Serious Adverse Events

Reporting and Updates

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Quality Assurance Assistant Manager

March 21, 2025

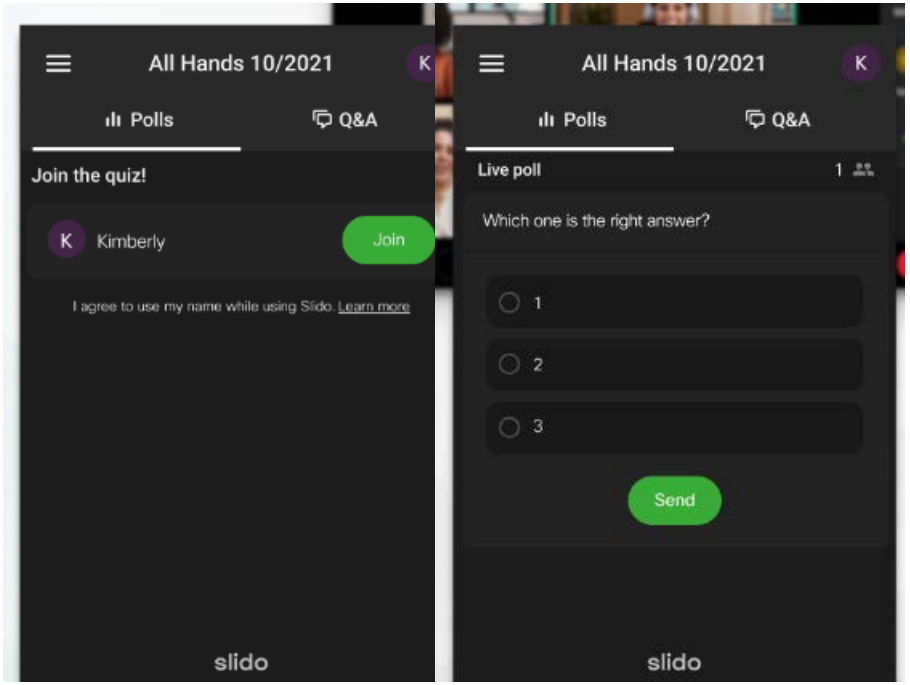
Disclosures:

SWOG plans to offer CEU credit for participation

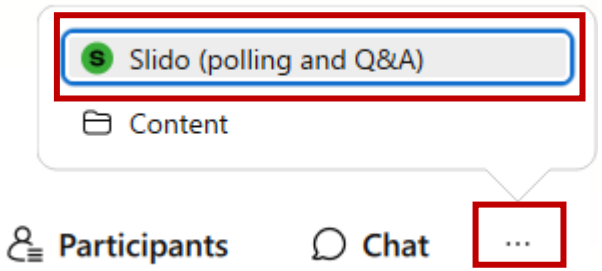
- This activity has been approved by the Maryland Nurses Association to award contact hours. Maryland Nurses Association is accredited as an approver of nursing continuing professional development by the American Nurses Credentialing Center's Commission on Accreditation.
  - No one with the ability to control content of this activity has a relevant financial relationship with an ineligible company.
- **To receive 1 CEU contact hour for webinar attendance, participants must:**
  - Enroll to the QA Webinar March 21, 2025 -Serious Adverse Event Reporting & Updates course prior to the start of the webinar.
  - On 3/21/2025: Individually log in to ExpertusOne via the Serious Adverse Event Reporting & Updates course link that will be posted on the SWOG Quality Assurance Live Webinar Series webpage. The "join" option will become active just prior to the start of the webinar.
  - **Attend the entire educational activity and then complete and submit the post activity-evaluation form via Survey Monkey.** - The link to the post-activity evaluation will be provided via WebEx chat message at the conclusion of the webinar. The evaluation link will not be emailed.
    - CEU certificates will be batch-issued to all attendees who completed the post-activity evaluation approximately one week after the webinar.
- **Site staff who are not able to attend the entire webinar will be able to subsequently complete an online course (via a separate course link that will be published ~2 weeks after the webinar) to obtain 1 CEU contact hour for the same activity.**
- **For questions about SWOG ExpertusOne Course access, contact training@swog.org.**

Polling Questions Through Slido

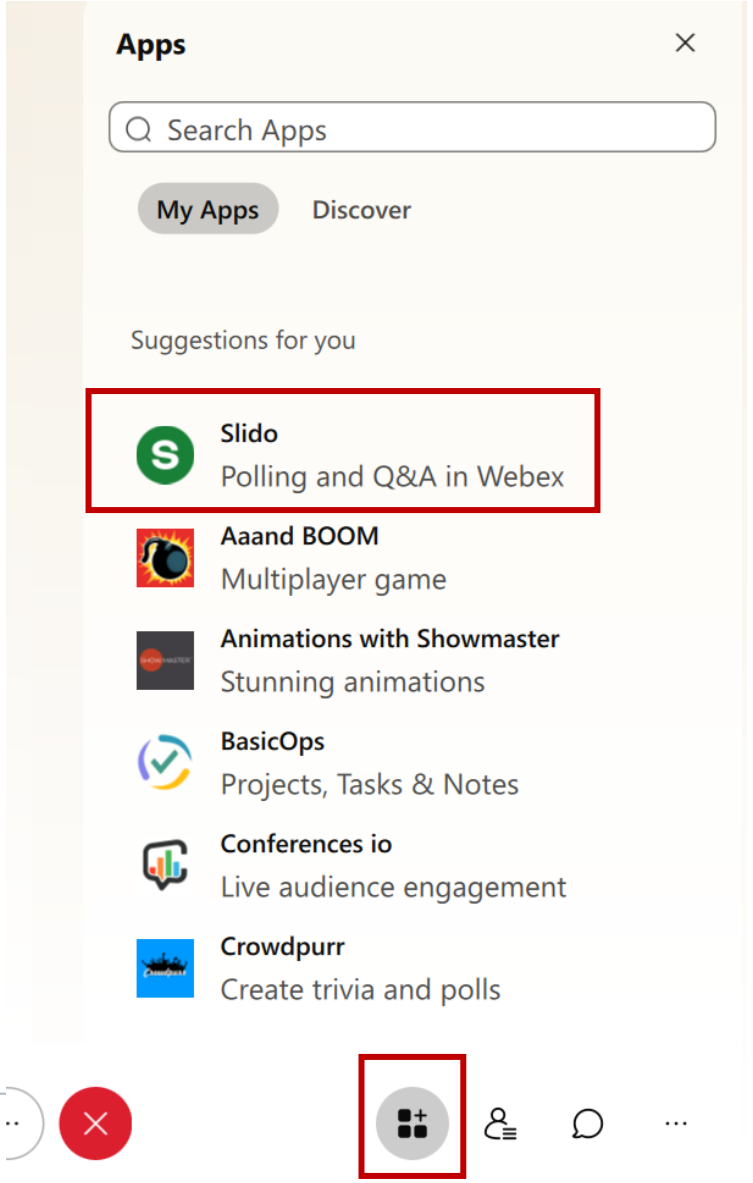
- Slido Panel should pop-up when the poll is launched, where you can join the poll and “send” your response.



