Module 2: The 13 Principles of ICH GCP

1. Module 2

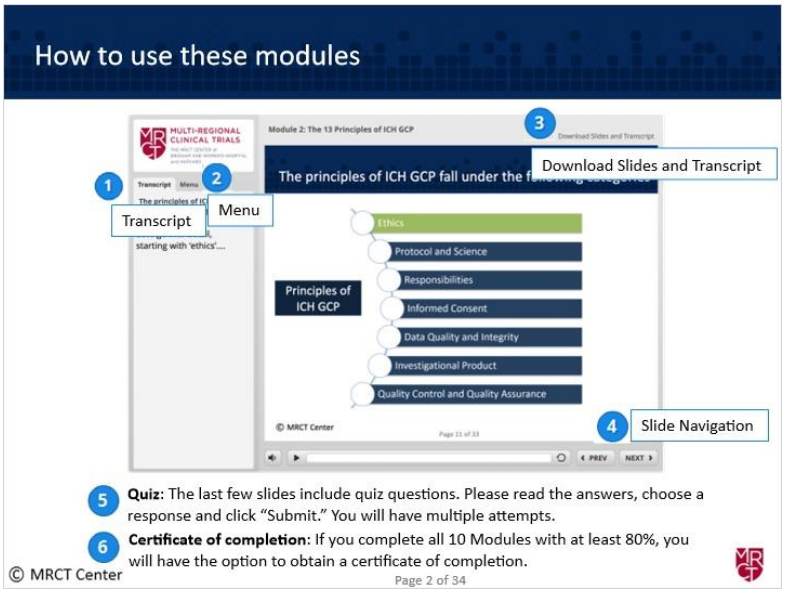
1.1 Interpretation and application of ICH E6(R2)

ICH E6(R2)的解读和应用

Notes:

Welcome to Module 2 of this training on the interpretation and application of ICH E6(R2)	欢迎来到ICH E6(R2)的解读和应用培训的第二讲

1.2 How to use these modules



1.3 Attribution

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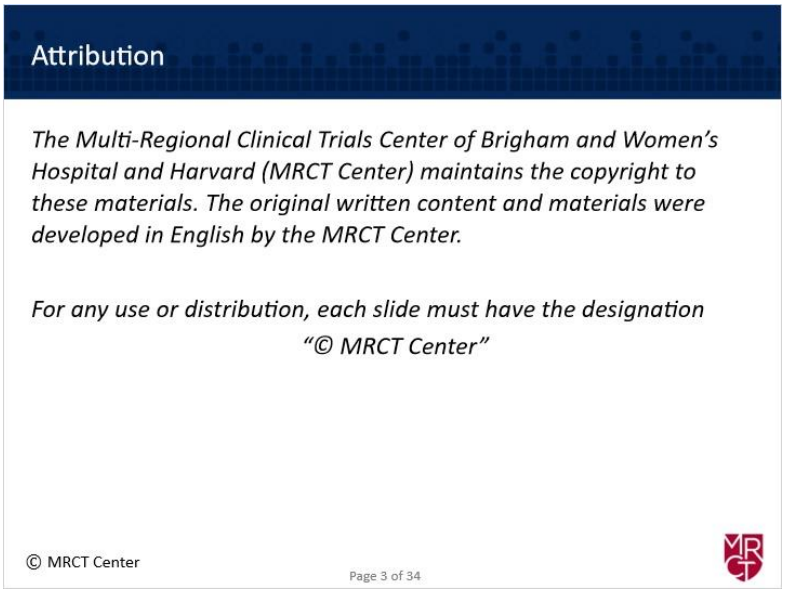

Notes:

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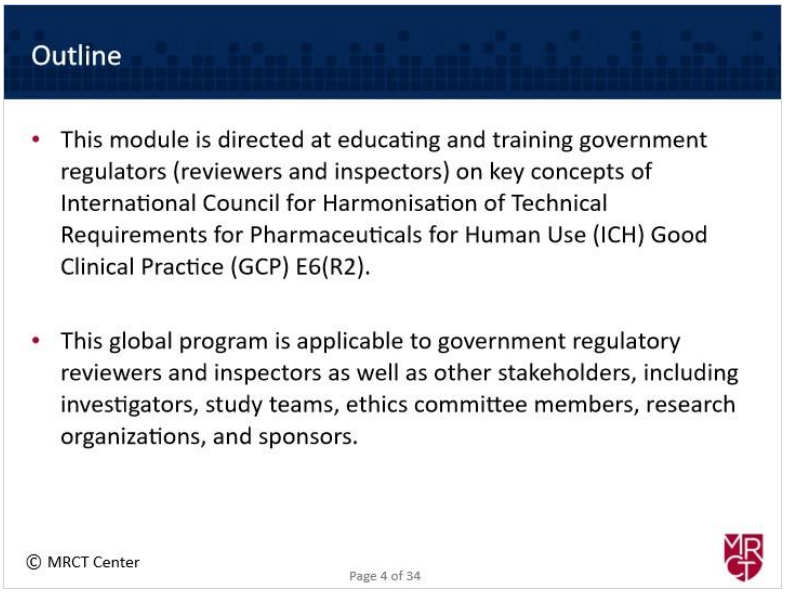
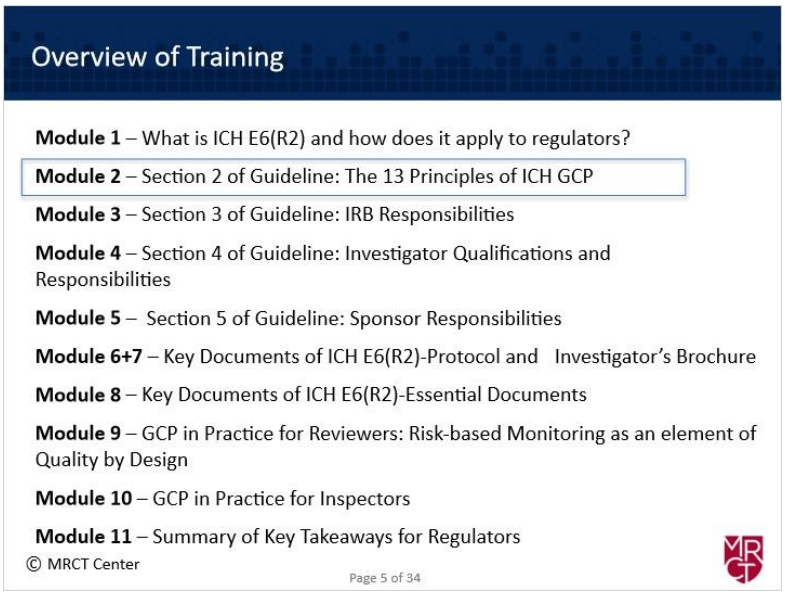
1.4 Outline



