Module 5: Sponsor Responsibilities

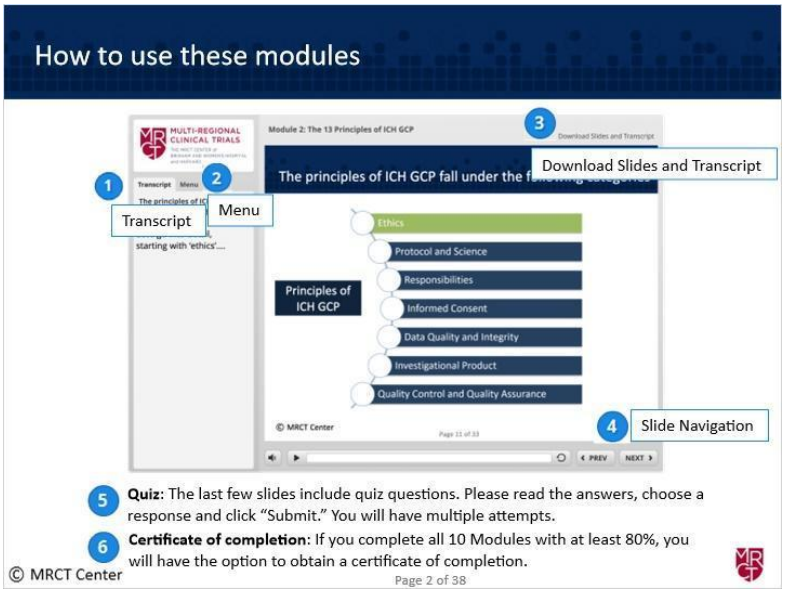
1.1 Interpretation and application of ICH E6(R2)

ICH E6(R2)的解读和应用

Notes:

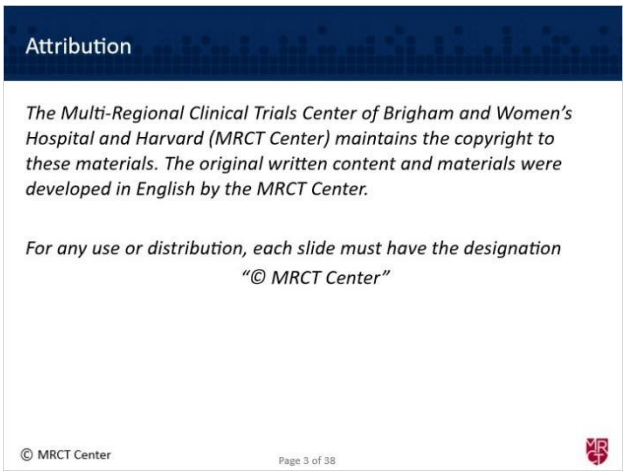
Welcome to Module 5 of this training on the interpretation and application of ICH E6(R2)	欢迎来到 ICH E6(R2)解读和应用培训的第五讲。

~~1.2 How to use these modules~~



1.3 Attribution

归属权



Notes:

Please note that our attribution policy stipulates The Multi-Regional Clinical Trials Center of Brigham and Women's Hospital and Harvard (MRCT Center) maintains the copyright to these training materials which were originally developed in English. For any use or distribution, each slide and the related information must include the MRCT Center copyright.	请注意，我们的归属权政策规定，哈佛大学医学院附属布里格姆和妇女医院多地区临床试验中心（MRCT中心）对这些最初以英文编写的培训材料拥有版权。 对于任何使用或分发，每张幻灯片和相关信息必须包括“MRCT 中心”字样明确版权归属。

1.4 Outline

Outline

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

1.5 Overview of Training

培训概览

Overview of Training

Module 1 – What is ICH E6(R2) and how does it apply to regulators?

Module 2 – Section 2 of Guideline: The 13 Principles of ICH GCP

Module 3 – Section 3 of Guideline: IRB Responsibilities

Module 4 – Section 4 of Guideline: Investigator Qualifications and Responsibilities

Module 5 – Section 5 of Guideline: Sponsor Responsibilities

Module 6+7 – Key Documents of ICH E6(R2)-Protocol and Investigator's Brochure

Module 8 – Key Documents of ICH E6(R2)-Essential Documents

Module 9 – GCP in Practice for Reviewers: Risk-based Monitoring as an element of Quality by Design

Module 10 – GCP in Practice for Inspectors

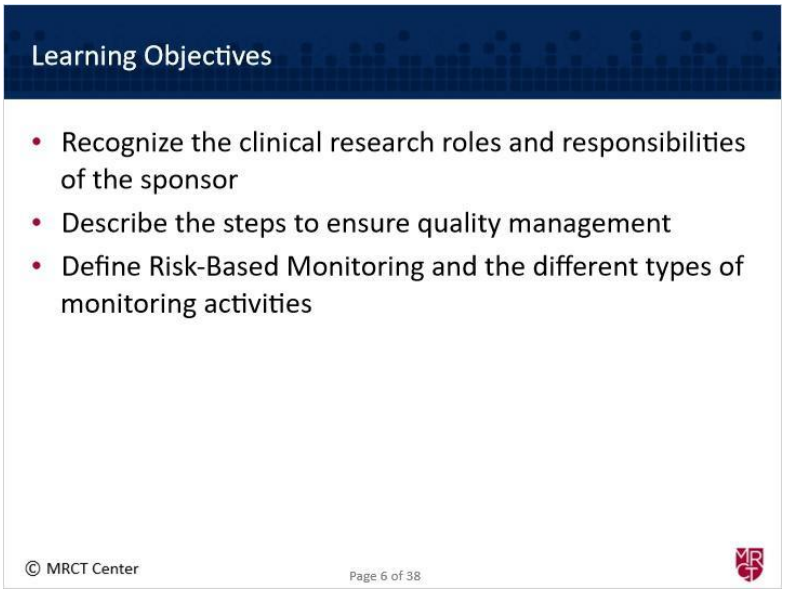
Module 11 – Summary of Key Takeaways for Regulators

Notes:

In Module 5 we will focus on describing the sponsor responsibilities of ICH GCP as outlined in the guideline.	第五讲的重点是 ICH GCP 指南对申办者的职责概述。

1.6 Learning Objectives

教学目标

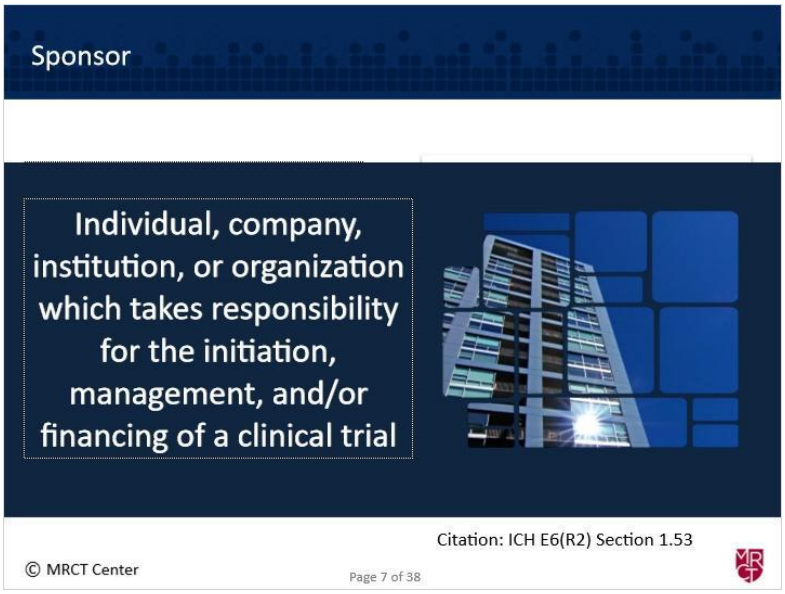


Notes:

By the end of this module you are expected to be able to: ● Recognize the clinical research roles and responsibilities of the sponsor ● Describe the steps to ensure quality management ● Define Risk-Based Monitoring and the different types of monitoring activities	当你学习完本讲以后，你应该能够： 认识申办者在临床研究中的角色与责任 描述确保质量管理的步骤 阐述基于风险的监查以及不同的监查活动

1.7 Sponsor

申办者



Notes:

A sponsor is defined as an Individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.	申办者的定义为：发起一项临床试验并负责管理和/或资助该试验的个人、公司、机构或组织。

1.8 Sponsor Responsibilities – Overview

申办者的责任-概述

Notes:

Sponsors responsibilities are varied and maintained throughout the clinical trial. This module will provide an overview of the responsibilities. Sponsors: ● Develop and prepare the protocol, case report form (CRF) and Investigator Brochure ● Develop and provide the tools (drug, protocol, CRF) to conduct the clinical investigation ● Conduct clinical trial oversight, which may include selecting monitors and auditors to oversee the clinical investigation ● Submit and maintain the Investigational New Product applications and New Product or marketing applications to regulatory authorities ● Manage quality throughout the clinical trial process by implementing and maintaining quality assurance and quality control systems Prior to initiating a trial, the sponsor should define, establish, and allocate all trial-related duties and functions (5.7)	申办者的责任会随临床试验的进行不断变化但始终存在。本讲概述申办者的职责，包括： 制定和准备临床试验方案、病例报告表和研究者手册 制定和提供实施临床研究的各类工具（如药品、临床试验方案、病例报告表） 监督临床试验，包括选择监查员和稽查员对临床研究进行监督 向监管机构提交和维护临床试验用新产品的临床试验申请和新产品注册上市申请 通过执行和维持质量保证和质量控制系统，管理试验过程所有阶段的质量 在开始一个试验前，申办者应当定义、规定和分配与试验相关的责任和职能。

1.9 Sponsor Responsibilities – Overview

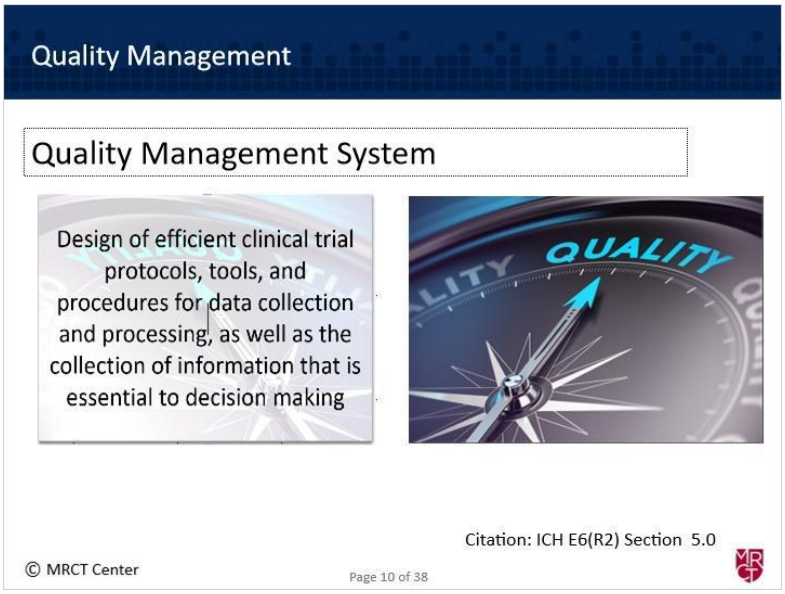
申办者的责任-概述

Notes:

The sponsor maintains clinical trial documentation demonstrating adherence to GCP obligations and manages quality throughout the clinical trial process by implementing and maintaining quality assurance and quality control systems with written SOPs, study plans, and monitoring plans. The Sponsor establishes requirements for completeness, accuracy, reliability, and consistent intended performance for electronic trial data handling systems The sponsor must ensure: ●The conduct of the trial and its data management is documented and reported in compliance with the protocol, regulations and regulator requirements ●Direct access to all trial related sites source data/document and reports for all parties involved for the purpose of monitoring, inspecting and auditing ●All data are processed correctly and is reliable ●All agreements are in writing with all parties involved in the trials ●Essential documents are retained for the appropriate length of time, i.e. 2 years in conformance with applicable regulatory requirements	申办者维护临床试验文件，证明其遵守了 GCP，并通过执行和维持遵照书面 SOP、研究计划和监查计划的质量保证和质量控制体系，对整个临床试验过程中的质量进行管理。申办者应设立对电子数据处理系统的完整性、准确性、可靠性和一致性预期性能的要求。 申办者必须确保： 临床试验的实施及其数据管理应按照临床试验方案、法规和监管机构的要求进行记录和报告 所有临床试验现场的相关源数据/文件和报告可供所有相关方直接访问，以进行监督、检查和稽查 所有的数据得到正确处理且数据可靠 与参与临床试验的各方达成书面协议 基本文件应保留足够长的时间，即与适用的管理规定一致，基本文件应保留两年。

1.10 Quality Management

质量管理

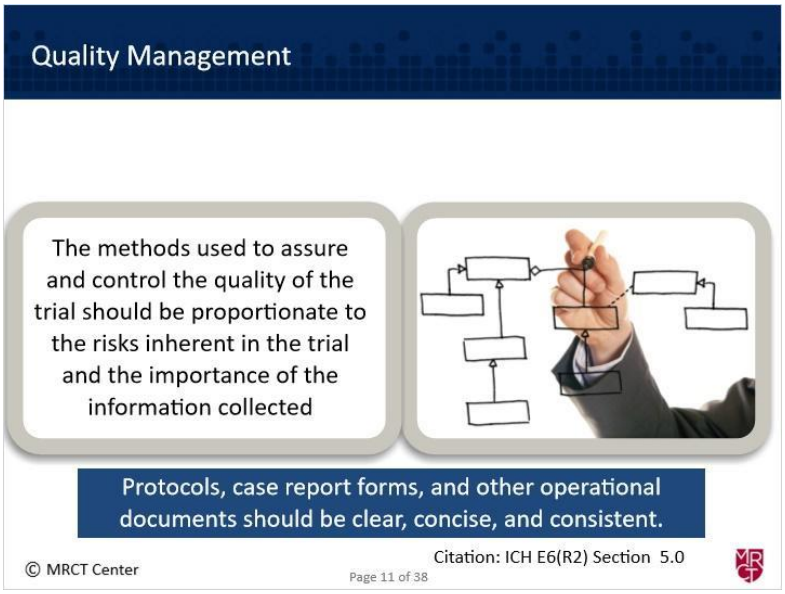


Notes:

The sponsor should implement a system to manage quality throughout all stages of the trial process and should focus on trial activities essential to ensuring human subject protection and the reliability of trial results. Quality management includes the design of efficient clinical trial protocols, tools, and procedures for data collection and processing, as well as the collection of information that is essential to decision making.	申办者应该建立系统来管理试验过程所有阶段的质量，并关注确保受试者得到保护和试验结果可靠性的试验活动。 质量管理包括有效的临床试验方案的设计，数据收集、处理的工具和程序的设计，以及临床决策必需信息的收集。

