



Adverse Event Reporting

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CALGB Statistical Center**

*CRA Committee: New CRA Session
2010 Summer Group Meeting*

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Objectives

- Define an adverse event
- Discuss terminology and grading of adverse events
- Differentiate between routine adverse events and serious adverse events
- Determine when and understand how to report adverse events
- Identify appropriate reference materials

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What is an Adverse Event?

- Any unfavorable sign, symptom, or disease associated with the use of medical treatment or a procedure that may or may not be attributed to the treatment or procedure
- Adverse Events are also known as:
 - Side effects
 - Toxicities

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How to Describe Adverse Events

- Terminology provided by the NCI
 - Common Toxicity Criteria (CTC) v2.0
 - Common Terminology Criteria for Adverse Events (CTCAE) v3.0 and v4.0
- Protocol specifies the correct version to use
Note: AE forms using CTCAE v4.0 will indicate this in the title.
- Provides:
 - Standard terminology
 - Grading criteria for adverse events
 - MedDRA codes

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MedDRA Codes

- Medical Dictionary for Regulatory Activities (MedDRA)
 - Provides a numeric code for every adverse event
 - Paired with the CTC
- CTC v2.0 uses MedDRA v5
- CTCAE v3.0 uses MedDRA v6
- CTCAE v4.0 uses MedDRA v12

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Where to find the CTC

**CALGB Member Web Site > Studies
Section > Quick Links**

[https://www.calgb.org/Private/COOP_Groups/
CALGB/studies/studies.php](https://www.calgb.org/Private/COOP_Groups/CALGB/studies/studies.php)

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Cancer and Leukemia Group B
 Tomorrow's Cancer Treatments Today

Home Member Site Studies Applications Directory Resources Training Policies Funding

Tuesday May 4, 2010

calgb.org > Member Site > Studies

CALGB Web Search
 Search

CALGB Site Navigation
 Site Navigation

Web Site Help
 PDF icon: *All documents require Adobe Acrobat PDF software. Download Adobe Acrobat Reader for free.

- Contact the Protocol Information Specialist
- Contact the CALGB Webmaster

Quick Links

- Common Toxicity Criteria MedDRA Codes v4
- Common Toxicity Criteria MedDRA Codes v3
- Common Toxicity Criteria MedDRA Codes v2

Protocols

Active Protocols (Updated - 04/15/2010)
 Index of [Active CALGB Protocols](#) available on-line.

Closed Protocols (Updated - 02/15/2010)
 Index of [Closed CALGB Protocols](#) available on-line.

Intergroup Access (Updated - 05/22/2008)
[Access to Intergroup Protocols](#) coordinated by other cooperative groups.

Monthly Protocol Postings (Updated - 04/15/2010)
[List of Protocol Updates](#), Activations, Notice of Closure/ Suspension, and Memoranda p 1999.

Protocols in Development (Updated - 02/15/2010)
 Index of [CALGB Protocols in Development](#) as well as a model protocol available on-line.

Forms

Study Specific Forms for Active Studies
 CALGB [Study Specific Forms for Active Studies](#) used to collect patient data from various studies.

Study Specific Forms for Closed Studies
 CALGB [Study Specific Forms for Closed Studies](#) used to collect patient data from various studies.

Forms By Number
 CALGB C-xxx and flowsheet forms by number

Administrative Forms
 Miscellaneous CALGB [Administrative Forms](#) available on-line.

