Module 8: Essential Documents

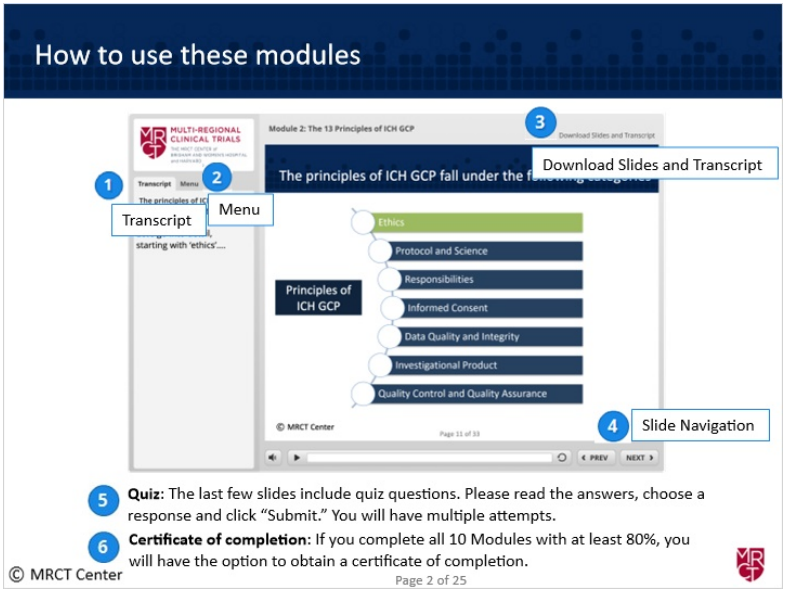
1. Essential Documents

1.1 Interpretation and application of ICH E6(R2)

Notes:

Welcome to Module 8 of this training on the interpretation and application of ICH E6(R2)

1.2 How to use these modules



Notes:

We want to familiarize you with how to use these modules. First, you can click on Transcript on the left side to read along with the audio. Second, if you click on Menu, next to Transcript, you can see where you are in this module. You can also go back to slides that you have previously viewed and listened to.

Third, you can click on the upper right on "Download Slides and Transcript" to view a printable PDF of the slides and transcript of the module. You can also click a link to the Guidelines for Good Clinical Practice.

Fourth, to move to the next slide, click "Next" after you listen to the audio. Click "Prev" to go to the previous slide.

Fifth, the last few slides include quiz questions. Please read the answers, choose a response and click "Submit." You will have multiple chances to answer correctly.

Sixth, if you complete all 10 Modules with at least 80%, you will have the option to obtain a certificate of completion.

1.3 Attribution and Disclaimer

Notes:

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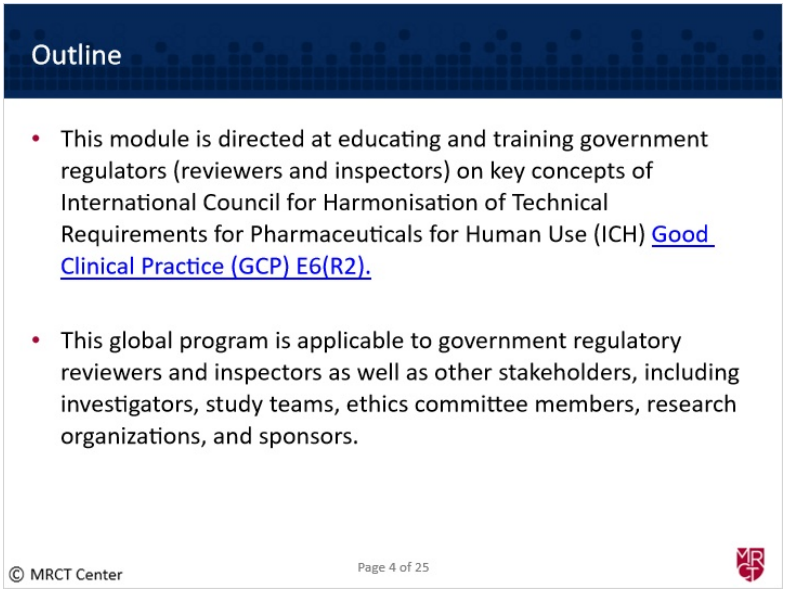
This training programme is recognised by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).

