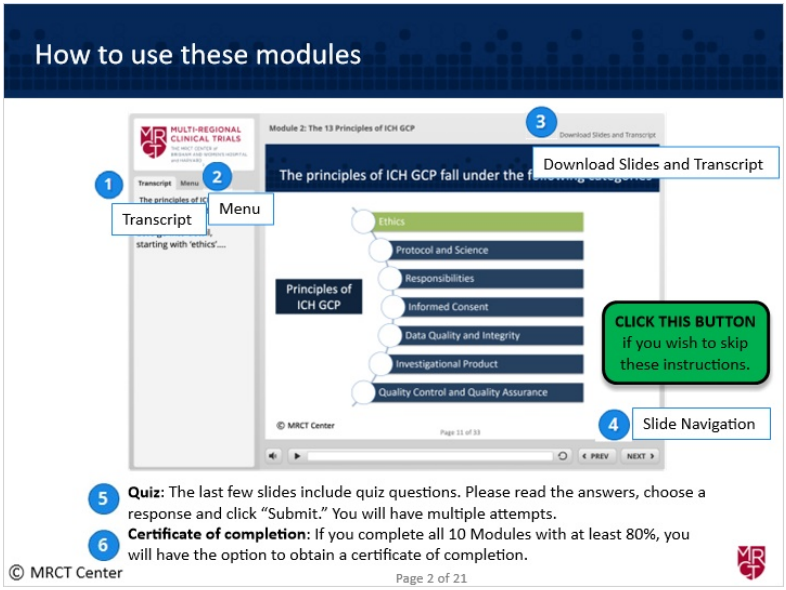
Module 11: Key Takeaways of this Training

1.1 Interpretation and application of ICH E6(R2)

Notes:

Welcome to Module 11 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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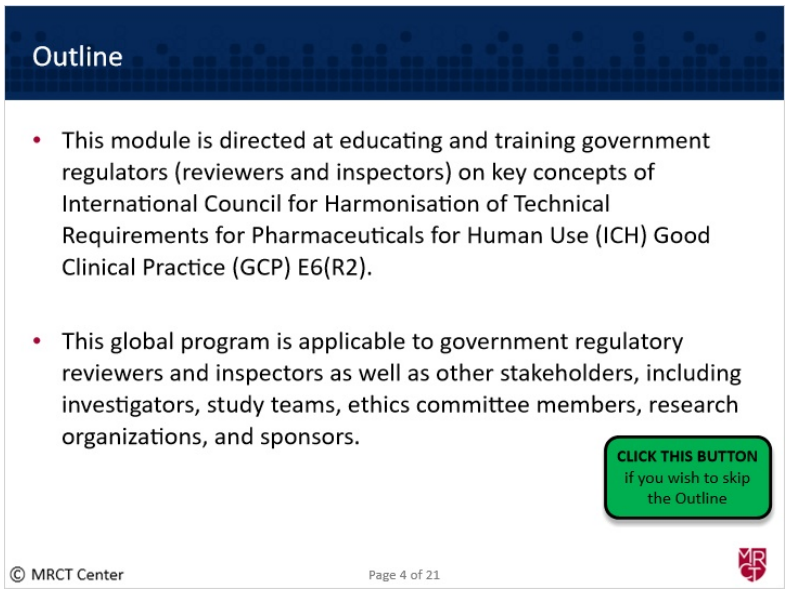
This training programme is recognised by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).

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.

