FDA Registration Trials

Aisha Shah

CRP Information Meeting, Conducting FDA Registration Trials

November 1, 2018

Goals

- Registration Trial Considerations
- DTL and RCR
- AE Submissions
- Essential Documents
- Protocol Training
- Auditing and Monitoring
- PI Oversight
- FDA Inspection

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REGISTRATION TRIAL CONSIDERATIONS

Alliance and NCI Initiatives: IND/NDA Trials

- Initiatives and Process Changes Implementation 2017-2018
- Improve regulatory authority inspection readiness; implement risk-based monitoring approach
  - Centralized Monitoring
  - Audits with TSDV in Rave
  - Centralized Delegation of Tasks Log (DTL)
  - Centralized Registration and Credential Repository (RCR)
  - CTEP-AERS/Rave Integration
- Alliance standardized approach to registration trials for all pharmaceutical partners

Delegation of Tasks Log (DTL) – *What is it?*

- NCI to focus on registration trials with central DTL
- Online application by CTSU that is used to define and maintain site personnel listing and their roles/responsibilities
- Via CTEP's *Registration & Credential Repository (RCR)*
  - Clinical Investigator per protocol
  - Study team per protocol per site
  - Verifies qualifications of study personnel – e.g. ICF, H&P, eligibility, toxicity, data entry, etc

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Delegation of Tasks Log (DTL) – *Why?*

- Ensures that there are no gaps at the site-level per FDA requirements (DTL is complete before enrollment)
- DTL + registration documents from RCR to create *Study Site Registration Packet*
  - Registration types – Investigator, Non-Physician Investigator, Associate Plus, Associate, Associate Basic
  - Documentation that responsibilities are delegated to qualified personnel
  - Protocol-specific training

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Delegation of Tasks Log (DTL) – *Why?*

- Audit – Per CTMB guidelines (August 2017), *The auditor will review the log to evaluate appropriate implementation and maintenance*
- Deficiencies:
  - Critical – any finding identified before or during an audit that is suspected to be fraudulent activity
  - Major – performing tasks not assigned to individual, failure to keep DTL current, individual not listed on DTL, etc
  - Lesser - other

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Delegation of Tasks Log (DTL) – *Who?*

- Site staff responsible for conduct of protocol leading submitted study data
- Clinical Investigator (CI) – responsible for overseeing the conduct of the protocol at the site. Must have active CTEP registration w/ investigator-type & be on a participating site roster

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Delegation of Tasks Log (DTL) – *Who?*

- Infusion nurses?
- Lab personnel?
  - The DTL is designed to capture individuals that significantly contribute to the protocol data at the site in the general task areas outlined on the DTL.
  - There is no formal definition of 'significant contributor', but guidance provided by the FDA on completion of the Form FDA 1572 can be found at *https://www.fda.gov/downloads/RegulatoryInformation/Gui dances/UCM214282.pdf*
  - In general, hospital staff providing ancillary or intermittent routine care are not considered significant contributors.

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Registration & Credential Repository (RCR)

- Self-service online registration application for study personnel
  - FDA Form 1572
  - Registration Types require different regulatory documentation – 1572, FDF, NCI Biosketch (education training, certification, license), CV, HSP & GCP training
  - Allows access to CTEP applications, e.g. Rave, OPEN, etc
  - DTL access for site/protocol maintenance

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Adverse Event Submission Requirements for Registration Trials

Shauna Hillman

CRP Information Meeting, Conducting FDA Registration Trials

November 1, 2018

AE Submission Requirements for Registration Trials

- Changes
  - Instead of reporting the maximum grade that occurred during the treatment cycle, all changes in grade must be reported
- Additions
  - Verbatim term
  - Start date of the AE
  - End Date of the AE
  - On-going status
- AE user guide is available on the CTSU website
  - Covers persistent, intermittent and recurrent AEs
  - A link to this user guide is available in the help text

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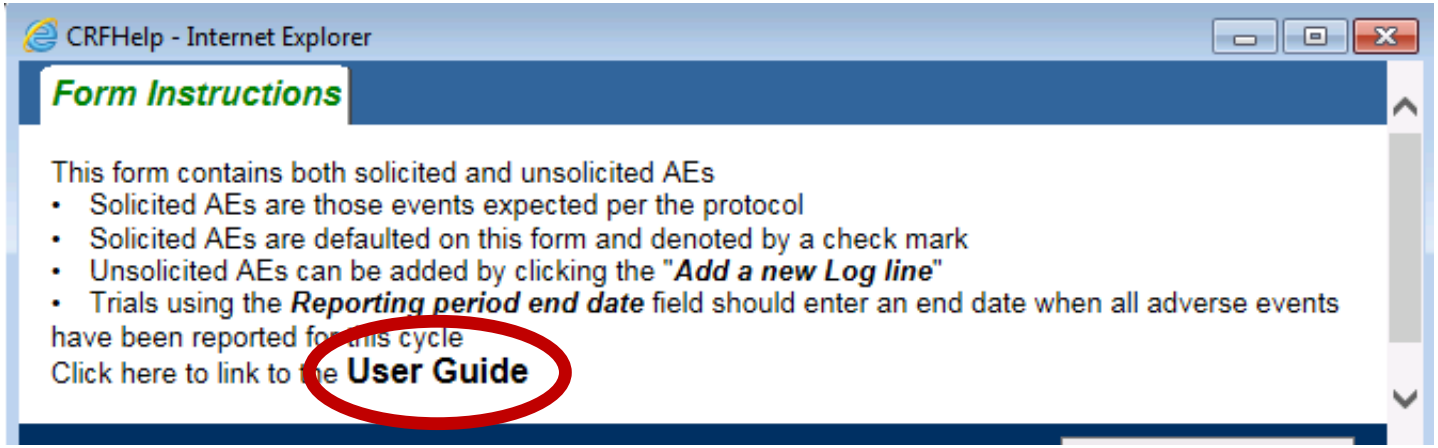
Example of Link to User guide