This presentation includes the author's views on "Interpretation and application of ICH E6(R2)" theory and practice. The presentation does not represent official guidance or policy of authorities or industry.

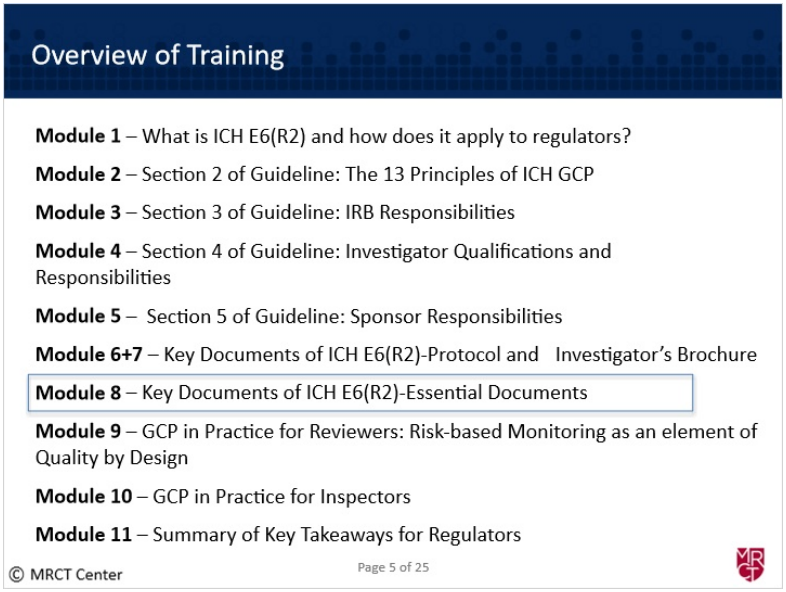
1.4 Outline



Notes:

Overall this training is directed at educating and training government regulatory reviewers and inspectors (as well as other stakeholders including investigators, study teams, ethics committee members, research organizations, and sponsors) on key concepts of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP) E6(R2).

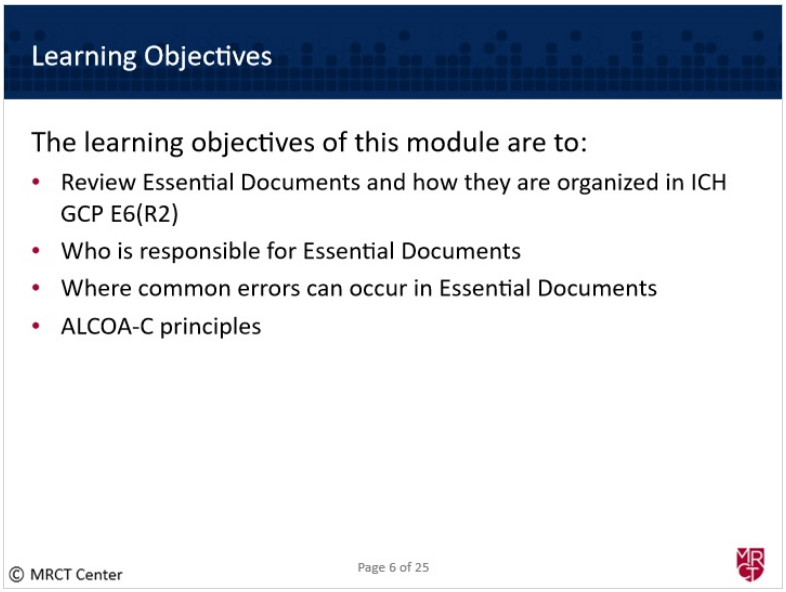
1.5 Overview of Training



Notes:

In Module 8 we will focus on the Essential Documents that are part of the Key Documents of ICH E6(R2) as outlined in the guideline.

