Adverse Events

Contents

Purpose

This eCRF is an ongoing form to capture all adverse events experienced by the patient regardless of the course.

An adverse event is any unfavorable or unintended sign, including abnormal laboratory findings, symptom or disease having been absent at baseline, or if present at baseline, appears to worsen, that has a temporal association with a medical treatment or procedure regardless of the relationship of the event to the medical treatment or procedure.

All adverse events will be coded using protocol specific version of NCI Common Terminology Criteria for Adverse Events (CTCAE) version. Every attempt to code the adverse event to a term using the standard terminology will be made before selecting the "other" term in a category.

Record all adverse events experienced by the patient, including laboratory abnormalities, regardless of relationship to the study medication.

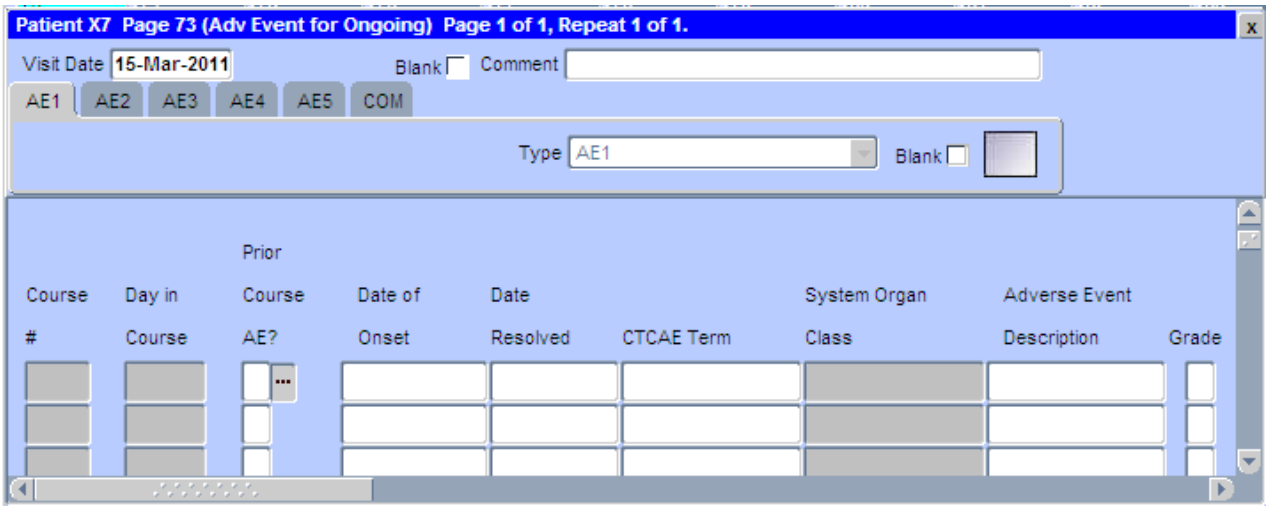
An adverse event entry is composed of both the adverse event term plus the grade. Complete a separate row for each adverse event entry to be recorded using the appropriate adverse event term and the appropriate codes for "grade", "attribution(s)", "serious", "action", "therapy", and "outcome" in the respective column for each event.

