

Serious Adverse Events

Reporting and Updates

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SWOG SAE Team

Contact first with all SWOG SAE questions, including technical support issues.

SAE Email: adr@swog.org

SAE Phone: 210-614-8808, Option 6

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Serious Adverse Events

- SAEs are a subset of all adverse events collected.
- The reporting of SAEs is in addition to, and does not replace, reporting routine adverse events.

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SAE Reporting Criteria Found In:

- 8/22/2024 CTEP Memo (overrides protocol for investigational treatment arms)
- Section 8 of SWOG Protocols
- Section 16 of SWOG Protocols (older protocols only)

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SAE Reporting Table

Example of SAE Reporting Criteria for Investigational Agents

- Step 1: Is the AE serious?
- Step 2: If serious, how quickly does it need to be reported?
- Step 3: If it's been > 30 days since the patient last received investigational study drug, refer to the bottom of the SAE Table.

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SAE Reporting Table

Example of SAE Reporting Criteria for Commercially Available Agents

Attribution	Grade 4		Grade 5 ^a	
	Unexpected	Expected	Unexpected	Expected
Unrelated or Unlikely			CTEP-AERS	CTEP-AERS
Possible, Probable, Definite	CTEP-AERS		CTEP-AERS	CTEP-AERS

Grade 4, Unexpected, and Possibly, Probably, Definitely Related OR Grade 5

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Expectedness

- **Expectedness for Investigational Drugs**
 - Expected = listed as a known risk in the Investigator's Brochure
 - Unexpected = not listed in the Investigator's Brochure
- **Expectedness for Commercial Drugs**
 - Expected = listed as a known toxicity in the Package Insert
 - Unexpected = not listed in the Package Insert

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How to Report an SAE

SAE Reporting is done electronically through CTEP-AERS.

- For older protocols, SAE reporting should be done directly in [CTEP-AERS](#).
- For newer protocols using the Rave/CTEP-AERS integration, the report will be generated through Rave, then completed in CTEP-AERS.

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How to Know if a Trial Uses Rave/CTEP-AERS Integration

www.ctsu.org

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Rave/CTEP-AERS Integration

- [Information on the Rave/CTEP-AERS integration](#)
 - Please contact adr@swog.org with any integration questions/issues
- When utilizing the Rave/CTEP-AERS integration, keep in mind that the system is only loaded with [basic rules](#) for reporting.
- The Rave/CTEP-AERS integration recommendation is just that - a recommendation; it is not a mandate to report.

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Rave Form Adverse Events: Report

#	Adverse Event (Description)	What is the event term (CTCAE v5.0)	Start Date	End Date	Ongoing	Relationship to Study Treatment	Hospitalization (Initial or prolonged)	Life Threatening	Death	Disability or Permanent/Significant Damage	Congestive or Birth Defect	Other Serious (Important taken with Medical Treatment?)	What action was taken with study treatment?	AE Number	SAE report recommended?	Date/Time of Collection
1	Back pain	Back pain (1) Mild pain	20 Oct 2023	20 Oct 2023	Yes	Unrelated	No	No	No	No	No	No	Discontinued	AE56: ED42922856D84E7DB88AF2E878DF834	No*	26 Oct 2023 01:44:31 PM
2	Dyspnea	Dyspnea (3) Shortness of breath at rest, limiting self care, etc.	20 Jan 2022	20 Jan 2022	Yes*	Unrelated	Yes	No*	No*	No*	No*	No*	Drug interrupted	AE11: D8ECAF792CF4E582D30F86078E5653	Yes*	24 Jan 2022 02:18:38 PM

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Rave Form Expedited Reporting Evaluation

- The Expedited Reporting Evaluation form must be run each time changes are made to the AE Report form.
- To run the evaluation, select the checkbox (highlighted here in green), then save the form.
 - If the checkbox does not display, click the pencil icon to run the evaluation.
- A recommended action will display (highlighted here in pink). This is only a recommendation, follow reporting guidelines in the protocol or [8/22/2024 CTEP Memo](#) or consult adr@swog.org.

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Rave Form Expedited Reporting Evaluation

NONE = no SAE report is being recommended by the automated rules engine

Recommended action for report (derived)

☐ An expedited report is NOT recommended. If the investigator believes an expedited report is warranted, use the link below to move to CTEP-AERS to complete the expedited report. (QC19) [View from System \(14 Feb 2015\)](#)

☑ Click this link to complete the safety report

NONE

CREATE = an SAE report is being recommended by the automated rules engine

Recommended action for report (derived)

☑ An expedited report is RECOMMENDED. If the investigator believes an expedited report is not warranted (e.g., per protocol, commercial agreement, etc.), use the Recommended action for report field to return NONE (QC19)

☑ Click this link to complete the safety report

CREATE

AMEND = an amended SAE report is being recommended because new/updated data has been reported on the AE Report form

Recommended action for report

☑ Click this link to complete the safety report

AMEND*

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Expedited Reporting Evaluation Form Tips

- Each time the AE Report form is updated, the Expedited Reporting Evaluation form must be manually run by sending all AEs for evaluation.
- Pop-up blockers must be disabled for the link on the Expedited Reporting Evaluation form to work.
- The CREATE, AMEND, and NONE recommendations are dynamic – they will change based on the current submitted data.
- A link to create or amend a report in CTEP-AERS is found on the Expedited Reporting Evaluation form, regardless of the recommendation. This allows sites to override the recommendations at any time.

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What is the deadline for submitting an SAE report to SWOG?