1.11 Quality Management

质量管理

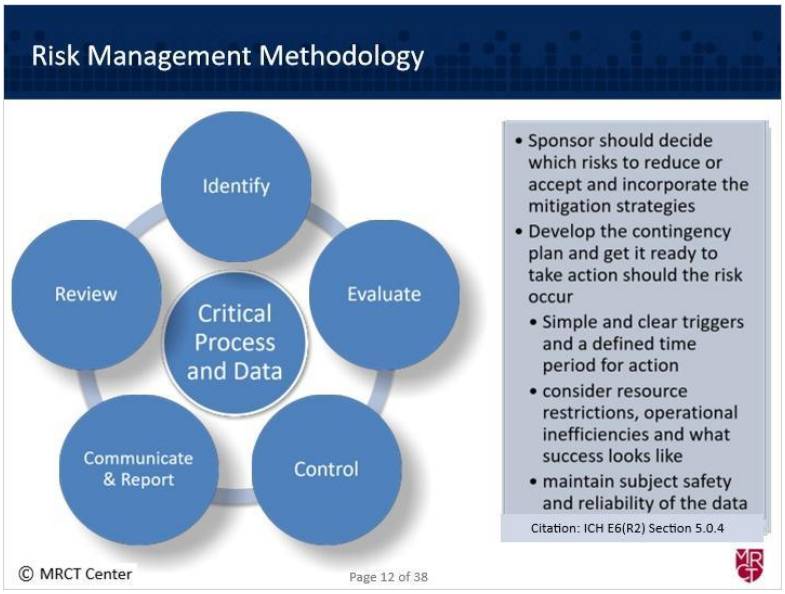


Notes:

The methods used to assure and control the quality of the trial should be proportionate to the risks inherent in the trial and the importance of the information collected. The sponsor should ensure that all aspects of the trial are operationally feasible and should avoid unnecessary complexity, procedures, and data collection. Protocols, case report forms, and other operational documents should be clear, concise, and consistent.	临床试验质控和质保的方法应与试验内在的风险和收集信息的重要性相称。 申办者应确保试验的所有方面都是可操作的，避免不必要的复杂性、程序和数据收集。临床试验方案、病例报告表和其它操作文件应清晰、简洁、前后一致。

1.12 Risk Management Methodology

风险管理方法



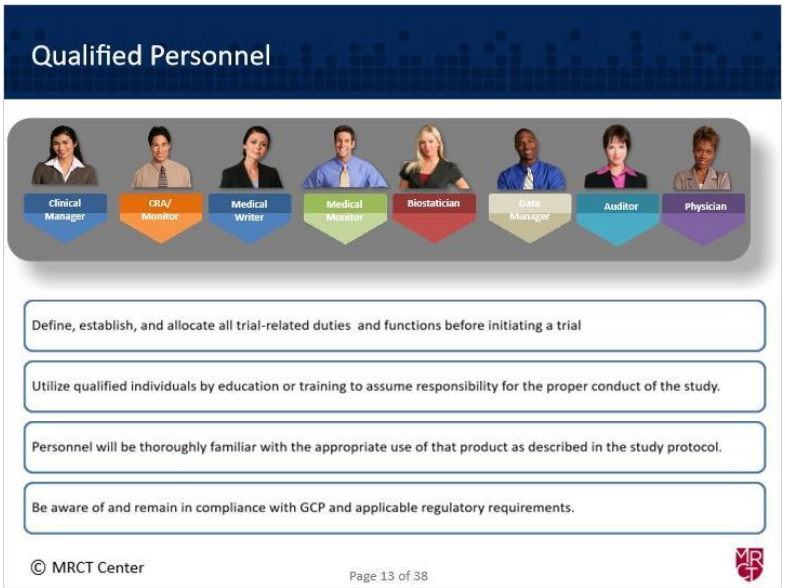
Notes:

Sponsors should develop a quality management system using a risk based approach. Risk Management methodology uses Critical Process and Data Identification to ensure human subject protection and the reliability of trial results. This includes: *Risk Identification* The sponsor should identify risks to critical trial processes and data. Risks should be considered at both the system level (e.g., standard operating procedures, computerized systems, and personnel) and clinical trial level (e.g., trial design, data collection, and informed consent process). *Risk Evaluation* The sponsor should evaluate the identified risks, against existing risk controls by considering: The likelihood of errors occurring. The extent to which such errors would be detectable. The impact of such errors on human subject protection and reliability of trial results.	申办者应开发一套基于风险的质量管理体系。风险管理方法使用关键流程和数据识别来确保对人体受试者的保护和临床试验结果的可靠性。 风险管理方法包括： *风险识别* 申办者应识别关键流程和数据的风险。申办者应在两个层面考虑风险，系统层面（例如标准操作规程、计算机系统、人员）和临床试验层面（例如试验设计、数据收集、知情同意过程）。 *风险评估* 申办者可以通过考虑以下方面，评估已识别的风险，控制现有的风险： 错误发生的可能性 错误可被察觉的程度 错误的发生对受试者保护和试验数据可靠性的影响；

Risk Control The sponsor should decide which risks to reduce and/or which risks to accept. The approach used to reduce risk to an acceptable level should be proportionate to the significance of the risk. The Sponsor should develop the contingency plan and get it ready to take action should the risk occur as well as Simple and clear triggers and a defined time period for action. The Sponsor should: ●consider resource restrictions, operational inefficiencies and what success looks like ●maintain subject safety and reliability of the data	*风险控制* 申办者应决定降低哪些风险，接受哪些风险。将风险降低至可接受程度的方法应该与风险的重要性相称。 申办者应制定应急计划，并准备好在风险发生时采取行动，同时制定简单、明确的触发条件和明确的行动时间。 申办者应该： 充分考虑临床试验中可能资源受限，运营低效，以及成功效果的预期 维护受试者安全和数据可靠性
Risk Communication & Reporting The sponsor should communicate quality management activities to those who are involved in or affected by such activities, to facilitate risk review and continual improvement during clinical trial execution. The sponsor should document quality management activities, as well as summarize important deviations from the predefined quality tolerance limits and remedial actions taken in the clinical study report	*风险沟通和报告* 申办者应与相关人员或受其活动影响的人员沟通质量管理活动，在临床试验执行中促进风险回顾和持续改进。 申办者应记录质量管理活动，并在临床试验报告中总结严重偏离预先设定的质量容许限的事件及补救措施。
Risk Review The sponsor should periodically review risk control measures to determine whether the implemented quality management activities remain effective and relevant, taking into account emerging knowledge and experience. *Please refer to Module 9 of the training for additional details on risk management.*	*风险回顾* 申办者应定期回顾风险控制措施来确定所实施的质量管理活动依然有效、可行，并考虑新出现的知识和经验。 风险管理相关细节请参考本培训课程第九讲。

1.13 Qualified Personnel

合格的人员



Notes:

The sponsor should utilize qualified individuals (e.g., biostatisticians, monitors, and physicians) as appropriate, throughout all stages of the trial process, from designing the protocol and CRFs and planning the analyses to analyzing and preparing interim and final clinical trial reports. Sponsors must ● Define, establish, and allocate all trial-related duties and functions before initiating a trial ● Ensure personnel responsible for the execution of trial related duties must be qualified by education, training, and experience to assume responsibility for the proper conduct of the study ● Ensure personnel is thoroughly familiar with the appropriate use of the investigational product as described in the study protocol ● Ensure personnel is aware of and remain in compliance with GCP and applicable regulatory requirements.	在试验过程的各个阶段，从设计临床试验方案、病例记录表、计划分析到分析和准备中期及最终临床试验报告，申办者应任用有合格资质的人(如生物统计学家、监查员和医生)。 申办者必须： 在临床试验开始前，定义、规定和分配与试验相关的责任和职能 确保负责执行临床试验相关职责的人员应在教育、培训和经验方面有资质承担合理执行临床试验的责任 确保人员充分熟悉临床试验方案中描述的临床试验用产品 确保人员知晓并持续遵守 GCP 以及适用的法规要求