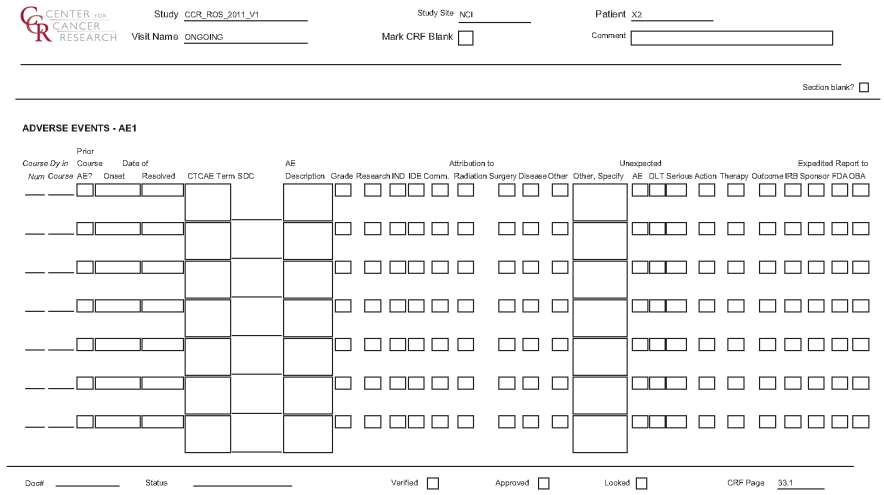
If an adverse event has not been resolved, leave the Resolved Date blank. The Resolved Date can be filled at a later time when the adverse event is considered resolved. Resolution means a change in grade to a higher or lower grade.

If a patient died on study then the death adverse event onset and resolved dates should be the same.

How to record baseline symptoms that change, either improve or worsen:
If a pre-existing condition resolves, it does not need to be reported as an adverse event since it would have been already recorded on the Baseline Symptoms case report form. Enter the resolution date on the corresponding symptom entry on the Baseline Symptoms case report form improves, no entry is made on the AE eCRF. See BL eCRF for instructions.
If a pre-existing condition worsens (i.e.: the grade of the baseline symptom increases), that constitutes an adverse event entry which must be reported in full detail..
If a pre-existing condition improves without a resolution, do not enter as an Adverse Event. When it resolves, enter the resolution date on the corresponding symptom entry on the Baseline Symptoms case report form.

Adverse Events eCRF





The second screen shot is the portion to the right of the Grade The third screen shot is the portion to the right of the DLT

Field Descriptions and Instructions

Field Name	Description / Instructions	Format
Visit Date	The Visit Date is optional on this case report form. Hit the "Tab" key to leave it empty and move to the Prior Course Adverse Event field.	DD-MMM-YYYY
Course # (d)	Indicates the course number that this adverse event started in as derived from the course initiation start date.Late adverse event (For CTMS and CDS monitored studies, it means the adverse event observed after the date of off treatment) have no associated Course #.	5 digits
Day in Course (d)	Indicates the day since the beginning of course that this adverse event started as derived from the course initiation start date.	5 digits

Prior Course Adverse Event (c)	For adverse events that begin on the first day of a course, indicate if related to the prior course by entering: • Y- Related to a prior course • N- Not related to a prior course For an adverse event that begins on the first day of the course PRIOR to any study medications being given, select "Y". For an adverse event that begins on the first day of the course AFTER study medications have been given, select "N". *Note: This field is optional for non-CTEP sponsored studies.*	Use pick list.
Date of Onset (m)	Enter the date of first observation of the adverse event and grade. If a patient died on study then start date and the resolve date for the death AE should be the same.	DD-MMM-YYYY
Date Resolved	Enter the date of resolution of the adverse event and grade. **Leave this field as well as the Outcome field blank if the adverse event is ongoing.** Resolution means a change in grade to a higher or lower grade.e.g, to the normal grade (grade zero) or the return to the baseline symptom grade.	DD-MMM-YYYY
CTC Term (m)	Using the pick list to select a CTCAE (Common Terminology Criteria for Adverse Events) Term. In the absence of a specific adverse event term, choose the "Other" term from the appropriate general category and be sure a meaningful adverse event description is entered in the "adverse event description" field. *Note: This pick list does not show all the CTCAE Terms. User must type in a search criterion and then click on the ellipsis perform the search and display the resulting matched CTCAE Terms. Ex: type % ypo% to list all the terms that include the lower characters 'ypo' somewhere in the CTCAE Term.* *Note: Visit CTEP's CTCAE webpage for latest version.*	Use pick list.
System Organ Class (d)	Broad classification of adverse events based on anatomy and/or pathophysiology. Within each category there is the adverse event term/description. *Note: This field is derived from the selected CTC Term*	40 Characters
Adverse Event Description	Enter a succinct clinical description of the adverse event. *Note: This field is mandatory, unless thelor} CTCAE term is the same as the description (e.g. nausea, diarrhea).* DO NOT enter raw data (i.e.: lab result). Use the term increase or decrease. DO NOT enter the attribution in this field. Use the Attribution field for this purpose.	100 characters(Only 33 characters are reported for CTMS monitored studies.)
Grade (m)	Grade adverse events using Common Terminology Criteria for Adverse Events (CTCAE) version indicated in the protocol. *Note: Note: Some grades are disallowed for some categories in the CTCAE. In the CTCAE tables this will be noted by the use of an em-dash "–".* For example, Hair loss/Alopecia can only be graded as a 1 or 2, so grade 3, 4, and 5 do not exist and will be noted in the table with a "–" verses a description. If the protocol does not use either CTC or CTCAE, grade according to the following general criteria: • 1. Mild - barely noticeable, does not influence functioning • 2. Moderate - makes subject uncomfortable, influences functioning • 3. Severe - severe discomfort, treatment given • 4. Life threatening - immediate risk of death • 5. Fatal - causes death of the patient - **Outcome must be 4-Died**	Use pick list.