1.5 Overview of Training

培训概览

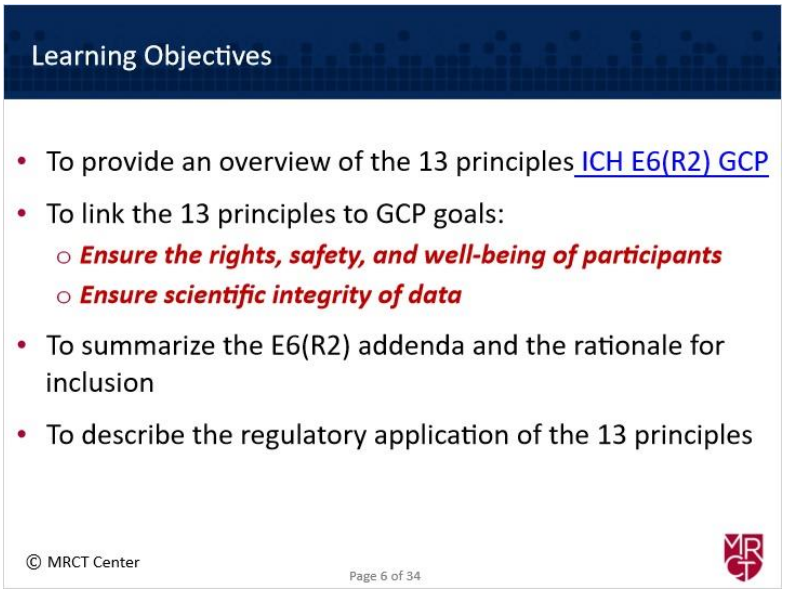


Notes:

In Module 2 we will focus on describing the 13 principles of ICH GCP as outlined in the guideline	在模块二，我们将重点讲解指南中概述的ICH GCP的13项原则

1.6 Learning Objectives

教学目标



Notes:

By the end of this module you are expected to be able to link those 13 principles to the goals of GCP, which are: • to ensure the rights, safety and well-being of participants, • to ensure the scientific integrity of the study data. By the end of this module you should have a more complete understanding of the addenda and their rationale, as well as an ability to describe the regulatory application of the 13 principles of GCP.	本模块的学习完成时，你应该能够将这 13 条原则与 GCP 的目标联系起来，即： • 确保受试者的权利、安全和福祉 • 确保研究数据的科学完整性 本模块的学习完成时，你应该对该附录及列入附录的理由有更全面的了解，并有能力描述 GCP 的 13 项原则在监管方面的应用。

1.7 Good Clinical Practice (GCP)

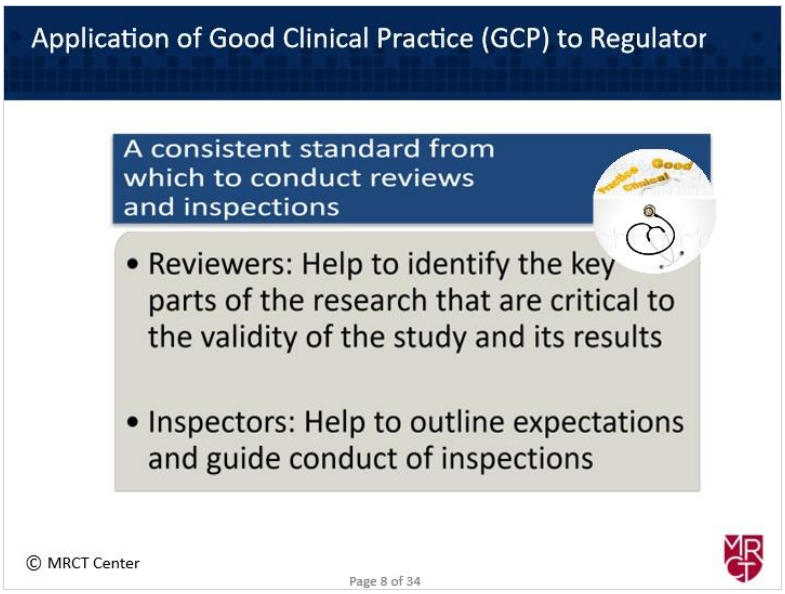
药品临床试验管理规范(GCP)

Notes:

As you know, GCP is an international standard for designing, conducting, performing, monitoring, auditing, recording, analyzing, and reporting clinical trials.	众所周知，GCP 是用于方案设计、组织实施、执行、监查、稽查、记录、分析和报告临床试验的国际标准。
It also provides public assurance that data and reported results are credible and accurate and that the rights and confidentiality of subjects are protected, facilitating mutual acceptance of data across regions.	它向公众保证临床试验的数据和报告的结果是可信和准确的，且受试者的权利和隐私得到了保护，促进不同地区临床试验数据的互认。
In addition to GCP, applicable international and national regulations and guidelines should be known and followed.	除 GCP 外，还应了解并遵守国内外相关法规和指南。