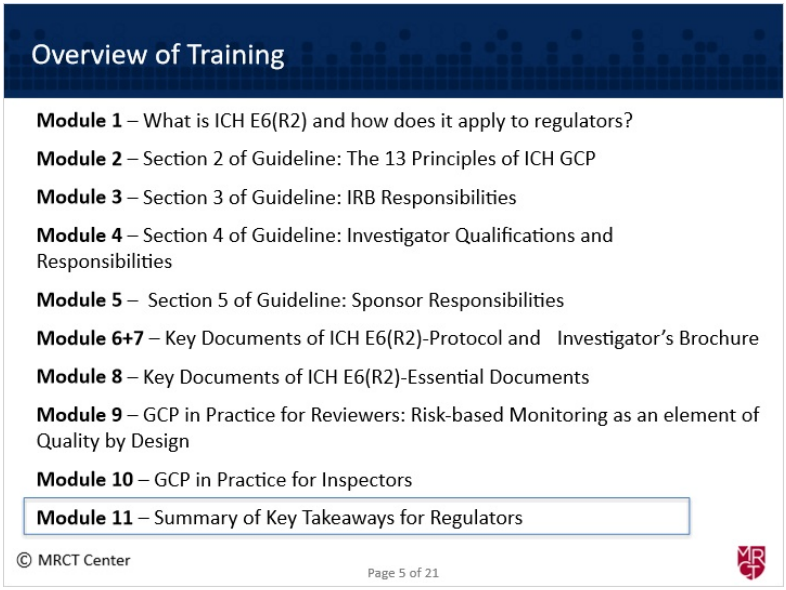
1.4 Outline



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).

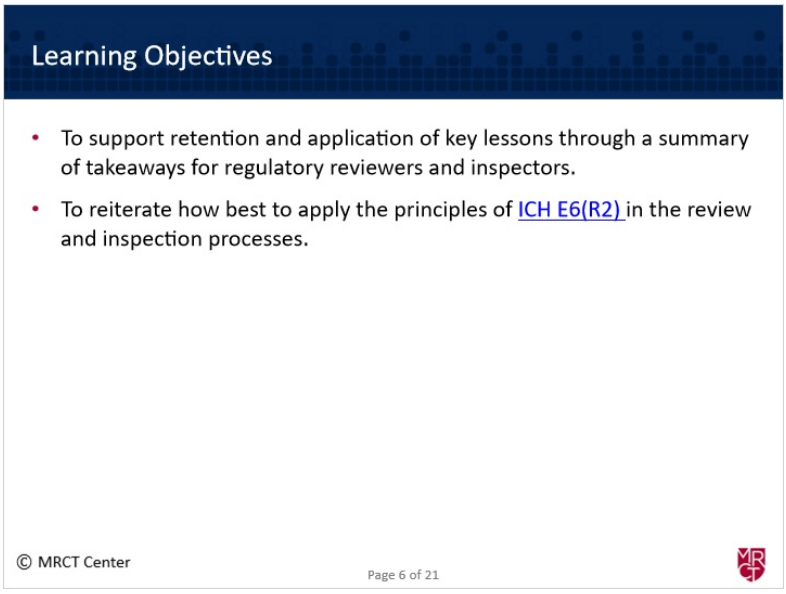
1.5 Overview of Training



Notes:

In Module 11 we will review the key lessons of ICH E6(R2) especially as they apply to the regulatory role.

1.6 Learning Objectives

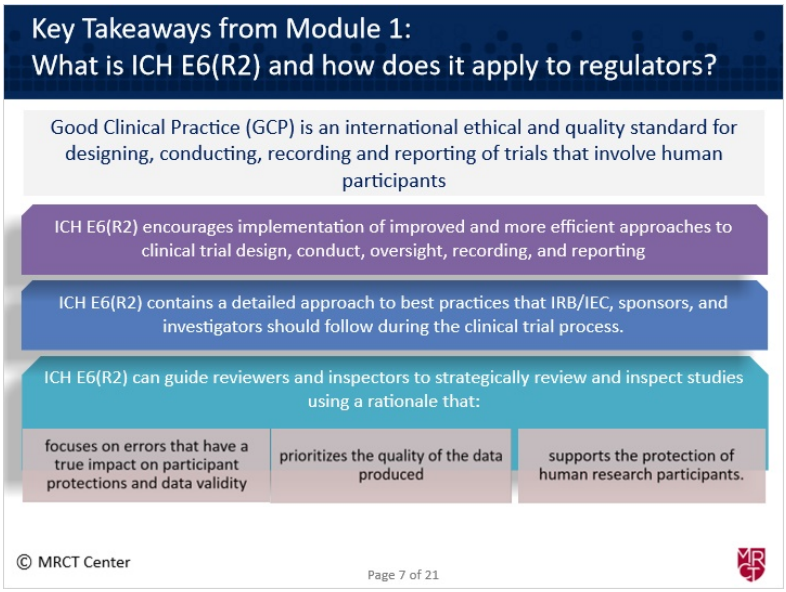


Notes:

In this module we wrap up our training. The learning objectives for this session are to:

- Support retention and application of key lessons of ICH E6(R2) for regulatory reviewers and inspectors.
- Reiterate how best to apply the principles of ICH E6(R2) in the review and inspection processes.

