National Cancer Institute

Cancer Therapy Evaluation Program Adverse Event Reporting System (CTEP-AERS)

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Learning Objectives

State the main features of CTEP-AERS:

- Why retire AdEERS?
- Updated ‘Look and Feel’
- Pre-submission evaluation/rules engine
  - Verbatim terms
- SAE Report Recipients
- SAE Report Amendments

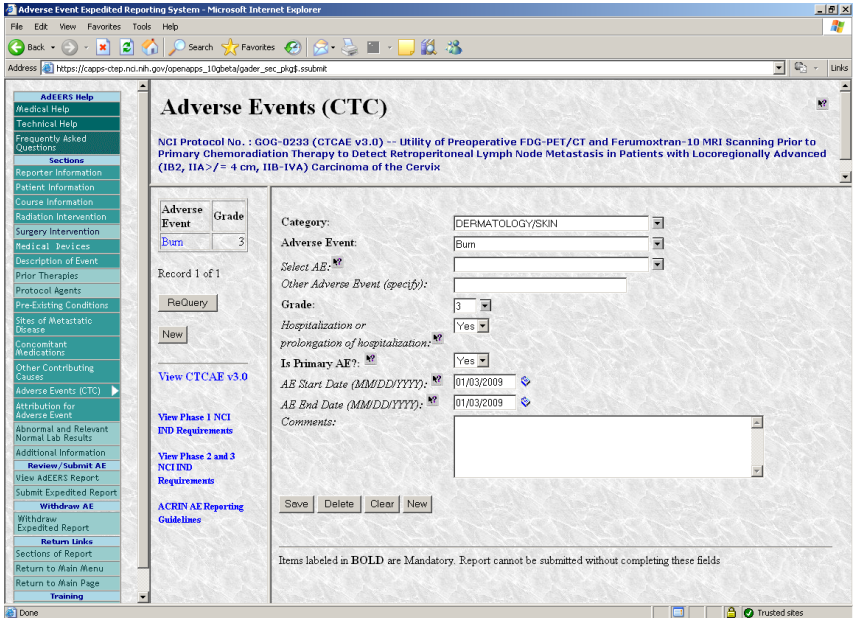
Why the switch to CTEP-AERS?

- Compliant with the FDA Final Rule
- Anticipated to save time and reduce workload
- More user-friendly and incorporates the large body of community input received during the development of caAERS

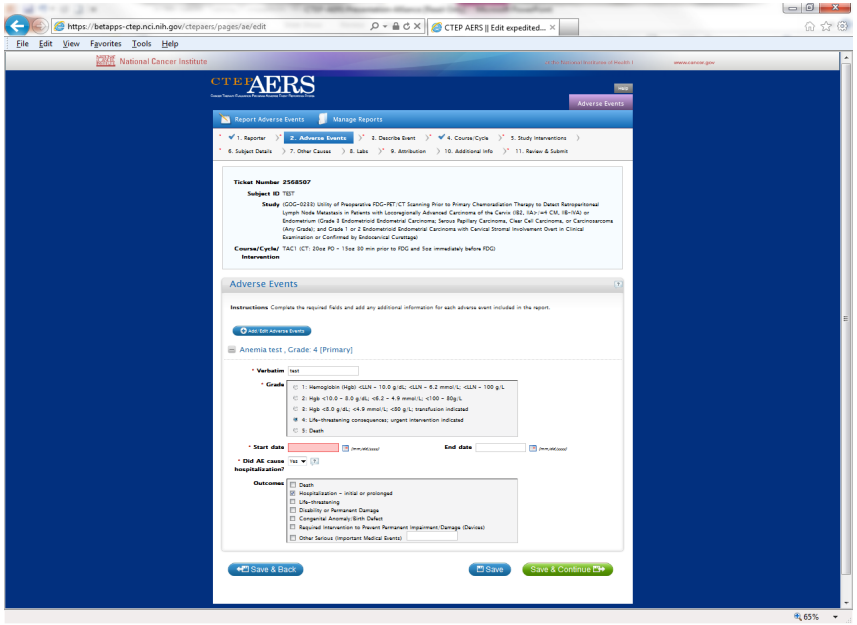
Updated ‘look and feel’