1.8 Application of Good Clinical Practice (GCP) to Regulators

监管人员对药品临床试验管理规范(GCP)的应用

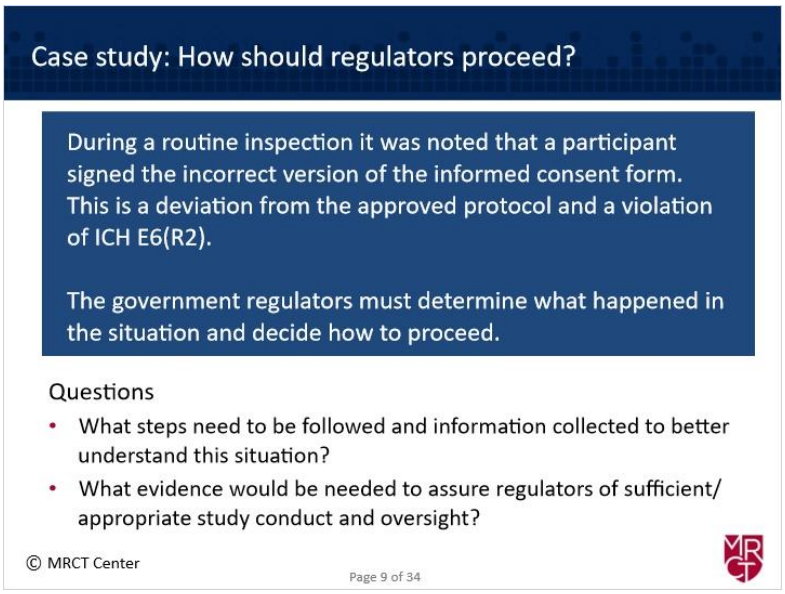


Notes:

So when we think of the regulator role and how GCP applies, consider that GCP is a consistent standard from which to conduct reviews and inspection, allowing reviewers to identify the key parts of the research that are critical to the validity of the study and its results [For example: Risks/safety concerns, data collection details, scientific/statistics plan, qualifications of study team], and providing inspectors with the expectations that guide the conduct of inspections [For example: ensure appropriate delegation/assignment of responsibilities, Identify deficiencies in following the protocol].	当我们考虑监管人员的角色以及如何应用 GCP 时，要把 GCP 当成审评和检查的统一标准，帮助审评人员识别对临床试验及其结果效度至关重要的信息（比如：风险/安全隐患、数据收集详情、科学/统计方案、研究团队的资质），并向检查员提供用以指导检查活动的参考（如：确保适当的责任/职责分工，确认临床试验方案执行中的缺陷]。

1.9 Case study: How should regulators proceed?

案例分析：监管人员应如何实施监管？

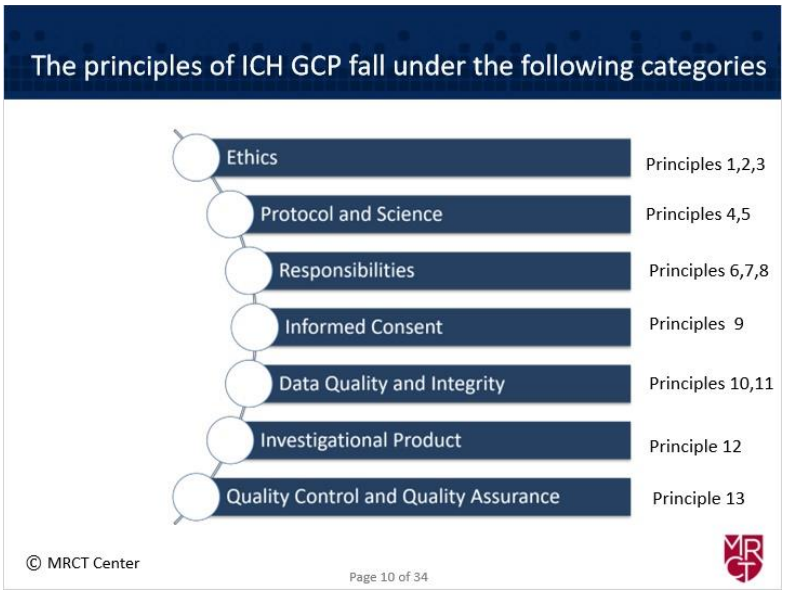


Notes:

Here is a case study. How should the regulator proceed? In this case, during a routine inspection it was noted that a participant signed the incorrect version of the informed consent form. This is a deviation from the approved protocol and a violation of ICH E6(R2). The government regulators must determine what happened in the situation and decide how to proceed. For this case, consider these questions: - What steps need to be followed and information collected to better understand this situation? - What evidence would be needed to assure regulators of sufficient/appropriate study conduct and oversight? We will return to this case later on in this module, but in the meantime, consider those questions.	案例：监管人员应如何实施监管？ 在一次例行检查中，检查员注意到一位受试者签署了错误版本的知情同意书。这是一项偏差，违反了 ICH E6(R2)。政府监管人员必须确认事情的经过并做出处理决定。这种情况，需要考虑以下问题： -为了更好地了解事情经过，政府监管机构需要采取哪些步骤，收集哪些信息？ -监管人员需要掌握何种证据证明临床试验得到了充分/适当的实施和监督？ 我们稍后再对此案例进行进一步分析，带着问题我们继续下面的内容。