1.7 Key Takeaways from Module 1:



Notes:

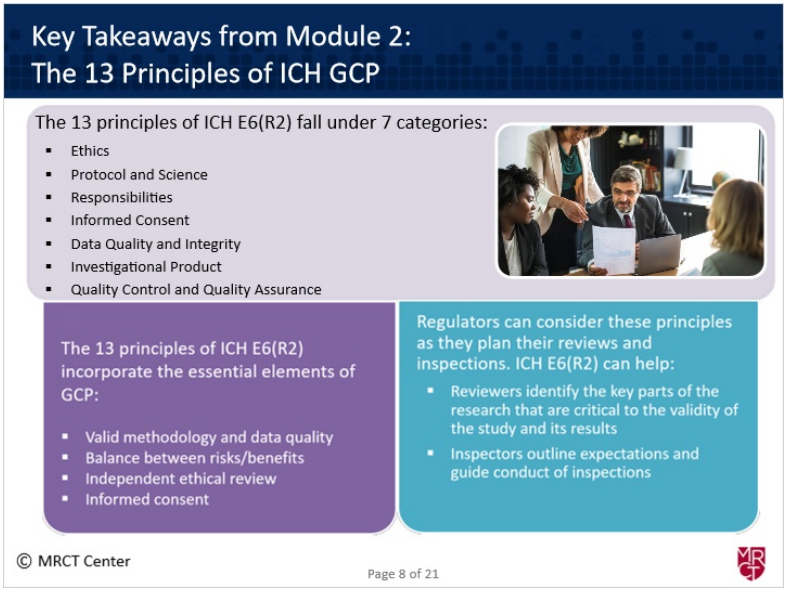
The ICH E6(R2) GCP guideline is an international ethical and quality standard for designing, conducting, recording and reporting of trials that involve human participants….
…. And encourages implementation of improved and more efficient approaches to clinical trial design, conduct, oversight, recording, and reporting.
The guideline contains a detailed approach to best practices that IRB/IEC, sponsors and investigators should follow during the clinical trial process.
The applicability of ICH E6(R2) to the regulatory role is as a guide for how to strategically review and inspect studies using a rationale that:

- focuses on errors that have a true impact on participant protections and data

validity

- prioritizes the quality of the data produced
- supports the protection of human research participants.

1.8 Key Takeaways from Module 2:



Notes:

In Module 2 we reviewed the 13 principles of ICH E6(R2) GCP which fall under 7 categories:

- Ethics
- Protocol and Science
- Responsibilities
- Informed Consent
- Data Quality and Integrity
- Investigational Product
- Quality Control and Quality Assurance

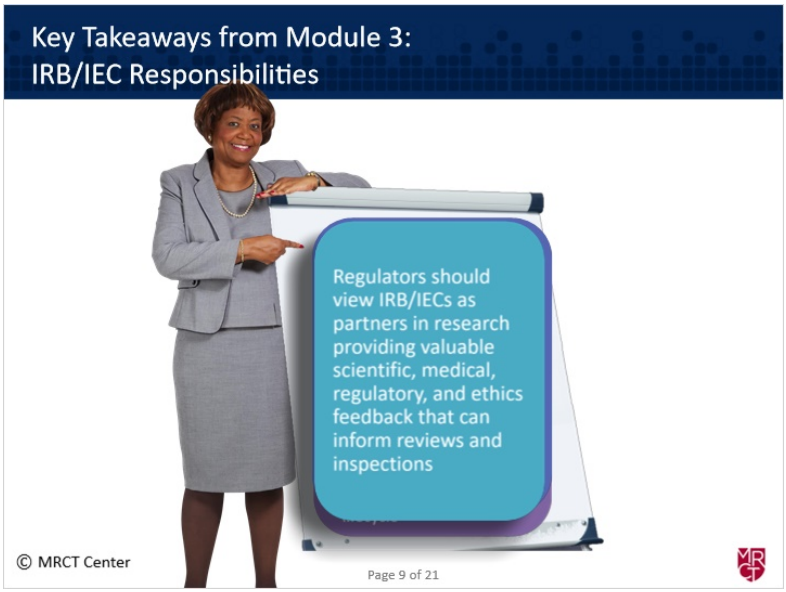
These 13 principles ensure ethics, quality and compliance in the conduct of clinical trials, incorporating the essential elements of GCP:

