

ACRINTM
AMERICAN COLLEGE OF
RADIOLOGY
IMAGING NETWORK

**ADVERSE EVENT
REPORTING MANUAL**

Prepared by the
American College of Radiology Imaging Network

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1.0 Adverse Event Terminology and Definitions

1.1 Adverse Event (AE)

An AE is any untoward medical occurrence in a patient that does not necessarily have a causal relationship with the study intervention. An AE can therefore be any unfavorable or unintended sign (including an abnormal laboratory finding), symptom or disease temporarily associated with the use of a medical treatment or procedure regardless of whether it is considered related to the medical treatment or procedure (attribution of unrelated, unlikely, possible, probable, or definite—see Section 1.7 below).

1.2 Life-Threatening Adverse Event

A life-threatening AE is any adverse event that places the patient at the discretion of investigator, at immediate risk of death.

1.3 Serious Adverse Event (SAE)

An SAE is defined as any untoward medical occurrence that: 1) results in death or is life-threatening at the time of the event, 2) causes inpatient hospitalization or prolongation of existing hospitalization (if applicable), 3) creates a persistent or significant disability/incapacity, or 4) leads to a congenital anomaly/birth defect (in an offspring).

1.4 Expected Adverse Event

An expected AE is an event that is listed in the protocol, the National Cancer Institute (NCI) Agent Specific Expected AE List, or the Investigator's Brochure.

1.5 Unexpected Adverse Event

An unexpected AE is an event that is NOT listed in the protocol, the NCI Agent Specific Expected Adverse Event List, or the Investigator's Brochure.

1.6 Unexpected-Indirect Adverse Event

An unexpected-indirect AE is an event associated with a procedure/medical treatment performed as a result of a positive finding on a screening imaging study and NOT listed in the protocol, the NCI Agent Specific Expected Adverse Event List, or the Investigator's Brochure.

1.7 Attribution

Attribution is the determination of whether an AE is related to a medical treatment or procedure.

Attribution categories are:

Definite	The AE is <i>clearly related</i> to the treatment or procedure.
Probable	The AE is <i>likely related</i> to the treatment or procedure.
Possible	The AE <i>may be related</i> to the treatment or procedure.
Unlikely	The AE is <i>doubtfully related</i> to the treatment or procedure.
Unrelated	The AE is <i>clearly NOT related</i> to the treatment or procedure.

1.8 Grade

Grade is used to denote the severity of the AE. An AE is graded using the following categories unless the term is otherwise defined by a different grade system in the current version of the Common Toxicity Criteria (CTC):

- | | |
|----------|--------------------------------------|
| 1 | Mild |
| 2 | Moderate |
| 3 | Severe |
| 4 | Life-threatening or disabling |
| 5 | Fatal |

For terms listed in the CTC, the grade is still recorded as 1, 2, 3, 4 or 5; however, the definition of the various grades will be specific to the term being used.

1.9 Toxicity

Regulatory organizations have NOT clearly defined the term ‘toxicity.’ However, toxicity has been described as an AE that has an attribution of possibly, probably or definitely related to the investigational treatment. It is NCI’s recommendation NOT to use the term toxicity for AE reporting purposes. The Common Toxicity Criteria (CTC) continues to use the term ‘toxicity’ because of familiarity.

1.10 Adverse Event Expedited Reporting System (AdEERS)

AdEERS is a web-based system created by NCI for electronic submission of serious or unexpected AE reports.

1.11 Common Toxicity Criteria (CTC)

The CTC contains descriptive terminology that is to be used for AE reporting. A grading (severity) scale is provided for each AE term. As of June 2003, CTC for Adverse Events (CTCAE) version 3.0 is mandated for use in all protocols.

1.12 Investigational Agent

An investigational agent is any agent held under an Investigational New Drug (IND) application.

1.13 Commercial Agent

A commercial agent is any agent not supplied under an IND but obtained from commercial sources.

1.14 Clinical Data Update System (CDUS)

CDUS is the data collection system used by the NCI Division of Cancer Treatment and Diagnosis (DCTD) to capture clinical data.

2.0 Adverse Event Reporting

Prompt reporting of AEs is the responsibility of each principal investigator and/or investigator designee (e.g. clinical research associate and/or nurse engaged in clinical research). Anyone uncertain about whether a particular AE should be reported should contact the American College of Radiology Imaging Network (ACRIN) Headquarters at **(215) 574-3150** and ask for the ACRIN AE Coordinator for further assistance.

Most ACRIN imaging trials will perform imaging with approved devices (or non-significant risk devices) and approved imaging agents with known favorable safety profiles. Under these circumstances, ACRIN protocols will typically limit the reporting of AEs to specific events, many of which occur within 2 hours of the imaging procedure. However, study participants should be followed for the duration of their trial participation and up to 30 days after trial completion. The protocol will define the specific follow-up procedures and reporting requirements.

2.1 Three (3) Categories of Imaging Studies:

- Diagnostic
- Screening
- Interventional

2.1.1 Diagnostic: Typically these studies will use approved devices and imaging agents with known favorable safety profiles. Reporting will follow the imaging-only guidelines for reporting AEs.

2.1.2 Screening: Trials involving screening studies add a second dimension to monitoring and reporting of AEs. Two (2) additional categories of AEs should be considered “expected-indirect” and “unexpected-indirect” AEs. These are AEs that are associated with a procedure/medical treatment performed as a result of a positive finding on a screening imaging study.

2.1.3 Interventional: This type of study will be treated as a therapeutic trial. AE reporting therefore follows all NCI guidelines.

2.2 **Steps to Initiate an Adverse Event Report**

The following steps should be taken to initiate an AE report:

1. Identify the event.
2. Grade the severity of the event.
3. Determine attribution of the AE – is the event related to the medical treatment or imaging procedure?
4. If the AE is related to the medical treatment or imaging procedure, determine if the AE is expected or unexpected.
5. Determine how the event should be reported, given the information above and referencing the AE reporting section of the protocol.

2.3 **Expected Adverse Events**

An AE is determined to be expected when the event is listed in the protocol, the NCI Agent Specific Expected AE List (if an NCI-sponsored investigational agent is used) or the Investigator's Brochure.

Expected AEs include, but are not limited to:

- Contrast reactions
- Machine failure
- Injury from devices
- Misadministration of imaging agent/contrast agent
- Vasovagal reactions

Only expected AEs listed in the protocol will be reported using the appropriate AE case report forms provided for the study.

Per NCI AE Reporting Requirements, expedited reporting is required for any expected AE that is reported as fatal (Grade 5) occurring within 30 days of the study intervention (imaging procedure) regardless of attribution. This will depend on the reporting requirements for each specific protocol.

2.4 **Expected – Indirect Adverse Events: Screening Trials**

An AE is determined to be expected-indirect when the event is associated with a procedure/medical treatment performed as a result of a positive finding on a screening imaging study and is listed either in the protocol or the Investigator's Brochure.

Only expected-indirect AEs listed in the protocol will be reported using the appropriate AE case report forms provided for the study. This will depend on the reporting requirements for each specific protocol.

2.5 **Unexpected Adverse Events**

An AE is determined to be unexpected when the event is NOT listed in the protocol, NCI Agent Specific Expected AE List (if an NCI-sponsored investigational agent is used) or the Investigator's Brochure.

All unexpected AEs regardless of severity or attribution will be reported using the appropriate AE case report form provided for the study. This will depend on the reporting requirements for each specific protocol.

Per NCI AE Reporting Requirements, expedited reporting—by both telephone and mail—is required for any unexpected AE that is reported as life threatening (Grade 4) or fatal (Grade 5) occurring within 30 days of the study intervention (imaging procedure) regardless of attribution. This will depend on the reporting requirements for each specific protocol.

2.6 Unexpected – Indirect Adverse Events

An AE is determined to be unexpected-indirect when the event is associated with a procedure/medical treatment performed as a result of a positive finding on a screening imaging study, and it is NOT listed either in the protocol or the Investigator's Brochure.

Reporting requirements for any unexpected-indirect AEs will be specified in the ACRIN protocol.

2.7 Persistent or Recurring Adverse Events

Any AE that persists or recurs from one visit to another should only be reported once in an expected manner, unless the grade becomes more severe at a subsequent visit. An AE that resolves and then recurs during a subsequent visit should only be reported in a routine manner, unless the severity changes.

2.8 Baseline Adverse Events

An expedited AE report should NOT be submitted if a patient entered the study with a preexisting condition. However, if the preexisting condition worsens in severity, the investigator should determine attribution of the event and if the event should be reported.

2.9 Event(s) not Related to Treatment or Procedure

Any event that is judged NOT to be related to the treatment or procedure should NOT be reported as an AE. However, an AE report should be submitted if there is a reasonable suspicion of effect from the medical treatment or imaging procedure. Please note that ACRIN protocols specify what AEs are reportable. The ACRIN AE manual serves as general guidelines for NCI reporting requirements.

