Patient Case Records Review

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Alliance for Clinical Trials in Oncology

Audit Workshop - Alliance Group Meeting – November 1, 2018

6 Categories

- Informed Consent
- Eligibility
- Treatment
- Disease Outcome/Response
- Adverse Events/Study Parameters
- General Data Quality

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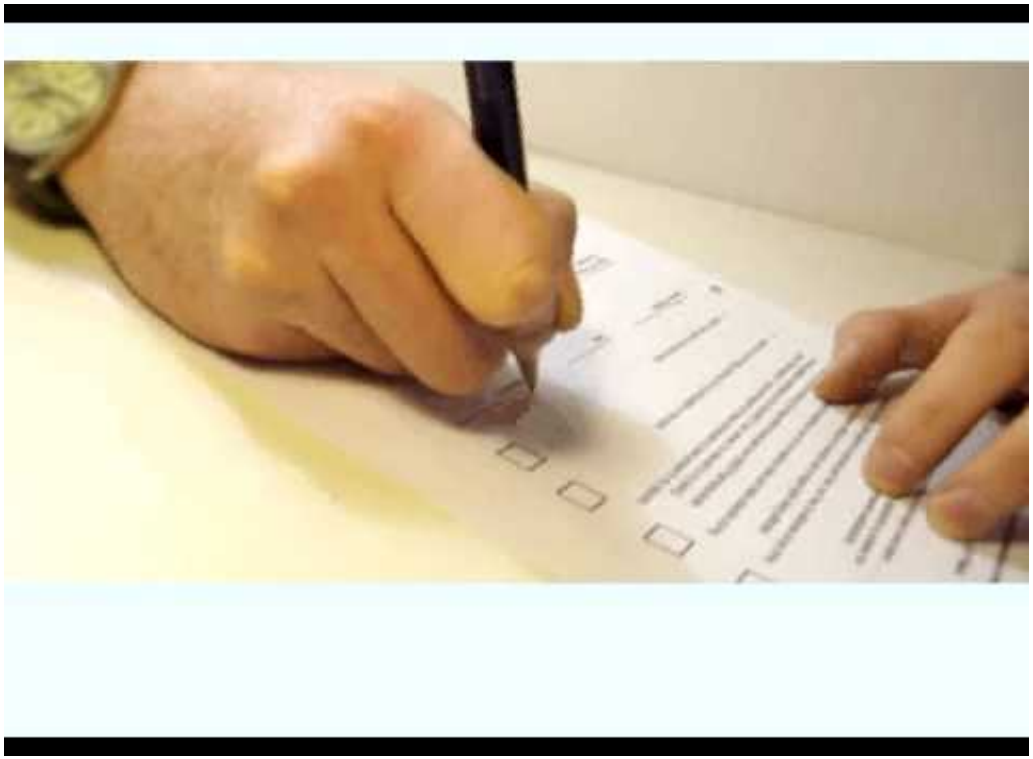
Informed Consent



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Informed Consent

- Participant signed, dated prior to undergoing any study related procedures
- All required signatures are present
- Current, IRB-approved CF was used
- Documentation of the informed consent process exists
- Any required re-consents
- Non English speaking subjects

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Eligibility

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Eligibility

- Documentation that all eligibility criteria have been met as specified by the protocol
- All required tests to confirm eligibility were performed prior to registration
- Tests done within protocol time limits

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Treatment

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Treatment

- Specific protocol treatment was given
- Treatment not given until after registration unless specifically allowed in the protocol
- Treatment given per protocol timeframe (cycle length, within window post-op, etc)
- Dose Deviations/Modifications
- Additional agent/treatment given?

