

## Legacy Expedited Reporting Tables for NCI IND/IDE Agents

### Legacy Table A:

Reporting Requirements for Adverse Events that occur within 30 Days<sup>1</sup> of the Last Dose of the Investigational Agent on Phase 1 Studies (valid ONLY for protocols approved prior to March 28, 2011)

	1	2	2	3		3		4 & 5 <sup>1</sup>
	Unexpected and Expected	Unexpected	Expected	Unexpected		Expected		Unexpected and Expected
				With hospitalization	Without hospitalization	With hospitalization	Without hospitalization	
<b>Unrelated Unlikely</b>	Not Required	Not Required	Not Required	10 Calendar Days	Not Required	10 Calendar Days	Not Required	24-Hour/5 Calendar Days
<b>Possible Probable Definite</b>	Not Required	10 Calendar Days	Not Required	24-Hour/5 Calendar Days	24-Hour/5 Calendar Days	10 Calendar Days	Not Required	24-Hour/5 Calendar Days
<p><sup>1</sup>AEs with attribution of, possible, probable, or definite that occur greater than 30 days after the last treatment with an agent/intervention under an NCI IND require reporting as follows:</p> <p>AdEERS 24-hour notification followed by complete report within 5 calendar days for:</p> <ul style="list-style-type: none"> <li>• Grade 3 unexpected AEs with hospitalization or prolongation of hospitalization</li> <li>• Grade 4 unexpected AEs</li> <li>• Grade 5 expected and unexpected AEs</li> </ul> <p><sup>2</sup>Although an AdEERS 24-hour notification is not required for death clearly related to progressive disease, a full report is required as outlined in the table.</p>								

### Legacy Table B:

Reporting Requirements for Adverse Events that occur within 30 Days<sup>1</sup> of the Last Dose of the Investigational Agent on Phase 2 and 3 Studies (valid ONLY for protocols approved prior to March 28, 2011)

	1	2	2	3		3		4 & 5	4 & 5 <sup>2</sup>
	Unexpected and Expected	Unexpected	Expected	Unexpected		Expected		Unexpected	Expected
				With hospitalization	With hospitalization	With hospitalization	Without hospitalization		
<b>Unrelated Unlikely</b>	Not Required	Not Required	Not Required	10 Calendar Days	Not Required	10 Calendar Days	Not required	10 Calendar Days	10 Calendar Days
<b>Possible Probable Definite</b>	Not Required	10 Calendar Days	Not Required	10 Calendar Days	10 Calendar Days	10 Calendar Days	Not required	24-Hour; 5 Calendar Days	10 Calendar Days
<p><sup>1</sup>AEs with attribution of, possible, probable, or definite that occur greater than 30 days after the last treatment with an agent/intervention under an NCI IND require reporting as follows:</p> <p>AdEERS 24-hour notification followed by complete report within 5 calendar days for:</p> <ul style="list-style-type: none"> <li>• Grade 4 and Grade 5 unexpected AEs</li> <li>• AdEERS 10 calendar day report:</li> <li>• Grade 3 unexpected AEs with hospitalization or prolongation of hospitalization</li> <li>• Grade 5 expected AEs</li> </ul> <p><sup>2</sup>Although an AdEERS 24-hour notification is not required for death clearly related to progressive disease, a full report is required as outlined in the table.</p>									

## Legacy Table C:

Phase 0 Studies: Expedited Reporting Requirements for Adverse Events that Occur on Studies under an IND/IDE within 30 Days of the Last Administration of the Investigational Agent/Intervention<sup>1, 2</sup>

