Patient Case Records Review

Debra Herzan, RN, BSN, OCN, CCRP
Alliance for Clinical Trials in Oncology

Audit Workshop - Alliance Group Meeting – November 3, 2016

6 Categories

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

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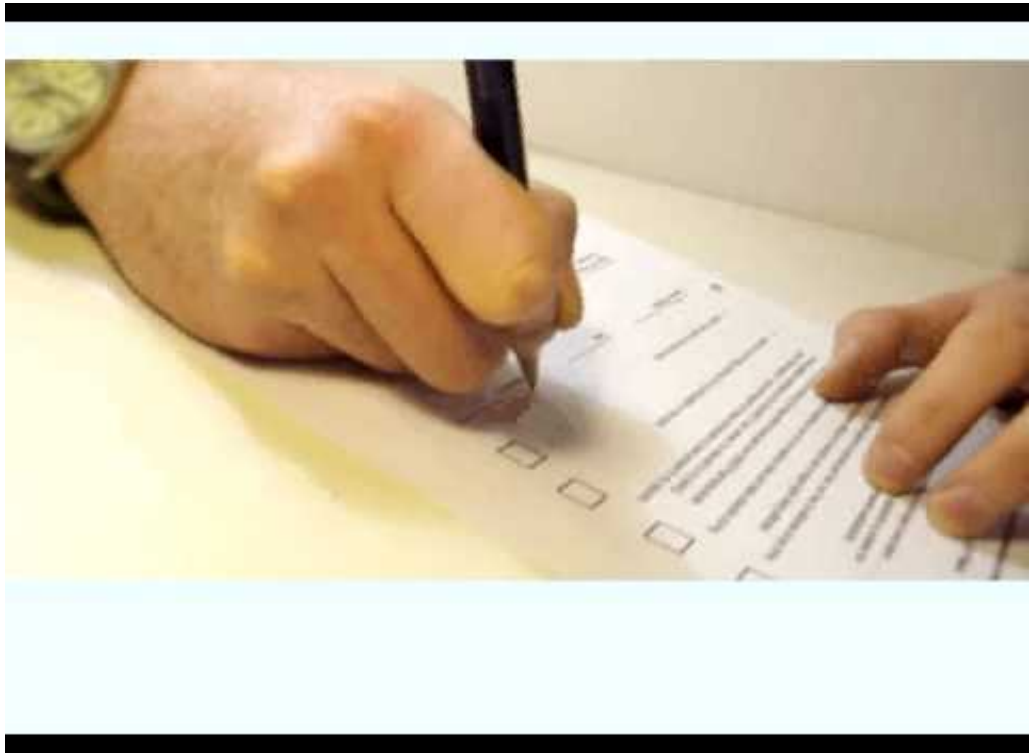
Informed Consent



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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 randomization
- 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
- Dose Deviations/Modifications
- Additional agent/treatment given?