3.0 Expedited Adverse Event Reporting

Expedited AE reporting is required for all unexpected Grade 4 (life threatening) AEs and all (unexpected and expected) Grade 5 (fatal) AEs regardless of attribution, unless otherwise specified in the protocol. The requirement for expedited AE reporting is also applicable to studies using imaging procedures only or imaging procedures with an investigational agent(s) or commercial agent(s). Further specific timeframes for occurrence and reporting requirements will be defined within the individual protocols.

The NCI's Cancer Imaging Program (NCI/CIP) has contracted Technical Resources International, Inc. (TRI) to head the expedited AE collection process.

3.1 Adverse Event Expedited Reporting Instructions: By Telephone

For SAEs that require 24-hour notification as outlined in the study-specific protocol, please call the following numbers to report the event:

1. TRI – SAE dedicated phone line at: 301-897-1704

- The TRI - SAE dedicated phone line is staffed Monday through Friday from 7:30am – 7:30pm.
- SAEs may be reported via voicemail during off hours.
- A TRI contact for AE/SAE reporting will return your call within 24 hours.

The following details are mandatory when reporting SAEs, so please collect this information and have it available prior to calling TRI:

- Your contact information including:
 - Name
 - Telephone number and e-mail address
- Your institution's name or ID number
- Protocol title and number
- Participant's case number and initials
- Principal investigator's (PI's) name and telephone number
- Date and time of the SAE
- Date and time you learned of the SAE
- Brief description of the SAE
- A statement regarding the PI's determination of the grade and attribution of the event

2. ACRIN – SAE dedicated phone line at: 215-717-2763

- The ACRIN – SAE dedicated phone line is staffed from Monday through Friday 8:30am – 4:30pm.
- SAEs may also be reported via voice mail during off hours.
- An ACRIN contact for AE/SAE reporting will return your call within 24 business hours.

The following details are mandatory when reporting SAEs, so please collect this information and have it available prior to calling ACRIN:

- Your contact information including:
 - Name
 - Telephone number and e-mail address
- Institution's name or Institution's number
- Protocol number
- Participant's case number
- Date and time of the SAE
- Date and time you learned of the SAE
- Brief description of the SAE
- PI's determination of the grade and attribution of the event

IMPORTANT: After calling the TRI - and ACRIN - SAE 24-hour phone notification lines, complete an "Adverse Event Expedited Report (AdEERS)—Single Agent v4.0" form (see AdEERS reporting instructions below).

3.2 Submitting an AdEERS Report: Paper and Electronic Submission

After completing the telephone notifications of SAEs, an AdEERS form must also be submitted. A completed AdEERS should be submitted within ten (10) working days or ten (10) calendar days of first knowledge of the AE. (Please refer to the protocol for specific reporting requirements.)

3.2.1 AdEERS for Imaging Trials: Paper Submission

Some information routinely included in AdEERS forms is not applicable to imaging trials, specifically the: "Course Information" (question # 4) and "Protocol Agent" (question # 10) sections. These questions should be omitted. Therefore, you **MUST** submit a paper copy of the AdEERS report because the electronically submitted reports are not accepted with omissions.

3.2.2 AdEERS for Imaging Trials with IND Agent(s): Electronic Submission

For imaging trials with IND agent(s), the AdEERS report can be submitted electronically. Please find the AdEERS application on the NCI/CTEP web page at: <http://ctep.cancer.gov/reporting/adeers.html>.

3.2.3 Completing an AdEERS Report

The NCI/CIP "Adverse Event Expedited Report (AdEERS)—Single Agent v4.0", is accessible at: http://ctep.cancer.gov/forms/34-AdEERSv4_SAT.pdf. You can also access the "Adverse Event Expedited Report (AdEERS)—Single Agent v4.0" document from the ACRIN web site (www.acrin.org). You will find an electronic copy within each protocol-specific web page and the Regulatory Resources' web page.

3.2.4 Assistance Completing an AdEERS Report

A TRI representative can assist you with the completion of the AdEERS report through the AdEERSMD help line at: 301-897-7497.

3.2.5 AdEERS Submission Requirements

1. Fax the completed AdEERS report to both TRI and ACRIN at:
TRI Fax Number: 301-897-7402
ACRIN Fax Number: 215-940-8819
2. Email TRI to notify them of the fax submission at:
CIPSAEReporting@tech-res.com
3. Mail the original, signed copy of the completed AdEERS report to ACRIN Headquarters:
American College of Radiology Imaging Network
Attn: ACRIN AE Coordinator
1818 Market Street, Suite 1600
Philadelphia, PA 19103
4. Please refer to your local IRB's policies regarding the reporting of AEs, SAEs and the submission of the appropriate paperwork to your institution.

Questions about the Adverse Event Reporting Process?

Please contact:

Cornelia (Lia) Tsikos
ACRIN AE Coordinator
Phone: (215) 574-3236
E-mail: ctsikos@phila.acr.org

Maria Oh
ACRIN Director of Protocol Development and Regulatory Compliance
Phone: (215) 574-3160
E-mail: moh@phila.acr.org

4.0 Reporting Requirements

4.1 ACRIN Protocol Compliance

ACRIN protocols are in compliance with NCI reporting requirements. Complete and accurate reporting of AEs is the obligation of investigators and/or investigator designees (e.g. clinical research associate and/or nurse engaged in clinical research). The accuracy and timeliness of reporting has implications both for the safety of research participants and for the validity of the data derived from clinical research.

4.2 An Expedited Report Is Required When:

1. Protocol uses an imaging procedure only:
 - Any AE requiring expedited reporting must be submitted using a **paper version** of the Adverse Event Expedited Report-Single Agent template.
2. Protocol uses an NCI-sponsored investigational agent:
 - Any AE requiring expedited reporting must be submitted via the AdEERS web application or the Adverse Event Expedited Report-Single Agent template.
3. Protocol uses both a commercial agent AND an NCI-sponsored investigational agent on the same treatment arm:
(Combination is considered investigational)
 - Any AE requiring expedited reporting must be submitted via the AdEERS web application or the Adverse Event Expedited Report-Multiple Agent template.
4. Protocol uses an investigational agent sponsored under a pharmaceutical company IND:
 - Protocol will define expedited reporting requirements determined in part by the pharmaceutical sponsor. The AdEERS web application may be used for non-NCI-IND agents.
5. Protocol uses a commercial agent on one treatment arm of the study AND an investigational agent or combination of investigational agent and commercial agent on the other arm:
 - Any AE requiring expedited reporting on either treatment arm must be submitted via the AdEERS web application or the Adverse Event Expedited Report-Single Agent or Multiple Agent templates. Previously MedWatch forms were required for reporting AEs for commercial agents. The FDA now accepts the AdEERS report in lieu of completing a MedWatch form. The NCI is responsible for

submitting a copy of the AdEERS report to the MedWatch division.

- 6. Protocol uses commercial agent(s) only:
 - An AE requiring expedited reporting must be submitted via the AdEERS web application or the Adverse Event Expedited Report-Single Agent or Multiple Agent templates. Previously MedWatch forms were required for reporting AEs for commercial agents. The FDA now accepts the AdEERS report in lieu of completing a MedWatch form. The NCI is responsible for submitting a copy of the AdEERS report to the MedWatch division.

4.3 Phase 2 and Phase 3 Studies - Imaging Procedures Only

4.3.1 What to Report

An expedited report is required for all unexpected Grade 4 (life-threatening) AEs and all (unexpected and expected) Grade 5 (fatal) AEs within 30 days of the date of imaging/study related procedures regardless of attribution, unless otherwise specified in the protocol. Any death after 30 days of the last study procedure attributed to the study intervention (possible, probable or definite) should be reported within **10 working days** of first knowledge of the event.

NOTE: The protocol-specific AE guidelines would supersede the standard guidelines for AE reporting.

<u>UNEXPECTED EVENT</u>			<u>EXPECTED EVENT</u>		
Grades 1 – 3 Regardless of Attribution *	Grade 4 Regardless of Attribution *	Grade 5 Regardless of Attribution *	Grades 1 – 3 Regardless of Attribution *	Grade 4 Regardless of Attribution *	Grade 5 Regardless of Attribution *
AE expedited reporting NOT required.	AE expedited report required within 10 working days of first knowledge of event.	Report by phone to NCI and ACRIN within 24 hrs of first knowledge of event. Expedited report submission completed within 10 working days of first knowledge.	AE expedited reporting NOT required.	AE expedited reporting NOT required.	Report by phone to NCI and ACRIN within 24 hrs. of knowledge of event. Expedited report within 10 working days.

(Grades 1-3 – AE Expedited Reporting is NOT required, unless it is otherwise specified in the protocol.)

* Unless it is otherwise specified in the protocol.

4.3.2 **How to Report**

Access CTEP Forms, Templates, and Documents at <http://ctep.cancer.gov/forms>. Scroll down to **Reporting Forms** then, click on the pdf of the AdEERS Single Agent Template.

Alternatively, The NCI/CIP “Adverse Event Expedited Report (AdEERS)—Single Agent v4.0”, is accessible at: http://ctep.cancer.gov/forms/34-AdEERSv4_SAT.pdf. You can also access the “Adverse Event Expedited Report (AdEERS)—Single Agent v4.0” document from the ACRIN web site. You will find an electronic copy within each protocol-specific web page and the Regulatory Resources web page.