- Color scheme
- Auto-complete fields
- Some AdEERS pages combined

AdEERS Color Scheme

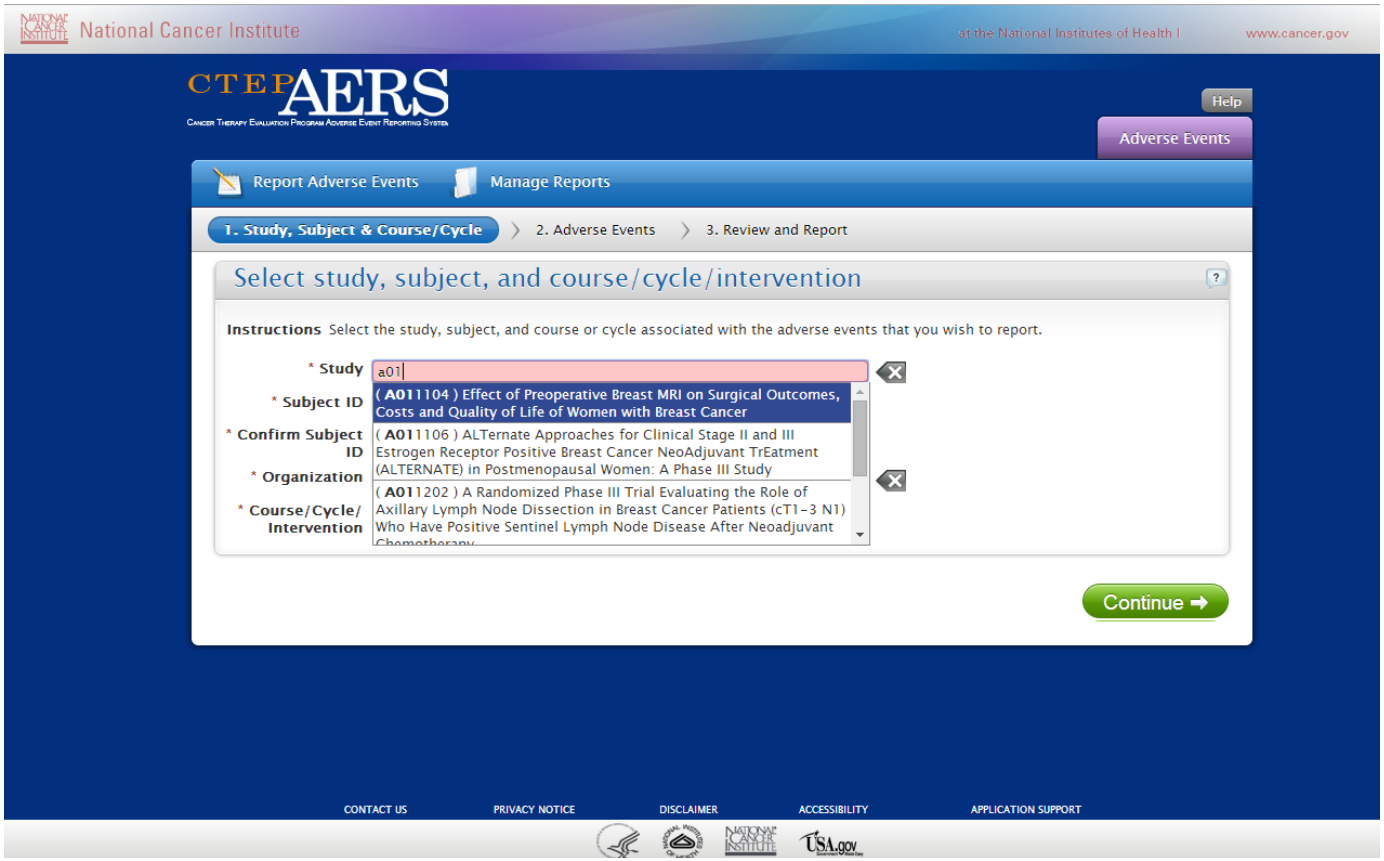


CTEP-AERS Color Scheme



Updated ‘look and feel’ (continued)