- If the panel does not pop-up: Go to the “3 dots” menu and then select “Slido (polling and Q&A)”



- OR, if Slido does not appear under the 3 dots menu, Go to: **Apps >> Slido >> Active session**



Slido Polling Question

Have you reported an SAE on a SWOG trial?

A. Yes

B. No

C. I have assisted with the process but was not the reporter.

D. I don't remember.

SWOG SAE Team

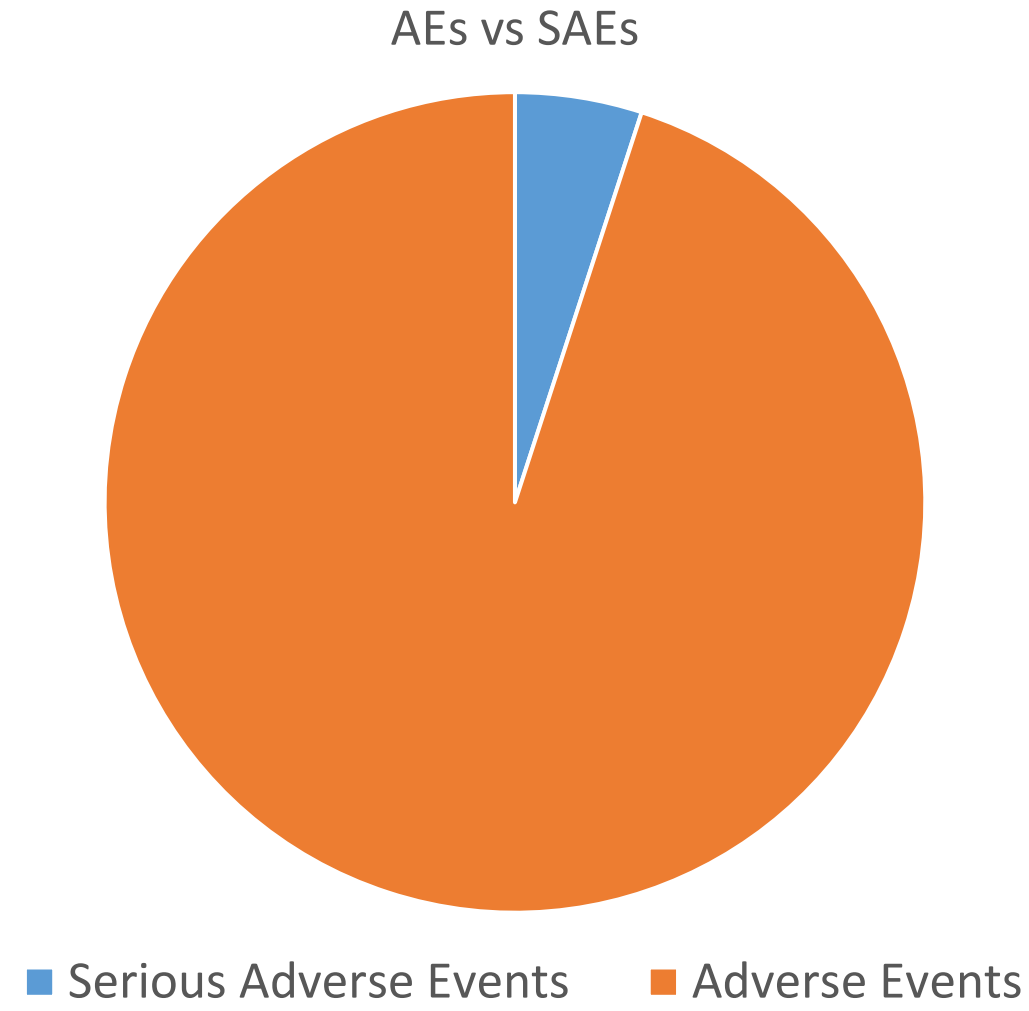
Contact first with all SWOG SAE questions, including technical support issues.

SAE Email: adr@swog.org

SAE Phone: 210-614-8808, Option 6

Serious Adverse Events

- SAEs are a subset of all adverse events collected.
- The reporting of SAEs is in addition to, and does not replace, the necessity of adequately reporting adverse events on the case report forms and in the final results of the clinical trial.



CTCAE Adverse Event Grades

- **Grade 1 -** Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
- **Grade 2 -** Moderate; minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL.
- **Grade 3 -** Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL.
- **Grade 4 -** Life-threatening consequences; urgent intervention indicated.
- **Grade 5 -** Death related to AE.

Attribution

RELATIONSHIP	ATTRIBUTION	DESCRIPTION
Unrelated to Investigational Agent / Intervention	Unrelated	The AE is clearly NOT Related to the intervention
	Unlikely	The AE is Doubtfully Related to the intervention
Related to Investigation Agent / Intervention	Possible	The AE May be Related to the intervention
	Probable	The AE is Likely Related to the intervention
	Definite	The AE is Clearly Related to the intervention

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

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)

Phase I and Early Phase II Trials

Current Table for Phase 1 and Early Phase 2 IND/IDE Studies

FDA REPORTING REQUIREMENTS FOR SERIOUS ADVERSE EVENTS (21 CFR Part 312)

NOTE: Investigators **MUST** immediately report to the sponsor (NCI) **ANY** SAEs, whether or not they are considered related to the investigational agent(s)/intervention (21 CFR 312.64)

An AE is considered serious if it results in **ANY** of the following outcomes:

1) Death
2) A life-threatening AE
3) An AE that results in inpatient hospitalization or prolongation of existing hospitalization for ≥ 24 hours
4) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
5) A congenital anomaly/birth defect.
6) Important Medical Events (IME) that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon 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. (FDA, 21 CFR 312.32; ICH E2A and ICH E6).

ALL SAEs that meet the above criteria MUST be immediately reported to the NCI via CTEP-AERS within the timeframes detailed in the table below.

Hospitalization	Grade 1 and 2 Timeframes	Grade 3-5 Timeframes
Resulting in Hospitalization ≥ 24 hrs	10 Calendar Days	24-Hour 5 Calendar Days
Not resulting in Hospitalization ≥ 24 hrs	Not required	

NOTE: Protocol-specific exceptions to expedited reporting of SAEs are found in the Specific Protocol Exceptions to Expedited Reporting (SPEER) portion of the CAEPR.

Expedited AE reporting timelines are defined as:

- "24-Hour; 5 Calendar Days" - The SAE must initially be reported via CTEP-AERS within 24 hours of learning of the SAE, followed by a complete expedited report within 5 calendar days of the initial 24-hour report.
- "10 Calendar Days" - A complete expedited report on the AE must be submitted within 10 calendar days of learning of the AE.

[1]SAEs that occur more than 30 days after the last administration of investigational agent/intervention and have an attribution of possible, probable, or definite require reporting as follows:

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

- All Grade 3, 4, and Grade 5 AEs

Expedited 10 calendar day reports for:

- Grade 2 AEs resulting in hospitalization or prolongation of hospitalization

[2] For studies using nuclear medicine or molecular imaging IND agents (NM, SPECT, or PET), the AE reporting period is limited to 10 radioactive half-lives, rounded UP to the nearest whole day, after the agent/intervention was last administered. Footnote "1" above applies after this reporting period.