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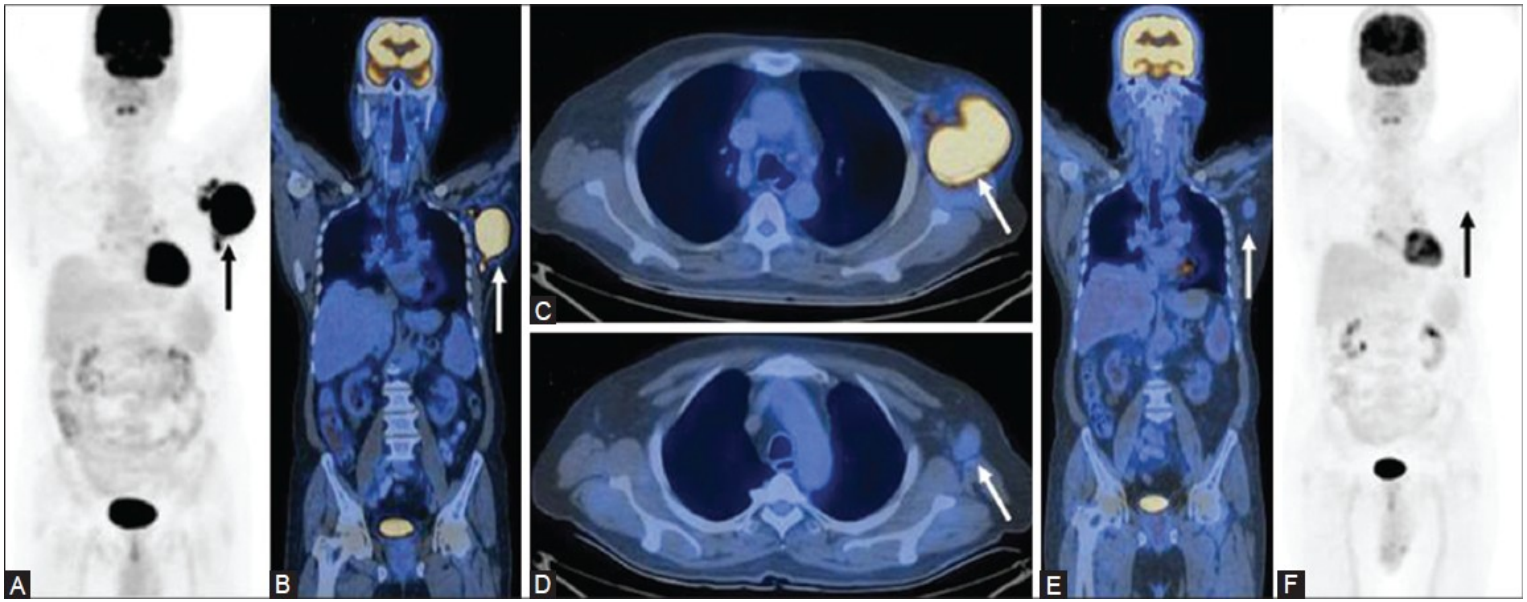
Disease Outcome/Response



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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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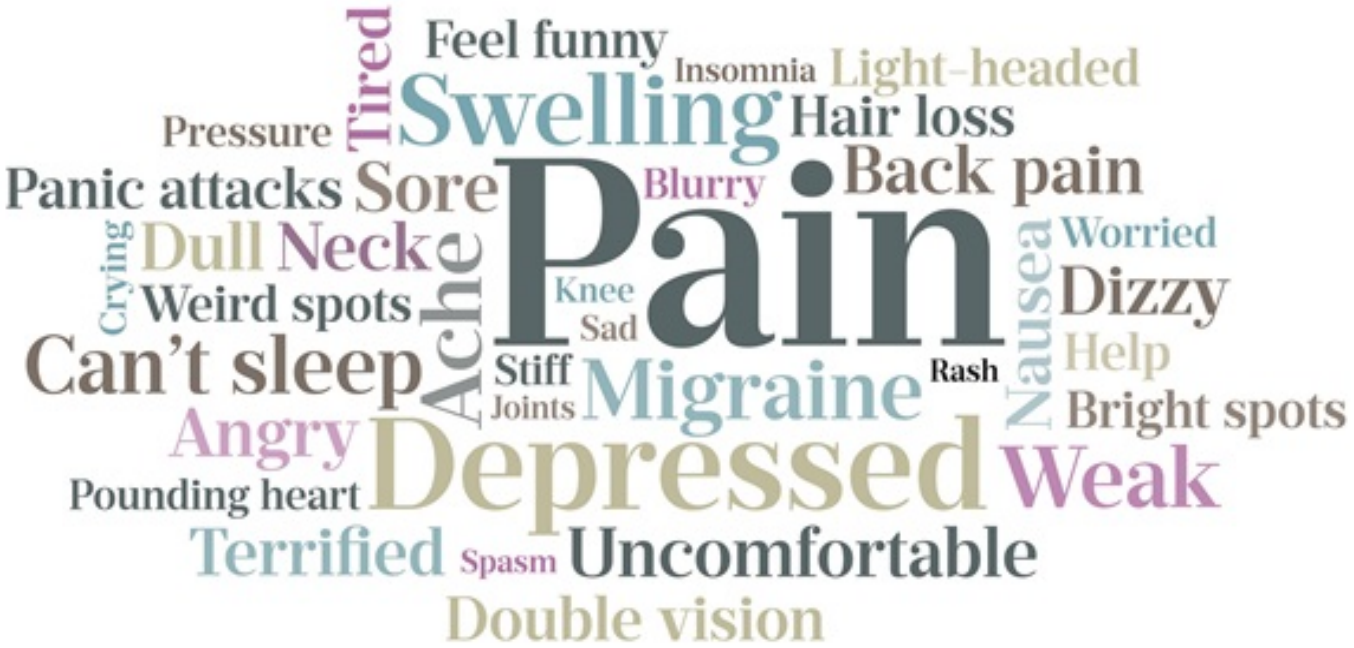
Adverse Events