- **Auto-complete fields**

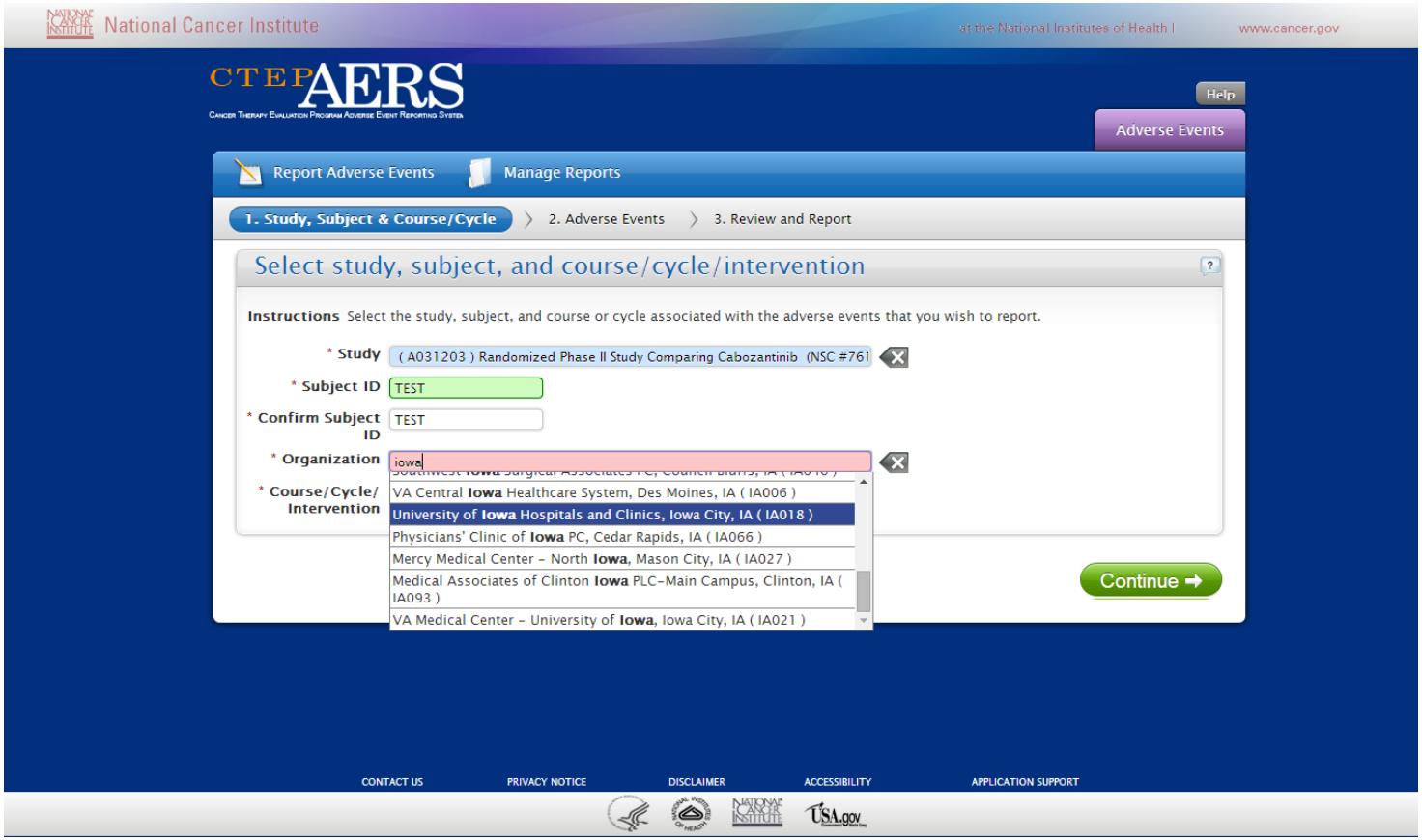


Pre-submission Evaluation

- CTEP-AERS Rules engine
  - Protocol-specific AE reporting level (i.e., AE Table)
  - Protocol-specific exceptions (PSEs) to expedited reporting
    - e.g., Specific Protocol Exceptions to Expedited Reporting (SPEER), etc.
- Action/No Action Recommendations
  - Feedback *prior to* report completion/submission
  - Limitations
  - Override
- Anticipated to reduce over-reporting

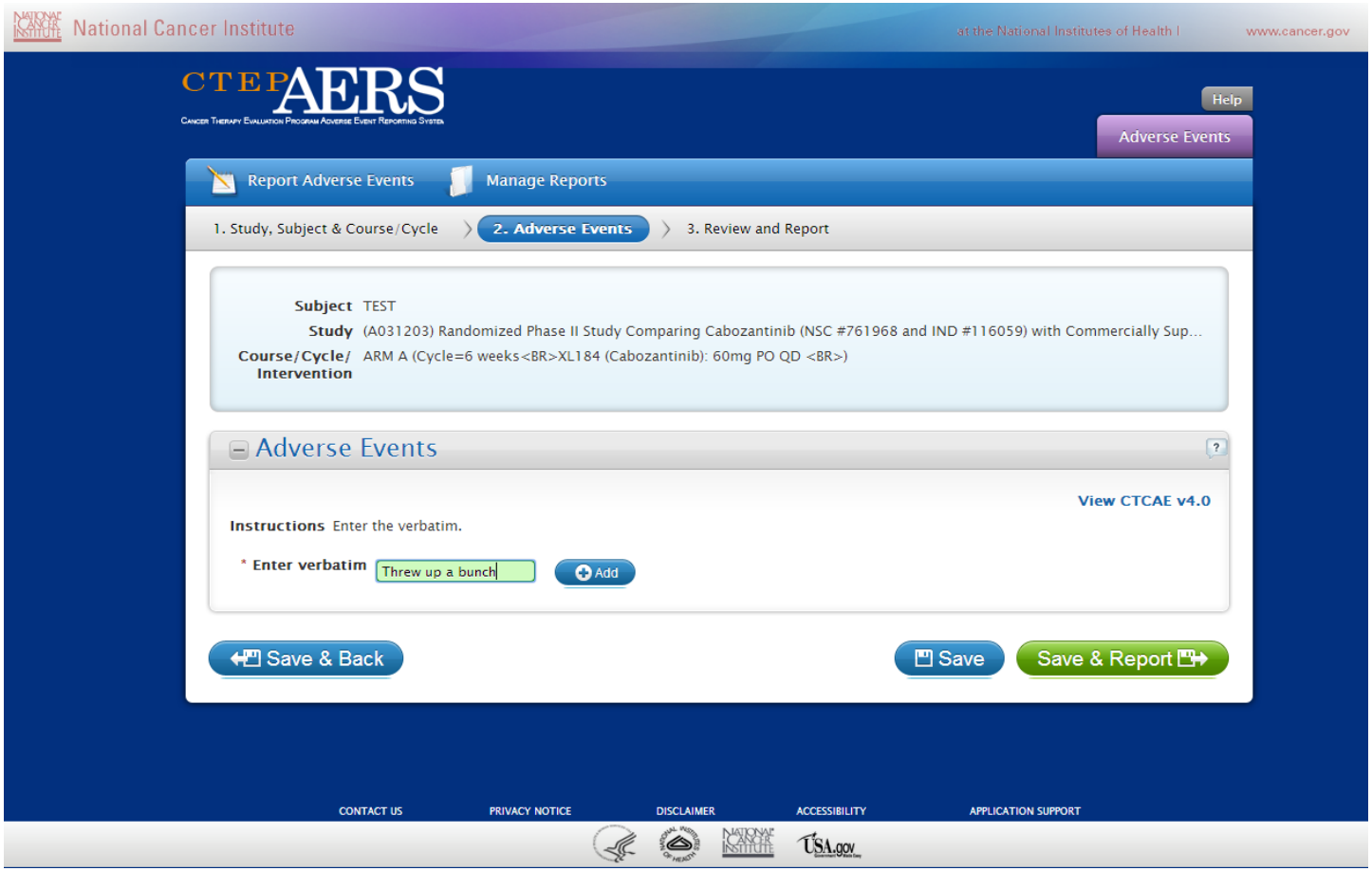
Pre-submission Evaluation (continued)