CTCAE v3.0 Codes

ALLERGY/IMMUNOLOGY							Page 1 of 1
Adverse Event	Short Name/MeDRA	Grade					5
		1	2	3	4		
Allergic reaction/hypersensitivity (including drug fever)	Allergic reaction 10020755	Transient flushing or rash; drug fever <38°C (<100.4°F)	Rash; flushing; urticaria; dyspnea; drug fever ≥38°C (≥100.4°F)	Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension	Anaphylaxis	Death	
REMARK: Urticaria with manifestations of allergic or hypersensitivity reaction is graded as Allergic reaction/hypersensitivity (including drug fever). ALSO CONSIDER: Cytokine release syndrome/acute infusion reaction.							
Allergic rhinitis (including sneezing, nasal stuffiness, postnasal drip)	Rhinitis 10039087	Mild, intervention not indicated	Moderate, intervention indicated	—	—	—	
REMARK: Rhinitis associated with obstruction or stenosis is graded as Obstruction/stenosis of airway – Select in the PULMONARY/UPPER RESPIRATORY CATEGORY.							
Autoimmune reaction	Autoimmune reaction 10003815	Asymptomatic and serologic or other evidence of autoimmune reaction, with normal organ function and intervention not indicated	Evidence of autoimmune reaction involving a non-essential organ or function (e.g., hypothyroidism)	Reversible autoimmune reaction involving function of a major organ or other adverse event (e.g., transient colitis or anemia)	Autoimmune reaction with life-threatening consequences	Death	
ALSO CONSIDER: Colitis; Hemoglobin; Hemolysis (e.g., immune hemolytic anemia, drug-related hemolysis); Thyroid function, low (hypothyroidism).							
Serum sickness	Serum sickness 10040400	—	—	Present	—	Death	
NAVIGATION NOTE: Splenic function is graded in the BLOOD/BONE MARROW CATEGORY.							
NAVIGATION NOTE: Urticaria as an isolated symptom is graded as Urticaria (hives, welts, wheals) in the DERMATOLOGY/SKIN CATEGORY.							
Vasculitis	Vasculitis 10047128	Mild, intervention not indicated	Symptomatic, non-steroidal medical intervention indicated	Steroids indicated	Ischemic changes; amputation indicated	Death	

CTCAE v4.0 Codes

Immune system disorders					
Adverse Event	Grade				
	1	2	3	4	5
Allergic reaction	Transient flushing or rash, drug fever <38 degrees C (<100.4 degrees F); intervention not indicated	Intervention or infusion interruption indicated, responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDs, narcotics), prophylactic medications indicated for <=24 hrs	Prolonged (e.g., not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement, hospitalization indicated for clinical sequelae (e.g., renal impairment, pulmonary infiltrates)	Life-threatening consequences, urgent intervention indicated	Death

Definition: A disorder characterized by an adverse local or general response from exposure to an allergen.

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Two Types of Adverse Event Reporting

- Routine reporting
 - Follow data submission schedule
 - Report using the CALGB AE Forms
- Expedited reporting for serious events
 - Report using AdEERS (or caAERS when released)
 - Submit CALGB AE form(s) per protocol

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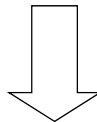
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Routine Adverse Event Reports

Reporting Routine AEs

Complete the Adverse Event Forms
and Supporting Documentation
(*C-260 Remarks Addenda, etc.*)
per the Data Submission Schedule



Submit to:
CALGB Statistical Center, Data Operations

Grading Adverse Events

- Some events do not have 5 grades
 - Represented as a dash (-) in the CTC
- Do not report baseline conditions unless they worsen
- If a solicited baseline event does not worsen then grade = -1

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AE Attribution Codes

- 1 = Unrelated to treatment
- 2 = Unlikely related to treatment
- 3 = Possibly related to treatment
- 4 = Probably related to treatment
- 5 = Definitely related to treatment

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Cancer as an AE

- ***A Secondary Malignancy*** is caused by protocol treatment
- ***A New Primary Cancer*** is not associated with protocol treatment

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Reporting Secondary Malignancies

Reported on several forms:

- Study specific adverse event form
- Some follow-up forms (for phase III studies)
- CALGB: New Malignancy Form (C-1001)*
**if required by protocol*
- NCI AML/MDS Form

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Reporting New Primary Cancers

Study specific reporting:

- CALGB: New Malignancy Form (C-1001)
- Follow-Up Form

Note: *New primary cancers are not reported as AEs or progression*

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Adverse
Event
Expedited
Reports
(AdEERS)

AdEERS = Adverse Event Expedited Reporting System

- Should I report?
- When should I report?
- How do I report?
- To whom do I report?