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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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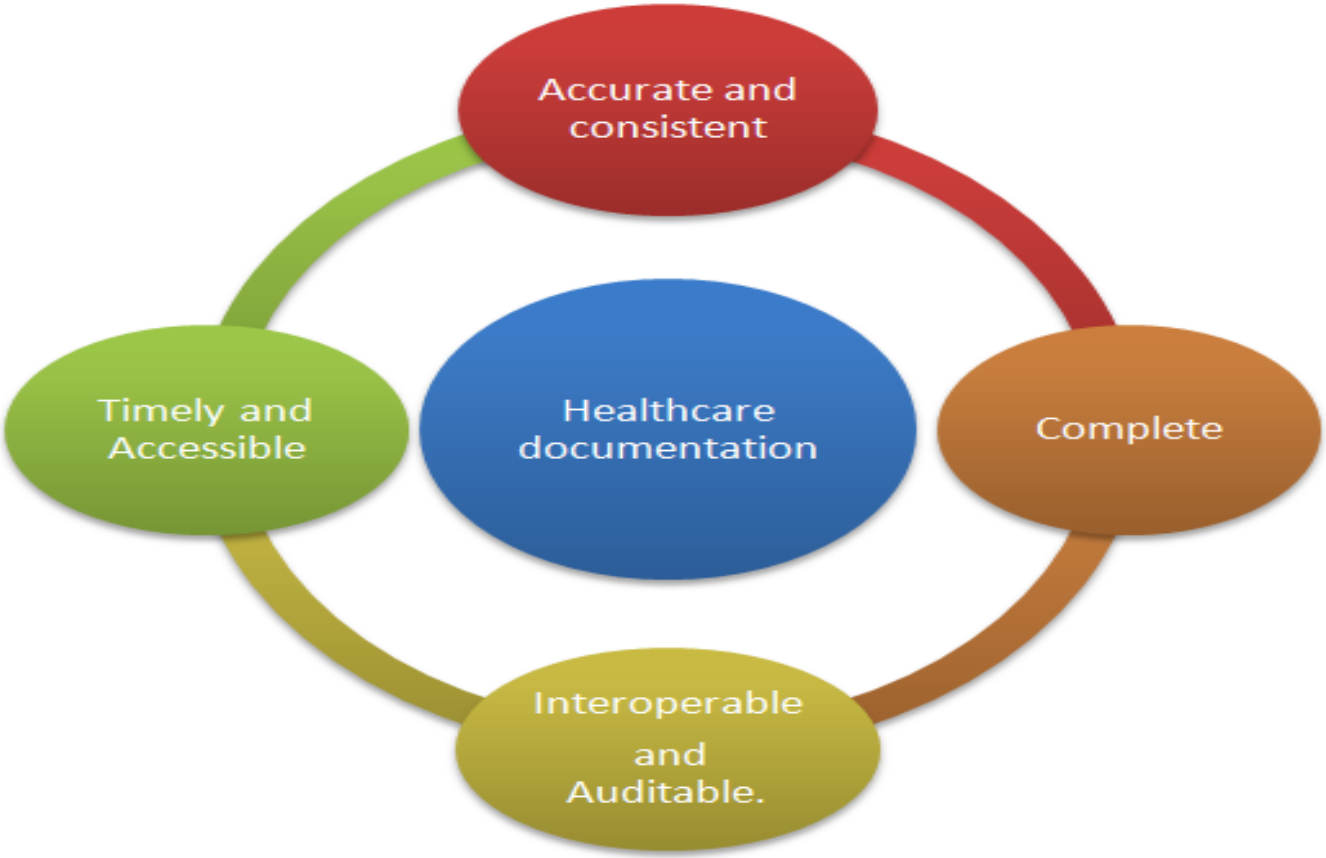
General Data Quality



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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
- Specimens submitted

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Source Documents

EMR: must have a local staff person as the “driver”;
official back-up for research folders

Paper records, Research folders:

Attributable: is it obvious who wrote it?