Effective Date: May 5, 2011

REVISED Table for Phase 1 and Early Phase 2 IND/IDE Studies

FDA REPORTING REQUIREMENTS FOR SERIOUS ADVERSE EVENTS (21 CFR Part 312)

NOTE: Investigators **MUST** immediately report to the sponsor (NCI) **ANY** SAEs, whether or not they are considered related to the investigational agent(s)/intervention (21 CFR 312.64)

An AE is considered serious if it results in **ANY** of the following outcomes:

1) Death
2) A life-threatening AE
3) An AE that results in inpatient hospitalization or prolongation of existing hospitalization for ≥ 24 hours
4) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
5) A congenital anomaly/birth defect.
6) Important Medical Events (IME) that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon 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. (FDA, 21 CFR 312.32; ICH E2A and ICH E6).

ALL SAEs that meet the above criteria MUST be immediately reported to the NCI via CTEP-AERS within the timeframes detailed in the table below.

Grade 1-2 Timeframes	Grade 3-5 Timeframes
24-Hour notification, 10 calendar days	24-Hour notification, 5 calendar days

NOTE: Protocol-specific exceptions to expedited reporting of SAEs are found in the Specific Protocol Exceptions to Expedited Reporting (SPEER) portion of the CAEPR.

Expedited AE reporting timelines are defined as:

- "24-Hour notification, 5 Calendar Days" - The SAE must initially be reported via CTEP-AERS within 24 hours of learning of the SAE, followed by a complete expedited report within 5 calendar days of the initial 24-hour report.
- "24-Hour notification, 10 Calendar Days" - The SAE must initially be reported via CTEP-AERS within 24 hours of learning of the SAE, followed by a complete expedited report within 10 calendar days of the initial 24-hour report.

[1]SAEs that occur more than 30 days after the last administration of investigational agent/intervention and have an attribution of possible, probable, or definite require reporting as follows:

Expedited 24-hour notifications are required for all SAEs followed by a complete report

- Within 5 calendar days for Grade 3-5 SAEs
- Within 10 calendar days for Grade 1-2 SAEs

[2]For studies using nuclear medicine or molecular imaging IND agents (NM, SPECT, or PET), the SAE reporting period is limited to 10 radioactive half-lives, rounded UP to the nearest whole day, after the agent/intervention was last administered. Footnote "1" above applies after this reporting period.

Effective Date: August 30, 2024

Late Phase II and Phase III Trials

Current Table for Late Phase 2 and Phase 3 IND/IDE Studies

FDA REPORTING REQUIREMENTS FOR SERIOUS ADVERSE EVENTS (21 CFR Part 312)

NOTE: Investigators **MUST** immediately report to the sponsor (NCI) **ANY** SAEs, whether or not they are considered related to the investigational agent(s)/intervention (21 CFR 312.64)

An AE is considered serious if it results in **ANY** of the following outcomes:

1) Death
2) A life-threatening AE
3) An AE that results in inpatient hospitalization or prolongation of existing hospitalization for ≥ 24 hours
4) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
5) A congenital anomaly/birth defect.
6) Important Medical Events (IME) that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon 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. (FDA, 21 CFR 312.32; ICH E2A and ICH E6).

ALL SAEs that meet the above criteria **MUST** be immediately reported to the NCI via CTEP-AERS within the timeframes detailed in the table below.

Hospitalization	Grade 1 Timeframes	Grade 2 Timeframes	Grade 3 Timeframes	Grade 4 & 5 Timeframes
Resulting in Hospitalization ≥ 24 hrs	10 Calendar Days			24-Hour 5 Calendar Days
Not resulting in Hospitalization ≥ 24 hrs	Not required		10 Calendar Days	

NOTE: Protocol-specific exceptions to expedited reporting of SAEs are found in the Specific Protocol Exceptions to Expedited Reporting (SPEER) portion of the CAEPR

Expedited AE reporting timelines are defined as:

- "24-Hour; 5 Calendar Days" - The AE must initially be reported via CTEP-AERS within 24 hours of learning of the AE, followed by a complete expedited report within 5 calendar days of the initial 24-hour report.
- "10 Calendar Days" - A complete expedited report on the AE must be submitted within 10 calendar days of learning of the AE.

[1]SAEs that occur more than 30 days after the last administration of investigational agent/intervention and have an attribution of possible, probable, or definite require reporting as follows:

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

- All Grade 4, and Grade 5 AEs

Expedited 10 calendar day reports for:

- Grade 2 adverse events resulting in hospitalization or prolongation of hospitalization
- Grade 3 adverse events

[2] For studies using nuclear medicine or molecular imaging IND agents (NM, SPECT, or PET), the AE reporting period is limited to 10 radioactive half-lives, rounded UP to the nearest whole day, after the agent/intervention was last administered. Footnote "1" above applies after this reporting period.

Effective Date: May 5, 2011

REVISED Table for Late Phase 2 and Phase 3 IND/IDE Studies

FDA REPORTING REQUIREMENTS FOR SERIOUS ADVERSE EVENTS (21 CFR Part 312)

NOTE: Investigators **MUST** immediately report to the sponsor (NCI) **ANY** SAEs, whether or not they are considered related to the investigational agent(s)/intervention (21 CFR 312.64)

An AE is considered serious if it results in **ANY** of the following outcomes:

1) Death
2) A life-threatening AE
3) An AE that results in inpatient hospitalization or prolongation of existing hospitalization for ≥ 24 hours
4) A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
5) A congenital anomaly/birth defect.
6) Important Medical Events (IME) that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon 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. (FDA, 21 CFR 312.32; ICH E2A and ICH E6).

ALL SAEs that meet the above criteria MUST be immediately reported to the NCI via CTEP-AERS within the timeframes detailed in the table below.

Grade 1-3 Timeframes	Grade 4-5 Timeframes
24-Hour notification, 10 calendar days	24-Hour notification, 5 calendar days

NOTE: Protocol-specific exceptions to expedited reporting of SAEs are found in the Specific Protocol Exceptions to Expedited Reporting (SPEER) portion of the CAEPR.

Expedited AE reporting timelines are defined as:

- "24-Hour notification, 5 Calendar Days" - The SAE must initially be reported via CTEP-AERS within 24 hours of learning of the SAE, followed by a complete expedited report within 5 calendar days of the initial 24-hour report.
- "24-Hour notification, 10 Calendar Days" - The SAE must initially be reported via CTEP-AERS within 24 hours of learning of the SAE, followed by a complete expedited report within 10 calendar days of the initial 24-hour report.