1.6 Learning Objectives

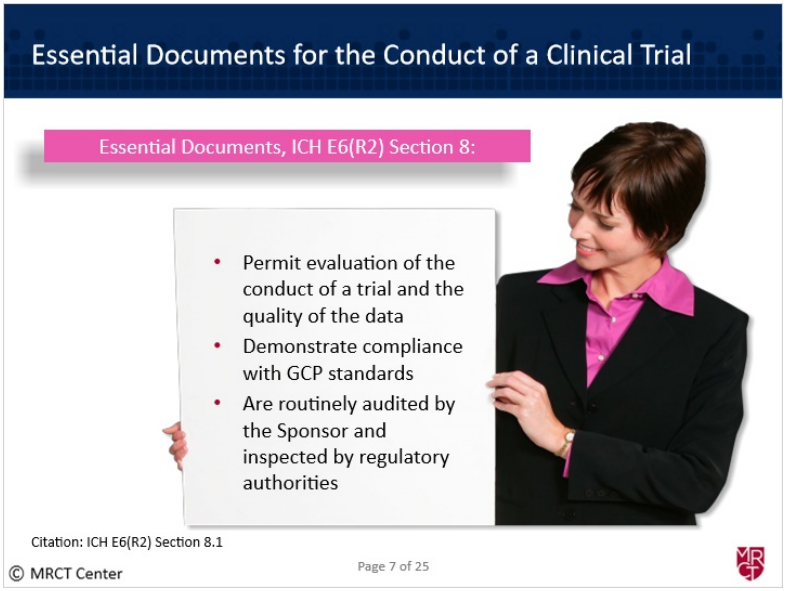


Notes:

At the end of this module, you are expected to understand:

- Essential Documents and how they are organized in the ICH GCP E6(R2) guideline
- Who is responsible for Essential Documents
- Where common errors can occur in Essential Documents
- What ALCOA-C principles are and how they are used by reviewers and inspectors in their activities.

1.7 Essential Documents for the Conduct of a Clinical Trial



Notes:

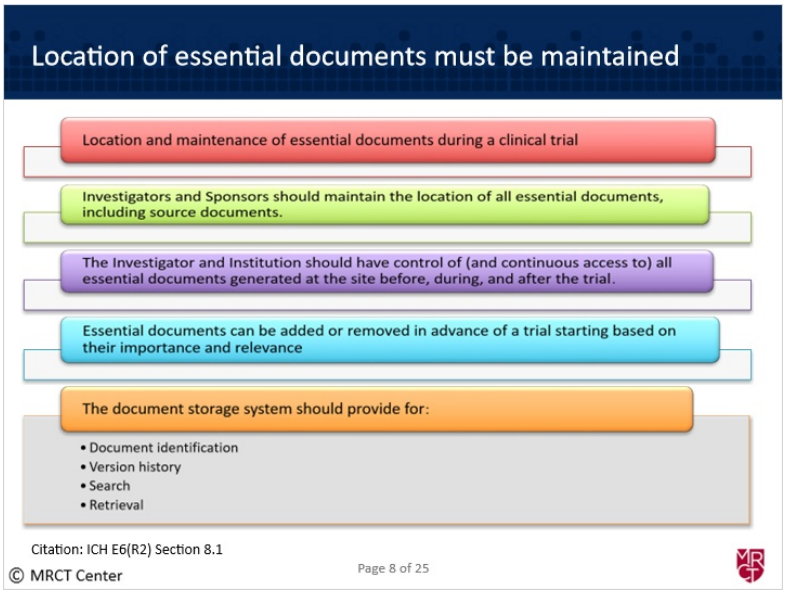
So let's begin by defining what Essential Documents are.

Essential documents are those documents that -- Individually and collectively -- permit evaluation of the conduct of a trial and the quality of the data produced.

These documents demonstrate the compliance of all the parties involved in the trial with GCP standards, including the Investigator, Sponsor, and Monitor.

Essential Documents are those documents routinely audited by the Sponsor and inspected by regulatory authorities to confirm the validity of the trial and integrity of the data.

1.8 Location of essential documents must be maintained



Notes:

Section 8 of the ICH E6(R2) GCP guidelines was revised to provide updated information that addresses the location and maintenance of essential documents during a clinical trial.

Investigators and Sponsors should maintain the location of all essential documents, including source documents.