Step 1: Identify the study, subject ID, treating institution, treatment course



Pre-submission Evaluation (continued)

Step 2a: Enter the adverse event verbatim term

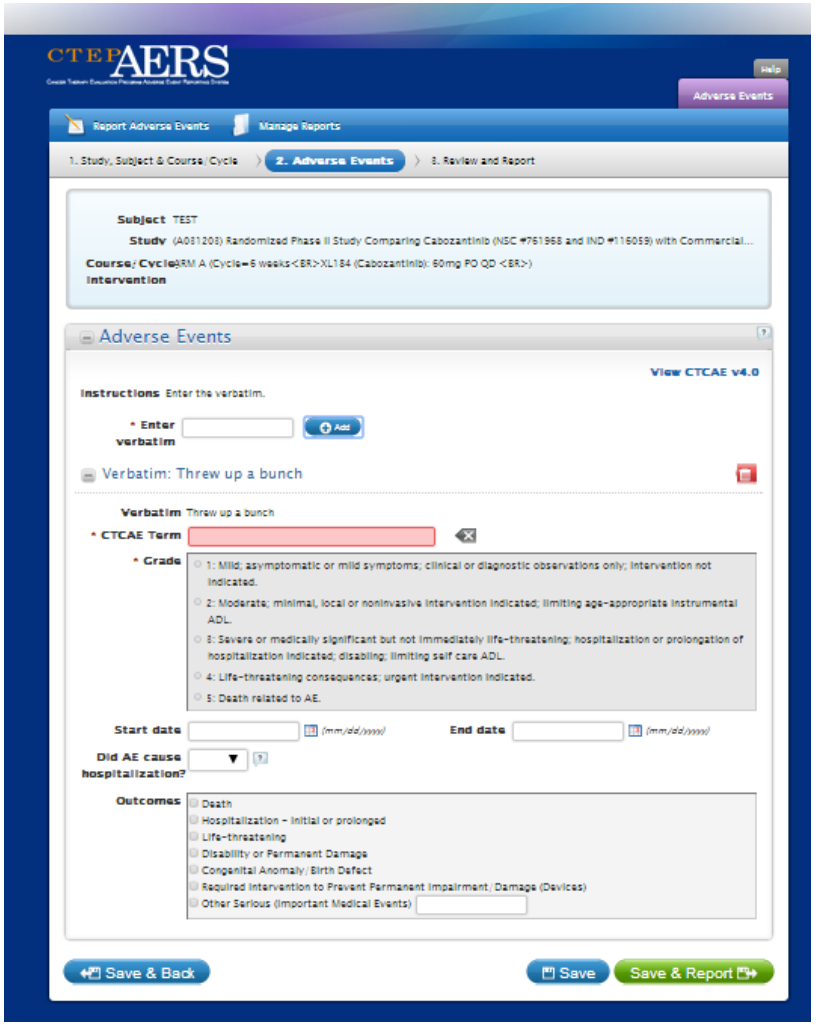


Verbatim

- Verbatim = what the patient said to describe the adverse event
  - Examples:
    - I threw up a bunch.
    - I'm very tired.
    - My chest hurts.
    - I went to the bathroom 10 times yesterday.
- What if there is no verbatim?
  - Use the CTCAE term or your own language
  - Examples
    - Laboratory reports
    - Patient unconscious
    - Secondhand SAE report