[1]SAEs that occur more than 30 days after the last administration of investigational agent/intervention and have an attribution of possible, probable, or definite require reporting as follows:

Expedited 24-hour notifications are required for all SAEs followed by a complete report

- Within 5 calendar days for Grade 3-5 SAEs
- Within 10 calendar days for Grade 1-2 SAEs

[2]For studies using nuclear medicine or molecular imaging IND agents (NM, SPECT, or PET), the SAE reporting period is limited to 10 radioactive half-lives, rounded UP to the nearest whole day, after the agent/intervention was last administered. Footnote "1" above applies after this reporting period.

Effective Date: August 30, 2024

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.

1

2

3

FDA REPORTING REQUIREMENTS FOR SERIOUS ADVERSE EVENTS (21 CFR Part 312)

NOTE: Investigators MUST immediately report to the sponsor (NCI) ANY Serious Adverse Events, whether or not they are considered related to the investigational agent(s)/intervention (21 CFR 312.64)

An adverse event is considered serious if it results in ANY of the following outcomes:

1) **Death**
2) **A life-threatening adverse event**
3) **An adverse event that results in inpatient hospitalization or prolongation of existing hospitalization for ≥ 24 hours**
4) **A persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions**
5) **A congenital anomaly/birth defect.**
6) **Important Medical Events (IME) that may not result in death, be life threatening, or require hospitalization may be considered serious when, based upon medical judgment, they may jeopardize the participant or subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. (FDA, 21 CFR 312.32; ICH E2A and ICH E6).**

ALL SERIOUS adverse events that meet the above criteria MUST be immediately reported to the NCI via CTEP-AERS within the timeframes detailed in the table below.

Grade 1-3 Timeframes	Grade 4-5 Timeframes
24-Hour notification, 10 Calendar Days	24-Hour notification, 5 Calendar Days

NOTE: Protocol specific exceptions to expedited reporting of serious adverse events are found in the Specific Protocol Exceptions to Expedited Reporting (SPEER) portion of the CAEPR or Section 8.8b.2.

Expedited AE reporting timelines are defined as:

- "24-Hour notification, 5 Calendar Days" - The SAE must initially be reported via CTEP-AERS within 24 hours of learning of the SAE, followed by a complete expedited report within 5 calendar days of the initial 24-hour report.
- "24-Hour notification, 10 Calendar Days" - The SAE must initially be reported via CTEP-AERS within 24 hours of learning of the SAE, followed by a complete expedited report within 10 calendar days of the initial 24-hour report.

Serious adverse events that occur more than 30 days after the last administration of investigational agent/intervention and have an attribution of possible, probable, or definite require reporting as follows:

Expedited 24-hour notification are required for all SAEs followed by a complete report

- Within 5 calendar days for Grade 4-5 SAEs
- Within 10 calendar days for Grade 1-3 SAEs

Effective Date: August 30, 2024

SAE Reporting Table

Example of SAE Reporting Criteria for Commercially Available Agent

Grade 4, Unexpected, *and* Possibly, Probably, Definitely Related

OR

Grade 5

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

CTEP-AERS: Indicates an expedited report is to be submitted via CTEP-AERS within 10 calendar days of learning of the event[b].

[a] **This includes all deaths within 30 days of the last dose of treatment with a commercial agent(s), regardless of attribution. Any death that occurs more than 30 days after the last dose of treatment with a commercial agent(s) and is attributed (possibly, probably, or definitely) to the agent(s) and is not due to cancer recurrence must be reported according to the instructions above.**

[b] **Submission of the on-line CTEP-AERS report plus any necessary amendments generally completes the reporting requirements. You may, however, be asked to submit supporting clinical data to the Operations Office in order to complete the evaluation of the event. If requested, the specified data should be sent within 5 calendar days by fax to 210-614-0006.**

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.

Slido Polling Question

Do you know how to look up protocols in CTSU?

A. Yes

B. No

C. I would need a refresher.

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

Home | Funding Information | Documents | Drug Safety Notification | Study Agent | Protocol Requirements

NCI National Clinical Trials Network
a National Cancer Institute program

S2302

IRBManager | Add to My Proto

Pragmatica - Lung: A Prospective Randomized Study of Ramucirumab (LY3009806; NSC 749128) Plus Pembrolizumab (MK-3475; NSC 776864) Versus Standard of Care for Participants Previously Treated with Immunotherapy for Stage IV or Recurrent Non-Small Cell Lung Cancer

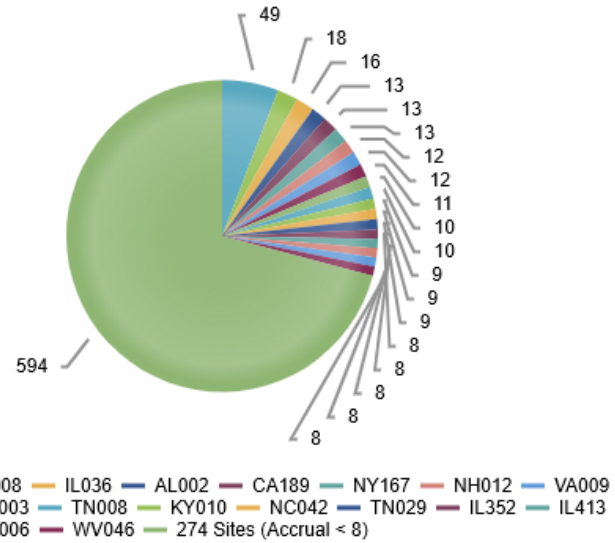
Protocol Status:	CLOSED TO ACCRUAL
Protocol Status Date:	20-Dec-2024
Activation Date:	06-Mar-2023
Lead Organization:	SWOG
NCI Program:	NCTN
Phase:	III
Country Participation:	
ClinicalTrials.gov Link:	NCT05633602
Patient Accrual:	As of 18-Mar-2025 12:30:18 PM

www.ctsu.org

Step Type	Step(s)	Planned	Actual
Intervention	1	800	838

Study Champions: Henick, S Brian NRG | Khalil, Maya ECOG-ACRIN

Patient Intervention Accrual by site



Supported By:

CIRB	DTL	OPEN	Rave	TSDV	IROC/ TRIAD	DQP	ePRO	SAE Int	CM	DCP-001	NINT	REG/LIC
✓	✓	✓	✓	✓	✗	✓	✗	✓	✗	✓	✗	✓

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.

Rave/CTEP-AERS Integration

- There will be times when the system recommends reporting an event via CTEP-AERS but per protocol, an event does not meet criteria for expedited reporting.
- The Rave/CTEP-AERS integration recommendation is just that - a recommendation; it is not a mandate to report.
- The opposite can also be true. The system may not recommend the reporting of an event via expedited report, but per protocol, the event meets criteria for expedited reporting. The event may also be an adverse event of special interest (AESI) that requires reporting per special instructions in the protocol.