Link is Available for Cabinet-Trial A021602



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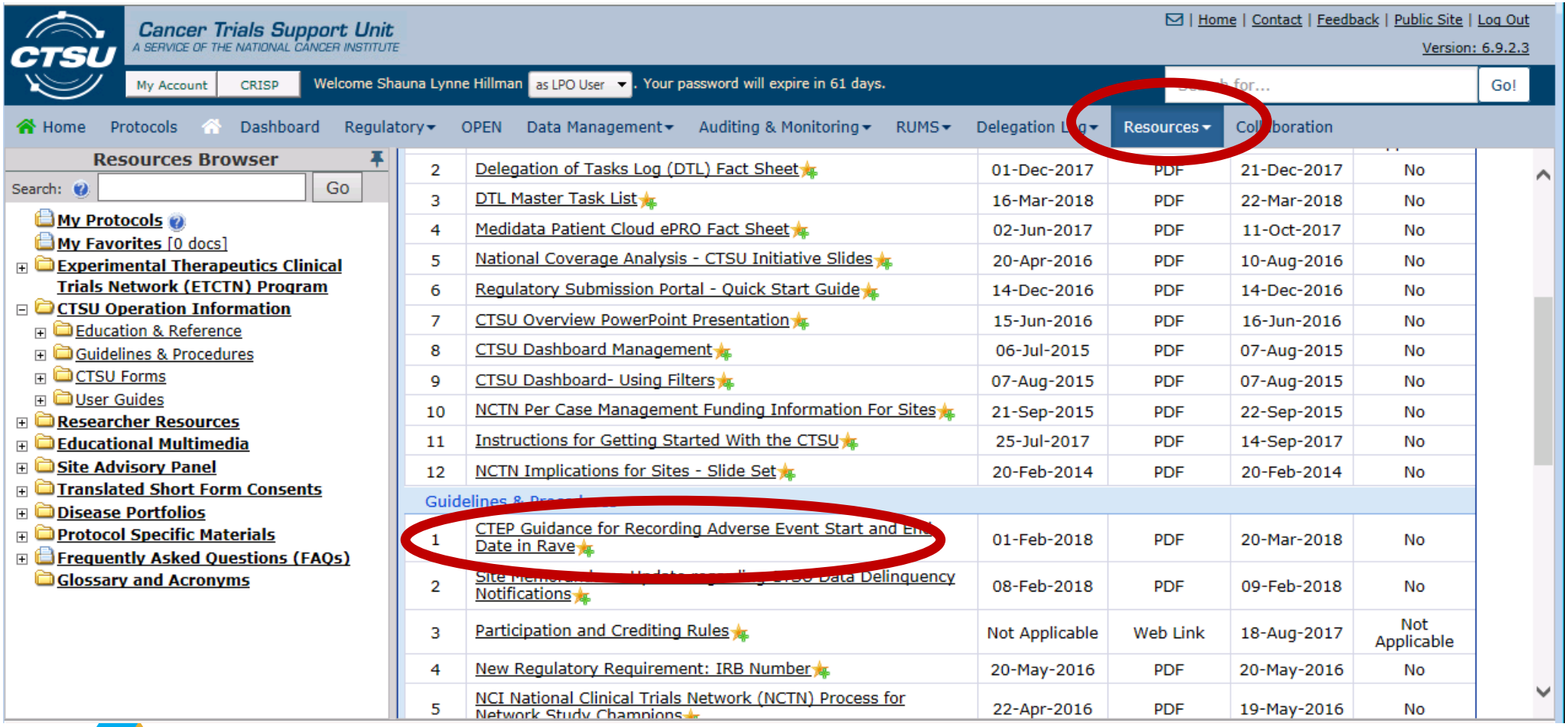
CTSU Website



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Rave – CTEP-AERs Integration

- Purpose: Synchronize routine and expedited Adverse Event (AE) data collection
- Purpose: Provide the site with guidance about whether an AE does/does not need to be submitted as a Serious AE in an expedited fashion
- Required for all trials where CTEP holds the IND starting October 2017
  - Implemented in A031501, A021502, A091605, A021602

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Rave - CTEP-AERs Integration