Please **print** and complete the paper template using the standard List of Values and submit the completed report.

NOTE: Please do NOT attempt to submit a completed form electronically through the AdEERS web site, as the system currently will not permit electronic submission of reports without the completion of Section 4 - Course Information and Section 10 - Protocol Agent .

For questions on how to complete the AdEERS report, call the AdEERSMD help line at 301-897-7497 for assistance from a TRI representative.

4.3.3 **When to Report**

The investigative site must report adverse events within **10 working days** of first knowledge. All fatal (Grade 5) adverse events should also be reported by telephone to both TRI and ACRIN within **24 hours** of first knowledge of the event, unless otherwise specified in the protocol.

4.3.4 Where to Report

<u>TRI</u>	<u>ACRIN</u>	<u>Local IRB</u>
<p><u>By phone:</u> 301-897-1704 TRI offers a 24-hour telephone reporting line. TRI representatives are available Mon. – Fri., 7:30 AM – 7:30 PM EST. If a representative is not available, leave a message and you will be contacted within 24 hours.</p> <p>Please have the following information:</p> <ul style="list-style-type: none"> ▪ Name ▪ Telephone number and e-mail address ▪ Your institution’s name or ID number ▪ Protocol title and number ▪ Participant’s case number and initials ▪ Principal investigator’s (PI’s) name and telephone number ▪ Date and time of the SAE ▪ Date and time you learned of the SAE ▪ Brief description of the SAE ▪ A statement regarding the PI’s determination of the grade and attribution of the event <p><u>AdEERSMD help line:</u> 301-997-7497 for AdEERS-related questions</p>	<p><u>By phone:</u> 215-717-2763 ACRIN offers a 24-hour telephone reporting line. An ACRIN representative is available Mon. – Fri., 8:30 AM – 4:30 PM EST. If a representative is not available, leave a message and you will be contacted within 24 business hours.</p> <p>Please have the following information available:</p> <ul style="list-style-type: none"> ▪ Name ▪ Phone number ▪ ACRIN study number ▪ Case number ▪ Description of event ▪ Date of event ▪ Investigator designated: <ul style="list-style-type: none"> ▪ Grade ▪ Attribution 	<p>Please refer to your local IRB policies regarding AEs/SAEs and safety reports.</p>
<p><u>By fax:</u> 301-897-7402 Once the AdEERS report has been completed and faxed, send a confirmation e-mail to TRI (see below).</p>	<p><u>By fax:</u> 215-940-8819 Attention: ACRIN AE Coordinator</p> <p>Please include a cover page with the following information:</p> <ul style="list-style-type: none"> ▪ Name ▪ Phone number ▪ ACRIN study number ▪ Case number 	
<p><u>By email:</u> CIPSAEReporting@tech-res.com</p> <p>To confirm that the AdEERS report was received by fax.</p>	<p><u>By mail:</u> Send the original signed copy of the completed AdEERS report to ACRIN Headquarters: American College of Radiology Imaging Network Attn: ACRIN AE/SAE Coordinator 1818 Market Street, Suite 1600 Philadelphia, PA 19103</p>	

4.4 Phase 2 and Phase 3 Studies- Commercial Agent(s) Only

Commercial agents are those agents not provided under the NCI IND, but obtained through a commercial source. Certain protocols may call for a commercial agent to be used for an indication that is not included in the package label. On some occasions, NCI may distribute commercial supplies for a trial. In either case, the agent is still considered a commercial agent.

4.4.1 What to Report

An expedited report is required for all unexpected Grade 4 AEs and all (unexpected and expected) Grade 5 AEs. Report submission must be completed within 30 days of the date of imaging and other study-related procedures regardless of attribution to the commercial agent or the study procedure, unless otherwise specified in the protocol. Any death after 30 days of the last study procedure that is attributed to the study intervention (possible, probable or definite) should be reported within **10 working days** of first knowledge of the event.

NOTE: ACRIN protocol-specific AE guidelines would supersede the standard guidelines for AE reporting.

<u>UNEXPECTED EVENT</u>			<u>EXPECTED EVENT</u>		
Grades 1 – 3 Regardless of Attribution *	Grade 4 Regardless of Attribution *	Grade 5 Regardless of Attribution *	Grades 1 – 3 Regardless of Attribution *	Grade 4 Regardless of Attribution *	Grade 5 Regardless of Attribution *
AE expedited reporting NOT required.	AE expedited report required within 10 working days of first knowledge of event.	Report by phone to NCI and ACRIN within 24 hrs. of first knowledge of event. Expedited AE report submission completed within 10 working days of first knowledge.	AE expedited reporting NOT required.	AE expedited reporting NOT required.	Report by phone to NCI and ACRIN within 24 hrs. of first knowledge of event. Expedited AE report submission completed within 10 working days of first knowledge.

(Grade 1-3 AE Expedited Reporting is NOT required, unless otherwise specified in the protocol.)

* Unless it is otherwise specified in the protocol.

4.4.2 How to Report

AEs were previously reported using the [MedWatch form](#). However, these events should now be reported using the [AdEERS web application](#).

4.4.3 When to Report

The investigative site must report the AE within **10 working days** of first knowledge of the event. All fatal (Grade 5) AEs should also be reported by telephone to both TRI and ACRIN within **24 hours** of first knowledge of the event, unless otherwise specified in the protocol.

4.4.4 Where to Report

<u>TRI</u>	<u>ACRIN</u>	<u>Local IRB</u>
<p><u>By phone:</u> 301-897-1704 TRI offers a 24-hour telephone reporting line. TRI representatives are available Mon. – Fri., 7:30 AM – 7:30 PM EST. If a representative is not available, leave a message and you will be contacted within 24 hours.</p> <p>Please have the following information:</p> <ul style="list-style-type: none"> ▪ Name ▪ Telephone number and e-mail address ▪ Your institution’s name or ID number ▪ Protocol title and number ▪ Participant’s case number and initials ▪ Principal investigator’s (PI’s) name and telephone number ▪ Date and time of the SAE ▪ Date and time you learned of the SAE ▪ Brief description of the SAE ▪ A statement regarding the PI’s determination of the grade and attribution of the event <p><u>AdEERSMD help line:</u> 301-997-7497 for AdEERS-related questions</p>	<p><u>By phone:</u> 215-717-2763 ACRIN 24-hour telephone reporting line. An ACRIN representative is available Mon. – Fri., 8:30 AM – 4:30 PM EST. If a representative is not available, leave a message and you will be contacted within 24 business hours.</p> <p>Please have the following information available:</p> <ul style="list-style-type: none"> ▪ Name ▪ Phone number ▪ ACRIN study number ▪ Case number ▪ Description of event ▪ Date of event ▪ Investigator designated: <ul style="list-style-type: none"> ▪ Grade ▪ Attribution 	<p>Please refer to your local IRB policies regarding AEs/SAEs and safety reports.</p>
<p><u>By fax:</u> 301-897-7402 Once the AdEERS report has been completed and faxed, send a confirmation e-mail to TRI (see below).</p>	<p><u>By fax:</u> 215-940-8819 Attention: ACRIN AE Coordinator</p> <p>Please include a cover page with the following information:</p> <ul style="list-style-type: none"> ▪ Name ▪ Phone number ▪ ACRIN study number ▪ Case number 	
<p><u>By email:</u> CIPSAEReporting@tech-res.com</p> <p>To confirm that the AdEERS report was received by fax.</p>	<p><u>By mail:</u> Send the original signed copy of the completed AdEERS report to ACRIN Headquarters: American College of Radiology Imaging Network Attn: ACRIN AE/SAE Coordinator 1818 Market Street, Suite 1600 Philadelphia, PA 19103</p>	

4.5 Phase 2 and Phase 3 Studies Using Industry-Sponsored Investigational Agent(s)

The protocol will define expedited AE reporting requirements as determined in part with the pharmaceutical sponsor. In some studies, the investigational drug may be distributed by NCI while the IND is held by the pharmaceutical sponsor. Under these circumstances AdeERS may be used to report AEs. Refer to the protocol for specific guidelines.

4.5.1 What to Report

An expedited AE report is required for all unexpected Grade 4 AEs and all (unexpected and expected) Grade 5 AEs. Report submission must be completed within 30 days of the date of imaging or other study-related procedures regardless of attribution to the investigational agent or the study procedure, unless otherwise specified in the protocol. Any death after 30 days of the last study procedure attributed to the study intervention (possible, probable or definite) should be reported within **10 working days** of first knowledge of the event.

NOTE: ACRIN protocol-specific AE guidelines would supersede the standard guidelines for AE reporting.

<u>UNEXPECTED EVENT</u>			<u>EXPECTED EVENT</u>		
Grades 1 – 3 Regardless of Attribution *	Grade 4 Regardless of Attribution *	Grade 5 Regardless of Attribution *	Grades 1 – 3 Regardless of Attribution *	Grade 4 Regardless of Attribution *	Grade 5 Regardless of Attribution *
AE expedited reporting NOT required.	AE expedited report required within 10 working days of first knowledge of event.	Report by phone to NCI and ACRIN within 24 hrs. of first knowledge of event. Expedited report submission completed within 10 working days of first knowledge.	AE expedited reporting NOT required.	AE expedited reporting NOT required.	Report by phone to NCI and ACRIN within 24 hrs. of first knowledge of event. Expedited report submission completed within 10 working days of first knowledge.