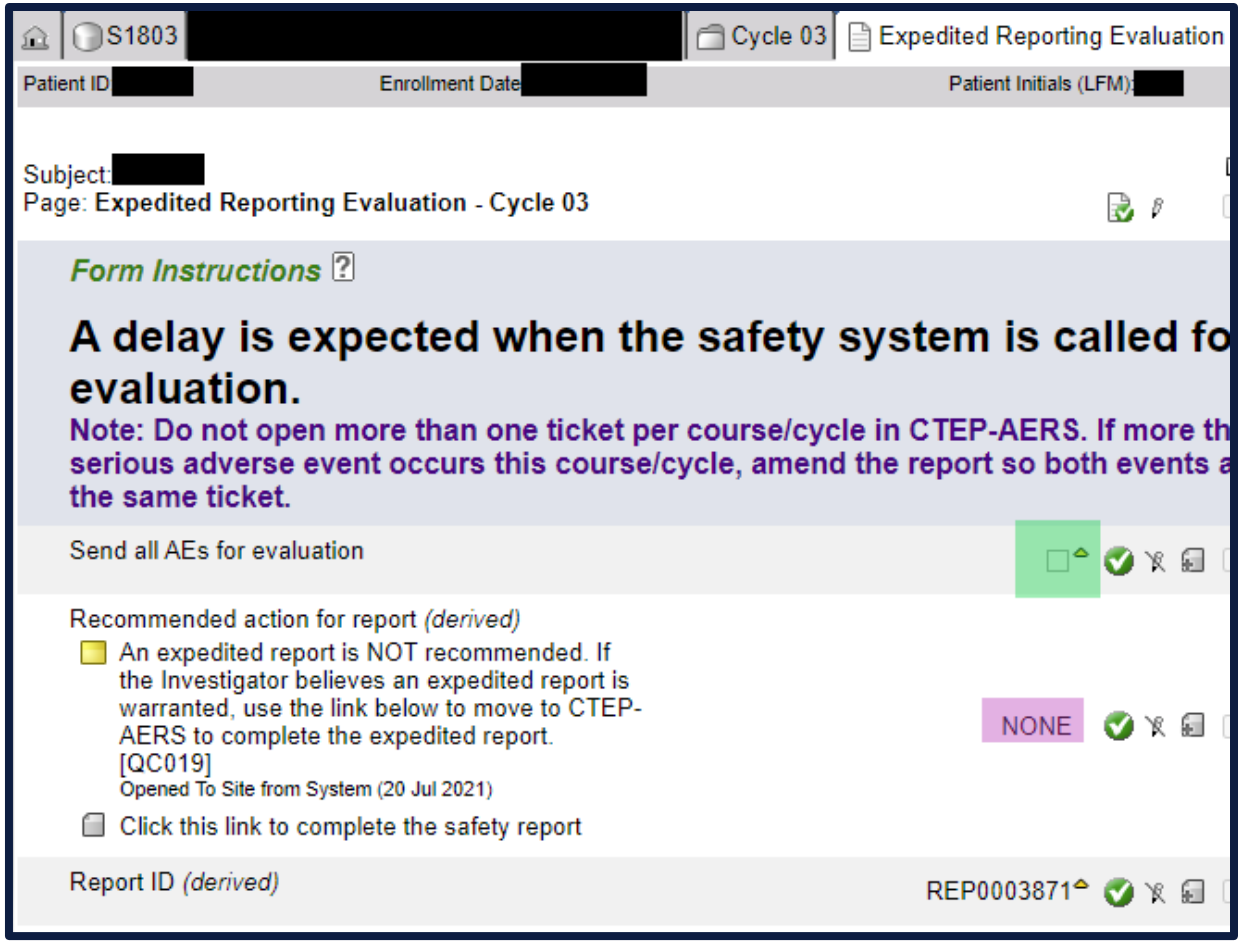
Rave Form

Adverse Events: Report

#	Adverse Event (Verbatim term)	*Adverse event term (CTCAE v5.0)	*What is the description of the toxicity? *(first 120 characters)*	Start Date	End Date	Ongoing	Relationship to Study Treatment	Hospitalization (initial or prolonged)	Life Threatening	Death	Disability or Permanent Damage	Congenital Anomaly or Birth Defect	Other Serious (Important Medical Events)	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 2021	–	Yes	Unrelated	No	No	No	No	No	No	Dose Not Changed	AE06-8D42262B58D84E7DB89AF2E673BDF834	No	26 Oct 2021 01 44 31 PM
2	dyspnea	Dyspnea	(3) Shortness of breath at rest; limiting self care ADL	20 Jan 2022	–	Yes	Unrelated	Yes	No	No	No	No	No	Drug Interrupted	AE11-D8EDA7F92CFC4E5882D38F86076B5653	Yes	24 Jan 2022 02 18 36 PM

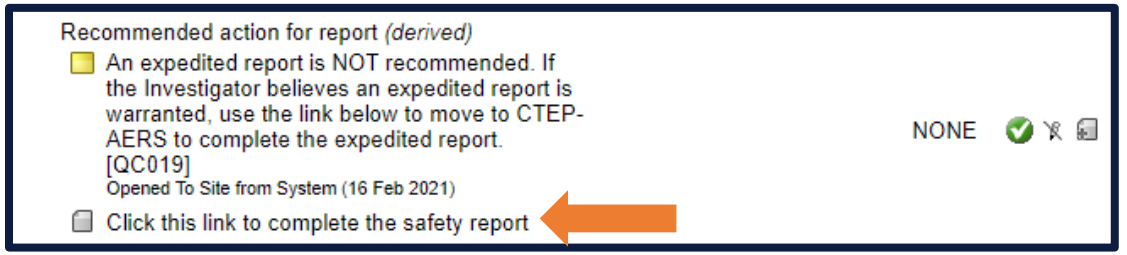
Rave Form
Expedited Reporting Evaluation

- 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.