- Main Changes
  - The timing of AE reporting
    - AE data must now be first reported in Rave
    - All updates to AE data must be first made in Rave, then resubmitted for rule evaluation
  - All AEs ≥ grade 0 must be sent for rule evaluation

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Rave - CTEP-AERs Integration

- Both solicited and “other” AEs are reported on the same form
- The report period end date should only be recorded when the cycle is complete as this drives querying
- An Expedited Reporting Evaluation Form must be submitted to send all AEs recorded on the AE form for rule evaluation to determine if any need to be reported in an expedited fashion via CTEP-AERs

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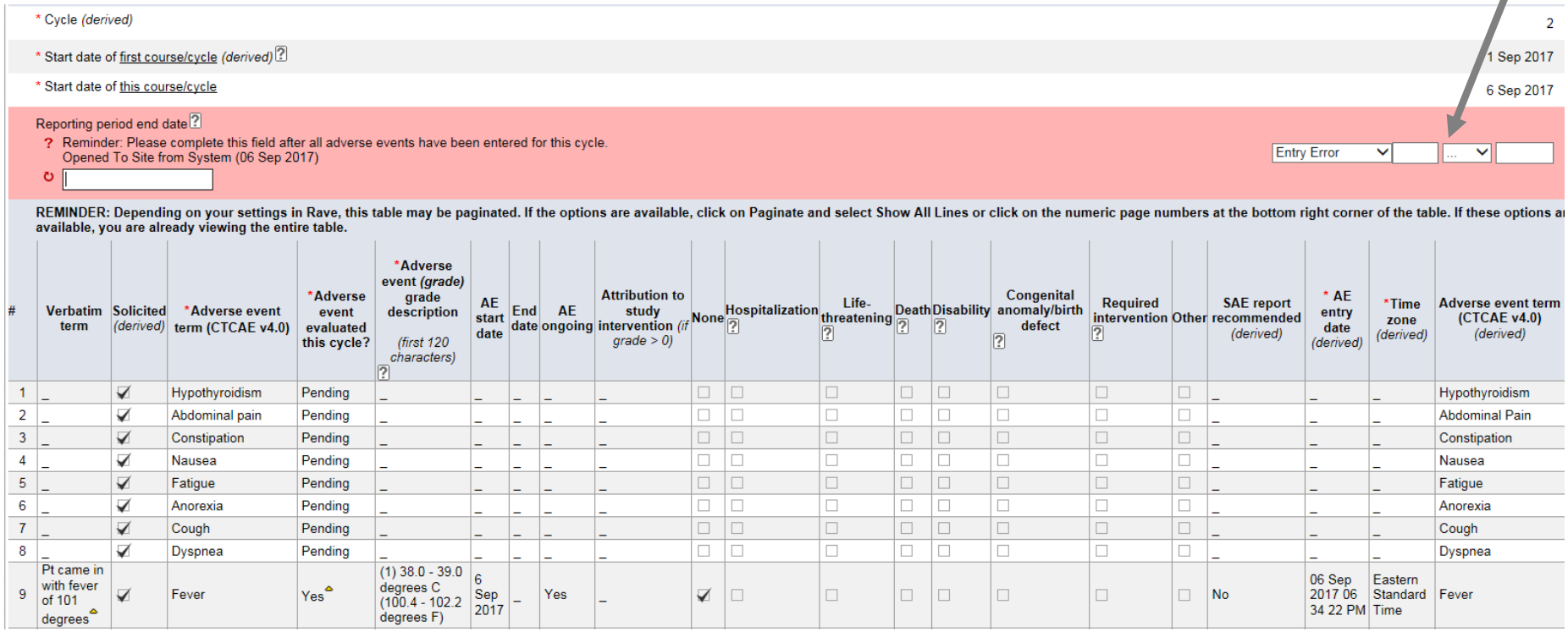
Tips for AE Form Submission

All fields required for rule evaluation are identified with a red asterisk

The site should leave report period end date missing until after completion of the entire cycle and form



* Cycle *(derived)* 2

* Start date of first course/cycle *(derived)* 1 Sep 2017

* Start date of this course/cycle 6 Sep 2017

Reporting period end date

? Reminder: Please complete this field after all adverse events have been entered for this cycle.
Opened To Site from System (06 Sep 2017)

