be associated with gene transfer product:  
Submit AE/ORIO report **within 15 calendar days** of determination. **Reporting to NIH OBA is required within same timeframe.**

Follow-up clinical and lab data relevant to a serious adverse event previously reported to NIH OBA:

Submit AE/ORIO report **within 15 calendar days** of sponsor's receipt of the information. **Reporting to NIH OBA is required within same timeframe.**

Any new information including animal test findings suggesting significant risk for human research participants including reports of mutagenicity, teratogenicity, or carcinogenicity: Submit AE/ORIO report **as soon as possible but not later than 15 calendar days after** sponsor's receipt of the information. **Reporting to NIH OBA is required within same timeframe.**

## SECTION 2: HOW TO REPORT ADVERSE EVENTS TO THE U-M IBC AND NIH OBA

### Reporting to the U-M IBC:

Reports of local adverse events are to be submitted to the U-M IBC through the AE/ORIO function of the IRB application within the timeframes noted in the chart above.

### Reporting to the NIH Office of Biotechnology Activities (NIH OBA):

- Timeframes for reporting: [See NIH Guidelines Appendix M-I-C](#), or refer to the chart above.
- Content and format of reports: [See NIH Guidelines Appendix M-I-C-4-a](#)

Submit reports to NIH OBA by email: [GeMCRIS@od.nih.gov](mailto:GeMCRIS@od.nih.gov)

General queries to NIH OBA: [oba-osp@od.nih.gov](mailto:oba-osp@od.nih.gov) or 301-496-9838

### Delegation of external reporting functions for human gene transfer clinical trials:

The role of reporting to NIH OBA may be delegated by the Principal Investigator to a third party (e.g., the sponsor) with written notification to NIH OBA (and the U-M IBC). The responsibility for all reporting remains with the Principal Investigator. [See NIH Guidelines Appendix M-I-C-4.](#)

## SECTION 3: DEFINITIONS

### From the [NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules](#):

<b>Serious Adverse Event</b>	A “ <b>serious adverse event</b> ” is any event occurring at any dose that results in any of the following outcomes: death, a life-threatening event, in-patient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect. Important medical events that may not result in death, be life-threatening, or require hospitalization also may be considered a serious adverse event when, upon the basis of appropriate medical judgment, they may jeopardize the human gene transfer research subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. ( <a href="#">NIH Guidelines Section I-E-8</a> )
<b>Related or Associated</b>	An adverse event is “ <b>associated with the use of a gene transfer product</b> ” when there is a reasonable possibility that the event may have been caused by the use of that product. Investigators should not await definitive proof of association before reporting such events. ( <a href="#">NIH Guidelines Section I-E-9</a> ; <a href="#">Appendix M-I-C-4</a> )
<b>Unexpected</b>	An “ <b>unexpected serious adverse event</b> ” is any serious adverse event for which the specificity or severity is not consistent with the risk information available in the current investigator’s brochure. ( <a href="#">NIH Guidelines Section I-E-10</a> )

### Criteria for Identifying Unanticipated Problems Involving Risks to Subjects or Others (UaPs):

<b>UaP Criteria</b>	<p>1) Is the event <b>unexpected</b> in nature, frequency, or severity?                  2) Is the event <b>related</b> to the research?                  3) Is there an <b>increased risk</b> of potential harm and/or actual harm than was previously known or recognized?</p> <p>If yes to <b>all three</b>, this is a potential UaP. Include “Potential UaP” in description of event when reporting.</p> <p><b>Note:</b> Some UaPs are not AEs. Report these events to IRB via an ORIO.</p>
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#### IBC-Related References:

[U-M Institutional Biosafety Committee](#)  
[NIH Office of Biotechnology Activities](#)  
[FAQ on NIH Review Process for Human Gene Transfer Clinical Trials](#)

#### IRB-Related 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](#)

Questions regarding U-M IBC reporting requirements for human gene transfer clinical trials: Contact [ibcstaff@umich.edu](mailto:ibcstaff@umich.edu) or 734-615-3960.