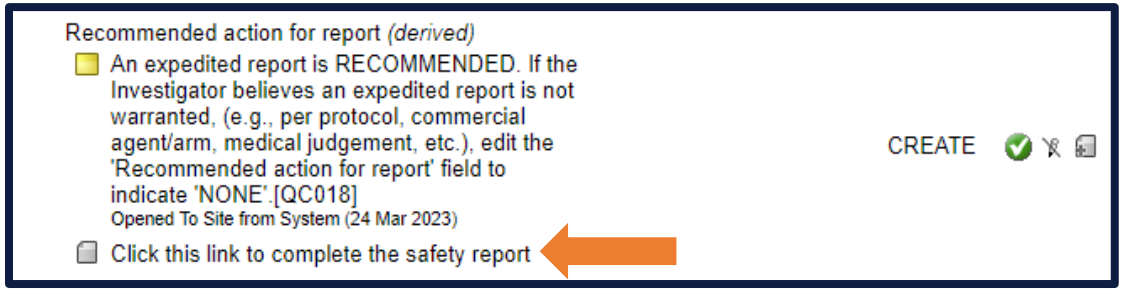


Rave Form
Expedited Reporting Evaluation

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



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



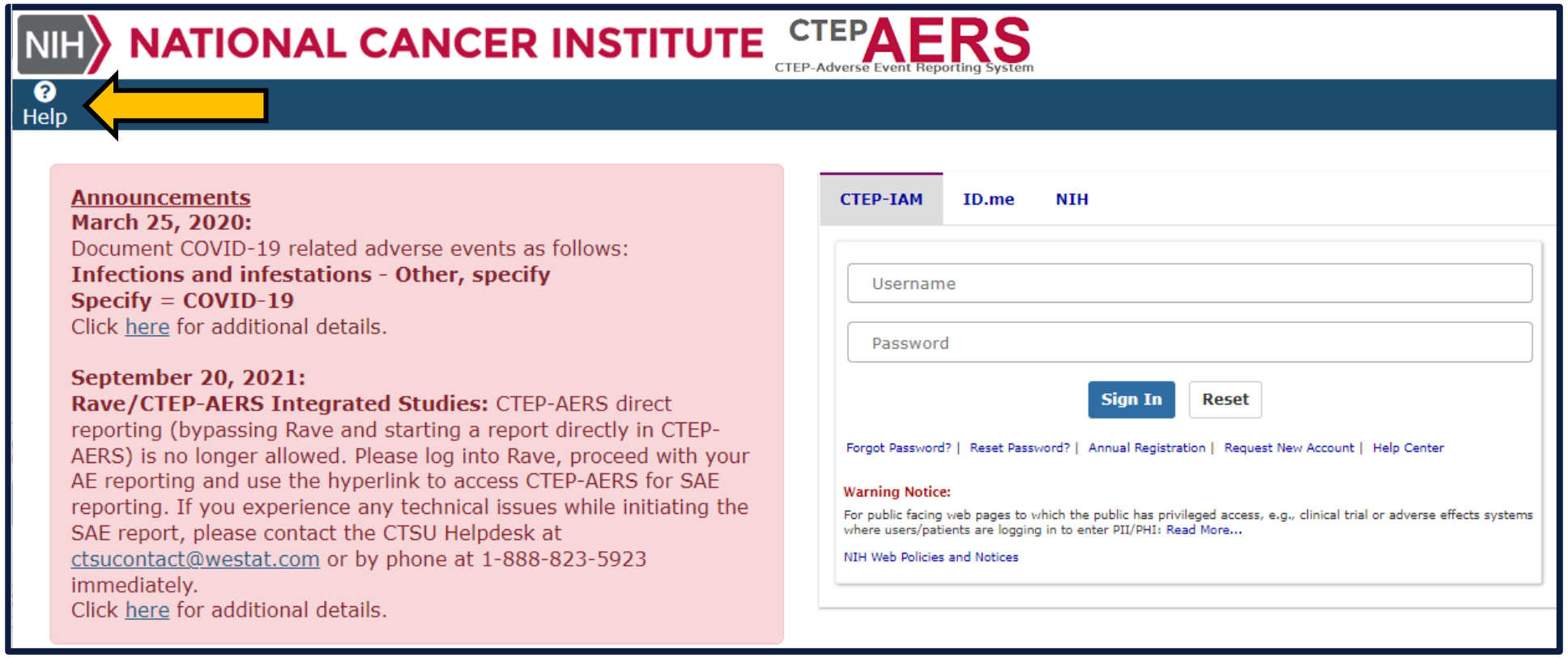
AMEND = an amended SAE report is being recommended because new/updated data has been reported on the AE Report form

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.

CTEP-AERS Home Page

[Link to CTEP-AERS Home Page]



CTEP-AERS

Completing the Report

- Outlined and colored tabs represent the page currently accessed.
- Tabs marked with "*" are mandatory and the section must be completely entered prior to report submission.
- Tabs marked with "✔" indicate that the section is completed.

Note that the **Reporter** page (Tab 1) must be completed and saved to generate the report ticket number.

CTEP-AERS Sections

01	Reporter	Enter the contact information for both the reporter and the Physician. If the treating physician is reporting the event, click in the box next to *If the Physician is the same as the Reporter.*
02	Adverse Events	Enter the verbatim term for those events to be included on the report. Deselect any events that should not be included in the report.
03	Describe Event	Enter detailed information to evaluate the event(s). Include information for all of the events included on the report. Detailed information can include presentation of the event, treatment of the event, clinical findings, and timing of the event in relation to study interventions. Be as complete as possible.
04	Course/Cycle	Enter the treatment information on the course the patient received at the time of the adverse event.
05	Study Interventions	Add any intervention used on the study that may have caused the adverse event. *In the event the patient does not receive the intended treatment, "0" can be entered for the *Total Dose Administered.*

CTEP-AERS Sections (continued)

06	Subject Details	Enter the following information: **General** - General information about the patient needed for the report **Disease Information** -disease information about the patient's primary, initial disease site **Metastatic Disease Site** - The location where the disease spread **Pre-Existing Conditions** - Medical conditions present in the patient prior to participating in the study **Concomitant Medications** - Prescription and over-the-counter drugs that are relevant to the SAE. **Prior Therapies** - Relevant prior therapies for the underlying cancer.
07	Other Causes	Enter information regarding any other circumstances possibly related to the event or other situations that may have contributed to the event.
08	Labs	Enter any labs pertinent to the adverse event(s).
09	Attribution	Enter the cause (attribution) of the adverse event. ***There must be a minimum of one attribution of at least possibly related***
10	Review & Submit	Review the report for accuracy. If the SAE has been assessed by the Investigator, you may check the *Physician Signoff* box and submit the report.