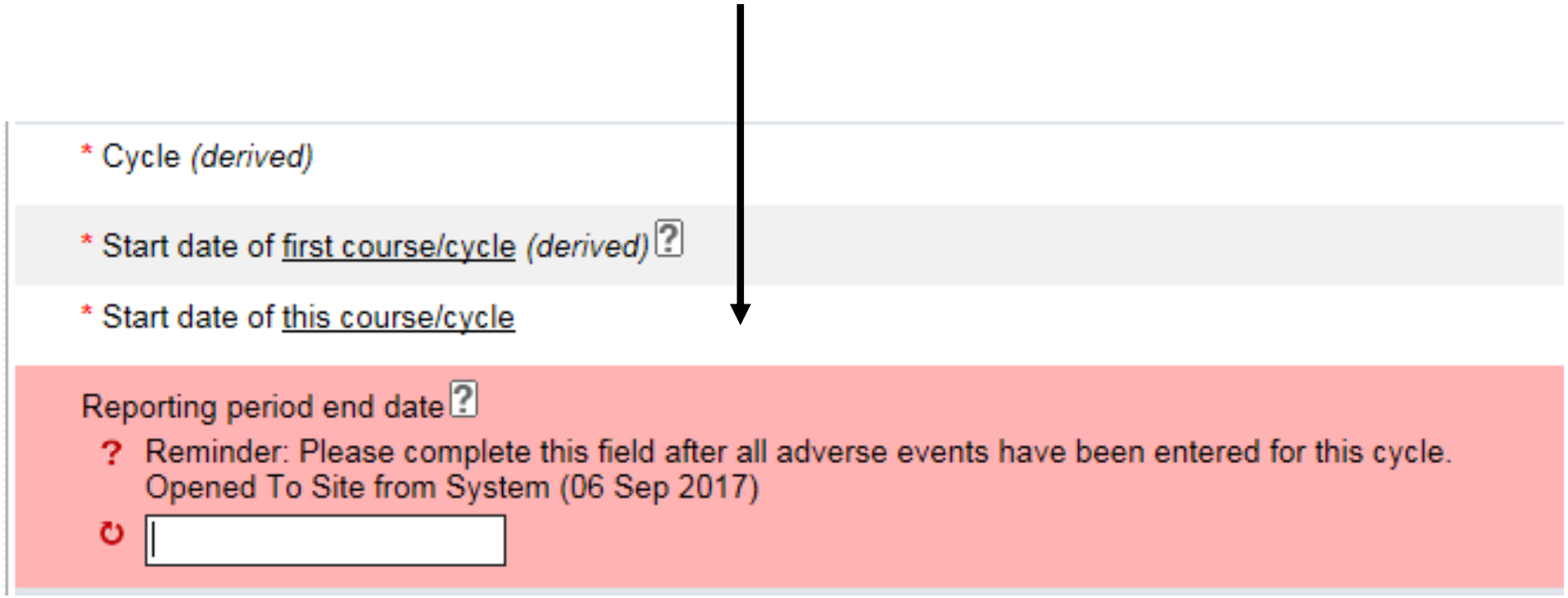
Entry Error

REMINDER: Depending on your settings in Rave, this table may be paginated. If the options are available, click on Paginate and select Show All Lines or click on the numeric page numbers at the bottom right corner of the table. If these options a available, you are already viewing the entire table.

#	Verbatim term	Solicited *(derived)*	*Adverse event term (CTCAE v4.0)	*Adverse event evaluated this cycle?	*Adverse event *(grade)* grade description *(first 120 characters)*	AE start date	End date	AE ongoing	Attribution to study intervention *(if grade > 0)*	None	Hospitalization	Life-threatening	Death	Disability	Congenital anomaly/birth defect	Required intervention	Other	SAE report recommended *(derived)*	* AE entry date *(derived)*	*Time zone *(derived)*	Adverse event term (CTCAE v4.0) *(derived)*
1	_	☑	Hypothyroidism	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Hypothyroidism
2	_	☑	Abdominal pain	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Abdominal Pain
3	_	☑	Constipation	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Constipation
4	_	☑	Nausea	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Nausea
5	_	☑	Fatigue	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Fatigue
6	_	☑	Anorexia	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Anorexia
7	_	☑	Cough	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Cough
8	_	☑	Dyspnea	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Dyspnea
9	Pt came in with fever of 101 degrees	☑	Fever	Yes	(1) 38.0 - 39.0 degrees C (100.4 - 102.2 degrees F)	6 Sep 2017	_	Yes	_	☑	☐	☐	☐	☐	☐	☐	☐	No	06 Sep 2017 06 34 22 PM	Eastern Standard Time	Fever

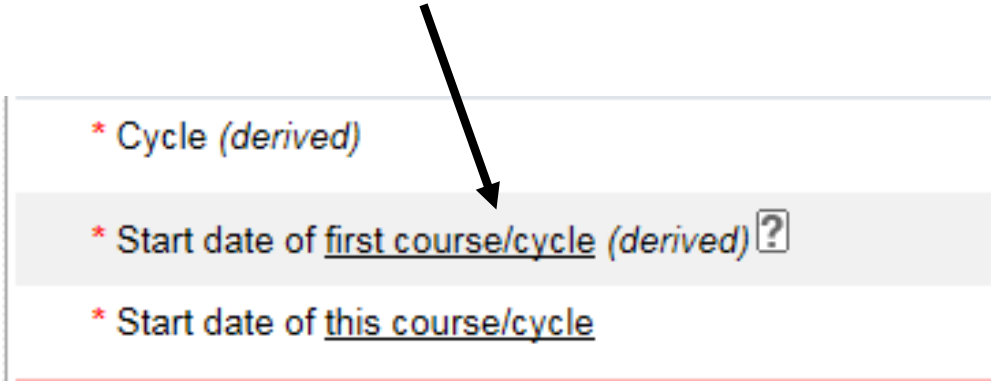
Tips for AE Form Submission

Do not respond to query, it will go away automatically when the report period end date is added. Please leave as a reminder that the form is not complete.



