



National Institutes of Health
National Cancer Institute
Bethesda, Maryland 20892

May 8, 2009

Dear Colleagues,

The CTEP, NCI Adverse Event Expedited Reporting Requirements are being revised in order to increase the efficiency of our reporting process both from an investigator and a CTEP perspective. The primary goal during this revision is to maintain patient safety and compliance with applicable FDA regulations. The new tables are being posted for a two-week public comment period.

The attached proposed tables pertain to all trials being conducted under a CTEP-held IND. We have developed a more progressive reporting scale in order to more closely tailor the reporting needs of a particular study based on (1) the extent of clinical experience with the agent(s), (2) the need to maintain patient safety and regulatory compliance, and (3) the Investigational Drug Branch/CTEP's collective medical experience. Thus, instead of the current AdEERS reporting tables (one for Phase 1 studies and one for Phase 2/3 studies), there will be four tables/levels that will cover agent development from Phase 0 all the way through Phase 3 of commercially-available agents. The appropriate level for a specific study will be determined by IDB staff but, in general, will be assigned as follows:

- Level 0: Phase 0
- Level 1: Phase 1 and Early Phase 2
- Level 2: Late Phase 2, and Phase 3
- Level 3: Phase 2 and Phase 3 Studies of Commercially-Available Agents

The Level 0 table is new to our guidelines, although it has already been used in NCI-sponsored Phase 0 studies. The Level 1 table is equivalent to the current Phase 1 table. The Level 2 table differs in minor ways from the current Phase 2/3 table. The Level 3 table, for trials of commercially-available agents, differs from the current tables based on the greater extent of clinical experience with these agents. Departures from the old tables are denoted by shading within the table, or by red font.

The new tables are being posted at this time for public comment. [Please e-mail any comments to NCIadeerscomments@mail.nih.gov](mailto:NCIadeerscomments@mail.nih.gov) (subject line: [Comments re Revised AdEERS Tables](#)) by May 22, 2009, so that they can be considered during finalization of these changes. Once the tables are finalized, the "CTEP, NCI Guidelines: Adverse Event Reporting Requirements" document will be revised accordingly.

Thank you in advance for your comments.

The AE Working Group, CTEP

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General Instructions to Accompany Tables

- Expedited AE reporting timelines are defined as:
 - “24-Hour; 5 Calendar Days” – The AE must initially be reported via AdEERS within 24 hours of learning of the event, followed by a complete AdEERS report within 5 calendar days of the initial 24-hour report.
 - “10 Calendar Days” -- A complete AdEERS report on the AE must be submitted within 10 calendar days of the investigator learning of the event.
- **All deaths on study require both expedited and routine reporting regardless of causality. Attribution to agent administration or other cause must be provided.**
- Any event that results in a persistent or significant disability/incapacity, or a congenital anomaly/birth defect, or is an important medical event which based upon medical judgment may jeopardize the patient and require intervention to prevent a serious adverse event, must be reported via AdEERS if the event occurs following investigational agent administration.
- Use the NCI protocol number and the protocol-specific participant ID assigned during trial registration on all reports.
- AdEERS Medical Questions/Help: *email:* adeersmd@tech-res.com, *phone:* (301) 897-7497, *fax:* (301) 230-0159
- AdEERS Technical Questions/Help: *email:* ncictephhelp@ctep.nci.nih.gov, *phone:* 1-888-283-7457, *fax:* (301) 948-2242

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Level 0: AdEERS Expedited Reporting Requirements for Adverse Events that Occur under a CTEP IND within 30 Days of the Last Dose of the Investigational Agent ¹

	Grade 1	Grade 2	Grade 3	Grades 4 & 5
Unrelated Unlikely	Not Required	10 Calendar Days	10 Calendar Days	24-Hour; 5 Calendar Days
Possible Probable Definite	10 Calendar Days	10 Calendar Days	24-Hour; 5 Calendar Days	24-Hour; 5 Calendar Days
April 29, 2009				

¹ Adverse events that occur more than 30 days after the last dose of the investigational agent and have an attribution of possible, probable, or definite require reporting as follows:

AdEERS 24-hour notification followed by complete report within 5 calendar days for-