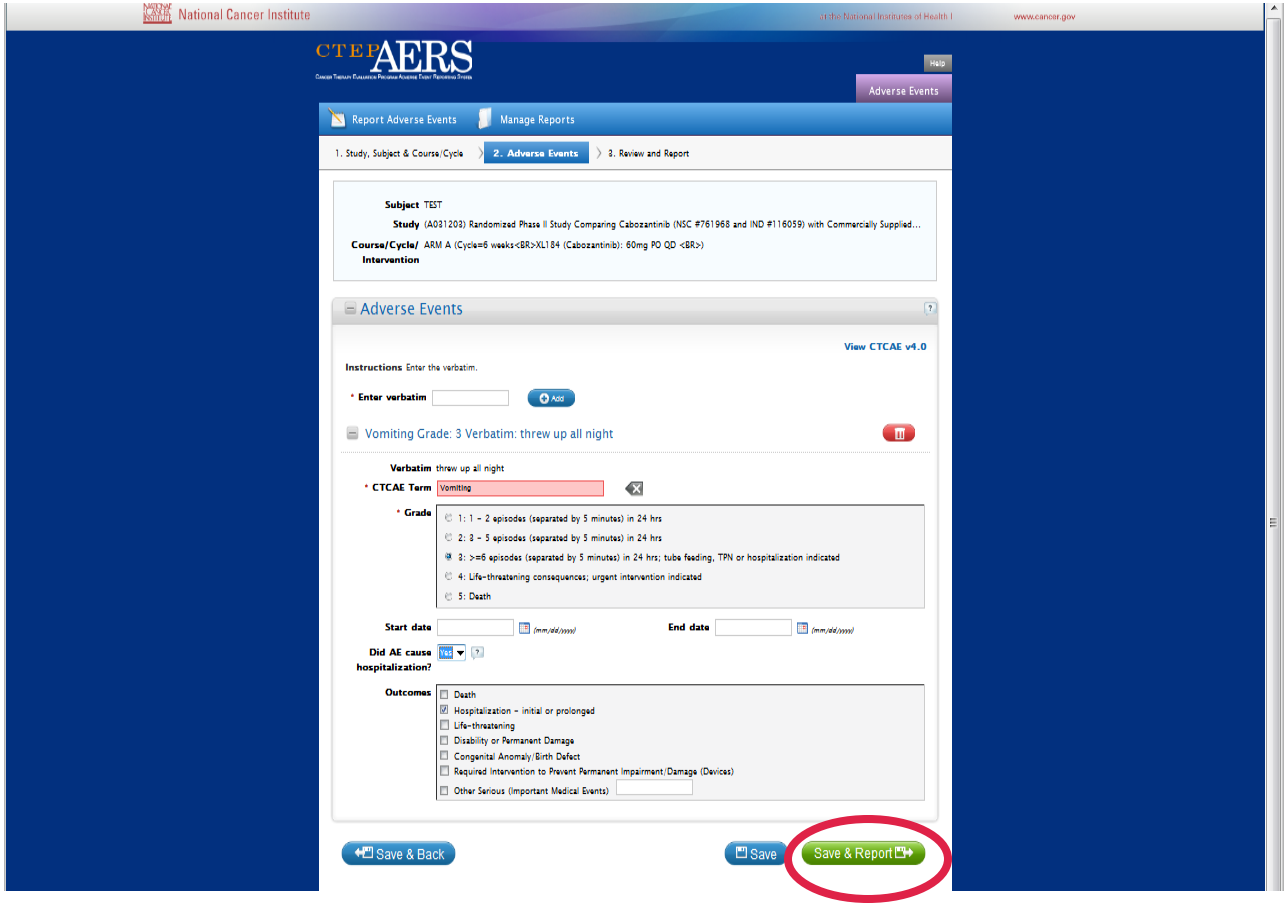
Pre-submission Evaluation (continued)

Step 2b: Enter the adverse event CTCAE term, grade, hospitalization status, dates and outcome(s)