Tips for AE Form Submission

This field is derived from the AE form for cycle 1, if missing enter on the cycle 1 AE form



Tips for AE Form Submission

Verbatim term is new

Indicator of whether AE is solicited

AE evaluated is defaulted to "Pending" and must be updated when AE is evaluated

AE start/stop dates and ongoing status are new, ongoing status is derived based on presence of AE stop date

After AE is submitted for rule evaluation the AE specific recommendation can be found here

REMINDER: Depending on your settings in Rave, this table may be paginated. If the options are available, click on Paginate and select Show All Lines or click on the numeric page numbers at the bottom right corner of the table. If these options are available, you are already viewing the entire table.

Verbatim term	Solicited *(derived)*	*Adverse event term (CTCAE v4.0)	*Adverse event evaluated this cycle?	*Adverse event *(grade)* grade description *(first 120 characters)*	AE start date	End date	AE ongoing	Attribution to study intervention *(if grade > 0)*	None	Hospitalization	Life-threatening	Death	Disability	Congenital anomaly/birth defect	Required intervention	Other	SAE report recommended *(derived)*	* AE entry date *(derived)*	*Time zone *(derived)*	Adverse event term (CTCAE v4.0) *(derived)*
_	☑	Hypothyroidism	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Hypothyroidism
_	☑	Abdominal pain	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Abdominal Pain
_	☑	Constipation	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Constipation
_	☑	Nausea	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Nausea
_	☑	Fatigue	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Fatigue
_	☑	Anorexia	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Anorexia
_	☑	Cough	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Cough
_	☑	Dyspnea	Pending	_	_	_	_	_	☐	☐	☐	☐	☐	☐	☐	☐	_	_	_	Dyspnea
Pt came in with fever of 101 degrees	☑	Fever	Yes	(1) 38.0 - 39.0 degrees C (100.4 - 102.2 degrees F)	6 Sep 2017	_	Yes	_	☑	☐	☐	☐	☐	☐	☐	☐	No	06 Sep 2017 06 34 22 PM	Eastern Standard Time	Fever

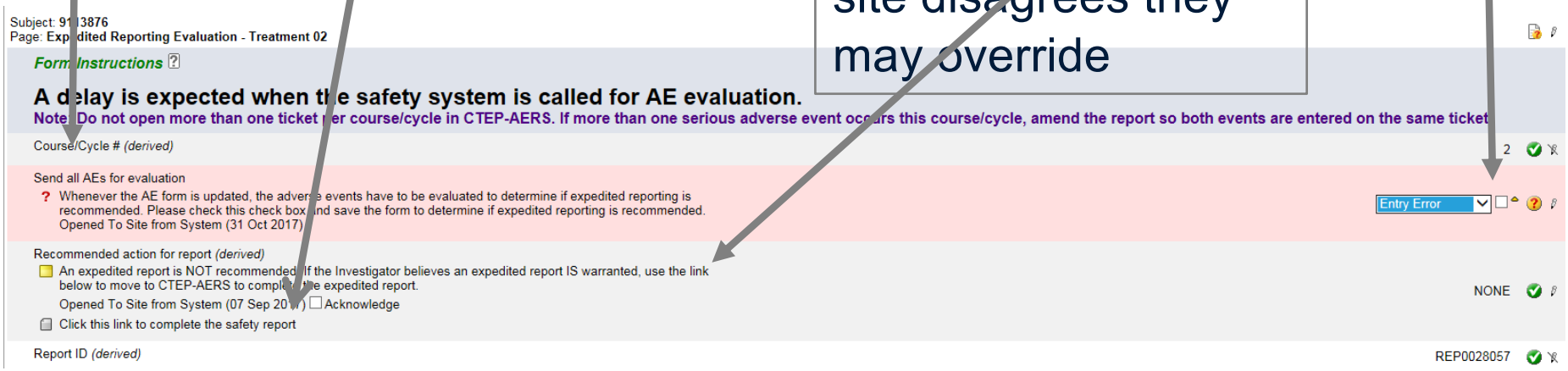
Expedited Reporting Evaluation Form

A query fires anytime a new AE is entered or an existing AE is updated. Check the checkbox and save the form to submit the AE for rule evaluation

If a query is present on the AE form, you will NOT be able to send the AE for rule evaluation until after the query is resolved, exception is the query that fires on the report period end date

Link to CTEP-AERs here

Recommendation provided here and is populated after form is submitted, if the site disagrees they may override