(Grade 1-3 AE Expedited Reporting is NOT required, unless otherwise specified in the protocol.)

* Unless it is otherwise specified in the protocol.

4.5.2 How to Report

AE were previously reported using the [MedWatch form](#). However, these events should now be reported using the [AdEERS web application](#).

4.5.3 When to Report

The investigative site must report the AE within **10 working days** of first knowledge. All fatal (Grade 5) AEs should also be reported by telephone to both TRI and ACRIN within **24 hours** of first knowledge of the event, unless otherwise specified in the protocol.

4.5.4 Where to Report

<u>TRI</u>	<u>ACRIN</u>	<u>Local IRB</u>
<p>By phone: 301-897-1704 TRI offers a 24-hour telephone reporting line. TRI representatives are available Mon. – Fri., 7:30 AM – 7:30 PM EST. If a representative is not available, leave a message and you will be contacted within 24 hours.</p> <p>Please have the following information:</p> <ul style="list-style-type: none"> ▪ Name ▪ Telephone number and e-mail address ▪ Your institution’s name or ID number ▪ Protocol title and number ▪ Participant’s case number and initials ▪ Principal investigator’s (PI’s) name and telephone number ▪ Date and time of the SAE ▪ Date and time you learned of the SAE ▪ Brief description of the SAE ▪ A statement regarding the PI’s determination of the grade and attribution of the event <p><u>AdEERSMD help line:</u> 301-997-7497 for AdEERS-related questions</p>	<p>By phone: 215-717-2763 ACRIN offers a 24-hour telephone reporting line. An ACRIN representative is available Mon. – Fri., 8:30 AM – 4:30 PM EST. If a representative is not available, leave a message and you will be contacted within 24 business hours.</p> <p>Please have the following information available:</p> <ul style="list-style-type: none"> ▪ Name ▪ Phone number ▪ ACRIN study number ▪ Case number ▪ Description of event ▪ Date of event ▪ Investigator designated: <ul style="list-style-type: none"> ▪ Grade ▪ Attribution 	<p>Please refer to your local IRB policies regarding AEs/SAEs and safety reports.</p>
<p>By fax: 301-897-7402 Once the AdEERS report has been completed and faxed, send a confirmation e-mail to TRI (see below).</p>	<p>By fax: 215-940-8819 Attention: ACRIN AE Coordinator</p> <p>Please include a cover page that includes the following information:</p> <ul style="list-style-type: none"> ▪ Name ▪ Phone number ▪ ACRIN study number ▪ Case number 	
<p>By email: CIPSAEReporting@tech-res.com</p> <p>To confirm that the AdEERS report was received by fax.</p>	<p>By mail: Send the original signed copy of the completed AdEERS report to ACRIN Headquarters: American College of Radiology Imaging Network Attn: ACRIN AE/SAE Coordinator 1818 Market Street, Suite 1600 Philadelphia, PA 19103</p>	

NOTE: If an IND is held by a pharmaceutical sponsor the protocol will define additional reporting requirements.

4.6 Phase 2 and Phase 3 Studies Using Industry-Sponsored Investigational Agent(s) and Commercial Agent(s)

When an investigational agent(s) is used in combination with a commercial agent(s), the combination should be reported as if it is an industry sponsored investigational agent. Expedited reporting of AEs should follow the guidelines defined in the protocol.

4.6.1 What to Report

An expedited report is required for all unexpected Grade 4 AEs and all (unexpected and expected) Grade 5 AEs. Report submission must be completed within 30 days of the date of imaging or other study-related procedures regardless of attribution to the investigational or commercial agent or the study procedure, unless otherwise specified in the protocol. Any death after 30 days of the last study procedure attributed to the study intervention (possible, probable or definite) should be reported within **10 working days** of first knowledge of the event.

NOTE: ACRIN protocol-specific AE guidelines would supersede the standard guidelines for AE reporting.

<u>UNEXPECTED EVENT</u>			<u>EXPECTED EVENT</u>		
Grades 1 – 3 Regardless of Attribution *	Grade 4 Regardless of Attribution *	Grade 5 Regardless of Attribution *	Grades 1 – 3 Regardless of Attribution *	Grade 4 Regardless of Attribution *	Grade 5 Regardless of Attribution *
AE expedited reporting NOT required.	Expedited AE report required within 10 working days of first knowledge of event.	Report by phone to NCI and ACRIN within 24 hrs. of first knowledge of event. Expedited report submission completed within 10 working days of first knowledge.	AE expedited reporting NOT required.	AE expedited reporting NOT required.	Report by phone to NCI and ACRIN within 24 hrs. of first knowledge of event. Expedited report submission completed within 10 working days of first knowledge.

(Grade 1-3 AE Expedited Reporting is NOT required, unless otherwise specified in the protocol.)

* Unless it is otherwise specified in the protocol.

4.6.2 How to Report

AEs were previously reported using the [MedWatch form](#). However, these events should now be reported using the [AdEERS web application](#).

4.6.3 When to Report

The investigative site must report the AE within **10 working days** of first knowledge. All fatal (Grade 5) AEs should also be reported by telephone to both TRI and ACRIN within **24 hours** of first knowledge of the event, unless otherwise specified in the protocol.

4.6.4 Where to Report

<u>TRI</u>	<u>ACRIN</u>	<u>Local IRB</u>
<p>By phone: 301-897-1704 TRI offers a 24-hour telephone reporting line. TRI representatives are available Mon. – Fri., 7:30 AM – 7:30 PM EST. If a representative is not available, leave a message and you will be contacted within 24 hours.</p> <p>Please have the following information:</p> <ul style="list-style-type: none"> ▪ Name ▪ Telephone number and e-mail address ▪ Your institution’s name or ID number ▪ Protocol title and number ▪ Participant’s case number and initials ▪ Principal investigator’s (PI’s) name and telephone number ▪ Date and time of the SAE ▪ Date and time you learned of the SAE ▪ Brief description of the SAE ▪ A statement regarding the PI’s determination of the grade and attribution of the event <p><u>AdEERSMD help line:</u> 301-997-7497 for AdEERS-related questions</p>	<p>By phone: 215-717-2763 ACRIN offers a 24-hour telephone reporting line. An ACRIN representative is available Mon. – Fri., 8:30 AM – 4:30 PM EST. If a representative is not available, leave a message and you will be contacted within 24 business hours.</p> <p>Please have the following information available:</p> <ul style="list-style-type: none"> ▪ Name ▪ Phone number ▪ ACRIN study number ▪ Case number ▪ Description of event ▪ Date of event ▪ Investigator designated: <ul style="list-style-type: none"> ▪ Grade ▪ Attribution 	<p>Please refer to your local IRB policies regarding AEs/SAEs and safety reports.</p>
<p>By fax: 301-897-7402 Once the AdEERS report has been completed and faxed, send a confirmation e-mail to TRI (see below).</p>	<p>By fax: 215-940-8819 Attention: ACRIN AE Coordinator</p> <p>Please include a cover page that includes the following information:</p> <ul style="list-style-type: none"> ▪ Name ▪ Phone number ▪ ACRIN study number ▪ Case number 	
<p>By email: CIPSAEReporting@tech-res.com</p> <p>To confirm that the AdEERS report was received by fax.</p>	<p>By mail: Send the original signed copy of the completed AdEERS report to ACRIN Headquarters: American College of Radiology Imaging Network Attn: ACRIN AE/SAE Coordinator 1818 Market Street, Suite 1600 Philadelphia, PA 19103</p>	

NOTE: If an IND is held by a pharmaceutical sponsor, the protocol will define additional reporting requirements.

4.7 Phase 2 and Phase 3 Studies Using Investigational Device(s)

The protocol will define expedited AE reporting requirements in part with the device sponsor. Sites will be provided with training for reporting requirements. Under these circumstances, the manufacturer will complete a mandatory FDA 3500A or electronic equivalent approved by the FDA. Refer to the protocol for specific guidelines.

5.0 Exceptions to Adverse Event Reporting

5.1 Adjuvant Systemic Therapy

Protocols may specify that patients may be treated with adjuvant systemic therapy (chemotherapy, hormonal, etc.) following or in addition to the study intervention. If adjuvant systemic therapy consists of a commercial agent, all expedited reporting must be completed using AdEERS. If a patient receives adjuvant systemic therapy as an investigational agent (through another protocol), the AE reporting guidelines for that specific protocol should be followed.

Expected Adverse Events: Expected AEs will not be listed in the protocol for possible adjuvant systemic therapy. Expected AEs reported as Grade 1, 2, 3 or 4 regardless of attribution* to the adjuvant systemic therapy should not be reported on the AE case report form(s) for the study. Expedited reporting is required for any expected AE that is reported as fatal (Grade 5) within 30 days of the last dose of the adjuvant systemic therapy regardless of attribution.*

Unexpected Adverse Events: Unexpected AEs related to adjuvant systemic therapy that are Grade 1, 2 or 3 do not require expedited reporting regardless of attribution.* An expedited report is required for all unexpected AEs that are Grade 4 regardless of attribution.* Expedited reporting is also required for any unexpected AE that is reported as fatal (Grade 5) within 30 days of the last dose of the adjuvant systemic therapy regardless of attribution.*

NOTE: ACRIN trials will provide study-specific reporting requirements in each protocol which supersede the general AE reporting requirements.