- Valid methodology and data quality
- Balance between risks/benefits
- Independent ethical review
- Informed consent

Regulators can consider these principles as they plan their reviews and inspections:

- ICH E6(R2) can help reviewers identify the key parts of the research that are critical to the validity of the study and its results; and
- help inspectors outline expectations and guide the conduct of inspections

1.9 Key Takeaways from Module 3:

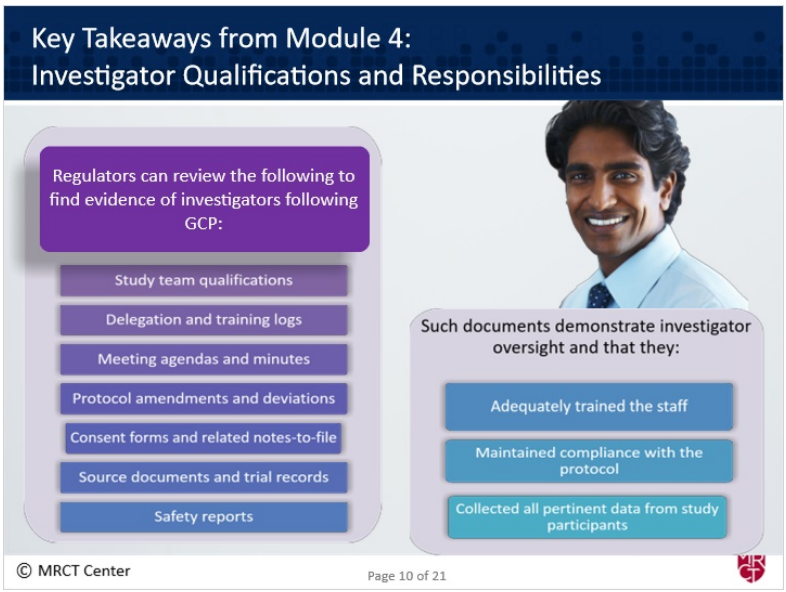


Notes:

In Module 3 we describe the role and responsibilities of the Institutional Review Board/Independent Ethics Committee (IRB/IEC) which is to protect the rights, safety, and well-being of clinical trial subjects.
While they are often referred to by various different terms and can take on different forms, IRB/IEC's general responsibilities, composition, and

functional requirements remain the same.
From a regulatory perspective, reviewers and inspectors should view IRB/IECs as partners in research providing valuable scientific, medical, regulatory, and ethics feedback that can inform reviews and inspections since a great deal of information that is reported to IRB/IECs can be informative to the regulatory process.

1.10 Key Takeaways from Module 4:



Notes:

In Module 4 we reviewed the role and responsibilities of the investigator as set forth in ICH E6(R2).

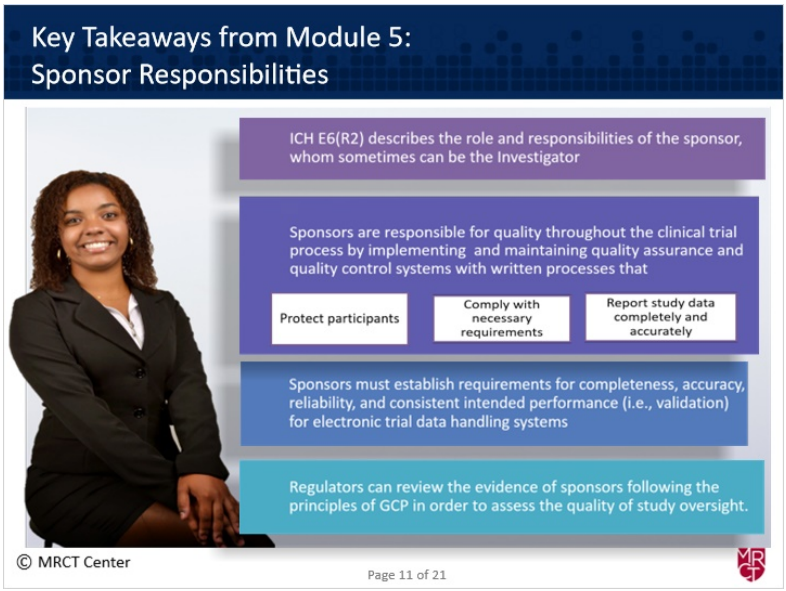
By understanding what investigators commit to by conducting research under ICH E6(R2), regulators can review with focused attention the various study materials, records and reports such as