Legible: can it be read?

Original: is it a copy; has it been altered?

Imaging: have access to images 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
    - **Alliance auditors will not complete site-specific training: 2.8.5.5**
      - **Auditors are current with Human Subjects training**
    - 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

- 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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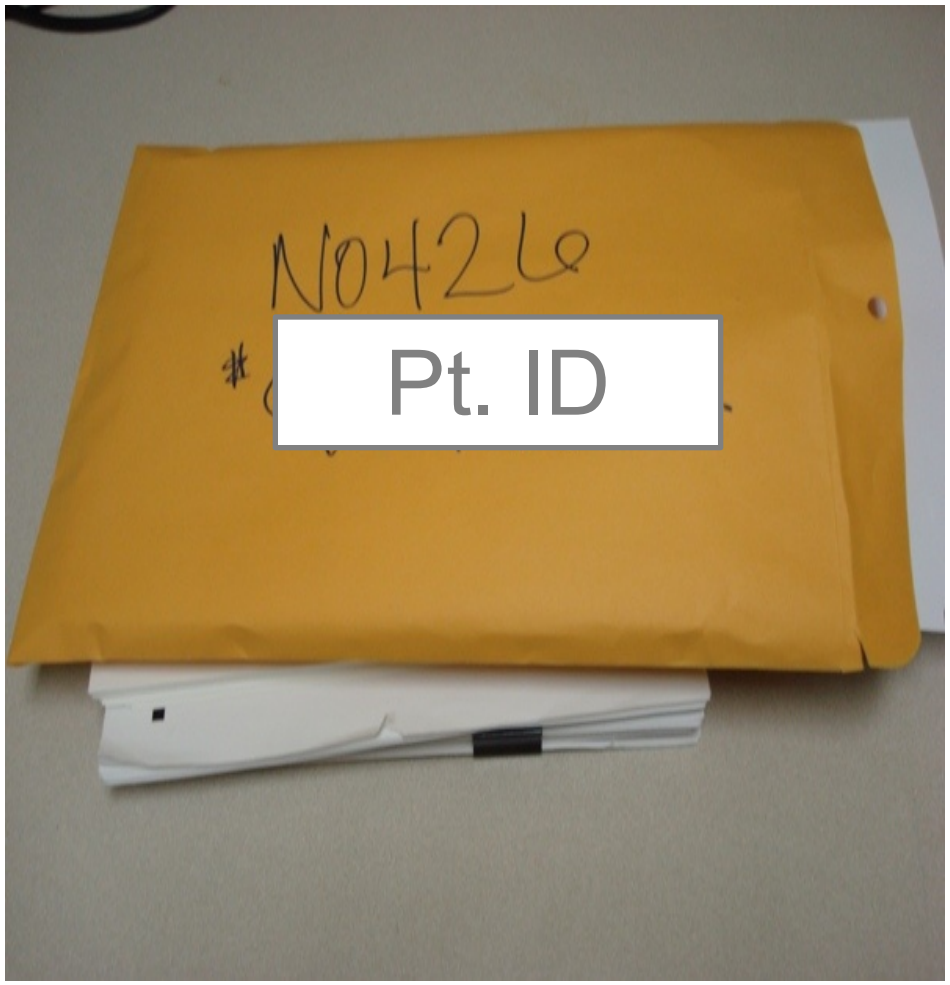