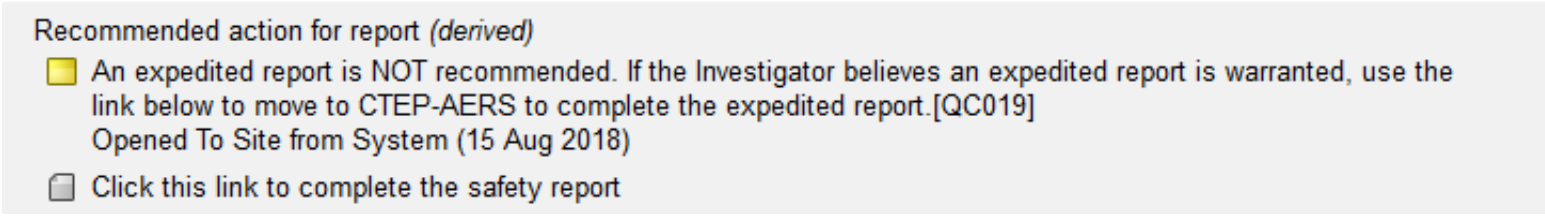


Rave – CTEP-AERs Integration

- All Alliance trials must use the new AE Form
  - verbatim term, AE start date, AE end date and ongoing status fields required for Registration trials only
  - All changes in AE grades must also be captured for Registration trials only
  - Integration required for all trials where CTEP holds the IND

Rave – CTEP-AERs Integration: Misc Notes

- The sticky notes found on the Expedited Reporting Evaluation Form are for instructional purposes only and there is no way to remove them from your Rave Task Summary



- The AE Start Date cannot be before the start date of cycle 1, if a pre-existing condition, enter the start date of cycle 1

Rave – CTEP-AERs Integration: Misc Notes

- You do not have to wait until all solicited AEs are evaluated to run the rule evaluation, the form is designed for you to evaluate AEs in real time
- If all AEs are reported, you do not have to submit each AE for rule evaluation, saving the Expedited Reporting Evaluation Form will result in all AEs on the AE form being evaluated.

Any Questions?

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Essential Documents at Sites (*ICH E6, Section 8)* –

1. Investigator Brochures
2. Protocol and amendments
3. ICF (and any other study info distributed to patient)
4. Subject recruitment info
5. IRB/Independent Ethics Committee
6. Investigator CVs
7. Lab certification/accreditation
8. IP - handling instructions & shipping records & DARF

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Essential Documents at Sites (*ICH E6, Section 8):*

1. Monitoring letters
2. Correspondences b/w IRB & Institution
3. AE/SAE/SUSAR/UPIRSO – site-specific SOPs, if applicable
4. Protocol-specific training
5. Screening/enrollment logs, per site SOP

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Essential Documents – *Don't Forget*:

- Sites should also have copies maintained of:

1. RCR – 1572, CV, License, FDF
2. DTL
3. Regulatory Support System (RSS) – regulatory approval, protocol amendments, continuing renewal, site termination letter from IRB, protocol-specific-training, +/- ICF templates
4. COI Disclosure Form

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Department of Health & Human Services

Public Health Service

National Institutes of Health
National Cancer Institute
Center for Cancer Research
Bethesda, Maryland 20892

Protocol Review Log

Protocol #:	Protocol Title:

The individuals listed below have reviewed the protocol with the PI or designee and understand their roles and responsibilities.

Name (Please Print or Type)	Role	Signature	Date	PI/Designee Signature	Date

Protocol Training

- Importance of maintaining log?
  - Protocol amendments
  - Staffing changes at the site
- FDA-inspection readiness
- Do you know your site's SOP?
  - Alternative/Back-up documentation
- Webinars for Alliance registration trials posted to Alliance website
  - Study-specific page -> supplemental materials

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Auditing & Monitoring

- Monitoring
  - Overseeing progress of a clinical trial and ensuring that it is conducted, recorded, and reported in accordance with the protocol, SOPs, GCP, and regulatory requirements
- Auditing
  - Systematic & independent examination of trial-related activities and documents to determine whether the evaluated trial-related activities were conducted, and the data were recorded, analyzed, and accurately reported according to the protocol, sponsor's SOPs, GCP, and regulatory requirements

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Monitoring

- Mandatory per federal regulations (21 CFR812.3 (j), 812.25, 812.40, and 312.50)
- During a US regulatory audit, FDA has access to monitoring reports and their associated action items
  - Importance of addressing action items on a monitoring letter/report in a timely fashion

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Monitoring

- Depending on the study-specific monitoring plan, the following is routinely monitored:
  - Informed consent Documents
  - Eligibility criteria
  - Protocol compliance
  - Source data verification for data accuracy
  - Query resolution
  - AEs – occurrence and reporting
  - IP accountability
  - Essential documents
  - Clinical Investigator (CI) & IRB oversight
- CI is adequately informed of responsibilities to recruit eligible subjects & collect high quality data

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Central Monitoring to Support Registration Trials

Shauna Hillman

CRP Information Meeting, Conducting FDA Registration Trials

November 1, 2018

Alliance Central Monitors

- Tiffany Schafer

- Sara Goodman

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Central Monitoring

- Introduction
  - Central Monitoring (CM) is performed by Lead Protocol Organizations (LPOs) to ensure protocol compliance by sites
  - It consists of remote review of source documents against data entered in Rave
  - The Source Document Portal (SDP) is an application on the CTSU website in the Auditing & Monitoring tab used to support the collection of source documents for CM review

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Central Monitoring-Current Status