1.10 The principles of ICH GCP fall under the following categories

ICH GCP 原则的分类

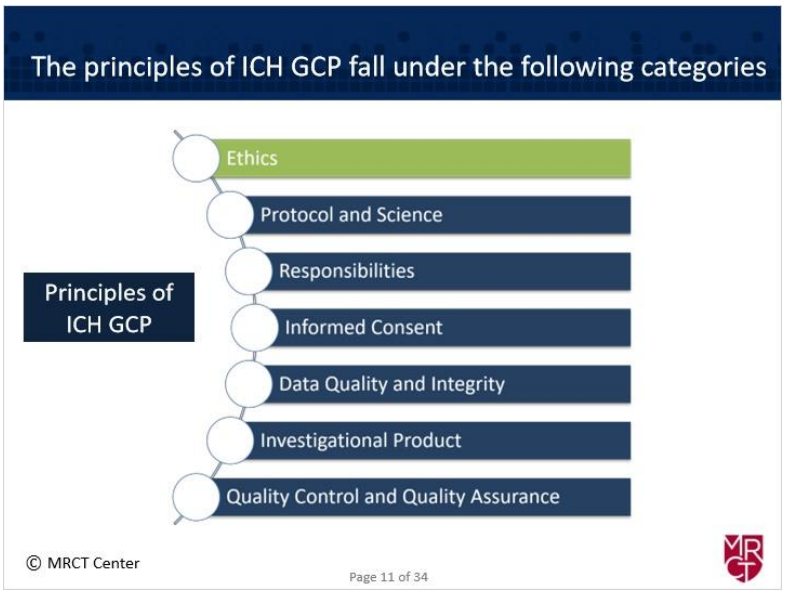


Notes:

The 13 principles of GCP generally fall under the following categories Ethics Protocol and science Responsibilities Informed Consent Data Quality and Integrity Investigational Product Quality Control and Quality Assurance	ICH GCP原则的分类 伦理 临床方案与科学 职责 知情同意 数据质量和完整性 试验用药品 质量控制与质量保证

1.11 The principles of ICH GCP fall under the following categories

ICH GCP 原则的分类

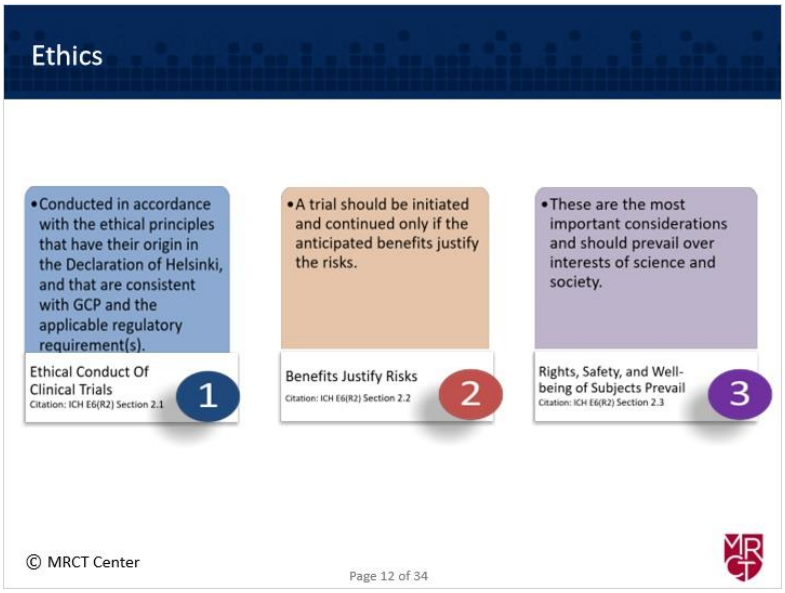


Notes:

Let's go into detail, starting with 'ethics'....	我们来细说每一类别，先从伦理开始。

1.12 Ethics

伦理



Notes:

Under this category, the three principles stipulate that the clinical trial conduct be ethical. The ethical principles have their origin in the Declaration of Helsinki and the Belmont Report that we will discuss later. These principles are consistent with GCP and the applicable regulatory requirement(s).	在伦理这一类别下，符合伦理的临床试验必须满足这三条原则。这三条原则的来源是我们稍后将讨论的《赫尔辛基宣言》和《贝尔蒙特报告》。这三条原则与 GCP 和适用的法规要求一致。
Second the benefits should justify the risks of the trial, so that before a trial is initiated, foreseeable risks and inconveniences are weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks.	其次，试验给受试者带来的获益应大于试验带来的风险，因此在一项试验开始之前应当权衡该临床试验对于个体受试者和社会的可预见的风险、不方便和预期的获益。只有当预期的获益大于风险时，方可开始和继续这项临床试验。
And third, the rights, safety and well-being of participants prevail as the most important	第三，受试者的权利、安全和福祉是最重要的考虑，应当高于对科学和社会的利益的考虑。

considerations, over the interests of science and society.	

1.13 Ethical Principles

伦理原则

Notes:

These GCP principles reflect those outlined in the Belmont Report – that research be designed and conducted with respect for persons, beneficence, and justice in mind.	这些 GCP 原则与《贝尔蒙特报告》中列示的原则一致—— 临床研究的设计和实施要时刻遵循尊重个人、行善、公平公正的原则。
First, research should have respect for persons (i.e. research participants). This means that participants should maintain their inalienable rights - autonomy and the right to make decisions for themselves and have complete information about participation and whether they want to participate. Participation should always be voluntary. Respect for persons is enacted by	首先，临床研究应该尊重个人(即尊重受试者)。这意味着维护受试者不可剥夺的权利 - 自主权及获取有关参与临床研究的完整信息并决定是否愿意参加的权利。受试者参与临床试验必须是自愿的。尊重个人可以通过充分的知情同意，不强迫或不用不恰当的方式去影响受试者的参与(比如告知危重病患者该临床研究是他们唯一可用的治疗方式)，来保障受试者的权利。受试者不应因参与