5.2 Adjuvant Radiation Therapy

Protocols may specify that patients may receive adjuvant radiation therapy either as part of the study or outside of the protocol following or in addition to the study intervention. If a patient receives adjuvant radiation therapy as an investigational agent (through another protocol), the adverse event AE reporting guidelines for that specific protocol should be followed.

Expected Adverse Events: Expected AEs will not be listed in the protocol for adjuvant radiation therapy. Expected AEs reported as Grade 1, 2, 3 or 4 regardless of attribution* to the adjuvant radiation therapy should not be reported on the AE case report form(s) for the study. Expedited reporting is required for any expected AE that is reported as fatal (Grade 5) within 30 days of the last dose of the adjuvant radiation therapy regardless of attribution.*

* Unless it is otherwise specified in the protocol.

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Unexpected Adverse Events: Unexpected AEs related to adjuvant radiation therapy that are Grade 1, 2 or 3 do not require expedited reporting regardless of attribution.* An expedited report is required for all unexpected events that are Grade 4 regardless of attribution.* Expedited reporting is also required for any unexpected adverse event that is reported as fatal (Grade 5) within 30 days of the last dose of the adjuvant radiation therapy regardless of attribution .*

NOTE: ACRIN trials will provide study-specific reporting requirements in each protocol which supersedes the general AE reporting requirements.

* Unless it is otherwise specified in the protocol.

6.0 Using AdEERS

The goal of AdEERS is to increase efficiency, completeness and accuracy of safety monitoring to the FDA. All report sections identified as mandatory must be completed before CTEP will accept and process the report.

Assistance in using the AdEERS program is available through the NCI CTEP via TRI (Technical Resources International, Inc.). A TRI representative can assist you with the completion of the AdEERS report through the AdEERSMD help line at **301-897-7497**. Computer based training is also available at http://ctep.cancer.gov/reporting/AdEERS_CBT_v3/welcome.html

6.1 Adverse Event Expedited Report – Single Agent Template

This template is used to report an AE for studies using only a surgical procedure and/or only one NCI-sponsored investigational agent.

6.2 Adverse Event Expedited Report – Multiple Agent Template

This template is used to report an AE for studies using more than one NCI-sponsored investigational agent. The template has additional space available to record up to four agents associated with the study.

6.3 Report Sections and Information Components

The AdEERS expedited report templates contain 18 report sections that are categorized as **MANDATORY** OR **Requisite**. **MANDATORY** sections are noted by the section title appearing in capital letters. **Requisite** sections are noted by the section title appearing in italics in the table on page 30.

There are seven **MANDATORY** sections that **MUST** be completed in order for the report to be properly processed. These sections must be completed regardless of whether an AE or Death Unrelated to an AE is being reported. The remaining sections of the report may be either **MANDATORY** or **Requisite** depending on the type of report or if the information is available.

NOTE: For imaging studies not employing the use of an investigational agent, **Section 4** - Course Information and **Section 10** - Protocol Agent will remain blank. **DO NOT** attempt to submit a completed form electronically through the AdEERS web site, as the system currently will not permit electronic submission of reports without the completion of Course Information and Protocol Agent sections.

All date information requires a four-digit year entry. The majority of date fields require a MM/DD/YYYY format. However, some date fields will accept “Month and Year” only.

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SECTION TITLE	MANDATORY			Requisite
	Mandatory when reporting an AE	Mandatory when reporting an <u>Imaging only AE</u>	Mandatory when reporting a <u>Death unrelated to an AE</u>	Required if relevant information is available
PROTOCOL INFORMATION	√	√	√	
REPORTER INFORMATION	√	√	√	
PATIENT INFORMATION	√	√	√	
COURSE INFORMATION	√	√	√	
DESCRIPTION OF EVENT	√	√	√	
DEATH UNRELATED TO AE	√	√	√	
PRIOR THERAPIES	√	√	√	
<i>Pre-Existing Conditions</i>		√		√
<i>Site(s) of Metastatic Disease</i>				√
PROTOCOL AGENT	√	√	√	
<i>Concomitant Medications</i>				√
<i>Other Contributing Cause(s)</i>				√
ADVERSE EVENT (CTC)	√			
ATTRIBUTION FOR AE	√	√		
<i>Abnormal /Normal Lab Results</i>				√
<i>Lab: Microbiology</i>				√
<i>Additional Information Attached</i>				√
Submitter Signature	√	√	√	√

7.0 Routine Adverse Event Reporting

7.1 Expected Adverse Event Reporting Through Case Report Form

Expected AEs listed in the protocol will be reported using the appropriate AE case report forms provided for the study. The protocol will define the timeframe for reporting.

7.2 Unexpected Adverse Event Reporting Through Case Report Form

All unexpected AEs regardless of severity or attribution will be reported (unless otherwise specified in the protocol) using the appropriate AE case report form provided for the study.

NOTE: ACRIN trials will provide study-specific reporting requirements in each protocol which, if differing, supersede the general AE reporting requirements presented in this manual.

7.3 CDUS Reporting

Currently ACRIN is required to use only the abbreviated CDUS report system for both Phase 2 and Phase 3 studies. CDUS reports are submitted to CTEP quarterly on January 31, April 30, July 31, and October 31. CDUS is not a substitute for submission of expedited reports. All AEs that require expedited reporting should be submitted as outlined previously.

Appendix

Additional Resources

- **NCI Reporting Guidelines**

<http://ctep.info.nih.gov/reporting/index.html>

- **AdEERS Computer Based Training:**

http://ctep.cancer.gov/reporting/AdEERS_CBT_v3/welcome.html

- **AdEERS Resources:**

<http://ctep.info.nih.gov/reporting/adeers.html>

- **AdEERS Single Agent Report:**

http://ctep.cancer.gov/forms/34-AdEERSv4_SAT.pdf

- **AdEERS Multiple Agent Report:**

http://ctep.cancer.gov/forms/34-AdEERS_v3-0_MAT_11-21-00.pdf



Adverse Event Expedited Report – Single Agent v4.0

INSTRUCTIONS: Use this form to submit an Expedited Report for an Adverse Event (AE) or Death Unrelated to an Adverse Event for NCI clinical trials using one investigational agent sponsored under an NCI IND. Refer to the protocol to determine if NCI IND agents are utilized on the study and how to submit the Expedited Report. **Use this form only when it is impossible to access the Adverse Event Expedited Reporting System (AdEERS) Web application.** The AdEERS Web application can be accessed at [https://webapps.ctep.nci.nih.gov/openapps/plsql/gadeers_main\\$.startup](https://webapps.ctep.nci.nih.gov/openapps/plsql/gadeers_main$.startup).

This form must be completed using the **AdEERS Template Instructions** available from the NCI CTEP Help Desk by phone at (301) 840-8202 or by fax at (301) 948-2242. Information components followed by "1," "LOV," "LOV/FT," or "CTC" must be entered using the special instructions below. Please see the **AdEERS Template Instructions** for a complete description of all components and instructions developed for this template.

- 1** Date information must be entered in MM/DD/YYYY format except where "MM/YYYY Only" (month and year only) instruction is given.
- LOV** Information must be entered using standardized values from the AdEERS List of Values (LOV) document available from the AdEERS Web site.
- LOV/FT** Information must be entered using the AdEERS LOV or, if an appropriate value cannot be found, using Free Text (values other than those listed in the LOV).
- CTC** Adverse Events are to be reported using the terminology and criteria of the NCI Common Toxicity Criteria (CTC), Version 2.0 (publish date April 30, 1999).

COMPLETING THE REPORT:

1. Complete all **MANDATORY COMPONENTS** in **MANDATORY SECTIONS**. Complete all *Requisite Components* in **MANDATORY SECTIONS** if relevant to the patient.
2. Determine which *Requisite Sections* apply to the patient and complete the **MANDATORY COMPONENTS** (if any) and *Requisite Components* if relevant to the patient.
3. If additional space is required to complete a report section, copy the page where the section appears, complete your entries, and attach to the final report.
4. Complete the form using black or blue ink and send to the Investigational Drug Branch (IDB), P.O. Box 30012, Bethesda, MD 20824 or fax to 301-230-0159.

1. PROTOCOL INFORMATION – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

NCI PROTOCOL NUMBER _____	IS THIS AN AMENDMENT TO A PREVIOUSLY SUBMITTED REPORT? <input type="checkbox"/> YES <input type="checkbox"/> NO	IF YES, CHECK AMENDMENT NUMBER: <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3	INITIAL EXPEDITED REPORT TICKET NUMBER (AMENDMENTS ONLY) _____
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PROTOCOL TITLE (Continue below)

2. REPORTER INFORMATION – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

REPORT DATE ¹ _____	LAST NAME _____	FIRST NAME _____	PHONE _____	FAX _____	E-MAIL _____
REPORTER _____					
PHYSICIAN INFORMATION (Physician to be consulted for questions) _____					

Fax is a requisite component for PHYSICIAN INFORMATION

3. PATIENT INFORMATION – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

A **PATIENT ID** is a unique identification code associated with each patient entered in the trial.