- Study team qualifications
- Delegation and training logs
- Meeting agendas and minutes

- Protocol amendments and deviations
- Consent forms and related notes-to-file
- Source documents and trial records
- Safety reports

Such documents can provide evidence of the investigator's oversight and compliance with GCP, including that the Investigator: adequately trained the staff, maintained compliance with the protocol, and collected all pertinent data from study participants.

1.11 Key Takeaways from Module 5:



Notes:

Module 5 describes the role and responsibilities of the sponsor as outlined in ICH E6(R2). Remember sometimes the investigator is also the sponsor and has to fulfill both sets of responsibilities

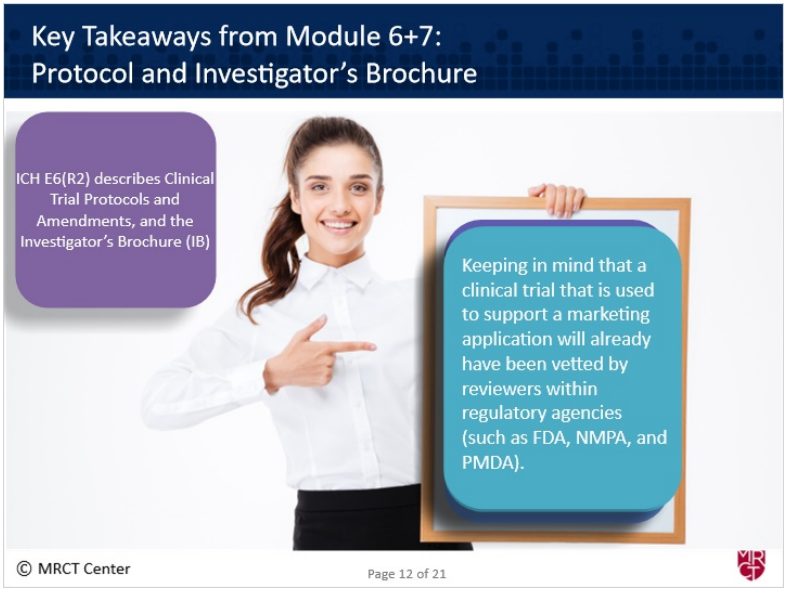
Sponsors are responsible for quality throughout the clinical trial process by implementing and maintaining quality assurance and quality control systems with written processes like SOPs, study plans and monitoring plans that:

- Protect participants
- Comply with the protocol, GCP, and regulatory requirements
- Report study data completely and accurately

Sponsors must establish requirements for completeness, accuracy, reliability, and consistent intended performance (i.e., validation) for electronic trial data handling systems

Regulators can review any of the written processes and procedures to find evidence of sponsors following the principles of GCP in order to assess the quality of study oversight.

1.12 Key Takeaways from Module 6+7:



Notes:

We combined the ICH E6(R2) sections 6 and 7 to describe Protocols, Amendments and the Investigator's Brochure.