safeguarding these rights through adequate informed consent and ensuring that the circumstances of the trial do not force or unduly influence an individual to participate (for example, if participants with a serious disease are told the trial is their only option for care). Participants should not give up any legal rights through trial participation. And, if a trial is to involve a **vulnerable population**, additional action to safeguard rights may be needed. (For example, in the case of enrolling children or decisionally-impaired individuals, requiring certain additions to the consent process such as having a guardian execute the informed consent or having an impartial witness during the process would be ideal.)	临床试验而放弃自己的任何权利。同时，如果临床试验涉及招募弱势对象，研究者 需要采取额外的行动保护他们的权利 （例如招募儿童或决策障碍者参与的临床试验，应在知情同意环节增加额外的步骤，如儿童由监护人签署知情同意书，决策障碍者在签署知情同意过程中有中立见证人在场更加理想。）
Second, research should satisfy the concept of beneficence. This means participants should only be subject to a clinical trial if such trial has an acceptable risk to benefit ratio, all risks have been minimized, and the trial is scientifically well-designed such that valid results will be derived. Of course, the scientific question should also be important.	第二，临床研究应符合行善原则。这意味着只有当临床试验具有可接受的风险获益比、所有风险已降至最低、临床试验的设计科学合理且能够得出有效结果时，才能招募受试者。当然，临床研究提出的科学问题也很重要。
Third, research should take into account justice. This means the burdens and benefits of research should be equally distributed to research participants. Justice is upheld by safeguarding participant well-being through study recruitment that makes sense. For example, there should be rationale for why certain populations are targeted and why other populations may be excluded. Also, one may have to consider issues like participant compensation to determine if such payment may cause an individual (or groups of individuals – like those who are economically disadvantaged) to act against their own best	第三，临床研究应该做到公平公正。这里要求对所有受试者公平地分配临床试验带来的负担与获益。公平公正可以通过合理的受试者招募、保障受试者福祉得以表 现。例如，临床研究受试者的入选和排除标准应当有依据。此外，还必须考虑受试者补偿等问题，以确定临床研究提供的经济补偿是否会导致个人（或群体 - 如经济状况不佳的人群）损害自己的最佳健康利益。

health interest.	

1.14 Benefits justify risks

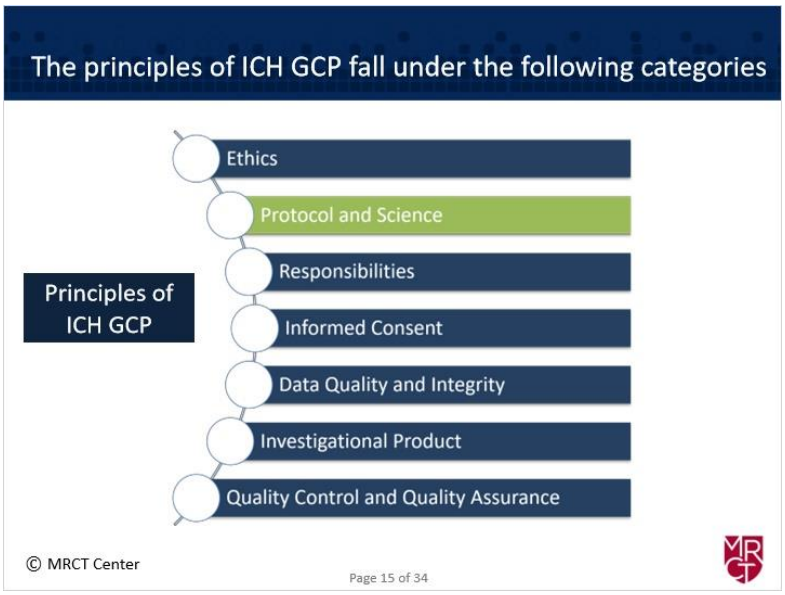
获益与风险相称

Notes:

The IRB/IEC must review the protocol to determine that risks have been minimized and that the anticipated benefits equal or exceed the anticipated risks. These determinations are dependent on the specifics of the study itself, and why each protocol must be reviewed individually by the IRB/IEC.	机构审查委员会(IRB)/独立伦理委员会（IEC）必须对临床方案进行审评，确定风险已降至最低，并且预期获益等于或超过可预见的风险。风险获益的评估决定与临床试验本身的具体情况紧密相关，所以每个临床方案均须经过机构审查委员会/独立伦理委员会审评。

1.15 The principles of ICH GCP fall under the following categories

ICH GCP 原则的分类

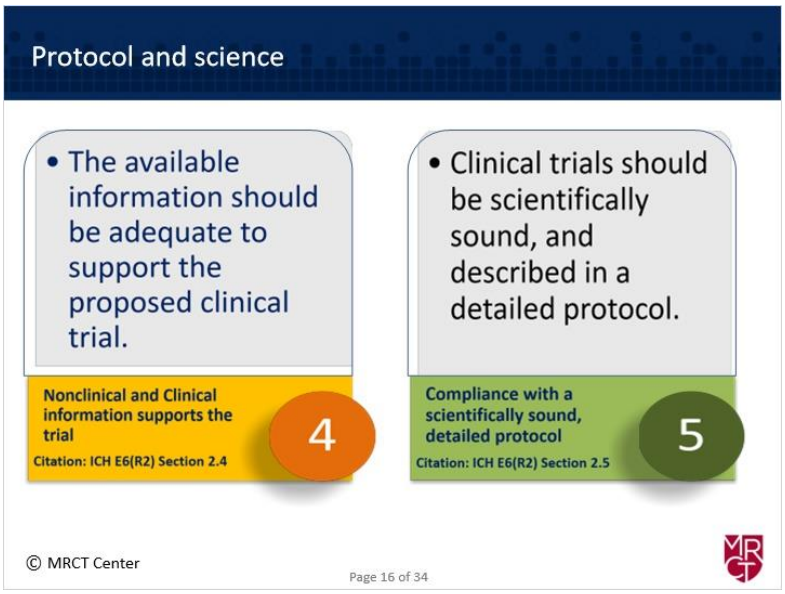


Notes:

The next of the 13 GCP principles fall under the category of protocol and science.	GCP13 条原则的下一个类别是临床方案与科学。

1.16 Protocol and science

临床方案与科学

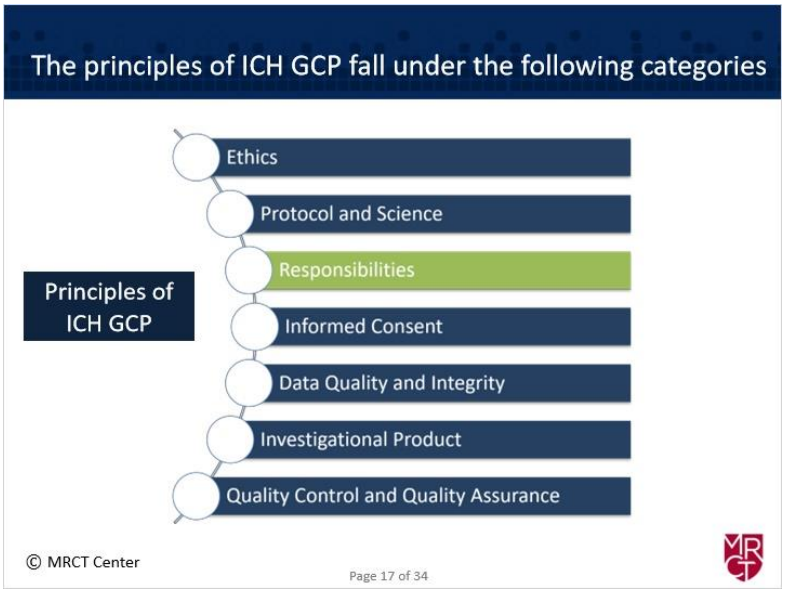


Notes:

The 4th principle stipulates that the available nonclinical and clinical information on an investigational product should be adequate to support the proposed clinical trial. And the 5th principle requires that clinical trials be scientifically sound and described in a clear, detailed protocol.	GCP 的第四条原则规定，关于试验用药品的非临床和临床资料，应该足以支持拟实施的临床试验。 第 5 条原则要求进行药物临床试验必须有充分的科学依据，应在临床试验方案中明确、详细地描述。

1.17 The principles of ICH GCP fall under the following categories

ICH GCP 原则的分类



Notes:

Under the next category of “responsibilities’ stakeholder roles are described.	GCP 原则的下一类别"职责"描述了各利益相关者的角色和作用。

1.18 Responsibilities

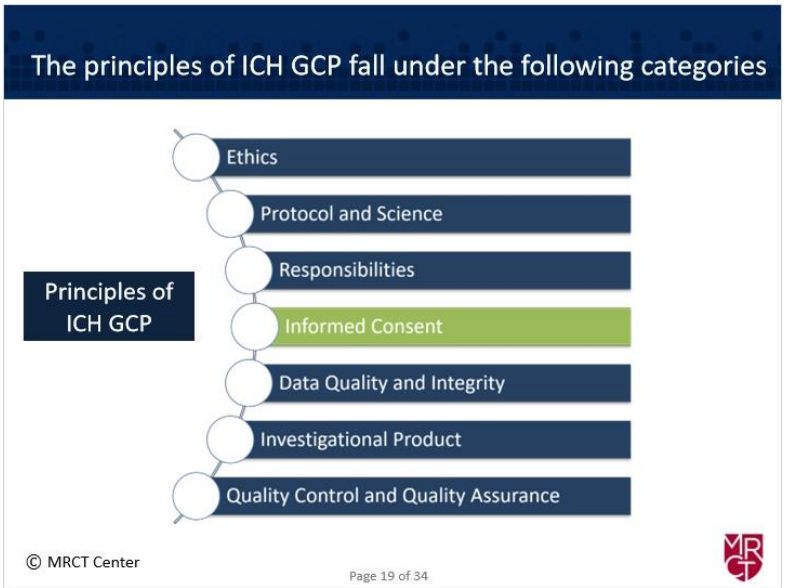
职责

Notes:

Principle 6 states that the IRB/IEC must approve the protocol prior to the initiation of the trial and that it be conducted as it has been approved. This principle implies that any changes to the protocol must also be reviewed and approved by the IRB/IEC prior to initiating the change, unless the change is for the immediate protection of participants.	GCP 的第 6 条原则规定，临床试验的实施应当遵循事先已经得到临机构审查委员会/独立伦理委员会（IRB/IEC）批准的试验方案。该原则意味着除了对受试者实施的紧急保护措施外，对临床方案的任何更改都必须事先获得 IRB/IEC 的审评和批准。
Principle 7 requires that medical decisions be made by appropriately qualified physicians or, as applicable, dentists.	第 7 条原则要求由合格的医生或（在适用时）合格的牙医作出医学决定。
While principle 8 refers to the investigators and their study teams requiring them to be qualified by education, training, and experience to perform their respective task(s).	而第 8 条原则要求研究者及其研究团队在教育、培训和经验方面具备执行各自任务的资格。