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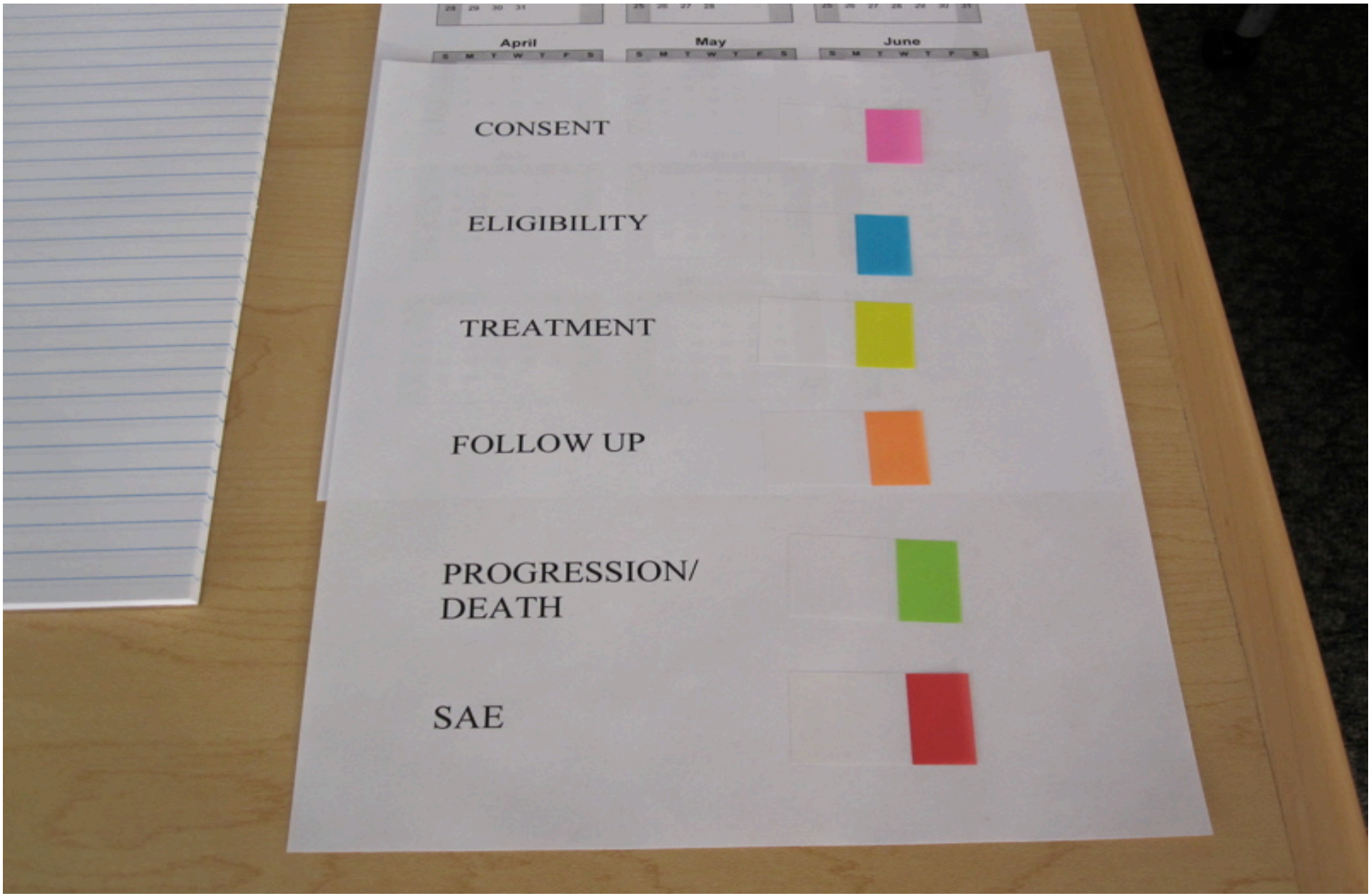