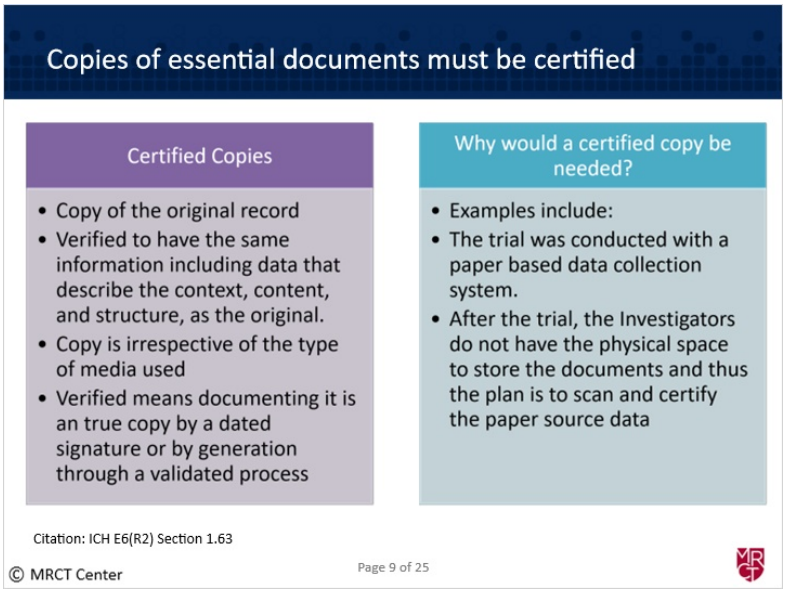
At all times, including before, during and after the trial, the Investigator and

Institution should maintain control of all essential documents generated at the site. The Sponsor should ensure the Investigator has control and continuous access of data reported to the Sponsor.

In advance of trial initiation, essential documents can be added, enhanced, or reduced based on the documents importance and relevance to the trial.

Regardless of whether a paper-based or electronically-based system is used, the document storage system should allow for each document to be identified, searched, and retrieved. Version history should be identified with each document.

1.9 Copies of essential documents must be certified



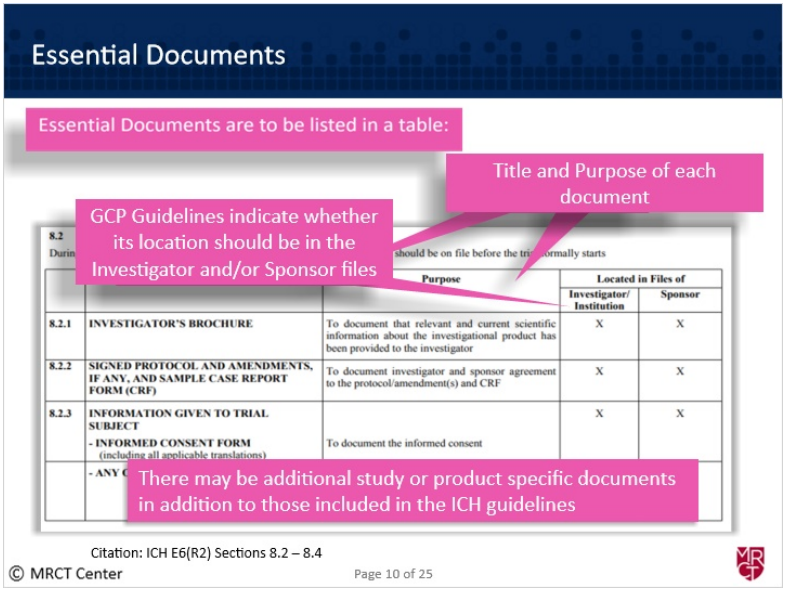
Notes:

The term ‘certified copy’ is now defined in the ICH E6(R2) GCP guidelines in section 1.63 as a copy of the orginal record that has been verified to have the same information, including data that describe the context, content, and structure as the original. A ‘certified copy’ is irrespective of the type of media

used, for example a paper copy or scanned electronic copy. Verifying a copy means documenting that the document is a true copy by a dated signature or by certifying via an electronic validated process.

This addition to the E6(R2) version reflects the need of many clinical trial sites to transition paper based source documentation to electronic documentation due to a lack of physical space to store the documents. This process allows trial sites to scan, certify, and then destroy the paper versions once electronic versions are certified. More specifically, if the trial was conducted with a paper based data collection system, and the Investigators, after the trial, do not have the physical space to store the documents, the Investigators could scan and certify the paper source data.