Attribution to Research	Evaluate the adverse event's relationship to the subject's participation in the study, including study-related therapy and procedures. Select one of the following codes to record this evaluation: • Adverse Event Unrelated • Adverse Event Related **Note:** In instances where protocols utilize the older 1-5 scale of attribution, please see the guidance and conversion scale below *Note: Attribution to Research must be the same as the highest Attribution to IND, IDE, Commercial, Surgery and Radiation.*	Use pick list.
Attribution to IND (m)	Evaluate the adverse event's relationship to the investigational agent. Select one of the following codes to record this evaluation: • Adverse Event Unrelated • Adverse Event Related **Note:** In instances where protocols utilize the older 1-5 scale of attribution, please see the guidance and conversion scale below	Use pick list.
Attribution to IDE	Evaluate the adverse event's relationship to the investigational device exemption. Select one of the following codes to record this evaluation: • Adverse Event Unrelated • Adverse Event Related **Note:** In instances where protocols utilize the older 1-5 scale of attribution, please see the guidance and conversion scale below *Note: This field is optional for some studies.*	Use pick list.
Attribution to Commercial	Evaluate the adverse event's relationship to the commercial agent. Select one of the following codes to record this evaluation: • Adverse Event Unrelated • Adverse Event Related **Note:** In instances where protocols utilize the older 1-5 scale of attribution, please see the guidance and conversion scale below *Note: This field is optional for some studies*	Use pick list.
Attribution to Radiation	Evaluate the adverse event's relationship to the Radiation therapy. Select one of the following codes to record this evaluation: • Adverse Event Unrelated • Adverse Event Related **Note:** In instances where protocols utilize the older 1-5 scale of attribution, please see the guidance and conversion scale below *Note: This field is optional for some studies.*	Use pick list.
Attribution to Surgery	Evaluate the adverse event's relationship to the surgery. Select one of the following codes to record this evaluation: • Adverse Event Unrelated • Adverse Event Related **Note:** In instances where protocols utilize the older 1-5 scale of attribution, please see the guidance and conversion scale below *Note: This field is optional for some studies.*	Use pick list.