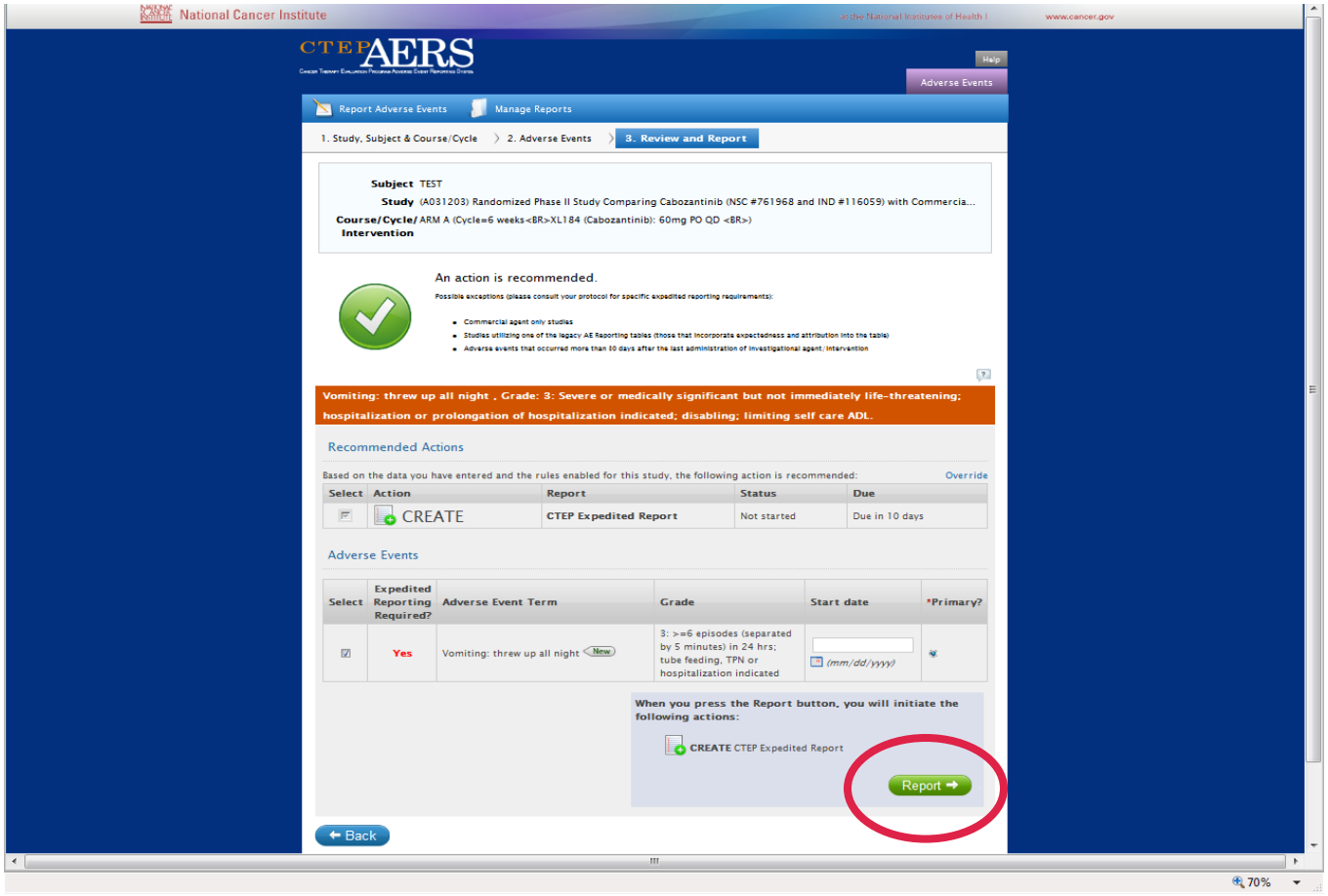
Pre-submission Evaluation (continued)

Step 3: Click Save & Report to trigger the Rules Engine



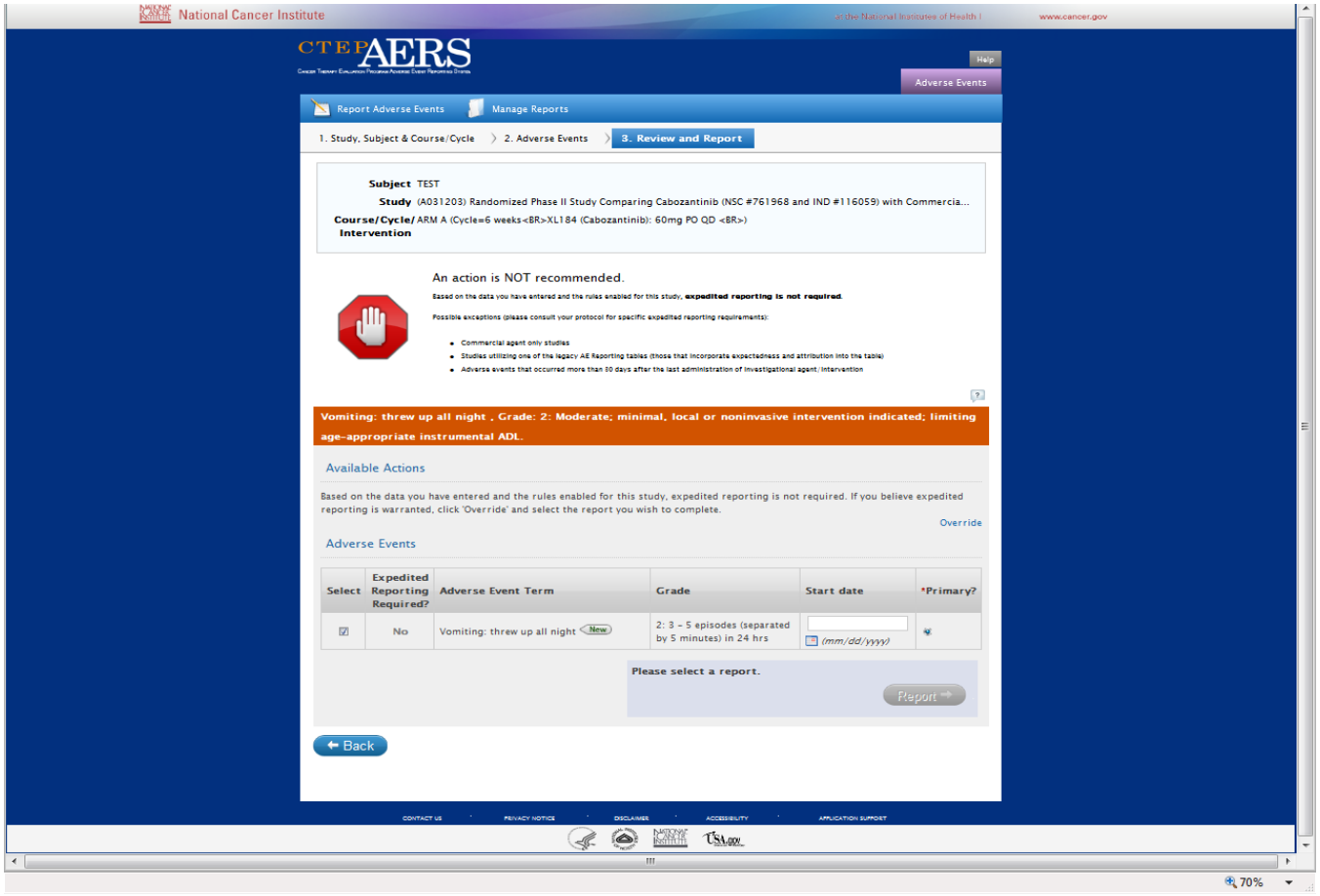
Pre-submission Evaluation (continued)