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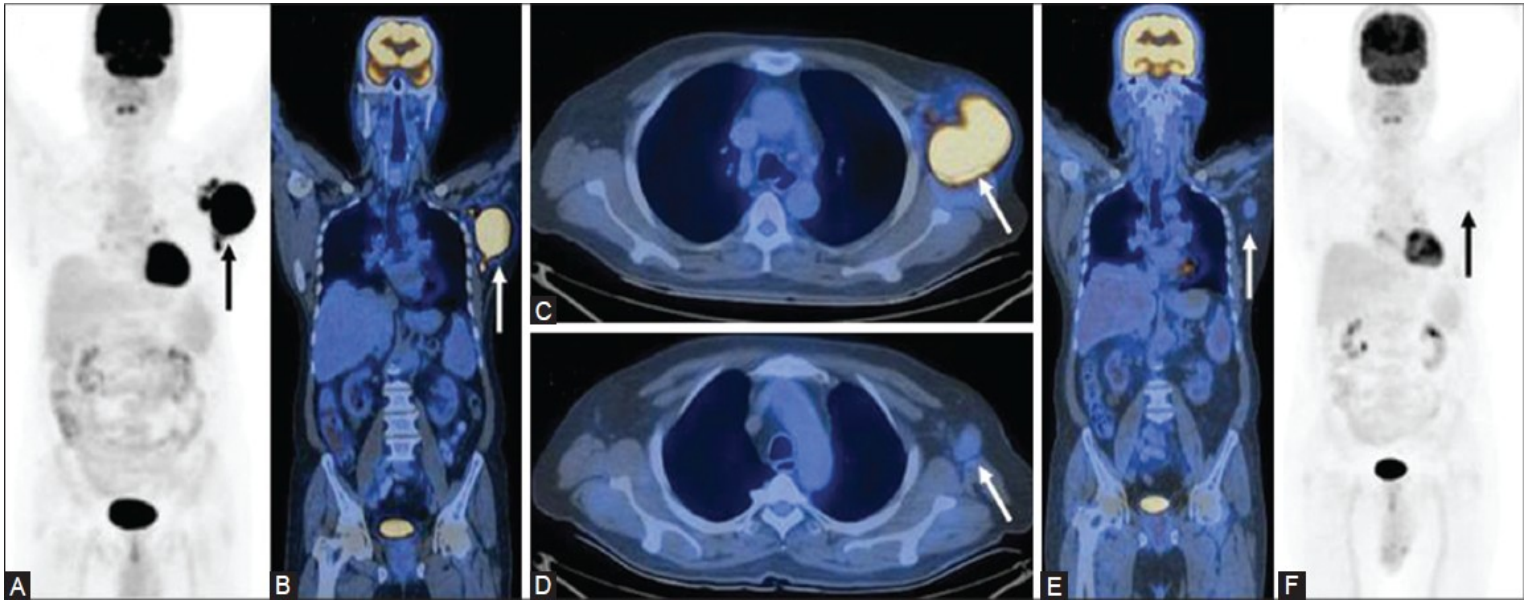
Disease Outcome/Response



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Disease Outcome/Response

- Accurate documentation of initial sites of involvement
- Re-evaluation of status performed according to protocol
- Protocol-directed response criteria followed
- Verify claimed response (PR, CR)

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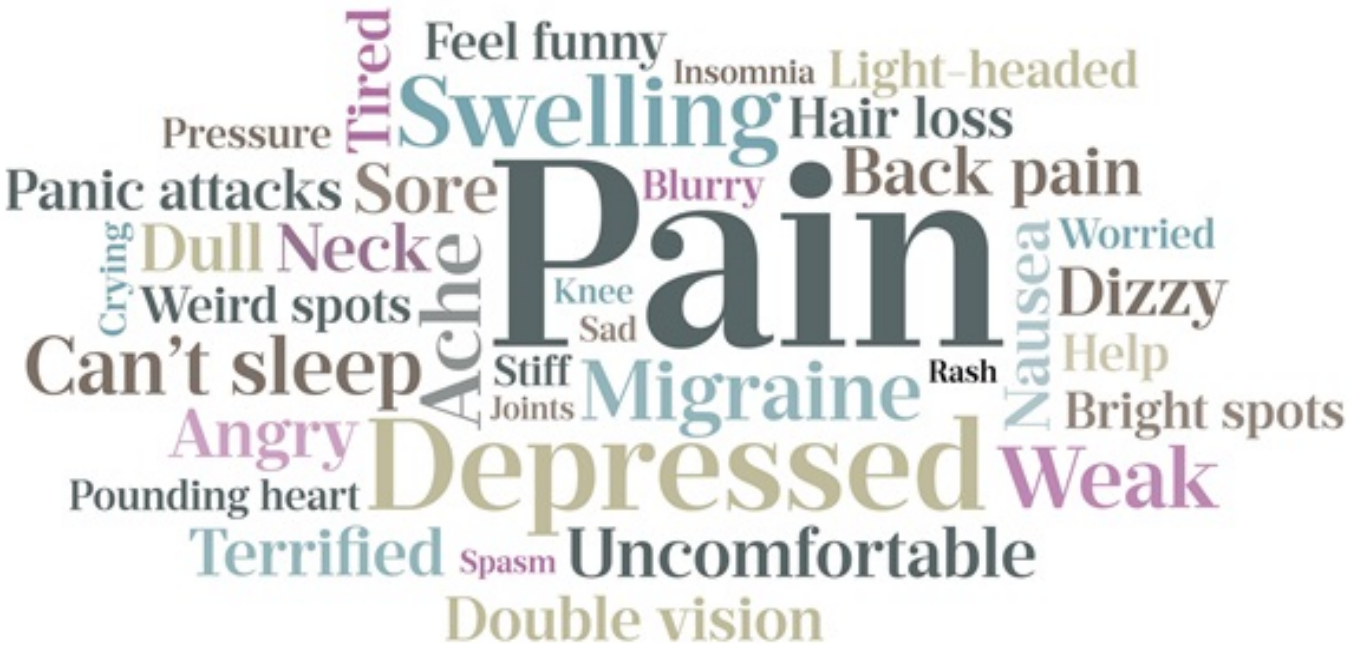
Adverse Events