- The CTSU SDP is not in use for any current Alliance trials
- Central Monitoring (CM) is being conducted for the following trials
  - A031501-Ambassador
  - A021502-Atomic
  - A021602-Cabinet
  - A041701-Future trial
- CM is currently being facilitated by uploading source documents on the Source Document Form within Rave

Example of Baseline Source Document Form for Atomic Trial

A021502 [redacted] Baseline | Supporting Documentation: Baseline

Subject: **9116633**
Page: **Supporting Documentation: Baseline - Baseline**

Cycle

#	Serial # of document	Date of assessment	Report type	Specify report type	Attachment *(max file size 10 MB)*
1	1	09 Feb 2018	H & P		A021502 HP 2.9.18_Redacted.pdf
2	2	09 Jan 2018	Colonoscopy Report		A021502 Colonoscopy 1.9.18_Redacted.pdf
3	3	09 Jan 2018	Pathology report from colonoscopy		A021502 Path 1.9.18_Redacted.pdf
4	4	19 Jan 2018	Pathology report from surgery		A021502 Path 1.19.18_Redacted.pdf
5	5	19 Jan 2018	Operative report		A021502 Op note 1.19.18_Redacted.pdf
6	6	12 Jan 2018	Imaging report	CT Ab/Pelvis	A021502 CT AbPel 1.12.18_Redacted.pdf
7	7	19 Jan 2018	dMMR testing results	Same Path report from Operation	A021502 Path 1.19.18_Redacted.pdf
8	8	09 Feb 2018	Informed Consent (redacted signature page)		A021502 Consent_Redacted.pdf
9	9	15 Feb 2018	Imaging report	Chest CT	A021502 CT Chest 2.15.18_Redacted.pdf
10	10				

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Source Document Reminders

- Redact all source documents before uploading
- The Informed Consent Document should include all indications to the optional correlative studies
- When ‘yes’ is provided for the disease assessment question, you must provide source documentation (imaging, biopsy, etc.)

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Source Document Reminders

- Source documents required for treatment may not be required for every cycle of treatment
  - Current requirements for Atomic

Treatment (first 3 cycles[1]; all cycles[2])	Treatment (Intervention)	Agent name Dose level Units of measure Dose (total) Units of measure Was protocol treatment modified? Was protocol treatment omitted? Was protocol treatment delayed? Start date Stop date
	Treatment (Intervention): Dose Modifications, Omissions and Delays	Dose modification reason Dose omission reason Dose delay reason

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Where to Find the Needed Source Documents

- Data Submission Schedule for A021502 & A021602, protocol for A031501

Data Submission Schedule for A021502:
Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Colon Cancer and Deficient DNA Mismatch Repair

SOURCE DOCUMENTATION REQUIREMNTS FOR MONITORING
The following data and documents will be reviewed through central/on-site data monitoring and source data verification (SDV) activities.

Domain	CRF	Data Fields/Section	Acceptable Source Documents
Informed Consent	Informed Consent[1]	Date of signature[3] Signature page[3]	Informed Consent Document
	Informed Consent[2]	Entire document	
Eligibility[1]	OPEN Registration Worksheet	All fields	Path report IHC report Operative report Radiology report Colonoscopy report Lab report (for registration eligibility) Clinic note Other relevant report
	On-study	Description of Primary Disease Section Mismatch Repair Testing Section Patient History Section (excluding NSAID usage) ECOG Performance Status Correlative Studies Section	
Treatment (first 3 cycles[1]; all cycles[2])	Treatment (Intervention)	Agent name Dose level Units of measure Dose (total) Units of measure Was protocol treatment modified? Was protocol treatment omitted? Was protocol treatment delayed? Start date Stop date	Relevant medical record (e.g., clinic note, other)
	Treatment (Intervention): Dose Modifications, Omissions and Delays	Dose modification reason Dose omission reason Dose delay reason	
Off Treatment [2]	Off Treatment	All fields	Relevant medical record (e.g., clinic note, other)
Disease Assessment[1]	Patient Status: Baseline, Patient Status: Treatment, Patient Status: Clinical Follow-up, Patient Status: Survival Follow-up	Survival Status Section Disease Status Section New Primary Section	Radiology report (conventional CT and MRI or chest x-ray) Lab report Colonoscopy report Relevant medical record (e.g., clinic note, other)
Disease Recurrence[1]	Notice of Recurrent Disease	All fields	Radiology report (conventional CT and MRI or chest x-ray) Lab report Colonoscopy report
New Primary[1]	Notice of New Primary	All fields	Radiology report (conventional CT and MRI or chest x-ray) Lab report Colonoscopy report
Adverse Events[2]	Adverse Events Late Adverse Events	All fields	Relevant medical record (e.g., clinic note, other)
Consent Withdrawal[2]	Consent Withdrawal (all types)	All fields	Relevant medical record (e.g., clinic note, other)

[1] Central and on-site monitoring
[2] On-site monitoring only
[3] For Central Monitoring: De-identified Informed Consent Document (ICD): Last page of signed and dated ICD (including page/s with options indicated by patient for additional studies). Patient's full signature should be redacted but date should be retained.