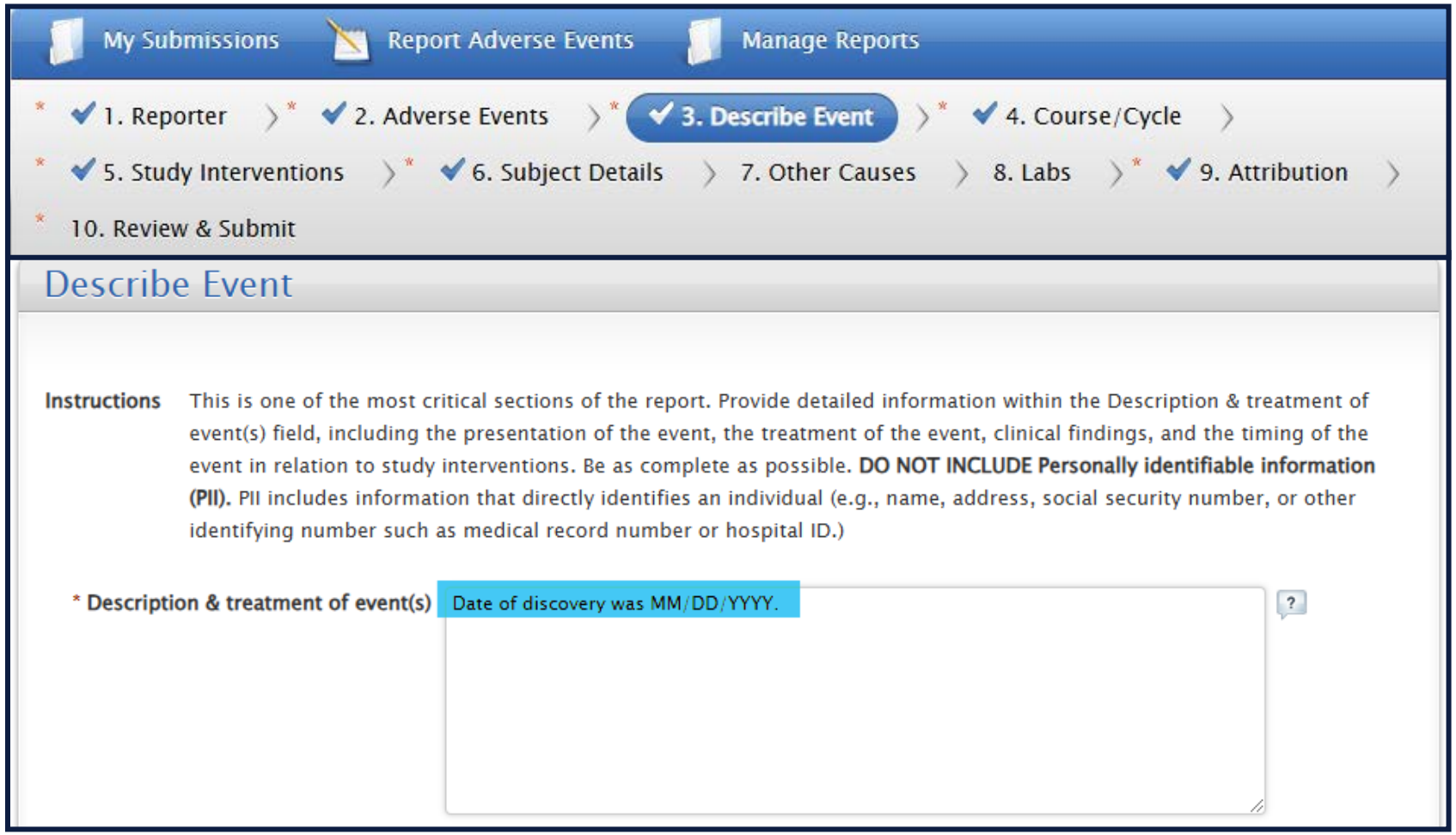
What is the deadline for submitting an SAE report to SWOG?

- 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.

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.

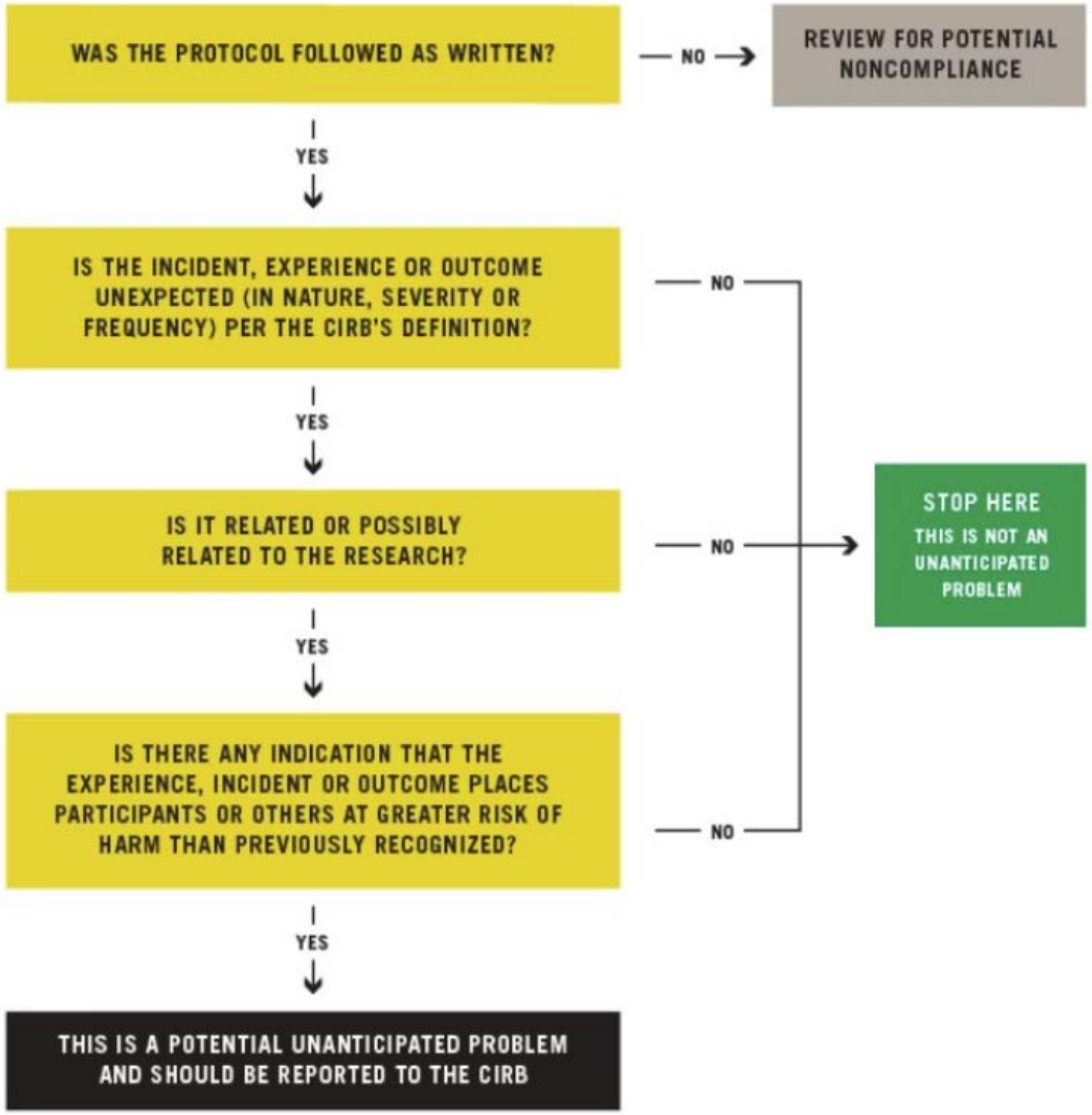
SAEs and Audits

- SAEs Reported Late
  - If no date of discovery is provided, SWOG uses the date the report was submitted to SWOG minus the start date of event to determine late reporting.
  - If the date of discovery is different from the start date of the event, please enter it in CTEP-AERS Section 3: Describe Event (narrative).

- SAEs Reportable to Local Institutional Review Board (LIRB)
  - Varies due to local IRB guidelines. Check with your IRB.

- SAEs Reportable to NCI Central Institutional Review Board (CIRB)
  - Use the CIRB algorithm to determine reporting.

CIRB Algorithm for Potential Unanticipated Problems



Slido Polling Question

Are you familiar with the SPEER?

