

CRA TRAINING
ADVANCED III

IP ACCOUNTABILITY, PROTOCOL DEVIATIONS, AND MISCELLANEOUS

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1

PROTOCOL DEVIATIONS LOG

- Either subject specific or Master deviation log
- Most common is master deviation log
- A deviation is anything not done in accordance with protocol
- Some deviations need to be reported to IRB if they are safety issues
- Some deviations are intentional (i.e., to reduce risk to a study subject)
- Most are inadvertent and require CRA discovery and retraining
- Source documents must be consistent with CRF entries with any discrepancies explained by NTF

2

QUERIES

- Source and CRF should match. If there are discrepancies, CRA should issue a query.
- Most queries are formatting issues such as data entered in pounds instead of kg, or other transcription errors such as date entered incorrectly or different format
- Commonly found by CRAs:
 - Spelling errors
 - Information captured on the same day that does not match in two different places (source and CRF)
 - Date does not match source in CRF
 - Story or Narrative of subject visit does not make sense

3

MISSING INFORMATION

- The cause of more queries
- ALCOA-C the final C is complete
- Missing assessments
- Missing data
- Headers incomplete
- Incomplete source capture
- Assessment not signed or dated
- Labs/ECG not marked with CS/NCS
- Data in EDC is not found in source

4

INTERACTIVE VOICE RESPONSE SYSTEM (IVRS) OR INTERACTIVE WEB RESPONSE SYSTEM (IWRS)

- 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

5

ELECTRONIC SOURCE

- Not all sites use paper source documents. Many sites are moving to electronic source documentation. As a side note, electronic regulatory is also possible.
- We use Clinical Research IO but there are many worthwhile vendors.
- Some of the typical costs involved with eSource:
 - Startup cost to program the system in accordance with the study - \$2,500
 - Charge per visit - \$12
 - Document storage - \$750 for 15 years

6

ELECTRONIC SOURCE: PAPER SOURCE

PROS

- As the study coordinator has to create this document (more likely) doing so will inflict a re-education on the study protocol, which gives him/her more readiness.
- Source documents are customizable and no training is required.
- Site can modify or improve the source documents right away without having to contact an external vendor to do so.

CONS

- Time consuming, tedious task
- If the CRC has not been properly trained, or is an inexperienced CRC, the source may have lots of mistakes. This will cause the site to inadvertently commit deviations.
- If any changes needed to be done the site is subject to the vendor's services

7

ELECTRONIC SOURCE: eSOURCE

PROS

- Electronic system makes obvious who created a record, when it was created, who made a change, when the change was made, and the reason a change was made. A compliant system will automatically track this information and enable electronic signatures. Data is attributable to a unique user with a secure password and role-based permissions, preventing changes from being made by unauthorized users.
- Reduces the opportunity for error
- Promotes real-time entry of electronic source data during subject visits.
- Ensures accuracy and completeness of data

8

ELECTRONIC SOURCE: eSOURCE

PROS (Continued)

- eSource has the ability to save time. Coordinators do not have to print out and manage paper templates, fill in subject headers, or initial and date for attribution purposes, furthermore the Study coordinator no longer have to spend long hours creating the source documents for a study.
- Automatic date and time stamps support this every time clinical data is entered, edited, or modified in an electronic system that has the appropriate controls in place to fully support compliance with 21 CFR Part 11.
- *With eSource, principal investigators (PIs) can have immediate access to source data wherever they are, thus enabling faster response times on lab sign-offs, serious adverse event assessments, etc. Information is easier and quicker to retrieve. A PI no longer has to be physically present in the office to review and sign off on source, enter progress notes, pull up a patient's medical history, etc.*

9

ELECTRONIC SOURCE: eSOURCE

CONS

- The study coordinators, PI, CRA and staff related to the study need to get trained in order to know how to use the eSource
- Study coordinator and site stuff that are using the eSource need to create yet another login credentials
- The site needs to spend time checking if this eSource has been done accordingly to the protocol.
- The study coordinator won't create the source document; therefore, it will not reeducate themselves with the protocol.
- Site needs to set aside extra budget for this eSource service.
- Rechecking the third parties for any discrepancies.

10

IP ACCOUNTABILITY

IPACCOUNTABILITY LOG

Investigator Name:	Units	Site Number	Subject Number	Subject Initials:
Protocol Number:	Capsules			

Date Dispensed to Subject (dd/mm/yyyy)	Kit # Dispensed to Subject	Quantity Dispensed (# Capsules)	Dispensed to Subject by (Initials)	Date Returned (dd/mm/yyyy)	Quantity Returned (# Capsules)	Accountability Performed by (Date & Initials)	Comments Document Discrepancies (i.e., missed doses, lost capsules, etc.)
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11

IP ACCOUNTABILITY... CONT'D

- Typically a Master IP Log and an Individual Subject IP Log
- CRAs to do IP accountability at every visit
- Check for subject compliance and verify with source, CRF, master log, individual log and physical counting of IP (tablets or infusion vials, etc.)
- Most protocols allow for a percentage compliance
- The logs usually include IP returned as well as IP lot #
- CRC usually counts and frequent counting errors

12

IP TEMPERATURE LOGS

- The storage area for IP will generally require temperature monitoring
 - ambient, refrigerated, frozen
 - Some studies require daily monitoring including weekends
 - Select a temperature monitoring device sufficient to cover requirements
- Frozen and refrigerated lab samples will also require temperature monitoring
- At our sites, this log is not initially kept in the regulatory binder
 - For convenience, it is kept on a clipboard in the drug room

13

LOST TO FOLLOW UP

- IP needs to be returned by subjects at end of each visit
- If subject is LTFU site must attempt 3 documented phone calls as well as send a certified letter by mail to attempt to collect IP

14

SAFETY FOLLOW UP

- Usually done after patient completes study or when withdrawn (ET visit)
- Assess con meds and ongoing AEs

15

SUSPECTED UNEXPECTED SERIOUS ADVERSE REACTION OR SUSAR

- A SUSAR is a serious adverse reaction that may or may not be caused by the IP but is unexpected.
- Most studies require SUSARs to be signed by the PI and possible even the SIs
- SUSAR vs SAE – A SUSAR is any SAE that is unexpected to occur. An SAE that occurs during research with a medicinal product may be a SAR or a SUSAR. SAR is the abbreviation for Serious Adverse Reaction, and SUSAR for Suspected Unexpected Serious Adverse Reaction.

16

STUDY SUPPLIES/INVENTORY/CALIBRATIONS

- CRA to check adequate supplies of:
 - Lab kits
 - IP
 - Other study supplies (patient reminder cards, patient diary tablets, etc.)
- Equipment Calibration (check with Site SOP)

17

LABS

- Central or Local Lab
- IATA Certificates
- Lab Certificate (CLIA, CAP, etc.)
- Reference Ranges

18

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