<b>FDA REPORTING REQUIREMENTS FOR SERIOUS ADVERSE EVENTS (21 CFR Part 312)</b> <b>NOTE:</b> Investigators <b>MUST</b> immediately report to the sponsor (NCI) <b>ANY</b> Serious Adverse Events, whether or not they are considered related to the investigational agent(s)/intervention (21 CFR 312.64) An adverse event is considered serious if it results in <b>ANY</b> of the following outcomes:	
1) Death 2) A life-threatening adverse event 3) An adverse event results in inpatient hospitalization or prolongation of existing hospitalization for ≥ 24 hours 4) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions 5) A congenital anomaly/birth defect. 6) Important Medical Events (IME) that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition (FDA, 21 CFR 312.32; ICH E2A and ICH E6).	
<b>ALL SERIOUS</b> adverse events that meet the above criteria <b>MUST</b> be immediately reported to the NCI via AdEERS within the timeframes detailed in the table below.	
Grade 1 and 2 Timeframes	Grade 3-5 Timeframes.
10 Calendar Days	24-Hour 5 Calendar Days
<b>Expedited AE reporting timelines are defined as:</b> <ul style="list-style-type: none"> <li>○ “24-Hour; 5 Calendar Days” - The AE must initially be reported via AdEERS within <u>24 hours</u> of learning of the AE, followed by a complete expedited report within <u>5 calendar days</u> of the initial 24-hour report.</li> <li>○ “10 Calendar Days” - A complete expedited report on the AE must be submitted within <u>10 calendar days</u> of learning of the AE.</li> </ul>	
<sup>1</sup> Serious adverse events that occur <b>more than</b> 30 days after the last administration of investigational agent/intervention require reporting as follows: Expedited 24-hour notification followed by complete report within 5 calendar days for <b>ALL</b> Grade 4 and 5 AEs and Grade 3 AEs with at least a possible attribution. <sup>2</sup> For studies using PET or SPECT IND agents, the AE reporting period is limited to 10 radioactive half-lives, rounded UP to the nearest whole day, after the agent/intervention was last administered. Footnote “1” above applies after this reporting period.  Effective Date: May 5, 2011 - August 29, 2024	

## Legacy Table D:

Phase 1 and Early Phase 2 Studies: Expedited Reporting Requirements for Adverse Events that Occur on Studies under an IND/IDE within 30 Days of the Last Administration of the Investigational Agent/Intervention <sup>1, 2</sup>

<b>FDA REPORTING REQUIREMENTS FOR SERIOUS ADVERSE EVENTS (21 CFR Part 312)</b>		
<p><b>NOTE:</b> Investigators <b>MUST</b> immediately report to the sponsor (NCI) <b>ANY</b> Serious Adverse Events, whether or not they are considered related to the investigational agent(s)/intervention (21 CFR 312.64)</p> <p>An adverse event is considered serious if it results in <b>ANY</b> of the following outcomes:</p> <ol style="list-style-type: none"> <li>1) Death</li> <li>2) A life-threatening adverse event</li> <li>3) An adverse event that results in inpatient hospitalization or prolongation of existing hospitalization for <math>\geq</math> 24 hours</li> <li>4) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions</li> <li>5) A congenital anomaly/birth defect.</li> <li>6) Important Medical Events (IME) that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. (FDA, 21 CFR 312.32; ICH E2A and ICH E6).</li> </ol>		
<p><b>ALL SERIOUS</b> adverse events that meet the above criteria <b>MUST</b> be immediately reported to the NCI via AdEERS within the timeframes detailed in the table below.</p>		
<b>Hospitalization</b>	<b>Grade 1 and Grade 2 Timeframes</b>	<b>Grade 3-5 Timeframes</b>
Resulting in Hospitalization $\geq$ 24 hrs	10 Calendar Days	24-Hour 5 Calendar Days
Not resulting in Hospitalization $\geq$ 24 hrs	Not required	
<p><b>NOTE:</b> Protocol-specific exceptions to expedited reporting of serious adverse events are found in the Specific Protocol Exceptions to Expedited Reporting (SPEER) portion of the CAEPR.</p> <p><b>Expedited AE reporting timelines are defined as:</b></p> <ul style="list-style-type: none"> <li>○ "24-Hour; 5 Calendar Days" - The AE must initially be reported via AdEERS within 24 hours of learning of the AE, followed by a complete expedited report within 5 calendar days of the initial 24-hour report.</li> <li>○ "10 Calendar Days" - A complete expedited report on the AE must be submitted within 10 calendar days of learning of the AE.</li> </ul>		
<p><sup>1</sup>Serious adverse events that occur more than 30 days after the last administration of investigational agent/intervention and have an attribution of possible, probable, or definite require reporting as follows:  <b>Expedited 24-hour notification followed by complete report within 5 calendar days for:</b></p> <ul style="list-style-type: none"> <li>• All Grade 3, 4, and Grade 5 AEs</li> </ul> <p><b>Expedited 10 calendar day reports for:</b></p> <ul style="list-style-type: none"> <li>• Grade 2 AEs resulting in hospitalization or prolongation of hospitalization</li> </ul> <p><sup>2</sup> For studies using PET or SPECT IND agents, the AE reporting period is limited to 10 radioactive half-lives, rounded UP to the nearest whole day, after the agent/intervention was last administered. Footnote "1" above applies after this reporting period.</p> <p>Effective Date: May 5, 2011 - August 29, 2024</p>		