1.19 The principles of ICH GCP fall under the following categories

ICH GCP 原则的分类

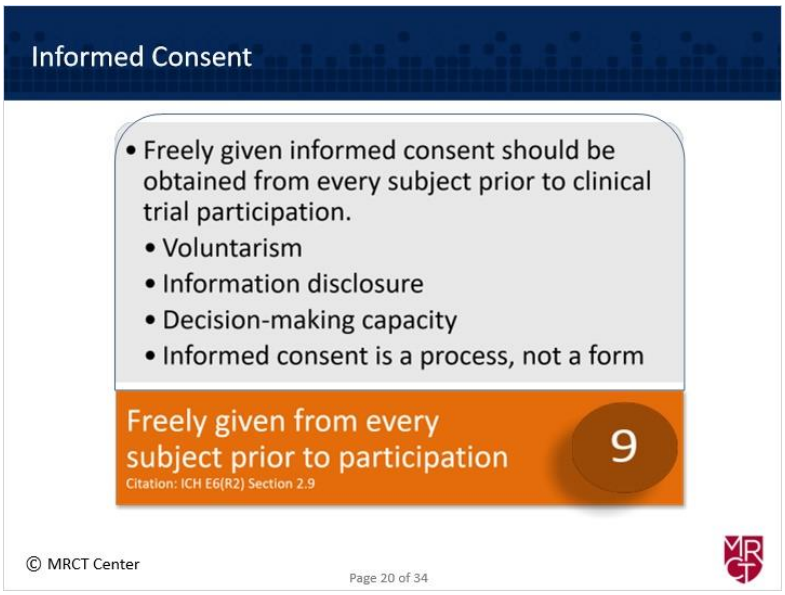


Notes:

Next, Principle 9 addresses the important category of informed consent.	接下来，第 9 条原则涉及知情同意这一重要类别。

1.20 Informed Consent

知情同意

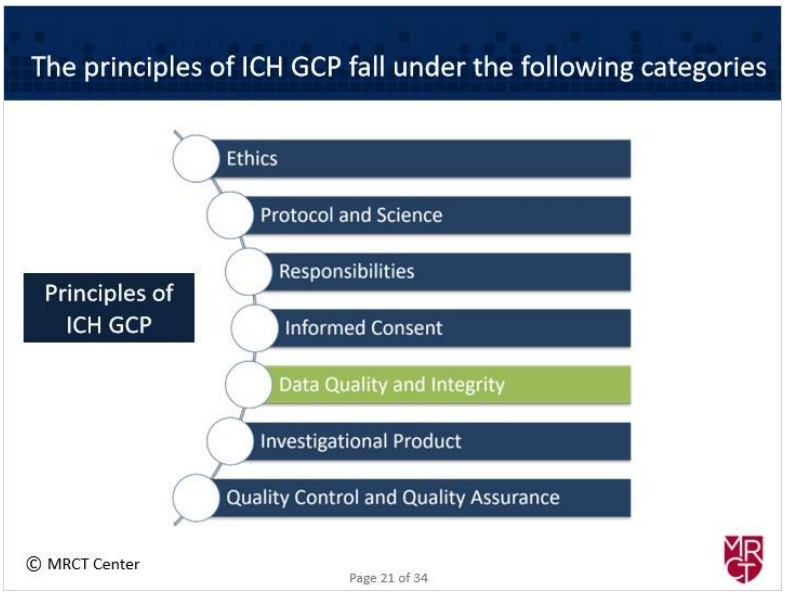


Notes:

The concept of freely given informed consent describes the necessity that consent is voluntary, that all necessary information is disclosed appropriately and in a language understandable to the potential participant, and that the potential participants are able to make an informed decision, in other words, that they are capable of rendering a independent decision. That every subject provide freely given informed consent prior to clinical trial participation goes beyond the signing of the form, and speaks to the process of engaging with potential participants about the study and their willingness to join.	自由的知情同意这一概念描述了同意必需是自愿的，所有必要的信息都以潜在受试者可以理解的语言适当地披露，并且潜在受试者能够做出知情决定，换句话说，他们有能力做出独立的决定。每位受试者在参与临床试验前都要提供自由的知情同意，这不只是知情同意书的签署，还包括研究者与潜在受试者就这项研究以及他们参与的意愿进行沟通的过程。

1.21 The principles of ICH GCP fall under the following categories

ICH GCP 原则的分类

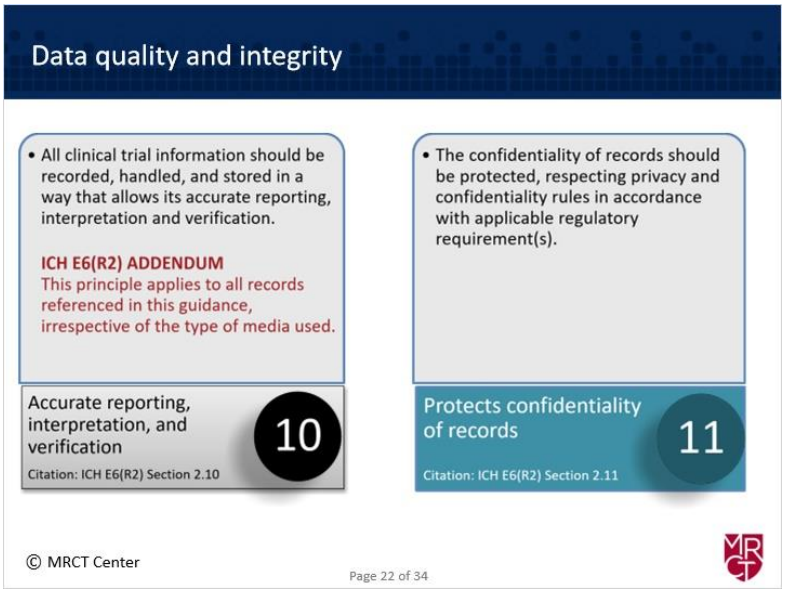


Notes:

Under the next category of 'data quality and integrity', we find two additional principles.	GCP 原则的下一类别"数据质量和完整性"有两条原则。