1.14 Clinical Research Organization (CRO)

临床合同研究组织

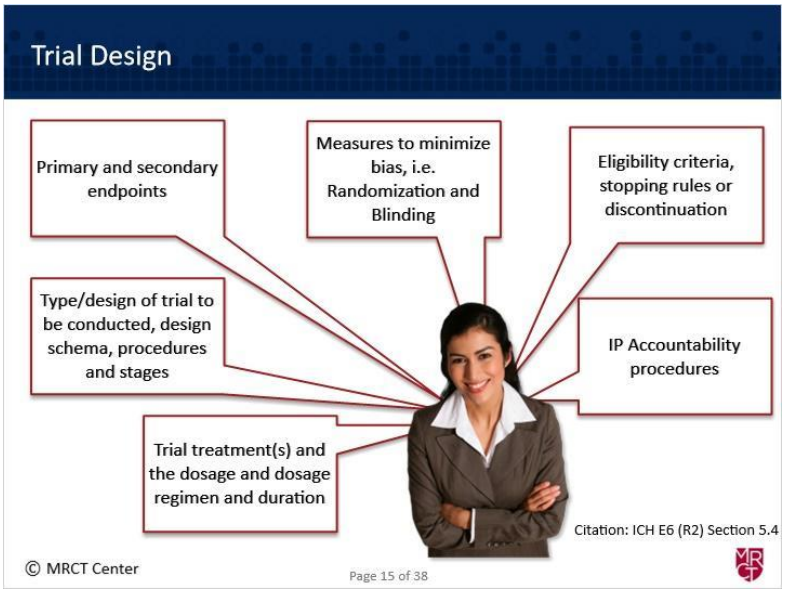
Notes:

A Clinical Research Organization or CRO is defined as a person or an organization (commercial, academic, or other) contracted by the sponsor to perform one or more of a sponsor's trial-related duties and functions. This includes all vendors to which trial-related duties have been contracted, such as site management organizations and data handling/processing companies.	临床合同研究组织(CRO)指的是与申办者订立契约，受委托完成其执行临床试验中的某些任务和工作的个人或组织(商业性的、学术的或其他)。合同研究组织包括与临床试验相关职责签订合同的所有供应商，如现场管理机构和数据处理公司。
A sponsor may transfer a portion of trial–related duties to a CRO. And in some cases a sponsor may transfer any or all of the sponsor's trial-related duties and functions to a CRO. It is important to remember the ultimate responsibility for the quality and integrity of the trial data always resides with the sponsor. Any trial-related duties and functions not specifically transferred to and assumed by a CRO are retained by the sponsor.	申办者可以将与试验有关的任务部分或全部转移给一个 CRO。在某些情况下，申办者可以将与试验有关的职能和任务的任何部分或全部转移给一个 CRO，但是试验数据质量和完整性的最终责任始终在申办者。没有明确转移给 CRO 或未由 CRO 承担的任何与试验有关的职能和任务仍然由申办者承担。
The CRO should implement quality assurance and quality control measures.	CRO 应实施质量保证和质量控制。
Any trial-related duty and function that is transferred to and assumed by a CRO should be specified in writing.	转移给 CRO 的或 CRO 承担的任何与试验有关的任务和职能应有书面说明。

The sponsor should ensure oversight of the trial-related duties carried out on its behalf by the CRO.	申办者应确保 CRO 实施的任何试验相关的任务都得到监督。

1.15 Trial Design

临床试验设计



Notes:

As stated before, the sponsor will design the protocol, the CRFs, conduct analysis and prepare interim and final clinical study reports. The scientific integrity of the trial and the credibility of the data from the trial depends substantially on the trial design. When designing clinical trials sponsors need to consider: ● Primary and secondary endpoints ● Type/design of trial to be conducted, design schema, procedures and stages ● Measures to minimize bias, i.e. Randomization and Blinding ● Trial treatment(s) and the dosage and dosage	如前所述，申办者将设计临床试验方案和病例报告表，分析并准备中期和最终临床研究报告。试验的科学完整性和数据可信度主要取决于试验设计。 申办者在设计临床试验时需要考虑： 主要终点和次要终点 要实施的临床试验的类型/设计描述，以及试验架构、程序及阶段的系统示意图。 减少偏倚的措施，即随机化和盲法 试验治疗及剂量、剂量方案和给药持续时间

regimen and duration ● Eligibility criteria, stopping rules or discontinuation ● Intellectual Property Accountability procedures Please see module 6 for more detailed information about the protocol.	入组标准、停止规则或终止标准 知识产权问责程序 更多临床试验方案相关内容请见本培训课程第六讲。

1.16 Trial Management, Data Handling, and Recordkeeping

试验管理、数据处理和记录保存

Notes:

Sponsors need to maintain the standard operating procedures (SOPs) for trial management, data handling, and recordkeeping. These SOPs should Ensure systems maintain an audit trail, data trail, edit trail Maintain a security system that prevents unauthorized access to the data. Safeguard the blinding, if any (e.g. maintain the blinding during data entry and processing).	申办者需要为临床试验的管理、数据处理及记录保存遵守标准操作规程（SOP） 这些 SOP 应： 确保系统能够保留审计追踪、数据痕迹和编辑痕迹 维护安保系统以防止未经授权访问数据 如采用盲法，保护盲法安全(如在数据输入和处理

Ensure the integrity of the data. This is particularly important when making changes to the computerized systems, such as software upgrades or migration of data. The sponsor should base their approach to validation of such systems on a risk assessment that takes into consideration the intended use of the system and the potential of the system to affect human subject protection and reliability of trial results.	期间维持盲态) 确保数据完整性。保证数据完整性特别重要，尤其是当计算机系统发生变化时，如软件升级或数据迁移。 申办者验证此类系统的方法应基于风险评估，该风险评估应考虑系统的使用目的，以及系统影响受试者保护和试验结果可靠性的可能。

1.17 Investigator Selection

研究者的选择

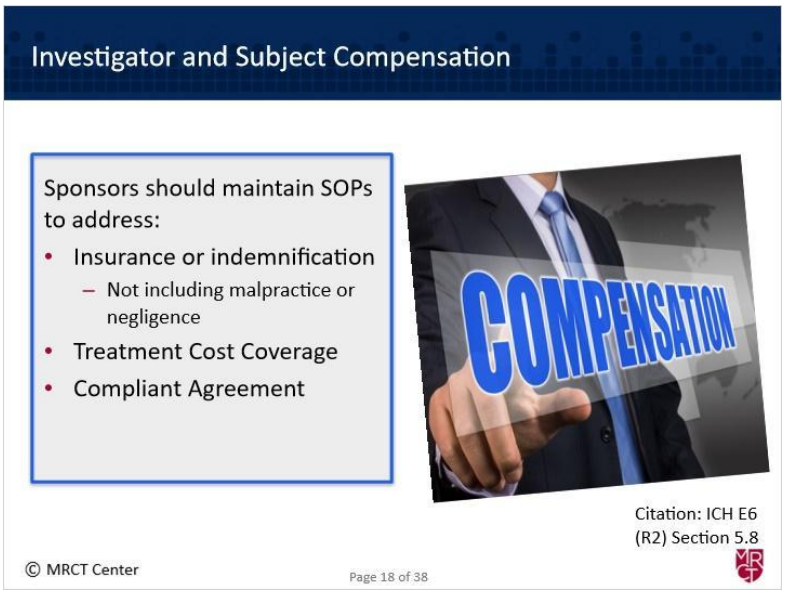
Notes:

Sponsors must select investigators whom by training or expertise will expertly oversee and conduct the trial. The Investigator should be based at the institutions/hospitals and have sufficient resources to properly conduct the trial. This include any third party retained by the investigator or institution to whom the investigator delegates trial-related duties	申办者必须选择经过培训或拥有专业知识能够熟练监督和实施临床试验的研究者。 研究者应驻扎在机构或医院，并有足够的资源来正确地实施临床试验。这包括由研究者或研究机构委托实施试验相关职能和任务的任何第三方。

and functions Sponsors use an Investigator Agreement to document that the investigator agrees to ●Conduct the trial in compliance with GCP ●Comply with procedures for data recording ●Allow monitoring, auditing and inspections ●Retain the trial related essential documents until the sponsor informs the investigator these documents are no longer needed ●Provide access to source data/documents	申办者与研究者通过签署协议记录研究者同意以下条款： 遵守 GCP 实施临床试验 遵循数据记录程序 允许监查、稽查和检查 保留与试验有关的基本文件直至申办者通知研究者不再需要这些文件 提供授权获取源数据和源文件

1.18 Investigator and Subject Compensation

受试者和研究者的补偿



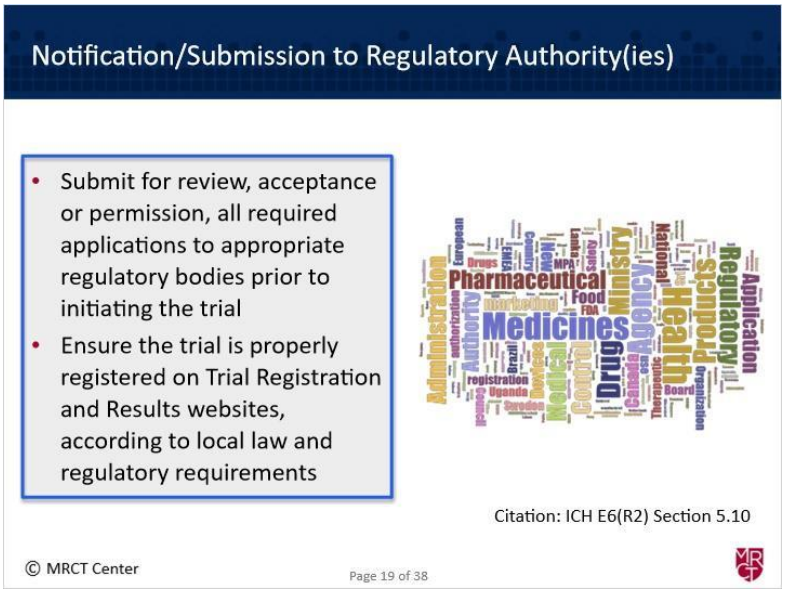
Notes:

The sponsor should maintain SOPs to: address insurance or indemnification against claims arising from the trial for the investigator/institution This does not include malpractice or	申办者应当遵照 SOP 为研究者/机构提供因临床试验引起的保险索赔或赔偿 但因治疗不当或疏忽所致的除外

negligence Address treatment cost in the event of trial-related injuries Ensure all compensation agreements are in compliance with regulatory requirements	支付临床试验相关的伤害事件的治疗费用 确保所有赔偿协议符合监管要求

1.19 Notification/Submission to Regulatory Authority(ies)

向管理当局通报/提交



Notes:

Before initiating a clinical trial, the sponsor should submit for review, acceptance or permission, all required applications to appropriate regulatory bodies. Sponsors are responsible for the Trial Registration on appropriate websites, according to local law, regulatory requirements and timeliness.	在启动临床试验之前，申办者应向相应的管理部门提交所需要的申请表，供审评、接受或许可。 申办者负责根据当地法律、监管要求和时间表在适当的网站上进行临床试验的注册。

1.20 Confirmation of Review by IRB/IEC

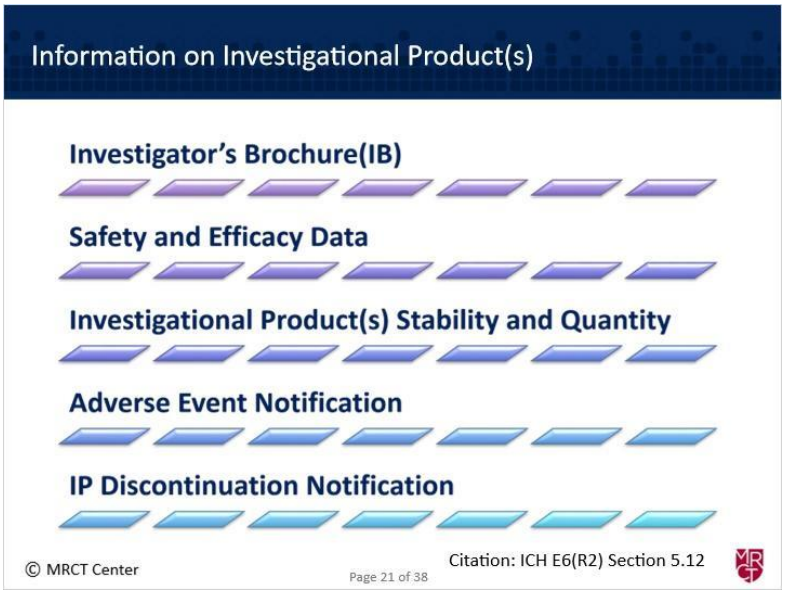
IRB/IEC 审评的确认

Notes:

Sponsors need to ascertain that all investigator sites have approval from their IRB/IEC to conduct the trial, and in addition, confirm that the IRB/IEC operates according to applicable local laws, regulations and GCP. The sponsor should maintain all relevant IEC/IRB documentation on file.	申办者需要确定所有临床研究现场均已获得其 IRB/IEC 的批准以进行试验，此外，还要确认 IRB/IEC 根据适用的当地法律、法规和 GCP 运作。申办者应将所有相关的 IEC/IRB 文件存档。

1.21 Information on Investigational Product(s)

有关试验用药品的资料



Notes:

When planning trials, the sponsor should ensure that sufficient safety and efficacy data from nonclinical studies and/or clinical trials are available to support human exposure by the route, at the dosages, for the duration, and in the trial population to be studied.	计划试验时，申办者应当保证有足够的非临床研究和/或临床研究的安全性与有效性数据支持所研究的试验人群暴露的给药途径、剂量和持续时间。
The sponsor should ensure that:	申办者应该确保：
The Investigator's Brochure(IB) is made available to the investigator(s) and the investigators are responsible for providing the up-to-date IB to the responsible IRBs/IECs.	研究者手册 (IB) 已经提供给研究者，研究者有责任将最新的 IB 提供给负责的 IRB/IEC。
Sufficient safety and efficacy data from nonclinical studies and/or clinical trials are available to support human exposure by the route, at the dosages, for the duration, and in the trial population to be studied	有足够的非临床研究和/或临床研究的安全性与有效性数据支持所研究的试验人群暴露的给药途径、剂量和持续时间。
The Investigational product(s) are stable over the period of use and that ongoing safety evaluations are performed on the investigational product(s)	临床试验用产品在整个使用期内是稳定的，并且对临床试验用产品进行了持续的安全性评估。
Notify all related parties of findings that may adversely affect subjects, trial conduct or approval from IRB/IEC or if the development of the Investigational Product is discontinued	临床试验用产品在整个使用期内是稳定的，并且对临床试验用产品进行了持续的安全性评估。