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Adverse Events/Study Parameters

- Follow-up studies necessary to assess adverse events (AEs) were performed (study calendar)
- Grades, types, and attribution of AEs are documented in source and are accurately recorded in CRFs
- Adverse Event Expedited Reporting filed for required toxicity (CTEP-AERs)

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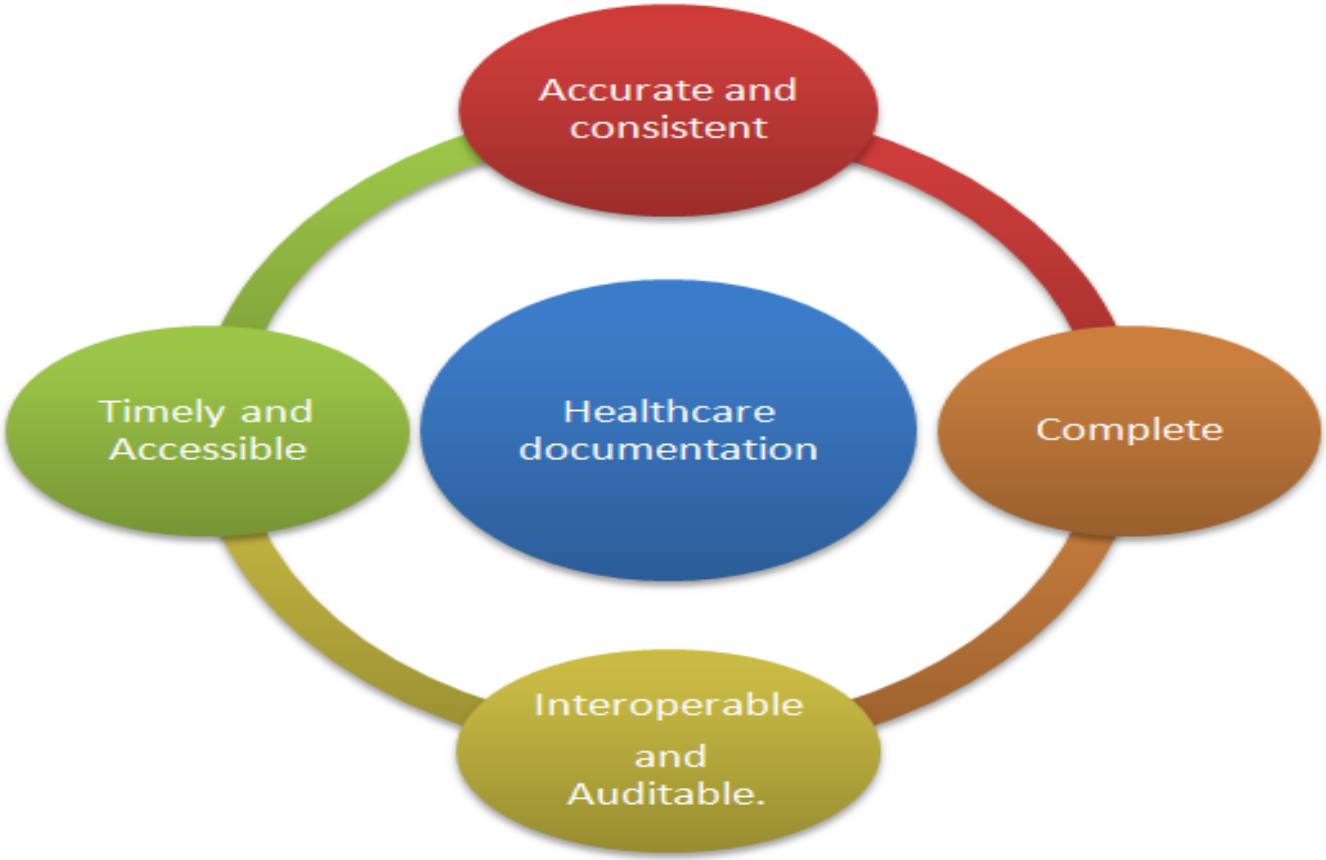
General Data Quality



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General Data Quality

- Data accurately reported on CRFs
- Forms complete
- Data submitted in a timely manner
- Concordance with source documentation
- Supplemental reports submitted
- Specimens submitted

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Source Documents

- **Accurate**: Is the document accurate?
- **Identifiable**: Is the document identifiable?
- **Legible**: Is the document legible?
- **Secure**: Is the document secure?