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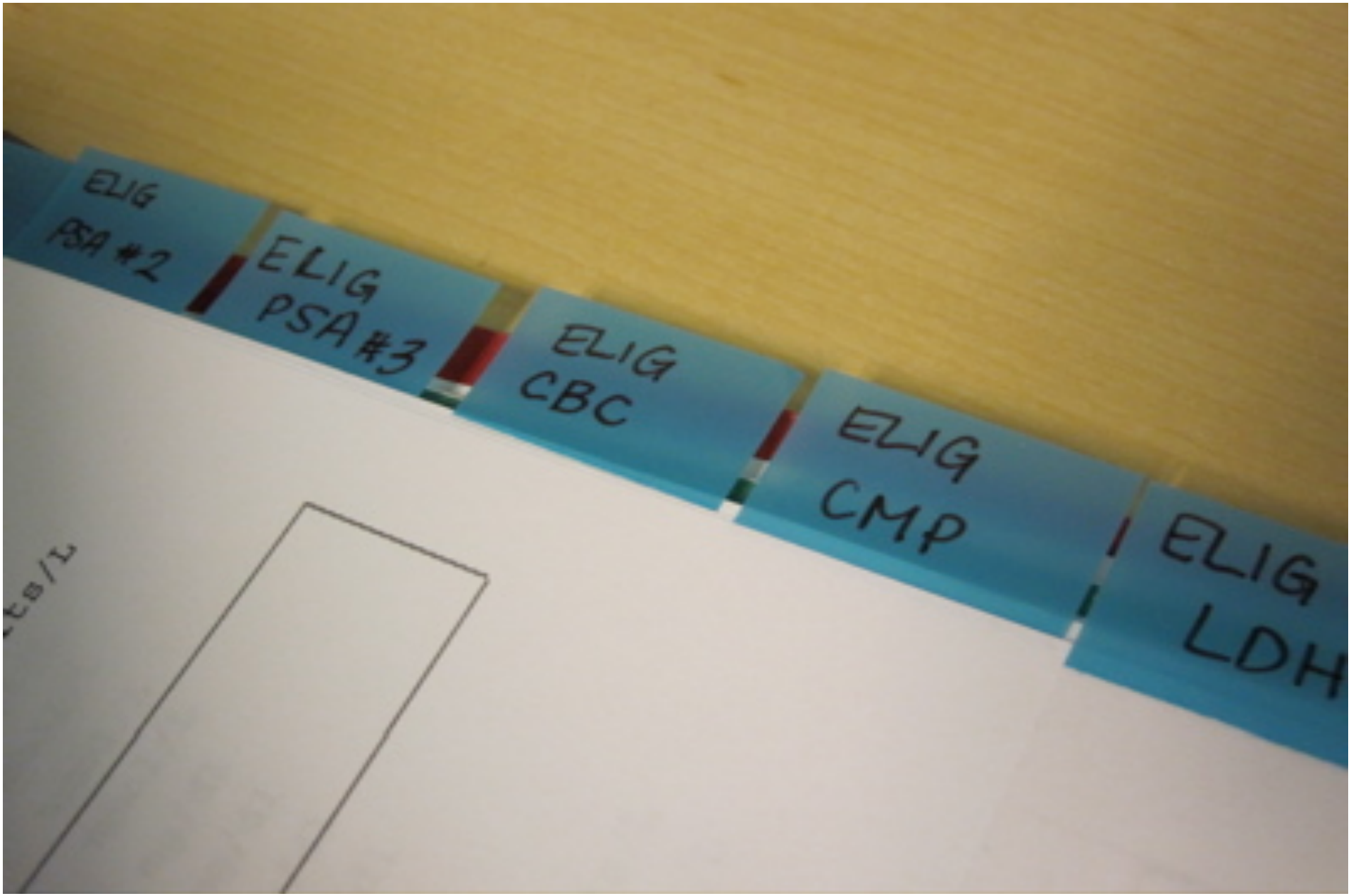