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Factors Affecting AdEERS Reporting

- Investigational or commercial agent
- Phase of trial
- Severity of event
- Hospitalization
- Expectedness
- Relation to treatment

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AdEERS Protocol-Specific Guidelines

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

¹ Adverse events with attribution of possible, probable, or definite that occur **greater** than 30 days after the last dose of treatment with an agent under a CTEP IND or non-CTEP IND 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 or prolongation of hospitalization
- Grade 5 expected events

² 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.

March 2005

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When to Report SAEs

Refer to the AdEERS table in the protocol to determine if you need to submit:

- Notification within 24 hours and the complete report within 5 calendar days

OR

- Complete report within 10 calendar days of learning of the event

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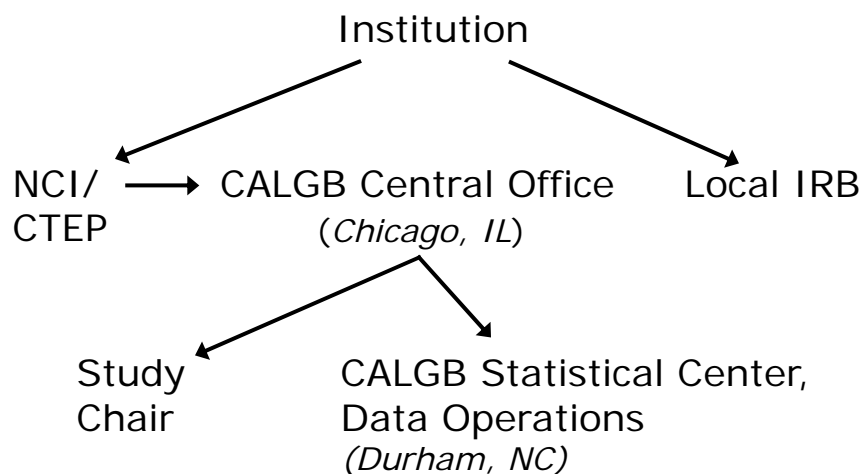
How to Report SAEs

- At the CTEP website: <http://ctep.cancer.gov>
- CALGB Adverse Event Form
- **Don't Forget!**
Send supporting documentation to:
 - NCI
 - CALGB Central Office
 - CALGB Statistical Center, Data Operations

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To Whom to Report SAEs



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AdEERS Help

- Policy-related, medical questions and administrative issues, contact:
 - AdEERS MD Help Desk: (301) 897-7497
 - AdEERS MD Email: AdEERSMD@TECH-RES.COM
- Technical and training issues, contact:
 - NCI CTEP Help Desk: (301) 840-8202
 - NCI CTEP Email: ncictephelp@ctep.nci.nih.gov

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Routine vs. Expedited Reporting

Routine Reporting

- Adverse Event Forms
 - Submit AE Forms to Stat Center
 - As required by protocol

Expedited Reporting

- AdEERS
 - As required by the protocol; refer to the AdEERS table to determine if/when reporting is required
 - Submit to your local IRB

NOTE: All events reported via AdEERS should be reported on the Routine AE Form

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Review

- Check the protocol Data Submission Schedule or AE form for the correct version of the CTC
- Use the CTC to determine the event name, grade, and MedDRA code
- Submit routine Adverse Event Forms per protocol
- Check the protocol and/or CALGB Web site for which events must be submitted via AdEERS

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Resources

- Protocol
- <http://ctep.cancer.gov>
- AdEERS/CTEP Help Desks
 - AdEERS MD Help Desk: (301) 897-7497
 - NCI CTEP Help Desk: (301) 840-8202
- AdEERS Computer-Based Training:
http://ctep.cancer.gov/reporting/AdEERS_CBT_v3/welcome.html
- Linda Bressler, PharmD, CALGB Director of Regulatory Affairs
 - Email: bressler@uic.edu
 - Phone: (773) 834-7973

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