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Source Documents

EMR: must comply with 21 CRF part 11 subpart B;
must have a local staff person as the “driver”;
official back-up for research folders

Paper records, Research folders:

please appropriately tag

Imaging: have access to images available when needed for assessing disease response

Delegation of Tasks Log (DTL) have copy available

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Audit Preparation

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Preparing for an Audit

- Attend the Audit Workshop!

- Review Alliance Audit Policies and Procedures
  - Institutional audits: Policy number 2.8
    - Audit preparation by the institution: 2.8.6
    - Conduct of an Alliance audit: 2.8.7
    - Review of patient case records: 2.8.7.4

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Preparing for an Audit

- **Alliance auditors will not complete site-specific training: 2.8.5.7**
  - **Auditors:**
    - **are current with Human Subjects training**
    - **have a signed Alliance Confidentiality agreement on file**
    - **have completed mandatory CTMB auditor training**

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Preparing for an Audit

- Ensure that arrangements have been made:
  - Reserve conference room
  - Notify appropriate personnel
  - Request all required materials including a paper copy of all protocols
  - Ensure Principal Investigator available for the Exit Interview
  - Review your records!

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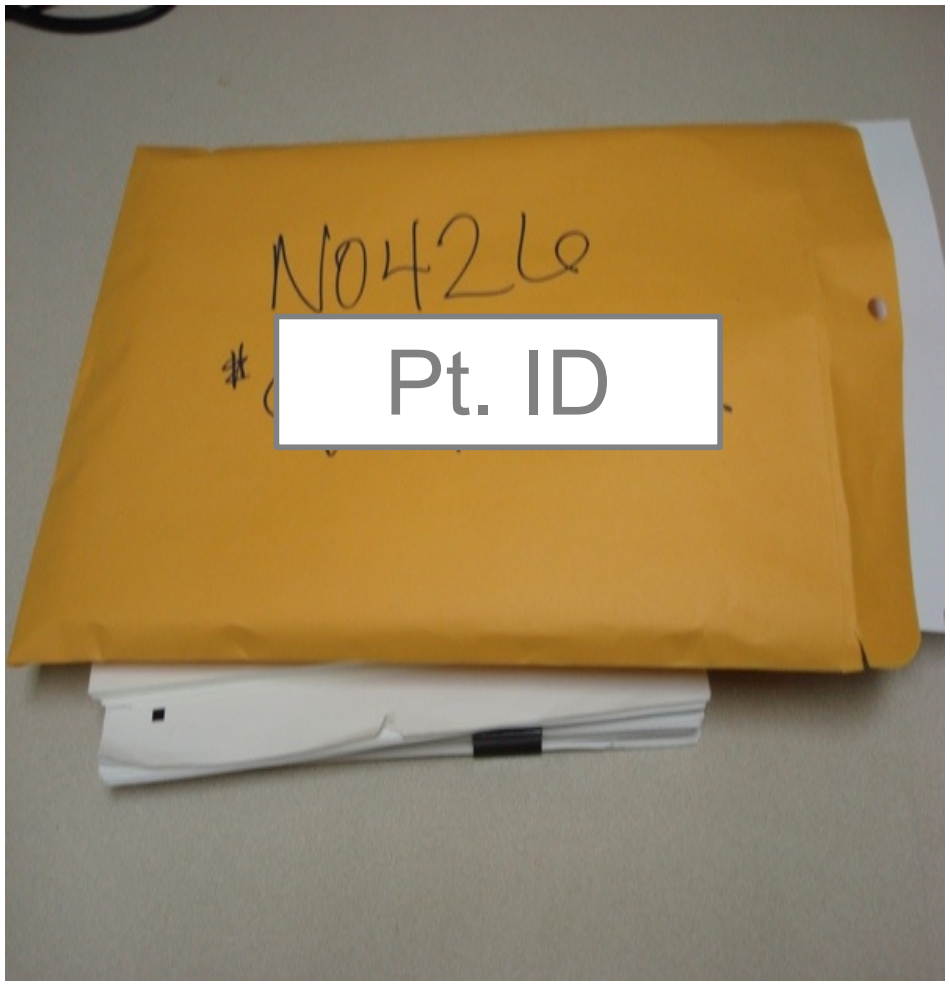