PATIENT ID _____	PATIENT'S INSTITUTION NAME, CITY, AND STATE (OR INSTITUTION CODE – Institution where patient is registered on the protocol or is currently being treated, see http://ctep.cancer.gov/guidelines/codes.html) _____
-------------------------	---

BIRTH DATE (MM/YYYY Only) _____	RACE ^{LOV} _____	GENDER ^{LOV} _____	HEIGHT (cm) _____	WEIGHT (kg) _____	Baseline Performance Status at Initiation of Protocol – ECOG/Zubrod Scale ^{LOV} _____
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DISEASE NAME ^{LOV} _____	<i>Disease Name Not Listed (Enter a specific disease name when "Solid Tumor NOS" or "Hematologic unspecified" is entered in the DISEASE NAME component)</i>
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PRIMARY SITE OF DISEASE ^{LOV} _____	<i>Other Primary Site of Disease (Enter only when an appropriate primary site is not found in the LOV)</i>
---	--

IS DATE OF INITIAL DIAGNOSIS KNOWN: YES NO **IF YES, ENTER THE DATE OF INITIAL DIAGNOSIS (MM/YYYY Only):** _____

4. COURSE INFORMATION – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

*A Treatment Assignment Code (TAC) is a unique identification code associated with each arm or dose level of the protocol.
Example: Drug ###mg / m2 IV over X hr D1-3 / every 3 weeks)*

Treatment Assignment Code (TAC)

If the appropriate TAC is unavailable from the LOV or is unknown, items A through D (below) are mandatory for the treatment arm or dose level.

A. Agent Name ^{LOV} B. Dose C. Administration Route ^{LOV} D. Duration and Schedule ^{LOV}

START DATE OF FIRST COURSE ¹ START DATE OF COURSE ASSOCIATED WITH EXPEDITED REPORT ¹ START DATE OF PRIMARY AE ¹

End Date of AE ¹ COURSE NUMBER ON WHICH AE OCCURRED TOTAL NUMBER OF COURSES TO DATE

WAS AN INVESTIGATIONAL AGENT(S) ADMINISTERED ON THIS PROTOCOL? YES NO

CROSSOVER STUDIES

The following information is required if this report is associated with a Crossover Study: a) Enter the date the Initial Crossover course started in the START DATE OF FIRST COURSE field (Section 4), b) Check YES to WAS AN INVESTIGATIONAL AGENT(S) ADMINISTERED ON THIS PROTOCOL? (Section 4), c) Enter the date the Investigational agent was last administered in the DATE LAST ADMINISTERED field (Section 10), and d) Enter the dose administered for the course in the TOTAL DOSE ADMINISTERED THIS COURSE field (Section 10), zero (0) is acceptable if the actual dose is unknown.

5. DESCRIPTION OF EVENT – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

DESCRIPTION AND TREATMENT OF EVENT(S) (Continue below)

HAS PATIENT BEEN RETREATED (TO DATE)? YES NO

PRESENT STATUS ^{LOV} (If you record Fatal/Death or Recovered/Resolved with or without Sequelae as PRESENT STATUS, then Date of Recovery or Death [see right] is mandatory) Date of Recovery or Death ¹

WAS PATIENT REMOVED FROM PROTOCOL TREATMENT (TO DATE)? YES NO
IF YES, ENTER THE Date Removed from Protocol Treatment (see right) Date Removed from Protocol Treatment ¹

6. DEATH UNRELATED TO ADVERSE EVENT – MANDATORY ONLY IF DEATH IS UNRELATED TO AN AE

Sections 1, 2, 3, 4, 5, 6, 7, and 10 are mandatory when reporting a death caused by suicide, accident, progressive disease, etc.

CAUSE OF DEATH ^{LOV} (If you record Progressive Disease as the CAUSE OF DEATH, then PRIMARY ORGAN SYSTEM FAILURE CAUSING DEATH [see right] is mandatory) PRIMARY ORGAN SYSTEM FAILURE CAUSING DEATH ^{LOV}

7. PRIOR THERAPIES – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

THERAPY ^{LOV} (FOR THE PRIMARY DISEASE) (If you record any of the following as THERAPY, then PRIOR THERAPY AGENT NAME(S) [In column 6] is mandatory: bone marrow transplant, chemotherapy [NOS], chemotherapy [single or multiple agent systemic], hormonal therapy, or immunotherapy)	THERAPY START DATE (if known) (MM/YYYY only)	Therapy End Date (MM/YYYY only)	Comments (Enter additional therapies, prior therapy for diseases other than primary disease, or agents not included in LOV, if needed)	PRIOR THERAPY AGENT NAME(S) ^{LOV} (See note in THERAPY column)
--	--	---------------------------------	---	--

8. Pre-Existing Condition(s) – This section is required if the patient has Pre-Existing Conditions

Identify any medical condition(s) the patient experienced prior to receiving current protocol therapy.

CONDITION A ^{LOV} CONDITION B ^{LOV} Pre-Existing Condition Not Listed (Enter only when an appropriate condition is not found in the LOV)

9. Site(s) of Metastatic Disease – This section is required if the patient has Sites of Metastatic Disease

SITE A ^{LOV} SITE B ^{LOV} Sites of Metastatic Disease Not Listed (Enter only when an appropriate site is not found in the LOV)

10. PROTOCOL AGENT – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

AGENT NAME ^{LOV}	DATE LAST ADMINISTERED ¹ (This is mandatory for crossover studies if an investigational agent was administered at any time, see Section 4)
TOTAL DOSE ADMINISTERED THIS COURSE (Amount of agent given for current dose or cycle, this is not total dose given to date)	UNIT OF MEASURE ^{LOV}

Comments _____

Agent Adjustment ^{LOV} _____ Was administration delayed? Yes No If yes, complete Duration Delay below

Duration Delay _____ sec min hrs days
 (Enter duration length and check Unit of Measure)

CROSSOVER STUDIES – Instruction is provided in Section 4 regarding required information for reports associated with Crossover Studies.

11. Concomitant Medication(s) – This section is required if any non-protocol medication may have contributed to the event(s)

CONCOMITANT MEDICATION A _____ CONCOMITANT MEDICATION B _____

CONCOMITANT MEDICATION C _____ CONCOMITANT MEDICATION D _____

12. Other Contributing Cause(s) – This section is required if Other Causes may have contributed to the Adverse Event

OTHER CONTRIBUTING CAUSE A _____ OTHER CONTRIBUTING CAUSE B _____

OTHER CONTRIBUTING CAUSE C _____ OTHER CONTRIBUTING CAUSE D _____

13. ADVERSE EVENTS (CTC) – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS EXCEPT DEATH UNRELATED TO AE

CATEGORY ^{CTC}	ADVERSE EVENT ^{CTC}	If AE is other, Specify: (If an appropriate AE term cannot be identified in the CTC, identify the CTC CATEGORY and provide AE information in this column)	GRADE ^{CTC} (If you record a GRADE 3 or higher, Hospitalization or Prolongation of Hospitalization [In column 5] is mandatory)	Hospitalization or Prolongation of Hospitalization (See note in GRADE column)	Comments (Enter other relevant information in this column)
AE A:	_____	_____	_____	<input type="checkbox"/> Yes <input type="checkbox"/> No	_____
AE B:	_____	_____	_____	<input type="checkbox"/> Yes <input type="checkbox"/> No	_____
AE C:	_____	_____	_____	<input type="checkbox"/> Yes <input type="checkbox"/> No	_____

14. ATTRIBUTION FOR ADVERSE EVENT – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS EXCEPT DEATH UNRELATED TO AE

Attribution is the determination whether an AE is related to a medical treatment or procedure. Evaluate each AE the patient experiences to determine what might have caused the event or what interventions or conditions the event might have been attributed to.

IMPORTANT: Every AdEERS report that includes Adverse Events must include for each Adverse Event at least one attribution of Possible, Probable, or Definite to either the Agent, the Disease, Other Causes, or Concomitant Medications. NCI will not accept reports without at least one attribution of Possible, Probable, or Definite to either the Agent, the Disease, Other Causes, or Concomitant Medications for each Adverse Event.

Write the AE term(s) you used in Section 13 in the heading area of columns 2, 3, and 4 (found on page 4). Complete the AGENT NAME, DISEASE, Concomitant Medication and/or Other Contributing Causes information in column 1 using the same information you provided in Sections 10, 3, 11, and 12. Circle the ATTRIBUTION CODE in each column for each AE based on its relationship to the AGENT NAME, DISEASE, Concomitant Medication and/or Other Contributing Causes information provided in column 1. An example is provided below.