These documents play an important role for all stakeholders.
The protocol explains:

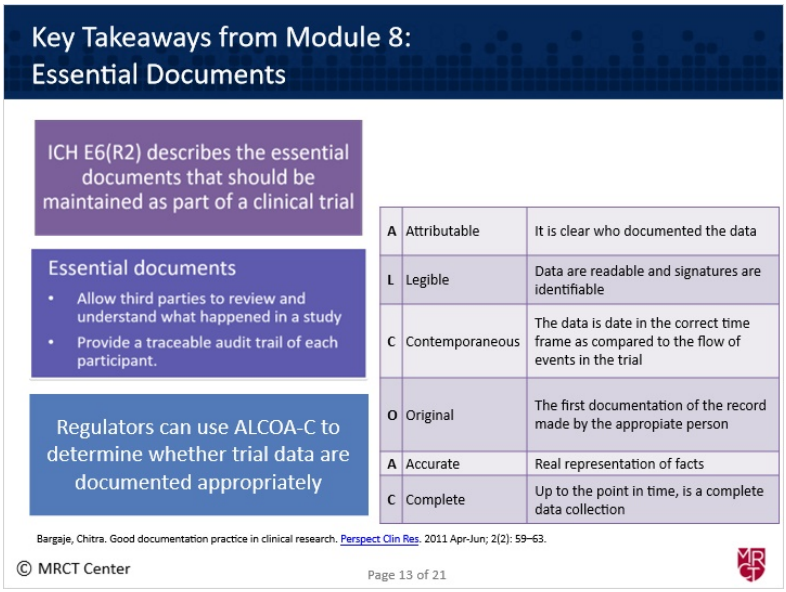
- The purpose of the study

- The methods, including safety and efficacy assessments and statistics
- Data handling and record keeping

The Investigator Brochure explains the investigational product and allows regulators to gain an overall summary of the background info that supports its safety and effectiveness.

Regulators should use the protocol and IB documents as the standard against which to review study conduct, keeping in mind that a clinical trial that is used to support a marketing application will already have been vetted by reviewers within regulatory agencies (such as FDA, NMPA, and PMDA).

1.13 Key Takeaways from Module 8:

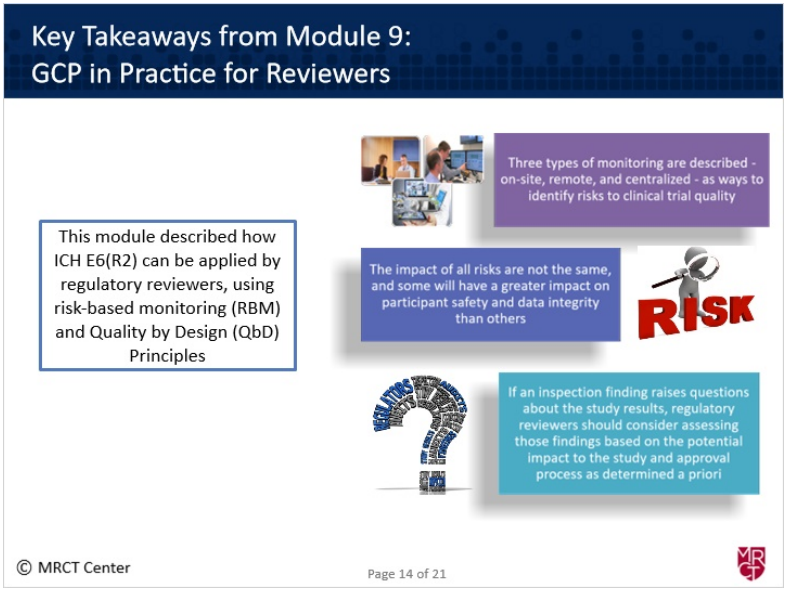


Notes:

In Module 8 we described ICH E6(R2)'s perspective on the essential documents that should be maintained as part of a clinical trial and allow third parties, such as regulators, to review and understand what happened in a study and provide a traceable audit trail of each participant.

In reviewing study documentation, regulators can use the principles of ALCOA-C to determine whether the data have been documented in acceptable ways.