## Legacy Table E:

Late Phase 2 and Phase 3 Studies: Expedited Reporting Requirements for Adverse Events that Occur on Studies under an IND/IDE within 30 Days of the Last

<b>Administration of the Investigational Agent/Intervention<sup>1, 2</sup></b>				
<b>FDA REPORTING REQUIREMENTS FOR SERIOUS ADVERSE EVENTS (21 CFR Part 312)</b>				
<b>NOTE:</b> Investigators <b>MUST</b> immediately report to the sponsor (NCI) <b>ANY</b> Serious Adverse Events, whether or not they are considered related to the investigational agent(s)/intervention (21 CFR 312.64)				
An adverse event is considered serious if it results in <b>ANY</b> of the following outcomes:				
<ol style="list-style-type: none"> <li>1) Death</li> <li>2) A life-threatening adverse event</li> <li>3) An adverse event that results in inpatient hospitalization or prolongation of existing hospitalization for ≥ 24 hours</li> <li>4) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions</li> <li>5) A congenital anomaly/birth defect.</li> <li>6) Important Medical Events (IME) that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. (FDA, 21 CFR 312.32; ICH E2A and ICH E6).</li> </ol>				
<b>ALL SERIOUS</b> adverse events that meet the above criteria <b>MUST</b> be immediately reported to the NCI via AdEERS within the timeframes detailed in the table below.				
Hospitalization	Grade 1 Timeframes	Grade 2 Timeframes	Grade 3 Timeframes	Grade 4 & 5 Timeframes
Resulting in Hospitalization ≥ 24 hrs	10 Calendar Days			24-Hour 5 Calendar Days
Not resulting in Hospitalization ≥ 24 hrs	Not required		10 Calendar Days	
<b>NOTE:</b> Protocol-specific exceptions to expedited reporting of serious adverse events are found in the Specific Protocol Exceptions to Expedited Reporting (SPEER) portion of the CAEPR <b>Expedited AE reporting timelines are defined as:</b> <ul style="list-style-type: none"> <li>○ “24-Hour; 5 Calendar Days” - The AE must initially be reported via AdEERS within 24 hours of learning of the AE, followed by a complete expedited report within 5 calendar days of the initial 24-hour report.</li> <li>○ “10 Calendar Days” - A complete expedited report on the AE must be submitted within 10 calendar days of learning of the AE.</li> </ul>				
<sup>1</sup> Serious adverse events that occur more than 30 days after the last administration of investigational agent/intervention and have an attribution of possible, probable, or definite require reporting as follows: <b>Expedited 24-hour notification followed by complete report within 5 calendar days for:</b> <ul style="list-style-type: none"> <li>• All Grade 4, and Grade 5 AEs</li> </ul> <b>Expedited 10 calendar day reports for:</b> <ul style="list-style-type: none"> <li>• Grade 2 adverse events resulting in hospitalization or prolongation of hospitalization</li> <li>• Grade 3 adverse events</li> </ul> <sup>2</sup> For studies using PET or SPECT IND agents, the AE reporting period is limited to 10 radioactive half-lives, rounded UP to the nearest whole day, after the agent/intervention was last administered. Footnote “1” above applies after this reporting period.				
Effective Date: May 5, 2011 - August 29, 2024				