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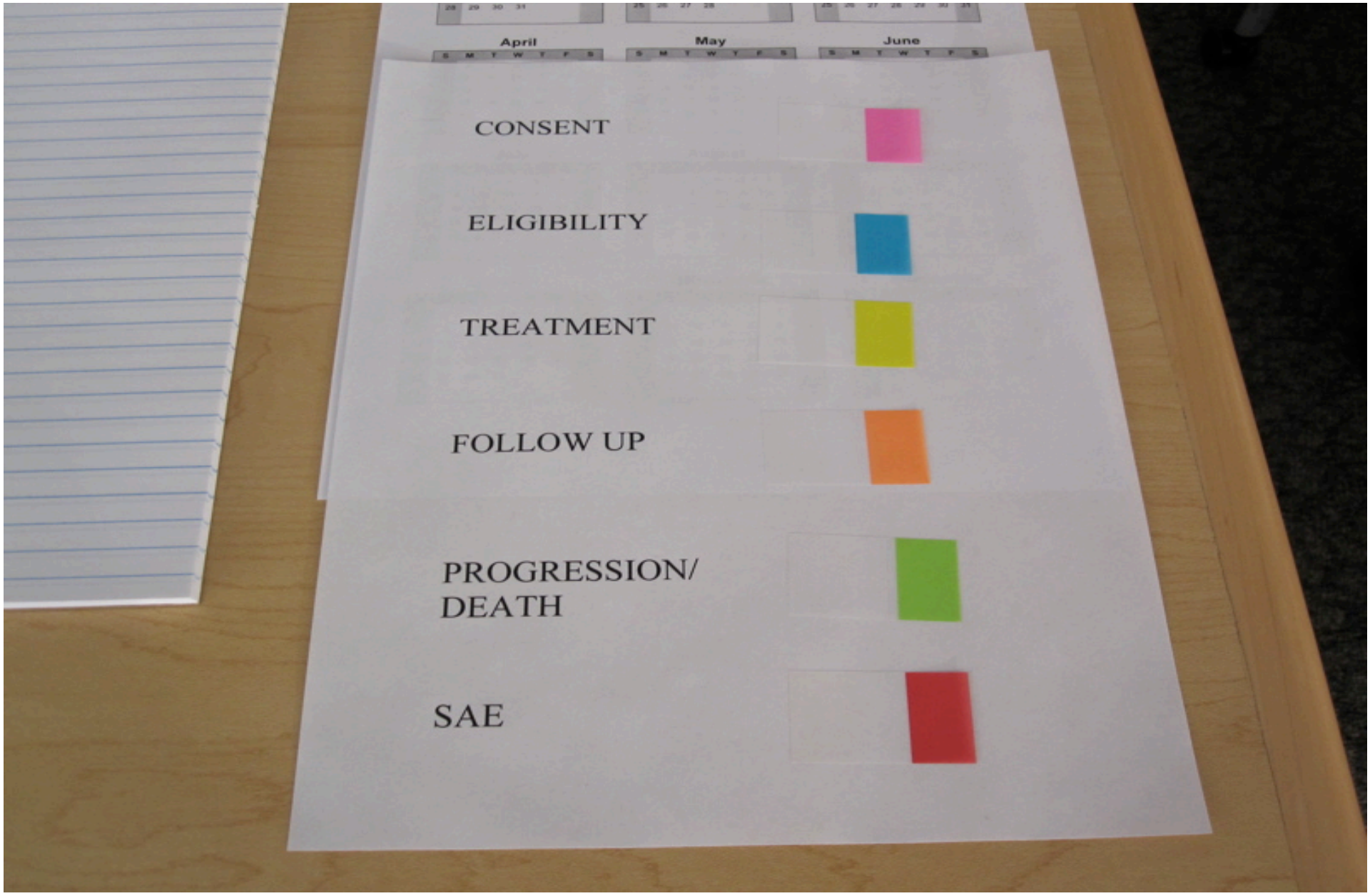