1.10 Essential Documents



Notes:

Section 8 of the ICH E6(R2) GCP guidelines presents Essential Documents in a tabular format and identifies which documents should be maintained. This is divided into three sub-sections:

- First: Before the trial begins participant enrollment (GCP E6(R2)

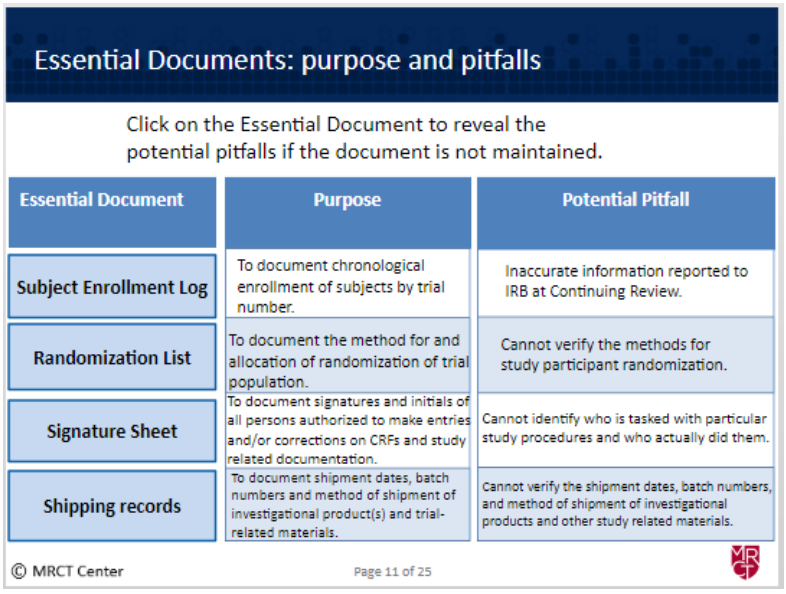
8.2)

- Second: During the conduct of the trial (GCP E6(R2) 8.3)
- Third: After completion/termination of the trial (GCP E6(R2) 8.4)

This slide presents an excerpt from ICH E6(R2) Section 8: Essential Documents. Note in addition to the title and purpose of each document, GCP Guidelines indicate if the document should be located in the Investigator and/or Sponsor files.

It is important to consider, during the review or inspection of a clinical trial, if there are additional documents beyond those included in the ICH guidelines that could and should be maintained to permit evaluation of the conduct of the trial and quality of data produced. These may be study or product specific.

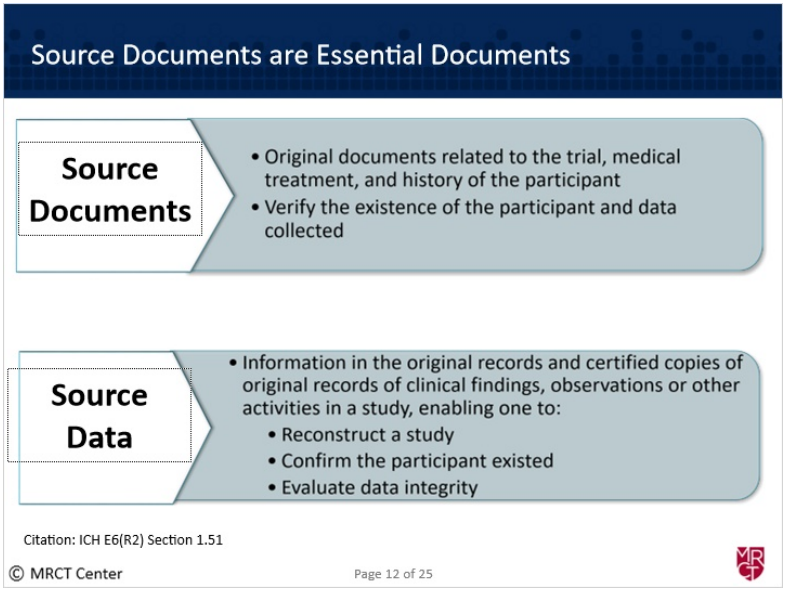
1.11 Essential Documents: purpose and pitfalls



Notes:

This interactive table has been designed for you to explore the purpose of some of the Essential Documents and the potential pitfall if that Essential Document is not maintained. After reading the purpose, click on the Essential Document to see the pitfall.

1.12 Source Documents are Essential Documents



Notes:

Source documents are the original documents related to the trial, medical treatment, and history of the participant. They verify, or document, the existence of the participant and integrity of the data collected about the participant.

Source documents are defined in Section 1.51 as “all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial.