## Legacy Table F:

FOR USE IN CIP STUDIES INVOLVING COMMERCIAL (NON-IND/IDE) AGENTS ONLY  
 CIP Commercial Agent Studies: Expedited Reporting Requirements for Adverse Events that Occur in a CIP Non-IND/IDE trial within 30 Days of the Last Administration of a Commercial Imaging Agent <sup>1, 2</sup>

<b>FDA REPORTING REQUIREMENTS FOR SERIOUS ADVERSE EVENTS (21 CFR Part 312)</b>				
<p><b>NOTE:</b> Investigators <b>MUST</b> immediately report to the sponsor (NCI) <b>ANY</b> Serious Adverse Events, whether or not they are considered related to the investigational agent(s)/intervention (21 CFR 312.64)</p> <p>An adverse event is considered serious if it results in <b>ANY</b> of the following outcomes:</p> <ol style="list-style-type: none"> <li>1) Death</li> <li>2) A life-threatening adverse event</li> <li>3) An adverse event that results in inpatient hospitalization or prolongation of existing hospitalization for <math>\geq</math> 24 hours</li> <li>4) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions</li> <li>5) A congenital anomaly/birth defect.</li> <li>6) Important Medical Events (IME) that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. (FDA, 21 CFR 312.32; ICH E2A and ICH E6).</li> </ol>				
<p><b>ALL SERIOUS</b> adverse events that meet the above criteria <b>MUST</b> be immediately reported to the NCI via AdEERS within the timeframes detailed in the table below.</p>				
<b>Hospitalization</b>	<b>Grade 1 Timeframes</b>	<b>Grade 2 Timeframes</b>	<b>Grade 3 Timeframes</b>	<b>Grade 4 &amp; 5 Timeframes</b>
Resulting in Hospitalization $\geq$ 24 hrs	10 Calendar Days			24-Hour 5 Calendar Days
Not resulting in Hospitalization $\geq$ 24 hrs	Not required	10 Calendar Days		
<p><b>NOTE:</b> Protocol-specific exceptions to expedited reporting of serious adverse events are found in the Specific Protocol Exceptions to Expedited Reporting (SPEER) portion of the CAEPR</p> <p><b>Expedited AE reporting timelines are defined as:</b></p> <ul style="list-style-type: none"> <li>○ "24-Hour; 5 Calendar Days" - The AE must initially be reported via AdEERS within 24 hours of learning of the AE, followed by a complete expedited report within 5 calendar days of the initial 24-hour report.</li> <li>○ "10 Calendar Days" - A complete expedited report on the AE must be submitted within 10 calendar days of learning of the AE.</li> </ul>				
<p><sup>1</sup>Serious adverse events that occur more than 30 days after the last administration of investigational agent/intervention and have an attribution of possible, probable, or definite require reporting as follows:</p> <p><b>Expedited 24-hour notification followed by complete report within 5 calendar days for:</b></p> <ul style="list-style-type: none"> <li>• All Grade 4, and Grade 5 AEs</li> </ul> <p><b>Expedited 10 calendar day reports for:</b></p> <ul style="list-style-type: none"> <li>• Grade 2 adverse events resulting in hospitalization or prolongation of hospitalization</li> <li>• Grade 3 adverse events</li> </ul> <p><sup>2</sup> For studies using PET or SPECT agents, the AE reporting period is limited to 10 radioactive half-lives, rounded UP to the nearest whole day, after the agent/intervention was last administered. Footnote "1" above applies after this reporting period.</p> <p>Effective Date: May 5, 2011 - August 29, 2024</p>				