Example	Anorexia					Bilirubin					Pain-Other				
	ADVERSE EVENT ^{CTC} (AE A from Section 13)					ADVERSE EVENT ^{CTC} (AE B from Section 13)					ADVERSE EVENT ^{CTC} (AE C from Section 13)				
Drug 1 <small>AGENT NAME ^{LOV} (from Section 10)</small>	1	2	③	4	5	1	2	③	4	5	1	②	3	4	5

ATTRIBUTION CODES are defined as:

- 1 Unrelated - The Adverse Event is clearly NOT related to the investigational agent, disease, concomitant medication, or other contributing cause.
- 2 Unlikely - The Adverse Event is doubtfully related to the investigational agent, disease, concomitant medication, or other contributing cause.
- 3 Possible - The Adverse Event may be related to the investigational agent, disease, concomitant medication, or other contributing cause.
- 4 Probable - The Adverse Event is likely related to the investigational agent, disease, concomitant medication, or other contributing cause.
- 5 Definite - The Adverse Event is clearly related to the investigational agent, disease, concomitant medication, or other contributing cause.

This section continues on page 4.

14. ATTRIBUTION FOR ADVERSE EVENT (Continued)

	ADVERSE EVENT ^{CTC} (AE A from Section 13)					ADVERSE EVENT ^{CTC} (AE B from Section 13)					ADVERSE EVENT ^{CTC} (AE C from Section 13)				
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
AGENT NAME ^{LOV} (from Section 10)															
DISEASE NAME ^{LOV} (from Section 3)															
Concomitant Medication (A from Section 11)															
Concomitant Medication (B from Section 11)															
Concomitant Medication (C from Section 11)															
Concomitant Medication (D from Section 11)															
Other Contributing Causes (A from Section 12)															
Other Contributing Causes (B from Section 12)															

15. Abnormal and Relevant Normal Laboratory Results – This section is required if Laboratory Results are relevant to the report
 This section is not required if Microbiology information is provided in Section 16.

Lab ^{LOV/FT}	Baseline			Nadir/Worst		Recovery/Latest	
	Date ¹	Value	Unit of Measure ^{LOV}	Date ¹	Value	Date ¹	Value
Lab A:							
Lab B:							
Lab C:							

16. Lab: Microbiology – This section is required for reporting infections
 Do not complete Section 15 if Microbiology information is provided below.

Infection Type: Bacterial Fungal Viral

Site _____ Date ¹ _____ Infectious Agent _____

17. Additional Information Attached – This section is required if relevant to the report
 Check those you have attached for submission with this report.

- Autopsy Report Consults Discharge Summary Flow Sheets/CRFs Laboratory Reports Other information, specify: _____
- Pathology Report Progress Notes Radiology Reports Referral Letters Summary Report Sent to IRB

18. Submitter Signature – This section required if submitter is someone other than reporter (from Section 2)

I certify that this Expedited Report has been reviewed and approved by a physician or the medically certified designee responsible for the care of this patient.

LAST NAME _____ FIRST NAME _____ PHONE _____ Fax _____ E-MAIL _____

SUBMITTER SIGNATURE _____ SIGNATURE DATE ¹ _____



Adverse Event Expedited Report – Multiple Agents

INSTRUCTIONS: Use this form to submit an Expedited Report for an Adverse Event (AE) or Death Unrelated to an Adverse Event for NCI clinical trials using more than one investigational agent sponsored under an NCI IND. Refer to the protocol to determine if NCI IND agents are utilized on the study and how to submit the Expedited Report. **Use this form only when it is impossible to access the Adverse Event Expedited Reporting System (AdEERS) Web application.** The AdEERS Web application can be accessed at <http://ctep.info.nih.gov/AdEERS/default.htm>.

REPORT SECTIONS: The template includes 18 report sections that are categorized as either MANDATORY or *requisite*. MANDATORY SECTION titles (see a through c, below) appear in CAPITAL LETTERS and must be completed for proper assessment of the report. *Requisite Section* titles (see d, below) appear in *italic letters* and must be completed if relevant to the patient for whom the report is being filed. Each section title is followed by a description of when they are MANDATORY and/or *requisite*:

- a. MANDATORY when submitting all Expedited Reports (SECTIONS 1, 2, 3, 4, 5, 7, AND 10)
- b. MANDATORY when submitting all Expedited Reports except for a Death Unrelated to an AE (SECTIONS 13 AND 14)
- c. MANDATORY when submitting an Expedited Report for a Death Unrelated to an AE (SECTION 6)
- d. *Requisite* if the report section is relevant to the patient for whom the report is being filed (*sections 8, 9, 11, 12, 15 or 16, 17, and 18*)

INFORMATION COMPONENTS: Within each report section is a set of information components that are also categorized as MANDATORY or *requisite*. The same formatting is used to identify MANDATORY COMPONENTS and *Requisite Components*. Note: *Requisite Sections* (type d, above) often include MANDATORY COMPONENTS that must be completed if relevant to the patient. Information components followed by "1," "LOV," "LOV/FT," or "CTC" must be entered using the special instructions below:

- 1 Date information must be entered in MM/DD/YYYY format except where "Month/Year Only" instruction is given.
- LOV Information must be entered using standardized values from the AdEERS List of Values (LOV) document available at <http://ctep.info.nih.gov/InfoForms/default.htm>.
- LOV/FT Information must be entered using the AdEERS LOV or, if an appropriate value cannot be found, entered using Free Text (a value other than those listed in the AdEERS LOV). Only five components allow Free Text entry, all others must be entered using values from the LOVs.
- CTC Adverse Events are to be reported using the terminology and criteria of the NCI Common Toxicity Criteria (CTC), Version 2.0 (publish date April 30, 1999). The List of Values for CATEGORY and ADVERSE EVENT are the same values as listed in the CTC. The most comprehensive approach to identify the appropriate CTC CATEGORY and ADVERSE EVENT term is to use the Index Search in the Interactive CTC Application available at <http://ctep.info.nih.gov/CTC3/default.htm>.

COMPLETING THE REPORT:

1. Complete all MANDATORY COMPONENTS in MANDATORY SECTIONS. Complete all *Requisite Components* in MANDATORY SECTIONS if relevant to the patient.
2. Determine which *Requisite Sections* apply to the patient and complete the MANDATORY COMPONENTS (if any) and *Requisite Components* if relevant to the patient.
3. If additional space is required to complete a report section, copy the page where the section appears, complete your entries, and attach to the final report.
4. Complete the form using black or blue ink and send to the Investigational Drug Branch (IDB), P.O. Box 30012, Bethesda, Maryland 20824 or fax to 301-230-0159.

Other References available from the AdEERS main page (<http://ctep.info.nih.gov/AdEERS/default.htm>) or the NCI CTEP Help Desk: NCI Guidelines: Expedited Adverse Event Reporting Requirements for NCI Investigational Agents (both the September 17, 1999 and the Effective Date: January 01, 2001 versions), AdEERS Templates Instructions, AdEERS Templates List of Values, AdEERS Application v3.0, AdEERS Application v3.0 Training Reference, and AdEERS Computer Based Training (CBT) v2.0.

1. PROTOCOL INFORMATION – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

NCI PROTOCOL NUMBER	IS THIS AN AMENDMENT TO A PREVIOUSLY SUBMITTED REPORT? <input type="checkbox"/> YES <input type="checkbox"/> NO	IF YES, CHECK AMENDMENT NUMBER: <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3	INITIAL EXPEDITED REPORT TICKET NUMBER (AMENDMENTS ONLY)
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PROTOCOL TITLE (Continue below, if needed)

2. REPORTER INFORMATION – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

REPORT DATE ¹	LAST NAME	FIRST NAME	PHONE	<i>Fax</i>	E-MAIL
REPORTER					
OTHER PHYSICIAN (Complete when a physician other than the PI is to be consulted for questions)					

PATIENT'S INSTITUTION NAME, CITY, AND STATE (OR INSTITUTION CODE – see <http://ctep.info.nih.gov/CtepInformatics/Instcode.htm>) (Institution where patient is registered on protocol or currently being treated)

3. PATIENT INFORMATION – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

A PATIENT ID is a unique identification code associated with each patient entered in the trial.

PATIENT ID	BIRTH DATE (Month/Year Only)	RACE ^{LOV}
GENDER ^{LOV}	HEIGHT (cm)	WEIGHT (kg)

Baseline Performance Status at Initiation of Protocol – ECOG/Zubrod Scale ^{LOV}

DISEASE NAME ^{LOV}	PRIMARY SITE OF DISEASE ^{LOV/FT}
IS DATE OF INITIAL DIAGNOSIS KNOWN: <input type="checkbox"/> YES <input type="checkbox"/> NO IF YES, ENTER THE DATE OF INITIAL DIAGNOSIS (Month/Year Only): _____	

4. COURSE INFORMATION – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

A Treatment Assignment Code (TAC) is a unique identification code associated with each arm or dose level of the protocol.