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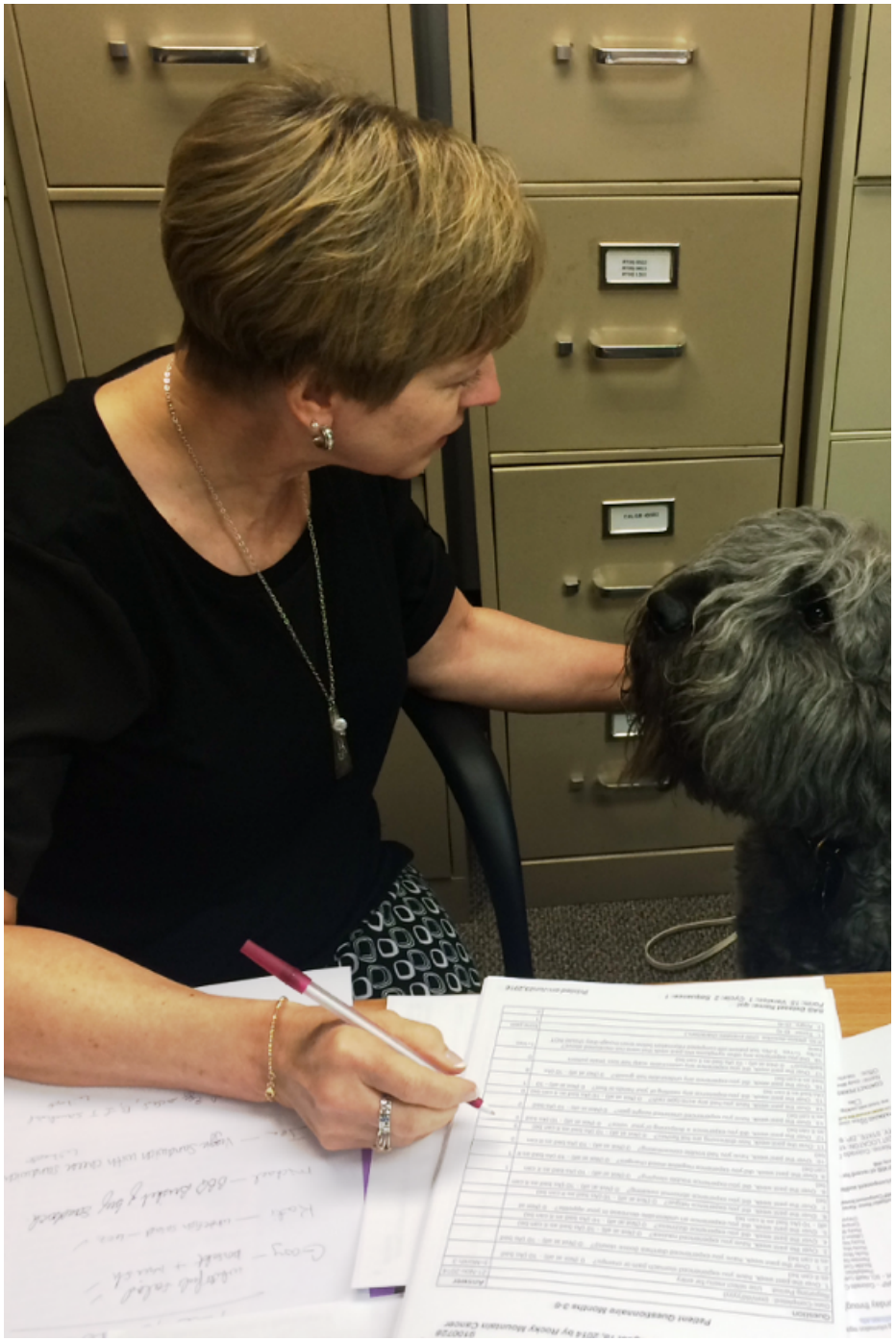

Sometimes we call in expert assistants!

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Deficiencies

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What is a Major Deficiency

CTMB Guidelines Section 5.4.1

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

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What is a Lesser Deficiency

CTMB Guidelines Section 5.4.2

- 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 or Major?

- Patient Case Review –

  Informed Consent

  Consent form used was not the current IRB-approved version at the time of patient registration; the correct version was signed 1 week after registration.

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Ok, Lesser or Major?

- Patient Case Review – Eligibility

  A pregnancy test was not done pre-randomization in this documented pre-menopausal patient. There was no documentation regarding sexual activity and/or use of contraceptives. Of note, a pregnancy test done after randomization but before treatment was negative.

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Ok, Lesser or Major?

- Patient Case Review – Eligibility

  The physician signed and dated an eligibility checklist indicating that all eligibility criteria are met. The required hemoglobin is >9.0 gm/dL, but the lab result printout indicates the hemoglobin is 8.9 gm/dL.

