

CRA TRAINING
ADVANCED I

SOURCE DATA & VERIFICATION

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AGENDA

- Definitions
 - ✓ Source Data Verification
 - ✓ Difference between source data verification and source data review (SDV vs SDR)
 - ✓ Other Definitions: Source Data, Source Documents, Monitor Responsibilities as per ICH GCP with regards to SDV
- ALCOA-C
- Source Document/Data Review as a Monitor/CRA

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DEFINITIONS: SOURCE DATA VERIFICATION (SDV)

- **What is source data verification (SDV)?**

- The on-site confirmation that Case Report Form (CRF)-required data is correctly transcribed from source material or data to the CRF (eCRF) or any other data collection system.
- According to The Institute of Clinical Research SDV is performed by CRA because, “ it is (SDV) a regulatory requirement, and also commercially and ethically essential that the data collected during a clinical study can be verified as complete, accurate, and reliable. Subject data collected in case report forms (CRFs) by the investigator(s) and reported to the pharmaceutical companies form the basis on which approval to market a drug is sought.”
- Therefore there is a need to make sure that data is not misrepresented or transcribed incorrectly by the research team.

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SOURCE DATA VERIFICATION (SDV) VS. SOURCE DATA REVIEW (SDR)

- **Source Data Verification (SDV)** is different from **Source Data Review (SDR)**. According to C. Adler in a May 2015 article in Forte Research, SDV and SDR are two terms that are used interchangeably. Though certainly related, the two terms can mean different things.
- While “SDV is defined as the process by which data within the CRF (or other data collection system) are compared to the original source information, to confirm that the data was transcribed accurately,” “Conversely, SDR refers to the review of the source document to check on quality, compliance, staff involvement, and other areas that aren’t associated with a CRF data field.”
- Alder’s point is that as CRAs or clinical research professionals it is important to consider weighing the importance of more high-value tasks like compliance (SDR), as against lower-value tasks such as checking for transcription errors (SDV)

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DEFINITIONS: SOURCE DATA, SOURCE DOCUMENTS

- **What is Source Data?**

- The ICH E6 document, section 1.51, defines source data as, “All information in original records and certified copies of original records or clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).”

- **What are Source Documents?**

- While Section 1.52 defines source documents as, “Original documents, data and records (e.g., hospital records, clinical and office charts, laboratory notes, memoranda, subjects; diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm of magnetic media, x-rays, and records kept at the pharmacy, at the laboratories and at medico-technical departments involved in the clinical trial).”

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MONITOR'S RESPONSIBILITIES

- **Monitor's Responsibilities-** According to the ICH GCP, Section “5.18.4: Monitor's (CRAs) Responsibilities- k) Verifying that source documents and other trial records are accurate, complete, keep up to date and maintained. m) Checking the accuracy and completeness of the CRF entries, source documents and other trial-related records against each other.”

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ALCOA-C

- ALCOA-C: In the Forte Research article of April 25th, 2014 K. Lopienski stated that the FDA expects clinical study data to meet certain fundamental elements of quality. These elements of quality apply to all data, either recorded on paper or electronically. ALCOA-C, stands for the following:
 - A- Attributable: To regard as produced by or originating in the time, period, place, etc. Is it traceable to a person, date, and subject visit? Who collected the data?
 - Legible: Capable of being read or deciphered, especially with ease, as writing or printing; easily readable. Is it clear enough to read? No white-out and always in ink.
 - Contemporaneous: Existing, occurring, or living at the same time; belonging to the same time; of about the same date. Was it recorded as it happened? Data can only be assumed credible, if it is recorded at the time a measurement or action is taken.

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ALCOA-C... CONT'D

- Original: An original work, writing, or the like, as opposed to any copy or imitation. Is it the first place data is recorded? The very first time a data is recorded, that medium becomes the source document.
- Accurate: Free from error or defect; consistency with a standard, rule, or model; precise; exact. Are all the details correct? An accurate source document has data that is true and correct.
- Complete: Are source documents completed in their entirety?

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SOURCE DOCUMENT/DATA REVIEW AS A MONITOR/CRA

- Source Document/Data Review as a Monitor/CRA
 - Source document review is defined as the on-site examination of all source materials documenting a study subject's course in the trial.