Example: Drug 1 ###mg / m2 IV over X hr D1-3 / every 3 weeks

Treatment Assignment Code

If the Treatment Assignment Code is unknown, items A through D (below) are mandatory

A. Agent Name(s) ^{LOV}	B. Dose	C. Administration Route ^{LOV}	D. Schedule and Treatment Arm or Dose Level ^{LOV}

START DATE OF FIRST COURSE ¹	START DATE OF COURSE ASSOCIATED WITH EXPEDITED REPORT ¹	START DATE OF PRIMARY AE ¹
End Date of AE ¹	COURSE NUMBER ON WHICH AE OCCURRED	TOTAL NUMBER OF COURSES TO DATE

5. DESCRIPTION OF EVENT – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

DESCRIPTION OF REACTION AND TEMPORAL RELATIONSHIP TO INVESTIGATIONAL AGENT ADMINISTRATION (Continue below, if needed)

HAS PATIENT BEEN RETREATED (TO DATE)? YES NO

PRESENT STATUS ^{LOV} (If you record Fatal/Death or Recovered/Resolved with or without Sequelae as PRESENT STATUS, then Date of Recovery or Death [see right] is mandatory.) _____ Date of Recovery or Death ¹

WAS PATIENT REMOVED FROM PROTOCOL TREATMENT (TO DATE)? YES NO IF YES, ENTER THE Date Removed from Protocol Treatment (see right) _____ Date Removed from Protocol Treatment ¹

6. DEATH UNRELATED TO ADVERSE EVENT – MANDATORY ONLY IF DEATH IS UNRELATED TO AN AE

Sections 1, 2, 3, 4, 5, 6, 7 and 10 are mandatory when reporting a death caused by suicide, accident, progressive disease, etc.

CAUSE OF DEATH ^{LOV} (If you record Progressive Disease as the CAUSE OF DEATH, then PRIMARY ORGAN SYSTEM FAILURE CAUSING DEATH [see right] is mandatory.)	PRIMARY ORGAN SYSTEM FAILURE CAUSING DEATH ^{LOV}
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7. PRIOR THERAPIES – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

THERAPY ^{LOV/FT} (FOR THE PRIMARY DISEASE) (If you record any of the following as THERAPY, then PRIOR THERAPY AGENT NAME [in column 4] is mandatory: bone marrow transplant, chemotherapy [NOS], chemotherapy [single or multiple agent systemic], hormonal therapy, or immunotherapy)	THERAPY START DATE (If known) (Month/Year only)	Therapy End Date (Month/Year only)	Comments (Enter additional therapies, prior therapy for diseases other than primary disease, or agents not included in LOV, if needed)	PRIOR THERAPY AGENT NAME(S) ^{LOV} (See note in THERAPY column)

8. Pre-Existing Condition(s) – This section is required if the patient has Pre-Existing Conditions

Identify any medical condition(s) the patient experienced prior to receiving current protocol therapy.

CONDITION A ^{LOV/FT}:

CONDITION B ^{LOV/FT}:

9. Site(s) of Metastatic Disease – This section is required if the patient has Sites of Metastatic Disease

SITE A ^{LOV/FT}:

SITE B ^{LOV/FT}:

10. PROTOCOL AGENT(S) – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS

AGENT NAME(S) ^{LOV}

TOTAL DOSE ADMINISTERED THIS COURSE (Amount of agent given for current dose or cycle, this is not total dose given to date)

Comments

Agent Adjustment ^{LOV}

Was administration delayed?

Duration Delay (Enter duration length and check Unit of Measure)

AGENT NAME A ^{LOV}	AGENT NAME B ^{LOV}	AGENT NAME C ^{LOV}	AGENT NAME D ^{LOV}
UNIT OF MEASURE ^{LOV}	UNIT OF MEASURE ^{LOV}	UNIT OF MEASURE ^{LOV}	UNIT OF MEASURE ^{LOV}
<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, complete Delay Duration below	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, complete Delay Duration below	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, complete Delay Duration below	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, complete Delay Duration below
<input type="checkbox"/> sec <input type="checkbox"/> min <input type="checkbox"/> hrs <input type="checkbox"/> days	<input type="checkbox"/> sec <input type="checkbox"/> min <input type="checkbox"/> hrs <input type="checkbox"/> days	<input type="checkbox"/> sec <input type="checkbox"/> min <input type="checkbox"/> hrs <input type="checkbox"/> days	<input type="checkbox"/> sec <input type="checkbox"/> min <input type="checkbox"/> hrs <input type="checkbox"/> days

11. Concomitant Medication(s) – This section is required if the patient received Concomitant Medication

CONCOMITANT MEDICATION A:

CONCOMITANT MEDICATION B:

12. Other Contributing Cause(s) – This section is required if Other Causes may have contributed to the Adverse Event

OTHER CONTRIBUTING CAUSE A:

OTHER CONTRIBUTING CAUSE B:

13. ADVERSE EVENTS (CTC) – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS EXCEPT DEATH UNRELATED TO AE

CATEGORY ^{CTC}	ADVERSE EVENT ^{CTC}	If AE is other, Specify: (If an appropriate AE term cannot be identified in the CTC, identify the CTC CATEGORY and provide AE information in this column)	GRADE ^{CTC} (If you record a GRADE 3 or higher, Hospitalization or Prolongation of Hospitalization [in column 5] is mandatory)	Hospitalization or Prolongation of Hospitalization (See note in GRADE column)	Comments (Enter other relevant information in this column)
AE A:				<input type="checkbox"/> Yes <input type="checkbox"/> No	
AE B:				<input type="checkbox"/> Yes <input type="checkbox"/> No	
AE C:				<input type="checkbox"/> Yes <input type="checkbox"/> No	

14. ATTRIBUTION FOR ADVERSE EVENT – THIS SECTION IS MANDATORY FOR ALL EXPEDITED REPORTS EXCEPT DEATH UNRELATED TO AE

Attribution is the determination whether an AE is related to a medical treatment or procedure. Evaluate each AE the patient experiences to determine what might have caused the event or what interventions or conditions the event might have been attributed to.

Write the AE term(s) you used in Section 13 in the heading area of columns 2, 3, and 4 (found on page 4). Complete the AGENT NAME, DISEASE, Concomitant Medication and/or Other Contributing Causes information in column 1 using the same information you provided in Sections 10, 3, 11, and 12. Circle the ATTRIBUTION CODE in each column for each AE based on its relationship to the AGENT NAME, DISEASE, Concomitant Medication and/or Other Contributing Causes information provided in column 1. An example is provided below.

Example	Anorexia					Bilirubin					Pain-Other				
Drug 1	ADVERSE EVENT ^{CTC} (AE A from Section 13)					ADVERSE EVENT ^{CTC} (AE B from Section 13)					ADVERSE EVENT ^{CTC} (AE C from Section 13)				
AGENT NAME ^{LOV} (AGENT NAME A from Section 10)	1	2	③	4	5	1	2	③	4	5	1	②	3	4	5

This section continues on page 4.

14. ATTRIBUTION FOR ADVERSE EVENT (Continued)

ATTRIBUTION CODES are defined as:

- 1 Unrelated - The Adverse Event is clearly NOT related to the investigational agent.
- 2 Unlikely - The Adverse Event is doubtfully related to the investigational agent.
- 3 Possible - The Adverse Event may be related to the investigational agent.
- 4 Probable - The Adverse Event is likely related to the investigational agent.
- 5 Definite - The Adverse Event is clearly related to the investigational agent.

	ADVERSE EVENT ^{CTC} (AE A from Section 13)					ADVERSE EVENT ^{CTC} (AE B from Section 13)					ADVERSE EVENT ^{CTC} (AE C from Section 13)				
	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
AGENT NAME ^{LOV} (AGENT NAME A from Section 10)															
AGENT NAME ^{LOV} (AGENT NAME B from Section 10)															
AGENT NAME ^{LOV} (AGENT NAME C from Section 10)															
AGENT NAME ^{LOV} (AGENT NAME D from Section 10)															
DISEASE NAME ^{LOV} (from Section 3)															
Concomitant Medication (A from Section 11)															
Concomitant Medication (B from Section 11)															
Other Contributing Causes (A from Section 12)															
Other Contributing Causes (B from Section 12)															

15. Abnormal and Relevant Normal Laboratory Results – This section is required if Laboratory Results are relevant to the report

This section is not required if Microbiology information is provided in Section 16.

Lab ^{LOV/FT}	Baseline			Nadir/Worst		Recovery/Latest	
	Date ¹	Value	Unit of Measure ^{LOV}	Date ¹	Value	Date ¹	Value
Lab A:							
Lab B:							
Lab C:							

16. Lab: Microbiology – This section is required for reporting infections

Do not complete Section 15 if Microbiology information is provided below.

Infection Type: Bacterial Fungal Viral

Site _____

Date ¹ _____ Infectious Agent _____

17. Additional Information Attached – This section is required if relevant to the report

Check those you have attached for submission with this report.

- Autopsy Report
- Pathology Report
- Consults
- Progress Notes
- Discharge Summary
- Radiology Reports
- Flow Sheets
- Referral Letters
- Laboratory Reports
- Summary Report Sent to IRB
- Other

18. Submitter Signature – This section required if submitter is someone other than reporter (from section 2)

I certify that this Expedited Report has been reviewed and approved by a physician or the medically certified designee responsible for the care of this patient.

LAST NAME	FIRST NAME	PHONE	Fax	E-MAIL
SUBMITTER SIGNATURE		SIGNATURE DATE ¹		