Additional detail about the Investigator's Brochure is presented in Module 6	有关研究者手册的更多内容请见本培训课程第六讲。

1.22 Investigational Product Oversight

临床试验用产品的监督

Notes:

For investigational product oversight, the sponsor is required to ● Supply all required documentation including approval from IRB and regulatory authorities before supplying the investigator with the Investigational Products, including Comparator(s) and Placebo if applicable. This includes a mechanism that permits rapid identification of the product(s) in case of a medical emergency, but does not permit undetectable breaks of the	在对临床试验用产品的监督方面，申办者必须： 在向研究者提供包括对照产品和安慰剂(如适用)的临床试验用产品之前，提供所有必需的文件，包括 IRB 和监管机构的批准。这还包括一种机制，允许在医学紧急情况下迅速鉴别药品、但不会导致不可发觉的破盲。

blinding ● Sponsors must Maintain records of the quantities of Investigational Product with proper batch numbers, determine acceptable storage temperature, conditions, time, reconstitution fluids and procedures and devices for product infusion characterized as appropriate to the stage of development of the product(s) ● Ensure all product(s) are manufactured in accordance with any applicable GMP, appropriately coded, packaged to prevent contamination and unacceptable deterioration during transport and storage; and Labelled in a manner that protects the blinding, if applicable and that it complies with applicable regulatory requirement ● And finally sponsors ensure that the investigational product(s) are stable over the period of use and timely delivered to the investigator(s).	申办者必须保留临床试验用产品数量及批号记录， 确定允许储存温度、储存条件、储存时间、复溶液和程序，以及与产品开发阶段相适应的产品递送装置。 确保所有产品按照适用的 GMP 生产、合理编码，包装，以防止在运输和储存期间受污染和不可接受的变质；标签的方式应适合于保护盲法（如适用）并符合适用的监管要求。 最后，申办者应该确保临床试验用产品整个使用期内的稳定性，并及时运送至研究者处。

1.23 Adverse Drug Reaction Reporting

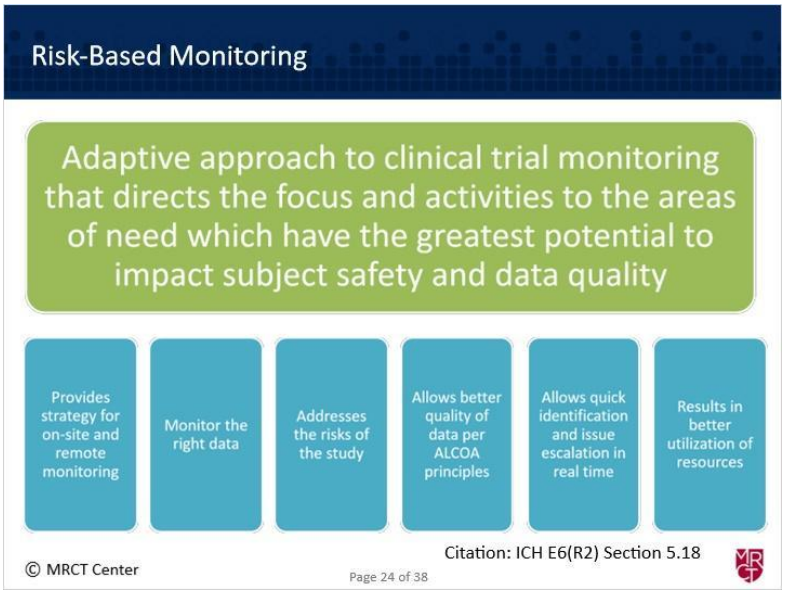
药品不良反应报告

Notes:

Sponsors submit to the regulatory authority all safety updates and periodic reports, as required by applicable regulatory requirements. All adverse drug reactions (ADRs) that are both serious and unexpected reporting must be expedited to all concerned investigators and institutions, where required, and to the regulatory authorities.	申办者应根据适用的管理要求向管理当局提交全部安全性更新和定期报告。 申办者应迅速向所有相关研究者和研究机构及管理当局报告所有非预期的严重不良反应。

1.24 Risk-Based Monitoring

基于风险的监查



Notes:

The sponsor should develop a systematic, prioritized, risk-based approach to monitoring clinical trials that directs the focus on activities to the areas of need which have the greatest potential to impact subject safety and data quality. The sponsor should document the rationale for the chosen monitoring strategy (e.g., in the monitoring plan). The monitoring plan needs to be tailored to the specific human subject protection and data integrity risks of the trial. No single approach is appropriate for every clinical trial, therefore risk-based monitoring approach ● Provides strategy for on-site and remote monitoring ● Allows sponsor Monitor the right data (Identified Risks) ● Addresses the risks of the study (Risk Mitigation Plan) ● Allows better quality of data per ALCOA principles – Accurate, Legible, Contemporaneous, Original and Attributable. ● Allows quick identification and issue escalation in real time	申办者应建立一个系统的、区分优先级别的，基于风险的方法来监查临床试验，将重点放在最可能影响受试者安全和数据质量的需要上。 申办者应该用文件记录其选择监查策略的依据（例如，在监查计划中写明）。监查计划需要与针对保护人体受试者及数据完整性的风险相适应。 没有一种放之四海而皆准的监查方法。基于风险的监查方法可以： 提供现场和远程监查策略 允许申办者对合适的数据（已被识别的风险）进行监查 对临床研究的风险进行处理（风险缓解计划） 根据 ALCOA 原则保证高质量的数据——准确、清晰、同步、原始、可追溯。 使问题的快速识别和实时上报成为可能

● Results in better utilization of resources	使资源得到更好的利用

1.25 Monitoring

监查

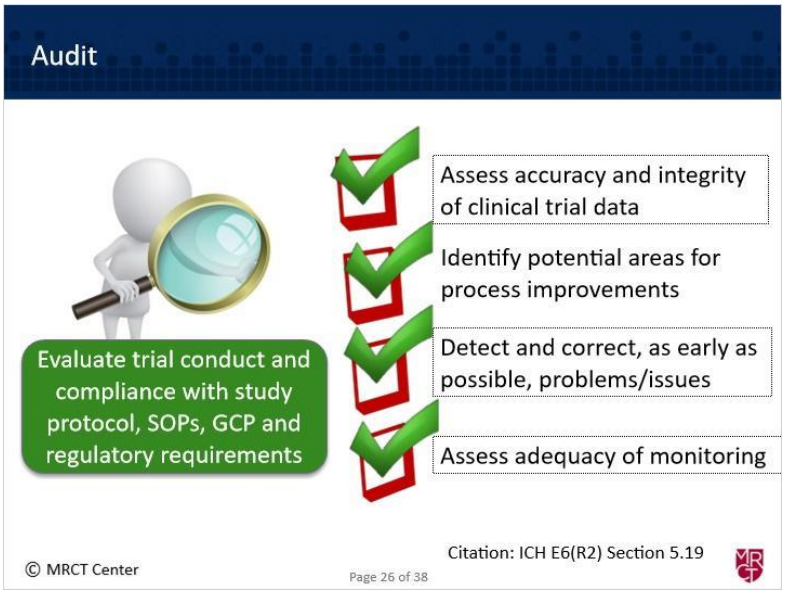
Notes:

Sponsors determine the extent and nature of monitoring activities to ensure that the trials are adequately monitored and document the rationale for the monitoring strategy in the monitoring plan. Included in the monitoring plan is the extent and nature of on-site, remote and central monitoring activities Activities may vary for a specific trial or the extent and nature of the monitoring activity. Included activities for on-site or remote monitoring may be: ●Schedule (Location visit or conferencing technology) ●Site Management ●Performance gaps ●Adherence to study documents and procedures ●Documentation	申办者应确定监查活动的范围和性质，以确保试验得到适当的监查， 并记录其监查策略的依据。监查计划还应包含现场的、远程的以及中心化监查活动的范围和性质。 监查活动会根据特定的临床试验或特定的监查活动范围和性质有所变化。现场和远程监查可能包含对以下活动的监查： 计划表（包括走访的地点或会议使用的技术） 临床现场管理 执行差距 临床试验与临床研究文件和流程是否一致

Centralized Monitoring is a remote evaluation of aggregated data and is generally different from on-site and remote monitoring. Activities include: ●Data Analytics (Examine data trends such as the range, consistency, and variability of data within and across sites, including analysis of site characteristics and other performance metrics) ●Outlier Oversight (Identify missing data, inconsistent data, data outliers, unexpected lack of variability and protocol deviations) ●Data Errors (Evaluate for systematic or significant errors in data collection and reporting at a site or across sites; or potential data manipulation or data integrity problems) ●Select sites and/or processes for targeted on-site monitoring The sponsor must confirm that all reports, Central or On-Site monitoring contain sufficient information to allow verification of compliance with monitoring plan, contain a summary of what was reviewed, significant findings, deviations and deficiencies, conclusions and actions recommended or taken to secure compliance	文件记录 中央化监查是对收集的数据进行远程评估，通常来说与现场和远程监查有所不同。中心化监查的活动包括： 数据分析（检查同一临床现场内和不同临床现场间的数据趋势，如数据的范围、一致性和变异性，包括分析临床现场特征和性能指标） 例外监管（识别丢失数据，不一致的数据，数据异常值，非预期的变异性缺失，方案偏离） 数据纠错（评估同一临床现场内或者不同临床现场间数据收集和报告系统的或显著的错误，或潜在的数据处理或数据完整性问题。） 选择临床现场和流程进行有针对性的现场监查 申办者必须确认中心化监查或现场监查的所有报告包含了足够信息以证明监查与计划的一致，报告还应包括检查内容的摘要、重大发现、偏离和缺陷项、结论，以及为确保符合性建议的和已采取的措施。

1.26 Audit

稽查

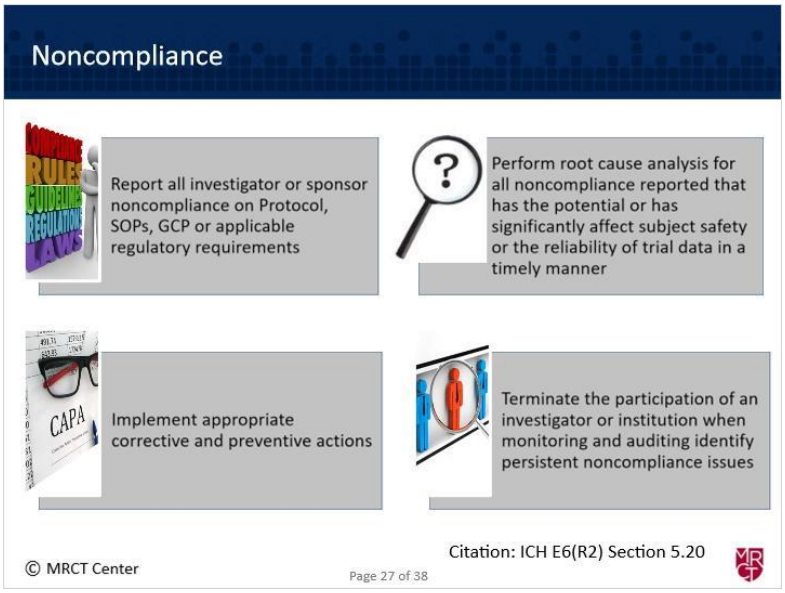


Notes:

A sponsor audit is an independent and separate activity from monitoring, and is usually a more formal approach to evaluating a study's conduct by professionals who are independent of the research. It evaluates the trial conduct and compliance with the protocol, SOPs, GCPs, and the applicable regulatory requirements. Sponsors appoint individuals qualified by training and experience to conduct audits. Auditors evaluate trial conduct and compliance with study protocol, SOPs, GCP and regulatory requirements to: ● Assess accuracy and integrity of clinical trial data ● Identify potential areas for process improvements ● Detect and correct, as early as possible, of problems/issues ● Assess the adequacy of monitoring	申办者稽查是有别于监查的一项独立活动，通常由独立于该临床研究的专业人员对临床试验进行评价。相对于监查，稽查更为正式。稽查评价试验的实施和对试验方案、SOP、GCP 及适用的监管要求的符合性。 申办者指派经过培训并有经验的合格人员实施稽查。稽查人员评价临床试验的实施和对试验方案、SOP、GCP 及适用的监管要求的符合性的目的包括： 评价临床试验数据的准确性和完整性 发现流程改进的潜在方面 尽可能早地识别和纠正问题 评价监查的充分性

1.27 Noncompliance

不符合性

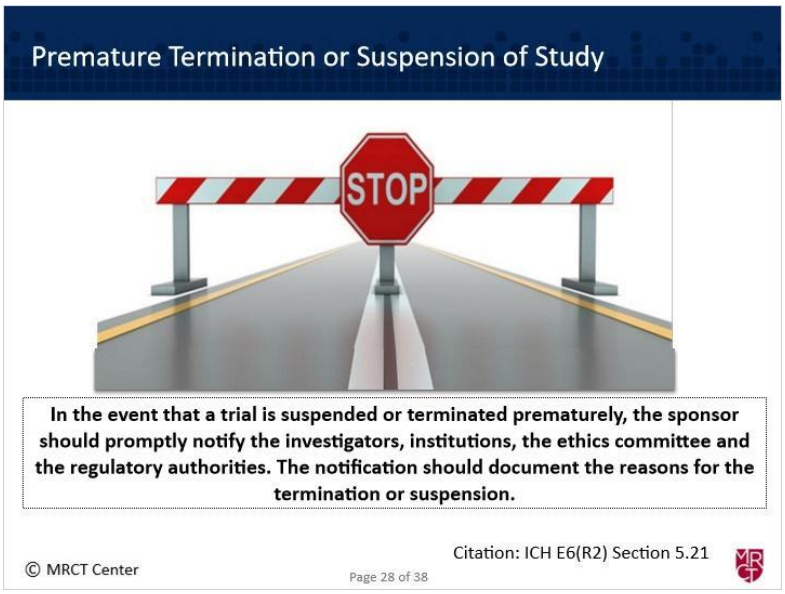


Notes:

Any non compliance with the protocol, SOPs, GCP, and/or applicable regulatory requirement(s) by an investigator/institution, or by member(s) of the sponsor's staff should lead to prompt action by the sponsor to secure compliance.	一个研究者/研究机构或申办者方的职员不符合试验方案、SOP、GCP 和/或适用管理要求时，申办者应立即采取措施保护符合性。
If noncompliance that significantly affects or has the potential to significantly affect human subject protection or reliability of trial results is discovered, the sponsor should perform a root cause analysis and implement appropriate corrective and preventive actions.	如果发现显著影响或可能显著影响受试者保护或实验结果可靠性的不符合性时，申办者应当进行根本原因分析，采取适当的纠正和预防措施。
If the monitoring and/or auditing identifies serious and/or persistent noncompliance on the part of an investigator/institution, the sponsor should terminate the investigator's/institution's participation in the trial. When an investigator's/institution's participation is terminated because of noncompliance, the sponsor should notify promptly the regulatory authority(ies).	如果监查和/或稽查发现研究者/研究机构的某一部门严重的和/或持续的不符合性，申办者应当停止该研究者/研究机构参加临床试验。某研究者/研究机构因为不依从被终止参加试验时，申办者应当立即通报管理当局。

1.28 Premature Termination or Suspension of Study

试验的提前终止或暂停



Notes:

In case the sponsor chooses or is required to terminate prematurely, or suspend the study, then the sponsor should notify the investigators, institutions, the ethics committee and the regulatory authorities accordingly. The notification should document the reasons for the termination or suspension.	在申办者决定或被要求提前终止或暂停临床研究的情况下，申办者应当立刻通知研究者、研究机构、伦理委员会以及相应的监管机构。通知应说明终止或暂停的原因。

1.29 Clinical Trial / Study Reports

临床试验/研究报告

Notes:

A clinical trial/study report is defined under Section 1.12 as a written description of a trial/study conducted in human subjects, in which the clinical and statistical description, presentations, and analyses are fully integrated into a single report. As trials conclude or are halted by the sponsor, clinical trial reports should be prepared and submitted to the regulatory agencies. Reports should: describe the quality management approach implemented in the trial in the clinical study report And Summarize important deviations from the predefined quality tolerance limits and remedial actions taken in the clinical study report Reports must meet ICH guidelines and submission schedules Finally, Sponsors are responsible for Results Posting on appropriate websites, according to local law, regulatory requirements	临床试验/研究报告在 1.12 节的定义为：在人类对象进行的试验/研究的书面描述， 包含临床和统计学描述、陈述和分析的报告。 当试验结束或被申办者停止时，应准备临床试验报告并提交给监管机构。 报告应该包含： 在临床研究报告中描述试验中实施的质量管理办法 并总结严重偏离预先设定的质量容许限的事件及补救措施 报告必须符合 ICH 指南和提交时限 最后，申办者应根据当地法律和法规的要求，在适当的网站上发布临床试验/研究报告

1.30 Multicenter Trials

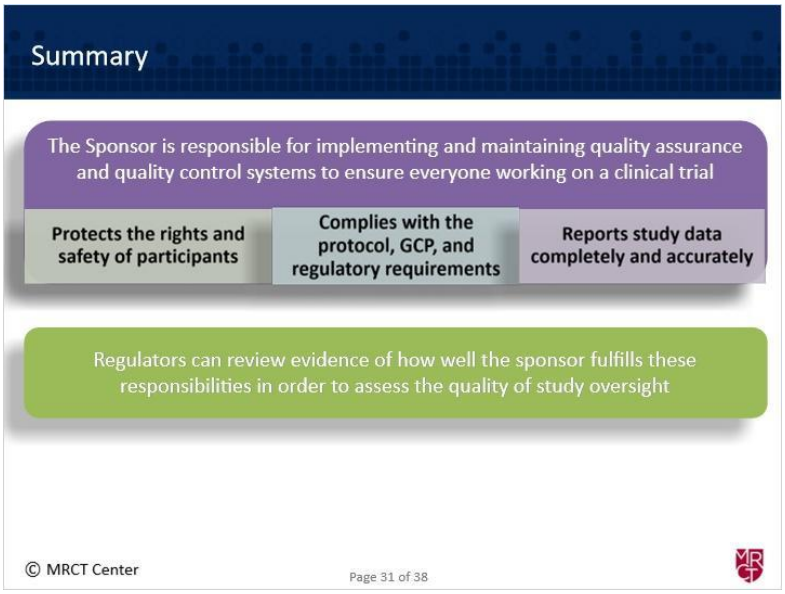
多中心临床试验

Notes:

A multicenter trial is defined in GCP guidelines as a clinical trial conducted according to a single protocol but at more than one site, and therefore, carried out by more than one investigator. Effective oversight of a multicenter trial includes: ensuring that all investigator and other institution personnel involved with the trials follows strict adherence to the trial protocol as well as GCP guidelines, The Investigators and site staff should receive adequate training and, comply with a uniform set of standards for trial Sponsors must ensure clear and consistent communications, and roles and responsibilities are clearly delineated for all sites.	多中心试验在 GCP 指南中的定义为：按照同一个试验方案，在多个试验现场实施，由多名研究者共同完成的临床试验。 对多中心试验的有效监督包括： 确保参与试验的所有研究者和其他机构人员严格遵守试验方案和 GCP 指南， 研究者和临床现场工的作人员应接受足够的培训，并遵守统一的试验标准 申办者必须与所有临床现场确保清晰和持续的沟通，并明确所有临床现场的角色和责任。

1.31 Summary

总结

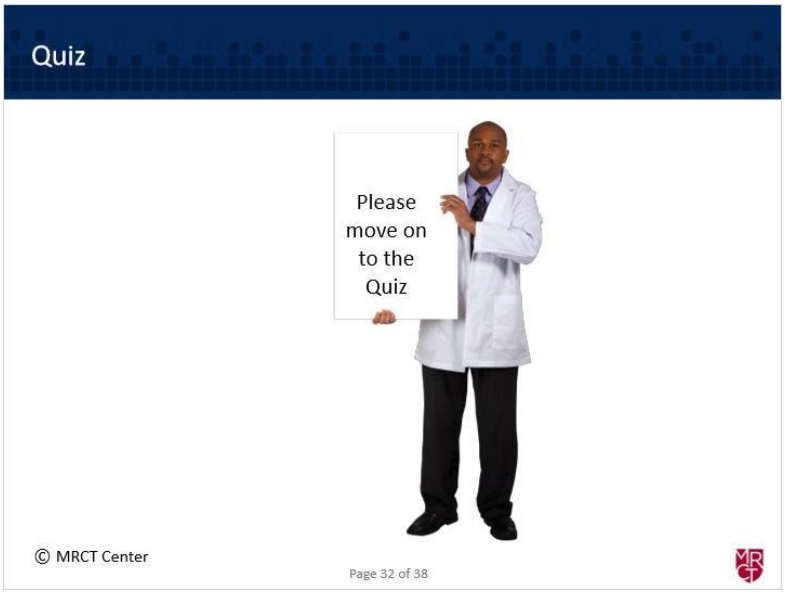


Notes:

In summary, The Sponsor is responsible for implementing and maintaining quality assurance and quality control systems to ensure everyone working on a clinical trial ● Protects the rights and safety of participants ● Complies with the protocol, GCP, and regulatory requirements ● Reports study data completely and accurately Regulators can review evidence of how well the sponsor fulfills these responsibilities in order to assess the quality of study oversight.	总而言之，申办者应负责实施和维护质量保证和质量控制体系，以确保参与临床试验的各方做到： 保护参与者的权利和安全 遵守临床试验方案、GCP 及监管要求 完整、正确地报告临床数据 允许监管机构审查申办者履行责任情况的证明，以评估研究监督的质量。

1.31 Thank you

感谢聆听



Notes:

Let us review of some of the key points of this module via the following case studies.
Please read the case at your own pace. Then take a moment to answer the questions. When complete, click Submit.