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CRA ACTIONS

- Determine if the PI is involved by evaluating PI documentation, progress notes, signatures, dates, etc
- Ensure the protocol is being strictly followed and any deviations are clearly documented
- Make sure the source document is adequate, complete, legible, and attributable
- Consent process is per ICH/GCP and fully documented
- Documentation of compliance with visits and dosing
- There are no unreported SAEs or AEs
- Visit procedures are completed as per the study protocol
- Investigator is documenting review of lab/ECGs by signing in a timely manner
- Staff are delegated responsibilities appropriate to their documented experience and training
- There is documentation that subjects are eligible for the trial
- Drug accountability records are present and accurate

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MEDICAL RECORDS

- Subjects must sign a release form to allow the site to access their medical records
- Most studies ask that subject medical records be acquired
 - Three attempts are sufficient (may not want to give since the process requires some time and that is something some people don't want to pay for)
 - Verification reports to show three attempts
- Some studies absolutely require subject medical records for the subjects to be randomized
- In either case listed above, this must be done prior to the subject randomizing

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PATIENT STIPEND

- Most studies offer some form of compensation for subject participation
- Sponsor or CRO may require proof of subject payment
 - Most do not
 - If your employer requires proof, make sure the subject is being paid as outlined in the ICF

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ADVERSE EVENT LOG

- To begin at the moment the subject signs the ICF
- Adverse Event Number
 - Corresponds to the sequence of occurrence during the trial
- Medical problem
 - Medical terminology is necessary
 - ✓ High cholesterol is not acceptable- hypercholesterolemia
- Serious/Non-serious
 - It is a serious adverse (SAE) or an adverse event (AE)
- Severity
 - AE= mild or moderate/SAE= severe

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ADVERSE EVENT LOG... CONT'D

- Action Taken
 - Drug interrupted - subject hospitalized did not receive study medication
 - Drug Withdrawn - study medication stopped for lack of efficacy or AE
 - Dose Reduced - dose is too high and causing the AE (e.g., somnolence)
 - Dose Increased - this would apply if there were exacerbation of the study indication
 - Dose not changed - no change in study drug
 - Not Applicable - the study does not involve an IP or prior to study drug being started
 - Unknown - should never be used unless the information was not gathered, hopefully never used

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CONCOMITANT MEDICATION LOG

- Medication number should correspond to the sequence of occurrences during the trial
- Medication - no brand names (e.g., Advair use fluticasone propionate)
- Dose - Amount
- Unit - how is it measured: milligrams for example, inhalers measured by puffs
- Frequency - How often does the patient take the medication: QD (once daily), BID (twice daily), TID (three times daily), QID (four times daily), QOD (every other day), QW (once weekly), QAM (in morning), QHS (once at night), PRN (as needed)
- Route - How does the patient take the drug? Oral, intramuscular, respiratory (inhalation), topical, subcutaneous, intraocular, intraperitoneal, nasal, vaginal, rectal

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IVRS OR IWRS

- Interactive Voice Response System (IVRS) or Interactive Web Response System (IWRS-more common)
 - The purpose of these systems is to enter study visits and to assign study drug.
 - Some of the many IWRS/IVRS systems
 - e-Portal, Bracket, Premier research, S-CLINICA, Veracity Logic, CENDUIT, Y-Prime, Suvoda, MEDPACE, ORACLE, ClinPhone*

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INCLUSION AND EXCLUSION CRITERIA

- Verify the subject meets all study criteria
- Compare data elsewhere in the source to make sure there is no contradictory information
- If a subject was enrolled/randomized without meeting the inclusion/Exclusion criteria, subject will most likely need to be withdrawn from the study. The medical monitor may need to be notified and so will the IRB.
- So any “NO” in the inclusion or any “YES” in the exclusion, disqualifies that subject

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PROGRESS NOTE

- Many CROs will not consider a visit was done unless the PI/SI have completed a Progress Note.
- It is necessary that the Screening Visit mentions the following in regards to the ICF process
 - Subject was given enough time to review ICF
 - Subject was given opportunity to ask questions and all questions were answered
 - No study procedures were performed prior to the subject consenting
 - Subject was given a copy
- Not a necessity but the following additional information should also be included
 - Subject has a good understanding of the ICF
 - Alternative treatments were discussed
 - The version of the ICF used (which should be latest IRB approved version)

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OTHERS

- Spirometry Results
 - Make sure these results are within the range specified in the inclusion Criteria #6
- Assessment or Scales
 - Rater administered or self administered
 - The person to complete the assessment must sign and date
 - Identifying information must be on all assessments to distinguish them from other subject's assessments
- Lab Results
 - Make certain the subject's results are not outside the acceptable range
 - The inclusion/Exclusion criteria should be blank, in regards to labs, until the results have been viewed.
 - Labs should be reviewed within two days of receipt

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OTHERS... CONT'D

- Patient Identifiers
 - Patient initials to match how they initialed the ICF
 - Date of birth
 - Patient number
 - ✓ Variation of typical format (example in intralinks)
 - Site number
 - Sequential in the number screened in the entire study
 - ✓ Typical format
 - Site number
 - Sequential in the number screened

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CRA Training:

- ❑ **Basic I: GCP for Site Monitors**
- ❑ **Basic II: Site Selection**
- ❑ **Basic III: Site Initiation**
- ❑ **Basic IV: Site Monitoring**
- ❑ **Basic V: Site Close-out**
- ❑ **Advanced: I: Source Documents**
- ❑ **Advanced II: Site Regulatory**
- ❑ **Advanced III: Protocol Deviations, IP Accountability, Miscellaneous**

THANK YOU