Action Recommendation



Pre-submission Evaluation (continued)

No Action Recommendation



Pre-submission Evaluation (continued)

Limitations

- 'Late' AEs (AE's that occur >30 days after the administration of the investigational agent)
- Protocol uses the old AE tables
- Protocols uses non-CTCAE terms to describe reporting exceptions
  - Example: Protocol states, "Do not use expedited reporting for all hematological AEs grade 3 or below."
- Some Commercial Agent only or non-CTEP IND studies
- Currently only encompasses ***exceptions*** to expedited reporting

Your protocol is always the correct source of truth for expedited reporting. If CTEP-AERS differs, the protocol wins. Always double check your protocol to ensure you are reporting correctly.

Pre-submission Evaluation (continued)

‘New’ AE Table

Late Phase 2 and Phase 3 Studies: Expedited Reporting Requirements for Adverse Events that Occur on Studies under an IND/IDE within 30 Days of the Last Administration of the Investigational Agent/Intervention[1, 2]

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 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 SERIOUS adverse events that meet the above criteria **MUST** be immediately reported to the NCI via AdEERS 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 serious adverse events 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 AdEERS 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]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 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 PET or SPECT IND agents, 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

‘Old’ AE Table

Legacy Table D: Reporting Requirements for Adverse Events that occur within 30 Days[1] of the Last Dose of the Investigational Agent on Phase 2 and 3 Studies

	1	2	2	3		3		4 & 5	4 & 5[2]
				Unexpected		Expected			
	Unexpected and Expected	Unexpected	Expected	With hospitalization	Without hospitalization	With hospitalization	Without hospitalization	Unexpected	Expected
Unrelated Unlikely	Not Required	Not Required	Not Required	10 Calendar Days	Not Required	10 Calendar Days	Not required	10 Calendar Days	10 Calendar Days
Possible Probable Definite	Not Required	10 Calendar Days	Not Required	10 Calendar Days	10 Calendar Days	10 Calendar Days	Not required	24-Hour; 5 Calendar Days	10 Calendar Days

[1]**AEs with attribution of, possible, probable, or definite that occur greater than 30 days after the last treatment with an agent/intervention under an NCI IND require reporting as follows:**