- All Grade 3, Grade 4, and Grade 5 Events

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Level 1: AdEERS Expedited Reporting Requirements for Adverse Events that Occur under a CTEP IND within 30 Days of the Last Dose of the Investigational Agent ¹

	Grade 1	Grade 2		Grade 3				Grades 4 & 5
	Unexpected and Expected	Unexpected	Expected	Unexpected		Expected		Unexpected and Expected
				with Hospitalization	without Hospitalization	with Hospitalization	without Hospitalization	
Unrelated Unlikely	Not Required	Not Required	Not Required	10 Calendar Days	Not Required	10 Calendar Days	Not Required	24-Hour; 5 Calendar Days
Possible Probable Definite	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
Hospitalization is defined as initial hospitalization or prolongation of hospitalization for \geq 24 hours, due to adverse event.								

¹ Adverse events that occur more than 30 days after the last dose of investigational agent and have an attribution of possible, probable, or definite require reporting as follows:

- AdEERS 24-hour notification followed by complete report within 5 calendar days for-
 - Grade 3 Unexpected Events with Hospitalization
 - Grade 4 Unexpected Events
 - Grade 5 Unexpected and Expected Events

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Level 2: AdEERS Expedited Reporting Requirements for Adverse Events that Occur under a CTEP IND within 30 Days of the Last Dose of the Investigational Agent ¹

	Grade 1	Grade 2			Grade 3				Grades 4 & 5	
	Unexpected and Expected	Unexpected		Expected	Unexpected		Expected		Unexpected	Expected
		with Hospitalization	without Hospitalization		with Hospitalization	without Hospitalization	with Hospitalization	without Hospitalization		
Unrelated Unlikely	Not Required	Not Required	Not Required	Not Required	10 Calendar Days	Not Required	Not Required	Not Required	10 Calendar Days	10 Calendar Days
Possible Probable Definite	Not Required	10 Calendar Days	Not Required	Not Required	10 Calendar Days	10 Calendar Days	10 Calendar Days	Not Required	24-Hour; 5 Calendar Days	10 Calendar Days

Hospitalization is defined as initial hospitalization or prolongation of hospitalization for ≥ 24 hours, **due to adverse event**.

1 Adverse events that occur more than 30 days after the last dose of investigational agent and have an attribution of possible, probable, or definite require reporting as follows:

AdEERS 24-hour notification followed by complete report within 5 calendar days for-

- Grade 4 and Grade 5 Unexpected Events

AdEERS 10 calendar day report-

- Grade 3 Unexpected Events with Hospitalization
- Grade 5 Expected Events

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Level 3: AdEERS Expedited Reporting Requirements for Adverse Events that Occur under a CTEP IND within 30 Days of the Last Dose of the Investigational Agent ¹

	Grade 1	Grade 2			Grade 3				Grade 4		Grade 5	
	Unexpected and Expected	Unexpected		Expected	Unexpected		Expected		Unex-pected	Expected	Unexpected	Expected
		with Hospital-ization	without Hospital-ization		with Hospital-ization	without Hospital-ization	with Hospital-ization	without Hospital-ization				
Unrelated Unlikely	Not Required	Not Required	Not Required	Not Required	Not Required	Not Required	Not Required	Not Required	10 Calendar Days	Not Required	10 Calendar Days	10 Calendar Days
Possible Probable Definite	Not Required	10 Calendar Days	Not Required	Not Required	10 Calendar Days	10 Calendar Days	Not Required	Not Required	24-Hour; 5 Calendar Days	10 Calendar Days	24-Hour; 5 Calendar Days	10 Calendar Days
<p>Hospitalization is defined as initial hospitalization or prolongation of hospitalization for ≥ 24 hours, due to adverse event.</p>												

1 Adverse events that occur more than 30 days after the last dose of investigational agent and have an attribution of possible, probable, or definite require reporting as follows:

AdEERS 24-hour notification followed by complete report within 5 calendar days for-

- Grade 4 and Grade 5 Unexpected Events

AdEERS 10 calendar day report-

- Grade 3 Unexpected Events with Hospitalization
- Grade 5 Expected Events