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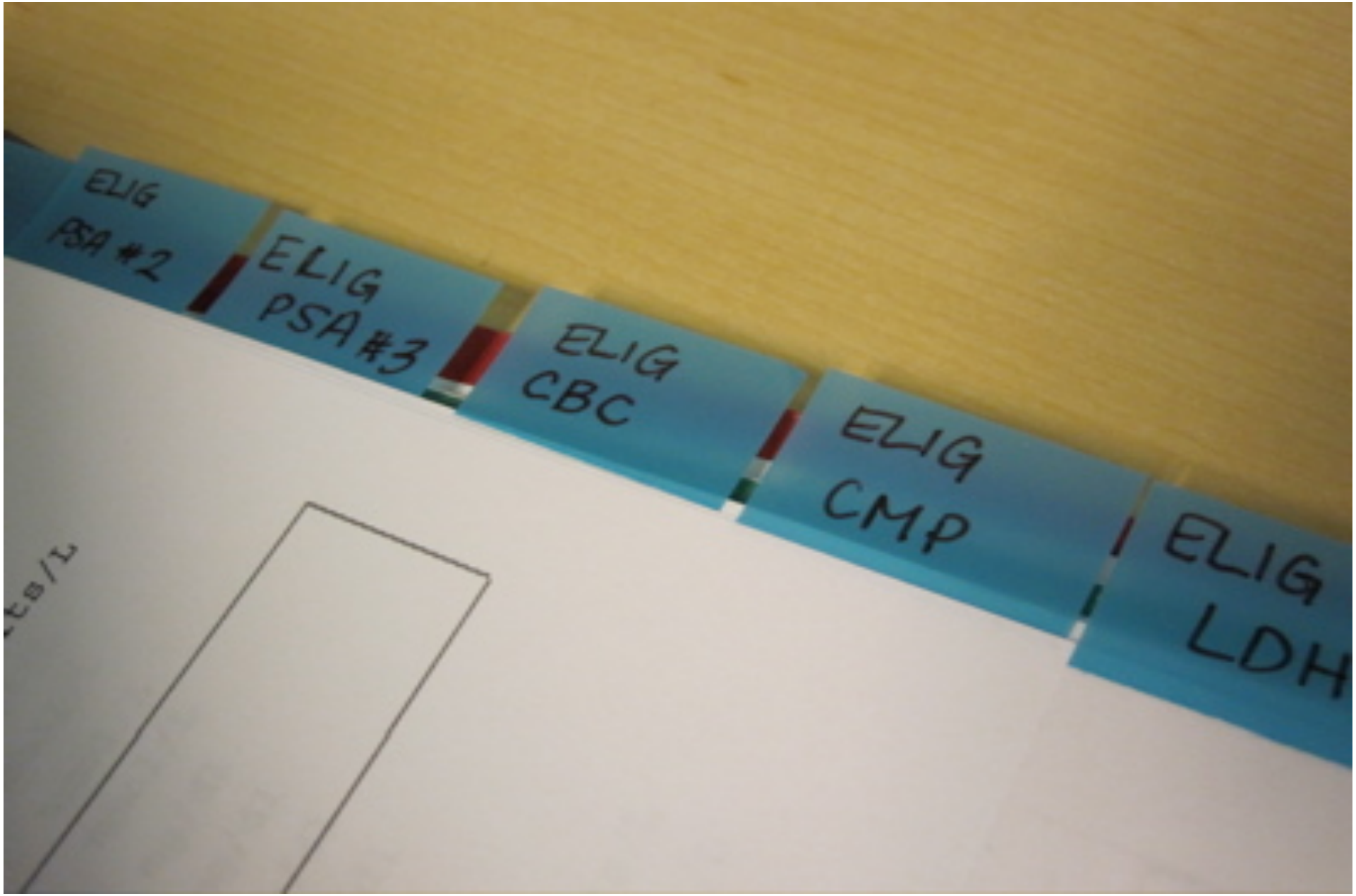