Attribution to Disease	Evaluate the adverse event's relationship to the disease. Select one of the following codes to record this evaluation: • Adverse Event Unrelated • Adverse Event Related **Note:** In instances where protocols utilize the older 1-5 scale of attribution, please see the guidance and conversion scale below *Note: This field is optional for some studies.*	Use pick list.
Attribution to Other	Evaluate the adverse event's relationship to other causes not listed above. Select one of the following codes to record this evaluation: • Adverse Event Unrelated • Adverse Event Related **Note:** In instances where protocols utilize the older 1-5 scale of attribution, please see the guidance and conversion scale below *Note: This field is optional for some studies*	Use pick list.
Other, Specify	Enter an explanation when 'Attribute to Other' is selected.	40 Characters
Unexpected?(m)	Indicate if the adverse event is unexpected as defined by the NCI IRB, by entering: • Y- Yes • N- No	Use pick list.
DLT (m)	Indicate if the adverse event is dose limiting, as defined in the protocol, by entering: • Y- Yes • N- No *Note: Refer to the protocol for the definition of a dose limiting toxicity which should include the grade of the events and the duration of the event.* *Note: Mandatory for Phase I Clinical Trials.*	Use pick list.
Serious (m)	Indicate if the adverse event was a "serious" event by selecting from the following codes, as per the Code of Federal Regulations 21 Part 312. If multiple categories are applicable, select the worst. • 1. Not a Serious Adverse Event • 2. Life-Threatening Event - An adverse event or suspected adverse reaction is considered "life-threatening" if, in the view of either the investigator or sponsor, its occurrence places the patient or subject at immediate risk of death. It does not include an adverse event or suspected adverse reaction that, had it occurred in a more severe form, might have caused death. • 3. Death • 4. Disability - Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions • 5. Hospitalized - Inpatient hospitalization or prolongation of existing hospitalization • 6. Congenital Anomaly - Congenital anomaly/birth defect • 7. Important Medical Event -Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.	Use pick list.

Action (m)	Indicate any changes made to the study regimen in response to the adverse event using the following codes. "Action" refers to the decision to reduce or continue the **investigational medication**. • 1. None • 2. Dose Reduced • 3. Regimen Interrupted • 4. Therapy Discontinued • 5. Interrupted & Reduced If the "Action" for any adverse event is recorded as 2, 3, 4, or 5, the changes in medication administration must be reflected on the Study Medication Administration form. *Note: Interrupted also means therapy was delayed.*	Use pick list.
Therapy (m)	Indicate if additional therapy is required to treat the adverse event. • 1. None • 2. Symptomatic (i.e.: required medications to treat event) • 3. Supportive (i.e.: required medications and/or IV fluids, blood products) • 4. Vigorous Supportive (i.e.: required surgery, intubation) A corresponding entry of the therapy given to treat the adverse event must be recorded on the Concomitant Measures/Medication form.	Use pick list.
Outcome	Select the final status of the patient when the adverse event is considered "resolved". • 1- Recovered - the event (CTCAE term + grade) has resolved to normal or changed to a lower or higher grade. The recovery may be due to the suspension of study treatment or due to concomitant treatments that have ended. • 4- Died - Record outcome of death only for adverse events that resulted in the patient's death. *Note: For ongoing adverse events, leave this and the Resolution Date fields empty.* *Note: For deaths on study, only the event which caused the death should have the outcome coded as a "4." The events that were still continuing at the time of the death would still be ongoing. Do not enter a resolved date, and outcome.*	Use pick list.
Expedited Report to IRB (m)	Indicate if an expedited adverse event report was sent to IRB by entering: • Y- Yes • N- No	Use pick list.
Expedited Report to Sponsor (m)	Indicate if an expedited adverse event report was sent to sponsor by entering: • Y- Yes • N- No For CTEP-sponsored studies, this means that an expedited adverse event report was sent to CTEP via CTEP's Adverse Event Expedited Reporting System (AdEERS). *Note: This field is optional for some studies.*	Use pick list.
Expedited Report to FDA (m)	Indicate if an expedited adverse event report was sent to FDA by entering: • Y- Yes • N- No For studies where the PI holds the IND, this means that the PI has sent an IND Safety Report to FDA. *Note: This field is optional for some studies.*	Use pick list.