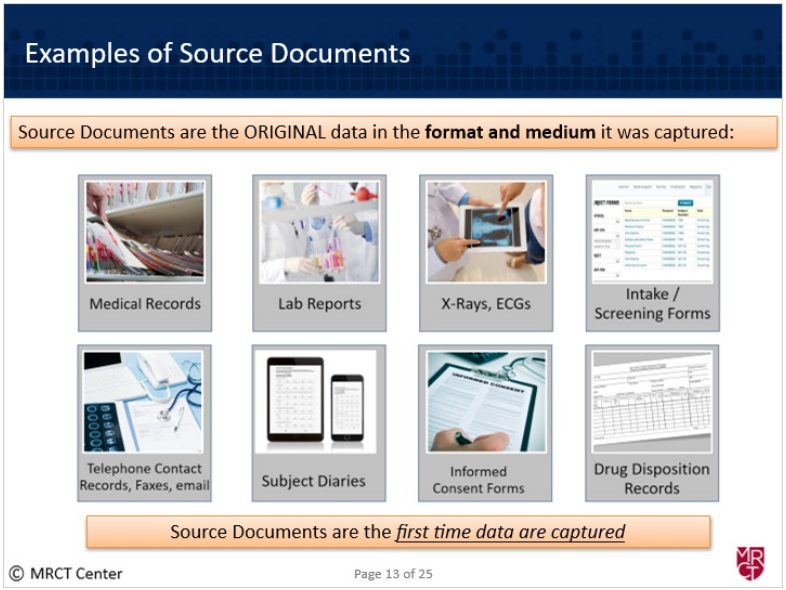
Source data are contained in source documents.

Source Data is the information in the original records and certified copies of original records of clinical findings, observations or other activities in a study,

enabling one to:

- Reconstruct a study
- Confirm the participant existed
- Evaluate data integrity

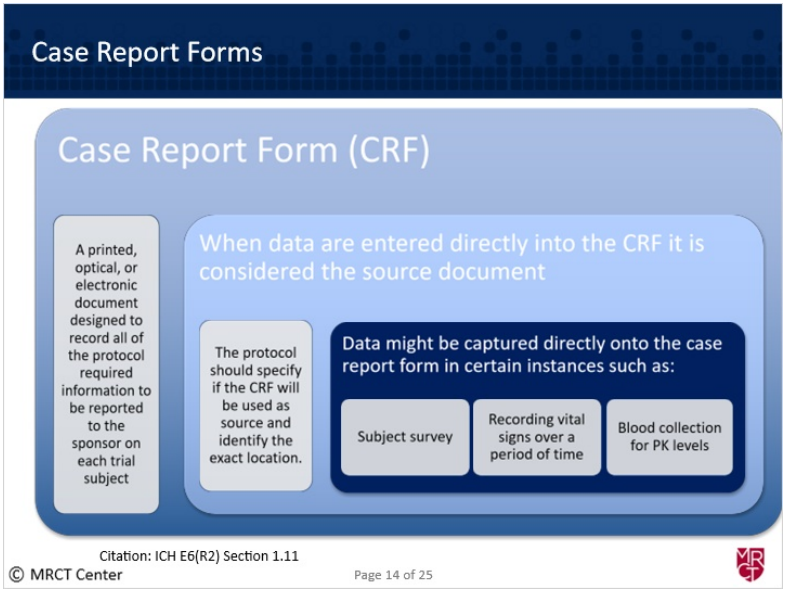
1.13 Examples of Source Documents



Notes:

Source documents are the first time data are captured and are in the original format and medium.
Examples of source documents include medical records, lab reports, x-rays, ECGs and other examples listed on this slide. It is important to remember that source documents are specific to the unique trial.