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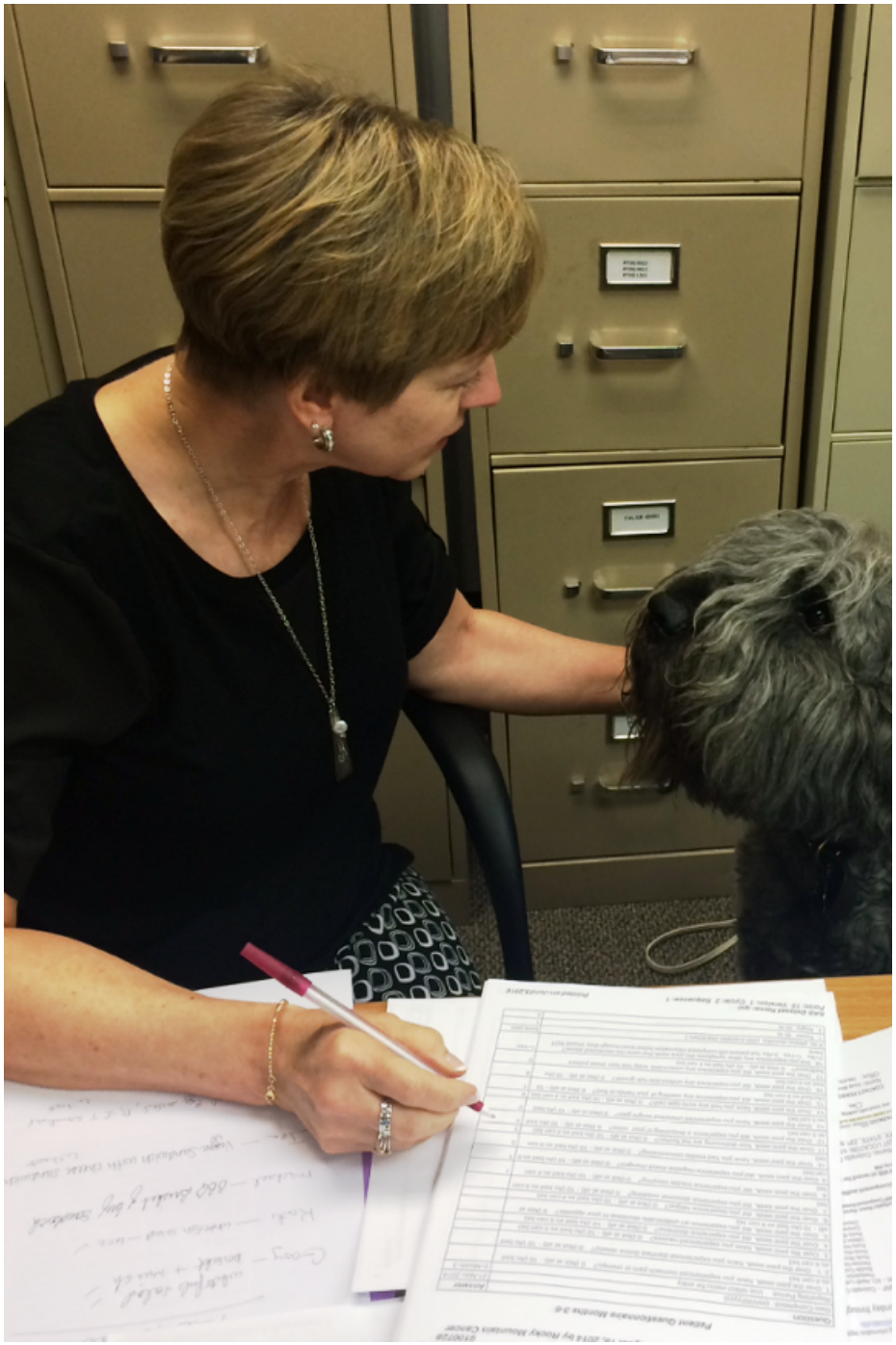

Sometimes we call in expert assistants!

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Deficiencies

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What is a Critical Deficiency

CTMB Guidelines Section 5.1

- Any condition, practice, process or pattern that adversely affect the rights, safety or well-being of the patient/study participant and/or the quality and integrity of the data; includes serious violation of safeguards in place to ensure safety of a patient/study participant and/or manipulation and intentional misrepresentation of data.

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What is a Major Deficiency

- A variance from protocol-specific procedures that makes the resulting data questionable.
- An unacceptable frequency of lesser deficiencies may be treated as a major deficiency.

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What is a Lesser Deficiency

- A deficiency that is judged not to have a significant impact on the outcome or interpretation of the study and is not described as a major deficiency.

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OK, Lesser, Major or Critical?

- Patient Case Review –

  Informed Consent

  The patient was enrolled into the study on 5/11/18. The consent form is dated 7/24/18.

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OK, Lesser, Major or Critical?

- Patient Case Review – Eligibility

  The physician signed and dated an eligibility checklist indicating that all eligibility criteria are met. The protocol requires a hemoglobin of ≥ 12.0 g/dl, but the lab result printout indicates the value is 11.8 g/dl.

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OK, Lesser, Major or Critical?

- Patient Case Review – Treatment

  The protocol treatment was not dose reduced per protocol guidelines. Blinotumumab 28 mcg/d was given for 8 days rather than 9 mcg/d.

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OK, Lesser, Major or Critical?

- Patient Case Review – Treatment

  Internal mammary lymph nodes were not included in the radiation field, as required by the protocol.

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OK, Lesser, Major or Critical?

- Patient Case Review –
  Adverse Event/Study Parameters

  Required labs were not done according to the study calendar.

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OK, Lesser, Major or Critical?

- Patient Case Review –
  Adverse Event/Study Parameters

A CTEP-AERs report (expedited adverse event reporting) was not submitted for cycle 1 hospitalization due to neutropenia.

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A041501

Additional Instructions or Exclusion to CTEP-AERS Expedited Reporting Requirements for Phase 2 and 3 Trials Utilizing an Agent Under a non-CTEP IND:

• All adverse events reported via CTEP-AERS (i.e., serious adverse events) should also be forwarded to your local IRB.

• Grade 3/4 hematosuppression and hospitalization resulting from such do not require CTEP-AERS, but should be submitted via routine AE reporting.

• Grade 1-3 fatigue and hospitalization resulting from such do not require expedited reporting via CTEP-AERS reporting, but should be reported via routine AE reporting.

• Grade 1-2 alopecia and hospitalization resulting from such do not require expedited reporting via CTEP-AERS reporting, but should be reported via routine AE reporting.

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OK, Lesser, Major or Critical?

