

CRA TRAINING

BASIC V

SITE CLOSE-OUT

CLOSE-OUT VISIT (COV)

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WHAT IS A CLOSEOUT VISIT?

- What does the ICH/GCP say?
 - According to The Institute of Clinical Research, the ICH/GCP stipulates that, "After completion or termination of the trial, all of the documents identified in sections 8.2 & 8.3 should be filed together with those in section 8.4." The three sections identified above include: documents needed before the trial (8.2), documents needed during the trial (8.3), and documents needed after the trial (8.4).
- In clear terms, the closeout visit is the final part of the monitoring process of a study and usually occurs after the last data queries have been completed, and the study database have been locked by data management.
 - Closing a clinical trial occurs only twice: once a clinical trial has been completed and also, when a decision has been made to terminate the study before completion.

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ROUTINE AND NON-ROUTINE COVS

- Routine COVs: As specified above a routine COV occurs when the clinical trial has been completed. In this case the following variables apply with this form of site closure:
 - All sites will need to be closed out.
 - Database lock, which occurs frequently and includes getting the EDC cleaned-up and all queries taken care of.
 - The EDC is signed-off by the PI.
 - The study drug (IP) is returned to the Sponsor (all unused ones).
 - Study records are archived by each site or at a central location.
 - Any outstanding protocol deviations, SAEs and AEs are taken care of.

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ROUTINE AND NON-ROUTINE COVS...CONT'D

- Non-Routine COV: A COV also happens when a decision has been made to terminate the study before its completion. A study can be terminated midterm for various reasons:
 - When a lot of protocol deviations are noted, i.e. non-compliance to protocol
 - Zero screening activity
 - IRB/Sponsor related issues; the IRB may see a site/some sites as been unable to carry out the trial and the Sponsor may decide to close a site due to the data gotten from the site
 - When no subjects have been enrolled into the study
 - A site may also be kicked out of a study if it does not screen as many subjects as all other participating sites and the Sponsor has other backup sites with promising subject base

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PRE-CLOSEOUT VISIT PREPARATION

- Send a confirmation letter to the site (CRC) to confirm the date and time of the visit. Request the presence of the PI, so that all necessary documents that need final attention, and all other study relative archive issues should be taken care of. This is the one visit the PI really can't miss!
- Ensure all AE's and SAE's are resolved. You need to make sure you have these documented
- Queries resolved and EDC signed off by PI
- Make sure IP accountability logs are completed- make sure that what the site is documenting is correct, counting bottles, matching blister cards to packets, etc. That is why if you were doing the IMV for the site you want to make sure you have been doing IP accountability thoroughly.
- Make sure all SUSARs (Suspected Unexpected Serious Adverse Reactions) are filled and filed. SUSARs basically refer to adverse reaction that is both unexpected (not consistent with the applicable product information) and also meets the definition of a Serious Adverse Event/Reaction.

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DAY OF VISIT

- Before you engage in any activity on site for the COV, make sure you will carry out activities that will include the following:
 1. Finalization of outstanding queries
 2. Drug accountability and return of clinical trial supplied
 3. Investigator's file review
 4. Meeting with the PI
- Within each of these you will be carrying out activities that may overlap at some point during your visit, but you should always make sure that you keep in mind the following sections so that you do not miss any documents or outstanding queries/issues that need to be resolved before the study is closed at that site. Below are a number of actions to take during the COV.

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DAY OF VISIT...CONT'D

- Sign into monitoring (visit sign in log) log- date it, name it as COV, then have someone from site counter-sign (usually the CRC or SC)
- Check IP Accountability Logs, returned IP, unused IP- This may be the most time-consuming activity
- Check SUSARs- you are going to get a lot of SUSAR reports. These should be filed in the Regulatory Binder under the SUSAR section. The PI's endorsement is needed for this as well.
- Go through all AE's and SAE's - either resolved with end date or checked as on-going.
- Ensure all e-diaries and other patient reported outcome (PRO's) tools are returned: Patients are provided with mobile devices that can be used by the patient to report their own health condition during the trial.

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DAY OF VISIT...CONT'D

- Ensure that the ECG/EKG or any other equipment provided by the Sponsor are returned
- The site will destroy the lab kits as per their SOP- usually sites are given an excess lab kits, which need to be destroyed because they have study-sensitive information on them.
- The unused IPs need to be returned to the Sponsor after accountability is complete
- Delegation logs are to be updated with end dates
- The EDC needs to be signed off by PI so that the database for the site can be locked/frozen
- Meet with PI and discuss EDC sign off
- Meet with PI and discuss Investigator responsibilities for archiving and maintaining source records or archive

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DAY OF VISIT...CONT'D

- Inform the PI that they will receive a CD-ROM with all EDC data
- Additional queries may still pop up after COV (check with data management)
- Submitting the IRB closeout form- you will not be doing this, and you will have the coordinator do this. Make sure that you can have them do this when you are there on site
- Tie up any loose ends in the regulatory binder/source documents

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POST CLOSEOUT VISIT

- “As always, try to write your closure visit report as soon as possible after the visit in order to ensure that you do not forget anything.
- Always send a follow up letter to the site after your visit, highlighting all issues discussed during your visit and reminding the PI of his/her responsibilities again
- Remember to finalize payments to the site, in accordance with the financial agreement (*in most cases you may not be taking care of this, depending on the site of the CRO or pharmaceutical company you work for*)
- Ensure all in house files are up to date in advance of archiving- in house files should be reviewed as thoroughly as the investigator file prior to archiving in anticipation of an audit once the study is terminated.”
- Ensure IRB “Closed” status has been obtained
- Ensure equipment has been returned

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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