Data Submission Schedule SD Requirements for Monitoring

Data Submission Schedule for A021502:
Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Colon Cancer and Deficient DNA Mismatch Repair

SOURCE DOCUMENTATION REQUIREMNTS FOR MONITORING
The following data and documents will be reviewed through central/on-site data monitoring and source data verification (SDV) activities.

Domain	CRF	Data Fields/Section	Acceptable Source Documents
Informed Consent	Informed Consent[1]	Date of signature[3] Signature page[3]	Informed Consent Document
	Informed Consent[2]	Entire document	

CRF

Data Field

Source Document:

Need a source document that will validate the data entered in the given CRF - data field

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Future Initiatives

- Alliance is in the process of selecting a future trial to implement the CTSU SDP
- There are no plans to implement the SDP for trials that are already activated
- Alliance is working out how to use the SDP to facilitate both source documents needed for central monitoring and source documents needed for eligibility reviews and case evaluations

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Any Questions?

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Auditing

- Quality assurance function
- Auditors can assess a wider study sample than monitors and can help evaluate trends at various levels
  - single or multiple sites and/or multiple studies
  - trial vendors/sponsors
- Evaluate compliance to recognized standards
  - FDA's Code of Regulations
  - International Conference on Harmonization
  - International Standards Organization
  - SOPs

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Auditing

- Compliance snapshot
- Can assist in determining effectiveness of:
  - Monitoring
    - importance of addressing action items on monitoring reports in a timely fashion
  - Study team
- Manage non-compliant sites
- Assess inspection readiness

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Investigator Oversight

- How often do you meet with your investigator?
- Are routine meetings established?
- Process for obtaining signatures/assessments?

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Investigator Oversight – *How to demonstrate?*

- Timely signatures on source documents
  - Diagnostic procedures –
    - Recist reads
  - Lab results
  - Eligibility criteria
  - Treatment authorization
- DTL – appropriate and qualified staff delegation
- SAE/SUSARs - evaluated and submitted in a timely manner

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Investigator Oversight – *How to demonstrate?*

- Feedback from the FDA suggests that they are concerned with **one Clinical Investigator covering multiple sites and protocols**
  - No hard rule as to how many sites/protocols a CI may cover
  - May be a reason for triggering an audit

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FDA Inspection Readiness

- On-going state of effectiveness and suitability monitored through periodic review an monitoring of compliance
  - Not a preparation activity
  - Requires Investigators and management to be actively involved and committed to culture of compliance
- FDA Bioresearch Monitoring (BIMO) Inspection Program
  - Protects the rights, safety, and welfare of human research subjects
  - Assures quality, reliability, and integrity of data collected

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FDA Inspection Focus at Sites:

- CI oversight
- Site management
- Data
- Investigational product (IP) management
- Adverse Events

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FDA Inspection Process:

1. Notification of inspection via FDA Form 482
2. Opening meeting
3. Interview of site staff
4. Review of study-related/source documents
5. Exit meeting
   - Review findings
   - Address issues or concerns
6. Response to inspection, as needed

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FDA Inspection – *What to do if issued FDA Form 482?*

- Alliance and/or pharmaceutical partner will:
  - Provide additional instructions & guidance for preparing
  - Provide a single point of contact (SPoC) at Alliance for any issues that may arise during the inspection
  - Site should also provide daily report to Alliance SPoC
  - SPoC will assist in preparing responses to the inspection findings, if needed

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FDA Inspection – *Role of Investigator/ Site*

- Ensure availability of staff during inspection
  - Alert other staff of section, so that they know to avoid lingering in areas hosting the inspection & to watch conversations near inspectors
- Ensure availability of study-related records & provide copies to HA as requested
- Answer questions regarding your role
- At the end of each day, request a summary from the inspector
  - Forward summary to Alliance SPoC
  - Respond to any inspection findings, as needed

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FDA Inspection – *Role of Alliance*

- Assign SPoC to site
- Provide daily status report to pharmaceutical partners
- Provide ongoing support to site/investigator before, during, and after

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FDA Inspection – *Tips for Interacting with Inspectors*

- When answering questions:
  - Honestly
  - Be concise & clear – only answer the question asked
  - Don't argue with inspector
  - Don't answer hypothetical questions
  - Wait until you have heard & understood the whole question
  - Beware of pauses – don't feel like you need to keep talking

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FDA Inspection – *Findings:*

- Criticality determined by deficiencies that:
  - Affects rights, safety, or welfare of subjects
  - Impacts data integrity
  - Indicates systematic problems within the study from the Sponsor
  - Indicates problems with the investigator/site that may impact other studies
- FDA Form 483, *Inspectional Observations*, documents & communicates concerns disovered during inspections
  - Forward to Alliance SPoC, immediately!

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FDA Inspection – *Resources:*

- FDA regulatory info for clinical trials: https://www.fda.gov/RegulatoryInformation/Guidances/ucm122046.htm
- FDA Cooperative Research Information Sheet: https://www.fda.gov/RegulatoryInformation/Guidances/ucm126422.htm
- FDA Bioresearch Monitoring Info: https://www.fda.gov/ICECI/EnforcementActions/BioresearchMonitoring/default.htm

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Any Questions?

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