A. Yes

B. No

C. Somewhat familiar

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 Term) [n= 2069]			Specific Protocol Exceptions to Expedited Reporting (SPEER)
Likely (>20%)	**Less Likely (<=20%)**	**Rare but Serious (<3%)**	
		Eye disorders - Other (optic neuritis retrobulbar)[3]	
		Eye disorders - Other (Vogt-Koyanagi-Harada)	
	Uveitis		
GASTROINTESTINAL DISORDERS			
	Abdominal pain		***Abdominal pain (Gr 2)***
	Colitis[3]		
		Colonic perforation[3]	
	Diarrhea Dry mouth		***Diarrhea (Gr 3)*** ***Dry mouth (Gr 2)***
		Enterocolitis	
		Gastritis	
		Mucositis oral	
	Nausea		***Nausea (Gr 2)***
	Pancreatitis[4]		

SPEER

Reminder that the SPEER column only applies to SAE reporting.

It does not apply to routine AE reporting.

Adverse Events with Possible Relationship to Nivolumab (CTCAE 5.0 Term) [n= 2069]			Specific Protocol Exceptions to Expedited Reporting (SPEER)
Likely (>20%)	Less Likely (<=20%)	Rare but Serious (<3%)	
		Eye disorders - Other (optic neuritis retrobulbar)[3]	
		Eye disorders - Other (Vogt-Koyanagi-Harada)	
	Uveitis		
GASTROINTESTINAL DISORDERS			
	Abdominal pain		***Abdominal pain (Gr 2)***
	Colitis[3]		
		Colonic perforation[3]	
	Diarrhea Dry mouth		***Diarrhea (Gr 3)*** ***Dry mouth (Gr 2)***
		Enterocolitis	
		Gastritis	
		Mucositis oral	
	Nausea		***Nausea (Gr 2)***
	Pancreatitis[4]		

Additional Reporting Requirements

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

16.1 Adverse Event Reporting Requirements

f. **Additional Instructions or Exceptions to CTEP-AERS Expedited Reporting Requirements for Phase 1 and Early Phase 2 Studies Utilizing an Agent under a CTEP-IND:**

1) **Group-specific instructions.**

Submission of the on-line CTEP-AERS report plus any necessary amendments generally completes the reporting requirements. In addition, you may be asked to submit supporting clinical data to the SWOG Operations Offices in order to complete the evaluation of the event. If requested, the supporting data should be sent within **5 calendar days** by fax to 210-614-0006. Supporting clinical data submitted should include:

- Printed copy of the first page of the CTEP-AERS Report.
- Copies of clinical sourced documentation of the event.
- If applicable, and they have not yet been submitted to the SWOG Data Operations Center copies of Off Treatment Notice and/or Notice of Death.

2) The adverse events listed below also require expedited monitoring for this trial:

- *Thromboembolic events, any Grade regardless of attribution*

3) For study arm(s)[applicable study arm(s)], the adverse events listed below do **not** require expedited reporting via CTEP-AERS:

- ≤ *Grade 4 myelosuppression*
- ≤ *Grade 4 Infection*

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

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 reporting unless otherwise specified in the protocol.

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

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

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

Prior QA Webinars Accessible for Review

Previous Webinars and Upcoming Webinar Information is posted at:
SWOG Quality Assurance Live Webinar Series | SWOG

CEU Courses now in CLASS:

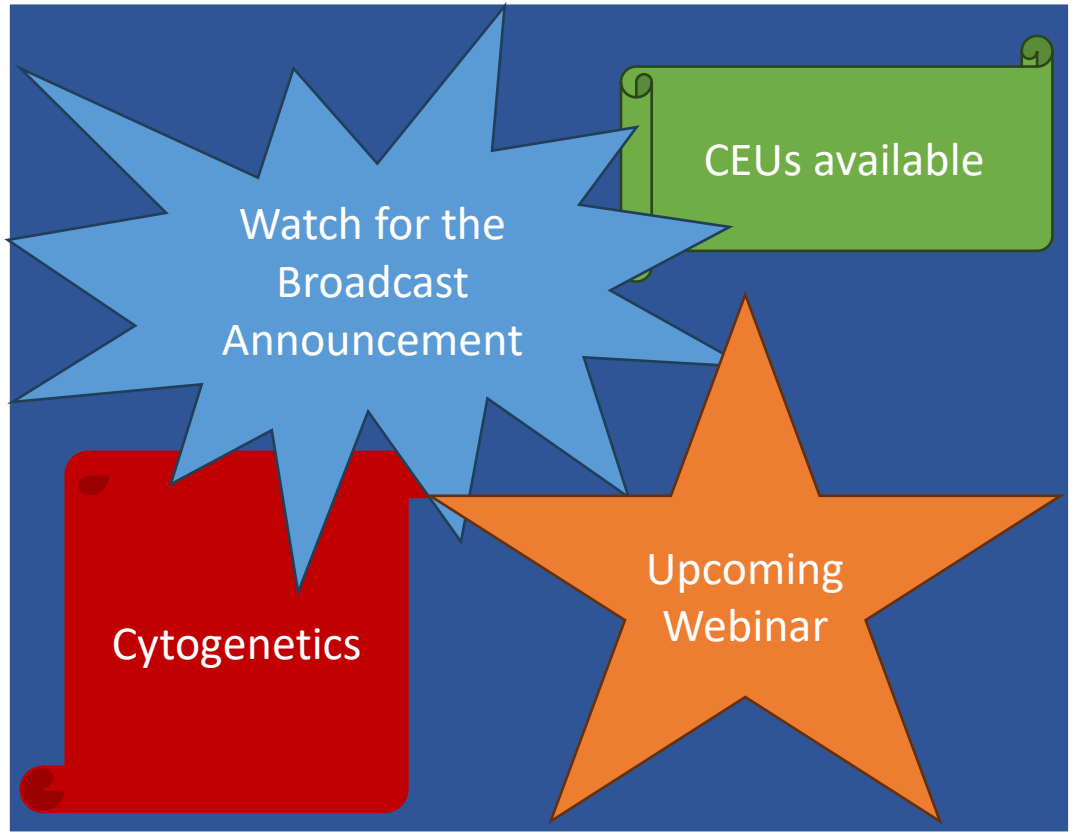
- **Disease Assessment in Solid Tumors**
  (1 contact hour)
- **Best Practices for Informed Consent**
  (1 contact hour)
- **Research Protocol Deviations vs Deficiencies**
  (1 contact hour)

CEU Courses in ExpertusOne:

- **Workload Prioritization in Clinical Trials**
  (1.5 contact hours)

Non-CEU Courses posted in CLASS:

- **Adverse Event Reporting**
- **Serious Adverse Event Reporting**
- **SWOG Audits: Preparing for Success and Audit Process**
- **How to Develop a CAPA Plan**



Upcoming QA Live Webinar

Cytogenetics Discussion

~Presented by:
Kathleen Calzone, PhD, RN, AGN-BC, FAAN
Research Geneticist
National Cancer Institute
Center for Cancer Research, Genetics Branch

Friday, June 20th, 2025
Time forthcoming

Registration information will be distributed via:

- SWOG Broadcast Emails,
- CTSU Broadcast Emails, and at
- SWOG's Spring Group Meeting in San Francisco.

This activity has been submitted to the Georgia Nurses Association for approval to award contact hours. Georgia Nurses Association is accredited as an approver of nursing continuing professional development by the American Nurses Credentialing Center's Commission on Accreditation.

Questions?