1.14 Case Report Forms



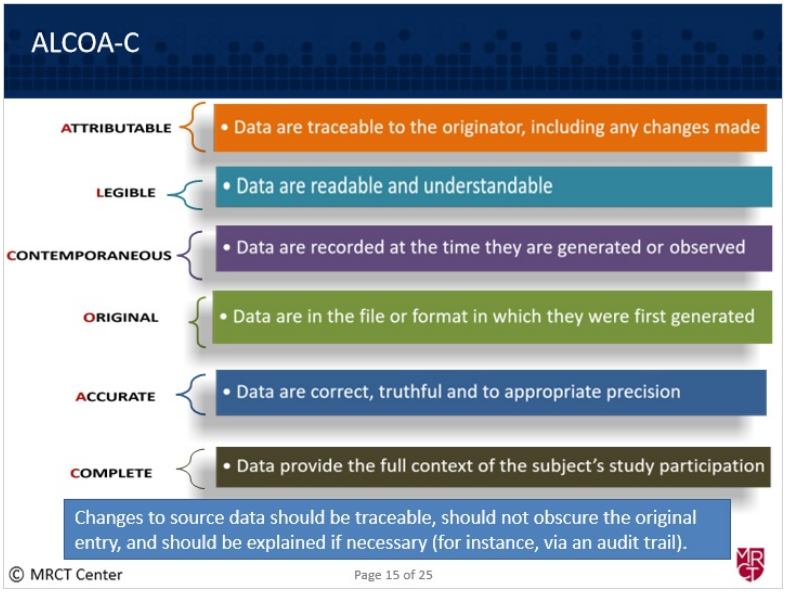
Notes:

Case report forms, or CRFs, are defined in E6(R2) as “a printed, optical, or electronic document designed to record all of the protocol required information to be reported to the sponsor on each trial subject”

When data are entered directly into the CRF, it is considered the source document. The GCP guidelines recommend that the protocol specify this practice as well as the exact location in the CRF that is the source (not the entire CRF as the source).

Examples of when data might be captured directly onto the CRF include a subject survey, when recording vital signs over a period of time, or blood collection for PK levels.

1.15 ALCOA-C



Notes:

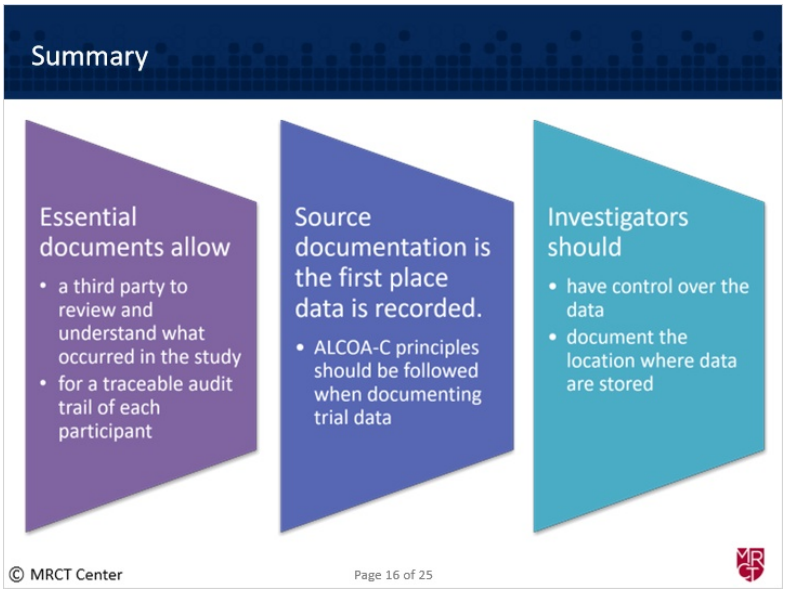
The investigator and institution are responsible for maintaining source documents and trial records that include all relevant observations on each of the site's trial participants.

Sponsors, Monitors, and Investigators frequently refer to the ALCOA-C system of source documentation. Using ALCOA-C as acronym, source data should be:

- Attributable: It should be clear who documented the data
- Legible: The data should be readable and signatures should be identifiable
- Contemporaneous: The data should be or dated in the correct time frame as compared to the flow of events in the trial.
- Original: The data should be the first documentation of the record made, or the original source data.
- Accurate. The data should be a real representation of facts
- And, Complete: The data should be complete up to the point in time that the source data is being reviewed.

Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (for instance, via an audit trail).

1.16 Summary



Notes:

In summary,

Essential documents allow both a third party to review and understand what occurred in the study and allow for a traceable audit trail of each participant. This is key for regulators to evaluate whether the trial was conducted properly and the data are good quality.

Source documentation is the first place data is recorded. ALCOA-C principles should be followed when documenting trial data.

Investigators should have control over the data and should document the location where data are stored as a means of demonstrating their oversight of the trial.