- Patient Case Review –
  Disease Response/Outcome

  The baseline tumor measurement form did not include a liver lesion that was 2 x 4 cm.

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OK, Lesser, Major or Critical?

- Patient Case Review –
  Disease Response/Outcome

  The subject has been non-compliant with follow-up scans and visits. There is good documentation of clinic scheduling and attempts to contact the subject.

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OK, Lesser, Major or Critical?

- Patient Case Review –
  General Data Quality

  The on-study form due at baseline (10/19/14) was submitted 3/12/15 (3-6 months late).

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OK, Lesser, Major or Critical?

- Patient Case Review –
  General Data Quality

  The research blood specimens due at disease progression were not collected.

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Common Findings

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Common Findings

- Informed Consent
  - Re-consenting not done
  - Use of out of date consent form
- Eligibility
  - Performance status not documented
  - Tests done out of window
- Treatment
  - Oral compliance not documented
  - Dose modifications not done or not within requirements of the protocol

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Common Findings

- Disease Outcome/Response
  - All initial sites of disease not reported at baseline
  - Imaging, physical exams etc not done per schedule
  - Lack of concordance between imaging report and RECIST flowsheet

- Adverse Events/Study Parameters
  - Toxicity assessments not performed or inconsistent
  - Unnecessary reporting of AEs < grade 3

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Adverse Events: Solicited

Adverse event term (v4.0)	**MedDRA AE code (CTCAE v4.0)**	**Adverse event not evaluated**	**Adverse event grade *(highest grade this reporting period)* INCLUDE GRADE 0's**	**AE attribution *(if grade >0)***	**Has an adverse event expedited report been submitted?**
Tinnitus	10043882	☐	0 1 2 3	☐Unrelated ☐Unlikely ☐Possible ☐Probable ☐Definite	☐Yes ☐No
~	~	~	~	~	~

Were *(other)* adverse events assessed during this reporting period? *(check one)*
☐Yes, and reportable adverse events occurred *(go to Adverse Events: Other CRF)*
☐Yes, but no reportable adverse events occurred
☐No

Adverse Events: Other

INSTRUCTIONS: Record all adverse events beyond those solicited; record grade 1 & 2 with attribution of possible, probable or definite and all grade 3, 4 and 5 regardless of attribution. (Both hematologic and non-hematologic adverse events must be graded on this form as applicable.)

Adverse event term (v4.0)	**MedDRA AE code (CTCAE v4.0)**	**Adverse event grade *(highest grade this reporting period)*** **INCLUDE GRADE 0's**	**AE attribution *(if grade >0)***	**Has an adverse event expedited report been submitted?**
		0 1 2 3 4 5 (death)	☐Unrelated ☐Unlikely ☐Possible ☐Probable ☐Definite	☐Yes ☐No
~	~	~	~	~

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Common Findings

- General Data Quality
  - Form instructions not followed
  - Delinquent data
  - Supplemental reports not submitted
  - Specimens not collected/submitted

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Component Evaluation

CTMB Guidelines Section 5.4.2

- Acceptable
  - No Major deficiencies found during the audit
- Acceptable needs follow-up
  - One or more Major deficiencies or multiple Lesser deficiencies found
- Unacceptable
  - Multiple Major deficiencies or a single critical deficiency found (re-audit required)

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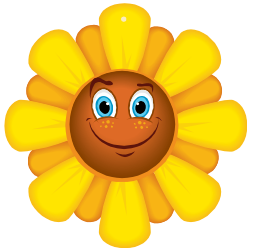
Want an easier audit day?



- Document!
  - If it is not documented, it did not happen
- Communicate!
  - Don’t be afraid to ask questions to your staff and/or the audit team
    - audit@alliancenctn.org
- Keep records audit ready!
  - Tag paper charts or keep summary sheet for electronic records as you go along

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Summary Sheet

Alliance Study

Patient

Signed ICF:
Enrolled:

Eligibility

Path:
H&P:
Labs:
CT chest & up abd:
Bone Scan:
Other:

Treatment

Cycle 1
Cycle 2
Cycle 3
Cycle 4
Cycle 5
Cycle 6

Response

Prior to Cycle 3 scan
Prior to Cycle 5 scan
End of treatment
Relapse

Last Follow-up

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Resources

The Alliance for Clinical Trials in Oncology

www.allianceforclinicaltrialsinoncology.org

FDA Code of Federal Regulations

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/cfrsearch.cfm

Cancer Therapy Evaluation Program (CTEP)

CTMB Audit Guidelines

http://ctep.cancer.gov/branches/ctmb/clinicalTrials/docs/ctmb_audit_guidelines.pdf

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Questions?

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2018 Fall Group Meeting

November 1-3/ Chicago, IL