Expedited Report to OBA (m)	Indicate if an expedited adverse event report was sent to OBA (Office of Biotechnology Activities) by entering: • Y- Yes • N- No *Note: This field is optional for some studies.*	Use pick list
Expedited Report to Manufacturer (m)	Indicate if an expedited adverse event report was sent to Manufacturer by entering: • Y- Yes • N- No *Note: This field is optional for some studies.*	Use pick list

Regarding the AE attribution fields:

For protocols that utilize the new system of AE attribution values (2 options only: “Adverse Event Unrelated” and “Adverse Event Related”), the following chart can be used to translate values in source documentation from the older system with 5 options to the new system. If the attribution in the source documentation is unclear the Data Manager should leave the attribution field in C3D/Rave blank until the source documentation is updated and clarified

Old System (numbers)	Old System	New System
0	Not Applicable	Adverse Event Unrelated
1	Unrelated	Adverse Event Unrelated
2	Unlikely	Adverse Event Unrelated
3	Possible	Adverse Event Related
4	Probable	Adverse Event Related
5	Definite	Adverse Event Related

Legend: (d) derived field, (m) RDC mandatory, (c) for CTEP reporting only.

Validations

Code	Description	Resolutions
AE01	Date Resolved is before Date of Onset.	Correct either the Date of Onset or Date Resolve.
AE03	Two Adverse Event records have identical values for Date of Onset, CTC Term and Grade.	If duplicate, delete one of the records. If not, manually resolve the discrepancy.
AE04, AE05, AE06, AE07	Two Adverse Event records with the same CTC Term and/or Description have overlapping Date of Onset and Date Resolved ranges.	Correct the Onset and Resolution Dates for the Adverse Events in question or review/correct the CTC term/description
AE08	Adverse Event Description missing for some certain CTC terms that require a clinical description.	Enter the Adverse Event Description or review/correct the CTC term/description.
AE09	A Baseline Symptom exists with the same CTC term and Grade as the Adverse Event and the Baseline Symptom has not been resolved.	Verify the Baseline Symptom resolution date, the Adverse Event onset date, or CTC Term. An Adverse Event with the same grade and CTC Term as the Baseline Symptom is only acceptable when the Baseline Symptom has been resolved and the AE onset date is after the Baseline Symptom resolution date.
AE10	The CTC Term for the ongoing Adverse Event has a specified lab, but a lab record with lab date = AE onset date and lab grade = AE grade does not exist.	Verify that the Averse Event is supported by appropriate lab test result.
AE11	Adverse Event is resolved and there is no supporting lab test result.	Review Adverse Event and related lab test result and their grades. A supporting lab result is one with the same date as the Adverse Event resolution date but with a different grade.

AE14, AE15	The Adverse Event Date of Onset or Date Resolved is in the future.	Correct the Onset or Resolution Dates. No future dates should be recorded.
AE16	The Adverse Event Date of Onset is less than the first Course Start Date.	Correct the Adverse Event Date of Onset to be equal to or after the first Course Start Date.
AE17	The Adverse Event CTC Grade is invalid.	Enter a Grade that is permissible for the CTC Term.
AE19	Resolution date has been entered, but Outcome is not provided or vice-versa.	A Date Resolved must be accompanied by an Outcome and vice-versa.
AE20	Adverse Event is the cause of death but Grade is not 5-Fatal and/or Outcome is not 4-Died and/or Seriousness is not 3-Death.	Change the Adverse Event Grade, Outcome and Seriousness.
AE21	Prior Course checked 'Y', but there is no Course with a Start Date the same as the Adverse Event Onset Date.	Change the Adverse Onset Date, the Prior Course or the Course Initiation Start Date.
AE22	Adverse Event 'Attribute to Other' and 'Other, Specify' are not present together.	Enter 'Other, Specify' if 'Attribute to Other' is associated.
AE23	Adverse Event Attribution to Research is not the same as the highest Attribution to IND, IDE, Commercial, Surgery, and Radiation	Review all Attributions to make sure that Attribution to Research is same as the highest Attribution to IND, IDE, Commercial, Surgery and Radiation.

Derivations

Code	Field Name	Description
AE1002	Course #	Course number is derived based on the course initiation start dates.
AE1003	Day in Course	Number of days since the beginning of the course is derived from the course initiation start date.
AE1004	CTC Category	Broad classification of the CTC Adverse Event Term derived from the pick list selection.