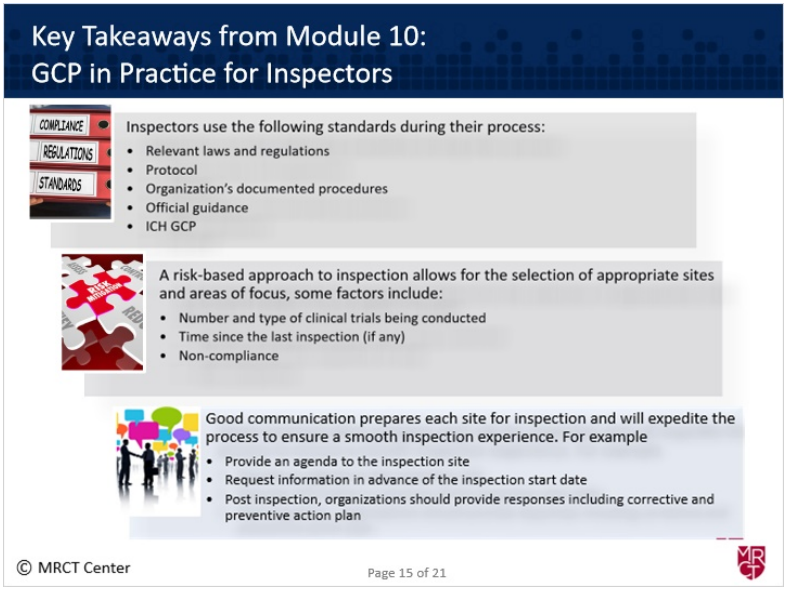
1.14 Key Takeaways from Module 9:



Notes:

In Module 9 we provided additional details on how ICH E6(R2) can specifically apply to the reviewer role, focusing in particular on risk-based monitoring and Quality by Design.
Three types of monitoring were described - on-site, remote, and centralized - as ways to identify risks to clinical trial quality.
It was noted, however, that the impact of all risks are not the same, and that some will have a greater impact than others
Thus, if an audit or inspection finding raises questions about the study results, regulatory reviewers should consider assessing those findings based on the potential impact to the study and approval process as determined in a priori discussions.

1.15 Key Takeaways from Module 10:



Notes:

And in Module 10 we focused on how inspectors can apply ICH E6(R2) to their activities. Inspectors use many standards during their process such as:

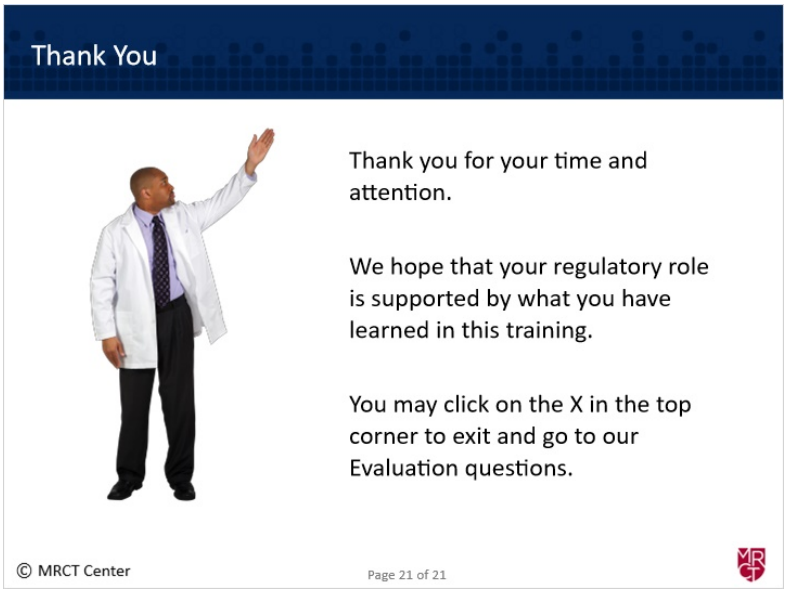
- Relevant laws and regulations
- The protocol itself
- Organization's documented procedures
- And official guidance
- In addition to ICH GCP

Again, using a risk-based approach to inspection allows for the selection of appropriate sites and areas of focus during the inspection process. Risk will depend on factors such as the number and type of clinical trials being conducted, time since the last inspection (if any), and any non-compliance. A wide range of organizations involved in clinical trials can be selected for inspection including Independent Ethics Committees or Institutional Review Boards.

In addition, advance communication that lays out inspection expectations expedites the process, ensures a smooth experience for all involved, and prepares each site for the inspection so that sufficient resources are available to meet the inspector's requests and timelines. Some examples include, providing an agenda to the inspection site,

requesting information in advance of the inspection start date, and planning for post-inspection activities like creating a corrective and preventive action plan as needed.

1.16 This completes Module 11



Notes:

Thank you for your time and attention.

We hope that your regulatory role is supported by what you have learned in this training.