- Reporting timeframes are found in the SAE reporting tables. SAE tables are found in the [8/22/2024 CTEP Memo](#), Section 8, or Section 16 of the protocol.
- It is important to note that the 'submission due dates' in Rave or in the automated CTEP-AERS emails are not true deadlines; these dates only reflect the date after which CTEP-AERS will automatically delete unsubmitted reports.
- SWOG makes every effort to notify sites if they have a pending report that will soon be deleted, but sites are responsible for reporting within timeframes specified in the protocol or the [8/22/2024 CTEP Memo](#).

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When reporting SAEs in CTEP-AERS, please add the date of discovery into CTEP-AERS Section 3: Describe Event.

Without this date, SWOG may assume the SAE was reported late, and this can lead to major deficiencies during audits.

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SPEER

- SPEER = Specific Protocol Exceptions to Expedited Reporting
- This subset of AEs (SPEER) is a list of events that are protocol-specific exceptions to expedited (SAE) reporting to NCI.
- Report AEs on the SPEER as SAEs only if 1) they exceed the grade noted in parentheses next to the AE in the SPEER and 2) the AE is serious.
- If the protocol uses multiple investigational agents and has an AE listed on different SPEERs, use the lower of the grades to determine if expedited reporting is required.

Adverse Events with Possible Relationship to Nivolumab (CTCAE 5.0 Terms) [see 2009]	Rare but Serious (<3%)	Specific Protocol Exceptions to Expedited Reporting (SPEER)
Likely (>20%)	Likely (≥20%)	Rare but Serious (<3%)
	Eye disorders - Other (optic neuritis, retinopathy)	
	Eye disorders - Other (high myopia, keratitis)	
Livedo		
GASTROINTESTINAL DISORDERS		
Abdominal pain		Abdominal pain (Gr 2)
Colitis ¹	Colonic perforation ²	
Diarrhea		Diarrhea (Gr 2)
Dry mouth		Dry mouth (Gr 2)
	Enterocolitis	
	Gastritis	
	Mucocutis oral	
Nausea		Nausea (Gr 2)
[Pharyngitis] ³		

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SPEER

Reminder that the SPEER column only applies to SAE reporting.

It does not apply to routine AE reporting.

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[Pharyngitis] ³		

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Additional Reporting Requirements

2) Additional expedited reporting requirements

The adverse events listed below also require expedited reporting via CTEP-AERS for this trial for all study arms:

- Infusion reactions \geq Grade 3
- Infections \geq Grade 4
- Cytopenias \geq Grade 4 excluding patients randomized to Arm-2 (high dose melphalan and autologous stem cell transplantation) during the period following stem cell infusion up to day 30 post-transplant.
- HBV Reactivation
- Other malignancies

A subsection that may contain information on events that are exceptions to expedited reporting as well as events that require expedited reporting regardless (AESI)



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Secondary Malignancies

- A secondary malignancy is a **cancer caused by treatment for a previous malignancy** (e.g., treatment with investigational agent/intervention, radiation, or chemotherapy). A secondary malignancy is *not* considered a metastasis of the initial neoplasm.
- SWOG requires all secondary malignancies that occur following treatment with an agent under an IND to be reported via CTEP-AERS. Three options are available to describe the event.
 - Leukemia secondary to oncology chemotherapy (e.g., Acute Myelocytic Leukemia [AML])
 - Myelodysplastic syndrome (MDS)
 - Treatment-related secondary malignancy



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Second Malignancies

- A second malignancy is one **unrelated to the treatment of a prior malignancy** (and is *not* a metastasis from the initial malignancy).
- Second malignancies require **ONLY** routine adverse event reporting unless otherwise specified in the protocol.



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Pregnancy Reporting

Refer to SAE Reporting Section of the Protocol

- Report via [CTEP-AERS](#)
- CTEP Pregnancy Reporting Form must also be completed and uploaded to SDP.
 - [CTEP Pregnancy Reporting Form](#)

CTCAE Terms:

- Pregnancy (Study Participant)
- Pregnancy Loss
- Death Neonatal



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Reporting a Death

Any death while on treatment or within 30 days of the last dose of study agent must be reported as a serious adverse event.

CTCAE Terms:

- Death Attributable to CTCAE Term
- Death, NOS (Only used if the death cannot be attributed to an existing Grade 5 CTCAE term.)
- Sudden Death NOS
- Disease Progression



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Serious Adverse Events - FAQ

I'm not sure if this AE requires SAE reporting, should I submit a report just in case?

- If unsure, the SWOG SAE Team would prefer that you contact us by email at adr@swog.org or phone at 210-614-8808 to confirm the need to report before spending time submitting an unnecessary report.



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Serious Adverse Events - FAQ

When a patient is on a treatment arm with both investigational and commercial agents, should both the investigational and commercial SAE reporting tables be used to determine reporting timeframes?

- No - when a commercial agent is used on the same treatment arm as an investigational agent, the entire combination is then considered an investigational intervention. In this situation, only the investigational SAE reporting table should be used to determine expedited reporting.

Source: National Cancer Institute. (2024). [Adverse Event Reporting Requirements for NCTD \(CTEP and GIP\) and DCF \(INDs and IDEs\)](#) [PDF], Section 5.5.



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SAE Resources

- [SWOG SAE Resource Page](#) – additional resources here
- [SWOG Expedited Reporting Submission Guide](#) – complete guide
- [SWOG SAE Reporting Flowchart](#)
- [8/22/2024 CTEP Memo re: Global Safety Update](#)
- [List of Trials Using Updated SAE Tables](#)
- [NCI Guidelines for Investigators: Adverse Event Reporting Requirements](#)
- [Information on the CTEP-AERS application](#)
- [Information on the Rave/CTEP-AERS integration](#)
- [SWOG SAE Escape Room](#)



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Questions?

Email adr@swog.org



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BREAK

10:25 AM – 10:40 AM



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