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Ok, Lesser or Major?

- Patient Case Review – Treatment

  Carboplatin dose given was 760 mg, but calculated dose was 693 mg.

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Ok, Lesser or Major?

- Patient Case Review – Treatment

  Documentation of patient counseling for lenalidomide was done at baseline, but not at the monthly dispensing of agent as required per protocol.

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Ok, Lesser or Major?

- Patient Case Review –
  Adverse Event/Study Parameters

  TSH/T4 levels were not checked at the required timepoints of 6 months and 12 months on treatment and during follow-up.

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Ok, Lesser or Major?

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

- All adverse events reported via AdEERS (i.e., serious adverse events) should also be forwarded to your local IRB.
- For the purposes of expedited adverse event reporting, the CAEPR for azacitidine may be found in Section 16.2 below.
- Grade 3/4 myelosuppression and hospitalization resulting from such do not require AdEERS, but should be submitted as part of study results. All other grade 3, 4, or 5 adverse events that precipitate hospitalization or prolong an existing hospitalization must be reported via AdEERS.
- AdEERS reports are to be submitted electronically (http://ctep.cancer.gov/protocolDevelopment/electronic_applications/adeers.htm) to the CALGB Central Office (CALGB@uchicago.edu). Faxed (312-345-0117) copies of the AdEERS paper template (downloadable from the AdEERS web page) will also be accepted, but electronic submission is preferred.
- The reporting of adverse reactions described in the tables above is in addition to and does not supplant the reporting of adverse events as part of the report of the results of the clinical trial, e.g., study summary forms or cooperative group data reporting forms (see Section 6.1 for required CALGB forms).
- All deaths within two years following protocol treatment that are not due to disease progression should be reported as adverse events.

16.2 Comprehensive Adverse Events and Potential Risks List (CAEPR) for Azacitidine (NSC 102816)

The Comprehensive Adverse Event and Potential Risks list (CAEPR) provides a single list of reported and/or potential adverse events (AE) associated with an agent using a uniform presentation of events by body system. In addition to the comprehensive list, a subset, the Specific Protocol Exceptions to Expedited Reporting (SPEER), appears in a separate column and is identified with bold and italicized text. This subset of AEs (SPEER) is a list of events

Ok, Lesser or Major?

- Patient Case Review –
  Adverse Event/Study Parameters

  Imaging reports were not available for auditors to review. Unable to confirm reported date of progression.

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Ok, Lesser or Major?

- Patient Case Review –
  Adverse Event/Study Parameters

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

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Ok, Lesser or Major?

- Patient Case Review –

General Data Quality

The eligibility form due at baseline (10/19/13) was submitted 3/12/14

(3-6 months late).

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Ok, Lesser or Major?

- Patient Case Review –

  General Data Quality

  The reported baseline value of AST is 43, but source documentation indicates value should be 53.

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Ok, Lesser or Major?

- Patient Case Review –

  General Data Quality

  The frozen specimens due at baseline were not submitted to the Pathology Coordinating Office by the time of the audit, 2 years later.

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Common Findings

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Common Findings

- Informed Consent
  - Re-consenting not done
  - Blanks remain blank
- 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
- General Data Quality
  - Corrections not done correctly
  - Delinquent data
- 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 any adverse event that leads to treatment discontinuation 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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Component Evaluation

CTMB Guidelines Section 5.4.3

- Acceptable
  - No Major deficiencies found during the audit
- Acceptable needs follow-up
  - One or more major deficiencies found
- Unacceptable
  - Multiple Major deficiencies or flagrant deficiencies found (re-audit required)

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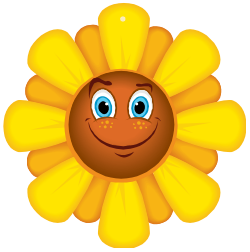
Want an easier audit day?



- Document!
  - If it is not documented, it did not happen
- Communicate!
  - Don’t be afraid to ask questions
- 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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Questions?

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2016 Fall Group Meeting

November 3 – 5 / Chicago, IL