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

- Grade 4 and Grade 5 unexpected AEs

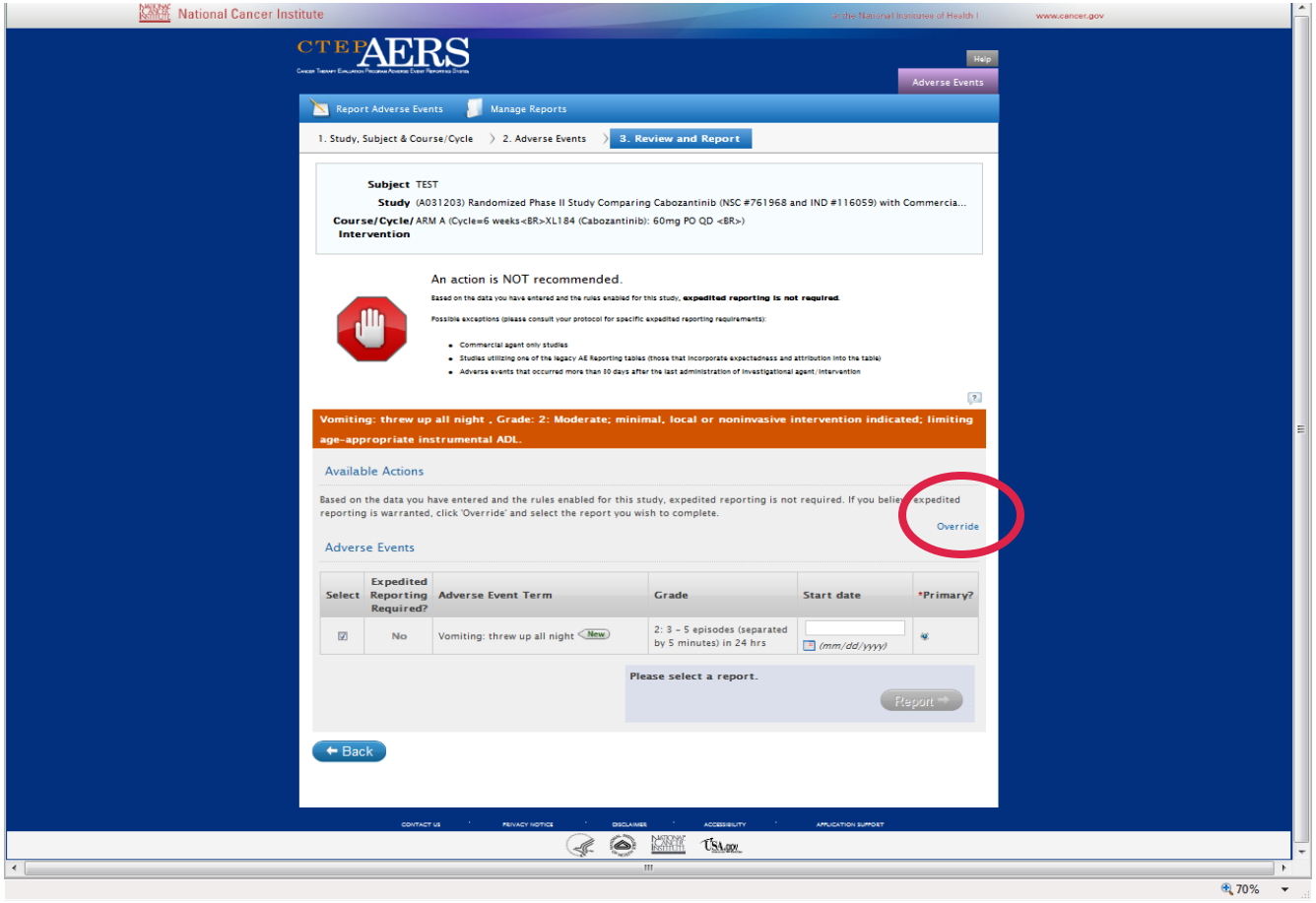
AdEERS 10 calendar day report:

- Grade 3 unexpected AEs with hospitalization or prolongation of hospitalization
- Grade 5 expected AEs

[2]Although an AdEERS 24-hour notification is not required for death clearly related to progressive disease, a full report is required as outlined in the table.

Pre-submission Evaluation (continued)

Override



Recipients

Always copied on Report Submissions:	
Contact info entered into CTEP-AERS during report creation	Reporter
	Submitter (often the same person as the Reporter)
	Treating Physician
	Any CCs added by the Submitter (optional)
Contact information housed at NCI (not viewed in CTEP-AERS)	Study PI
	Alliance Adverse Event Coordinators
	Others as added by Alliance Leadership
	NCI Adverse Event Notification System

Amendments to Reports

- All AdEERS Reports created since 1/1/2008 are available in CTEP-AERS and can be amended using CTEP-AERS
  - To amend a report created prior to 1/1/2008, please contact the CTEP Help Desk: ncictephelp@ctep.nci.nih.gov
- Amendments to CTEP-AERS reports or old AdEERS reports are created via the 'Manage Reports' tab on the CTEP-AERS home page
  - Study number, Subject ID, and Ticket number required for access

CTEP-AERS Resources

- CTEP-AERS Home Page
  - http://ctep.cancer.gov/protocolDevelopment/electronic_applications/adverse_events.htm
    - CTEP-AERS Application: https://eapps-ctep.nci.nih.gov/ctepaers
- Online resources
  - Comprehensive Training Guide
  - Training Presentations
  - Recorded Training Demo
  - FAQ Document
  - Practice Application: https://betapps-ctep.nci.nih.gov/ctepaers/public/login
- CTEP personnel available via email or phone
  - AEMD Help Desk (formerly known as the AdEERS MD Help Desk)
    - aemd@tech-res.com
    - (301) 897-7497
  - Technical Help Desk for technical, application-related issues
    - ncictephelp@ctep.nci.nih.gov
    - 1-888-283-7457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