1.22 Data quality and integrity

数据质量和完整性

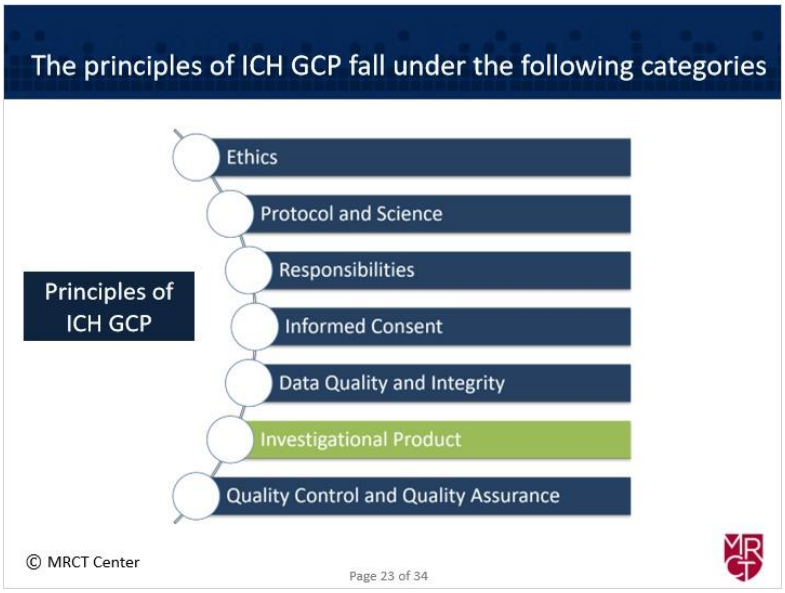


Notes:

Principle 10 describes the necessity of accurate reporting, documentation, interpretation, and validation of the data. We also see the first addendum of the section under Principle 10– expanding the Principle to all records regardless which type of media is used to record study data. This addendum was added specifically to call attention to the increasing use of digital data.	第 10 条原则描述了准确报告、记录、解释和核对数据的必要性。 我们还看到原则 10 下的第一个附录--将该原则扩展到所有的记录，无论使用哪种类型的媒介来记录研究数据。该附录是专门为呼吁关注使用日益增多的电子数据而增加的。
Principle 11 refers to the privacy and confidentiality of all records that could potentially identify subjects, and calls attention to applicable regulatory requirement(s) that may differ country to country.	第 11 条原则是确保所有可能识别受试者身份的记录的保密性应当得到保护，并提醒不同国家的相关法规要求可能有差异。

1.23 The principles of ICH GCP fall under the following categories

ICH GCP 原则的分类

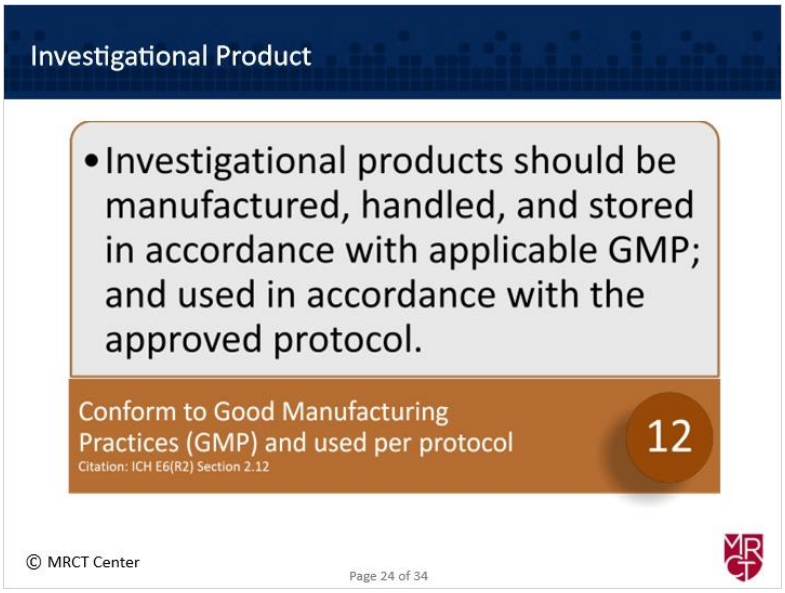


Notes:

The next category refers to the investigational product.	GCP 原则的下一类别是关于试验用药品的。

1.24 Investigational Product

试验用药品

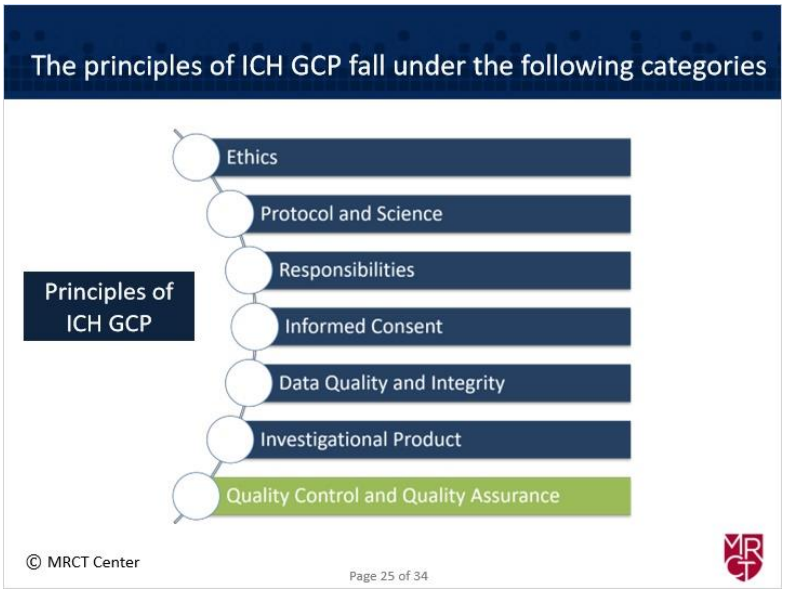


Notes:

It stipulates that all investigational products should be manufactured, handled, and stored in accordance with applicable Good Manufacturing Practices or GMP. Further, all investigational products should be used in accordance with the approved protocol.	该条原则规定，所有试验用药品应当按照适用的药品生产质量管理规范(GMP)生产、处理和储存。此外，所有试验用药品应按照已批准的临床方案使用。

1.25 The principles of ICH GCP fall under the following categories

ICH GCP 原则的分类

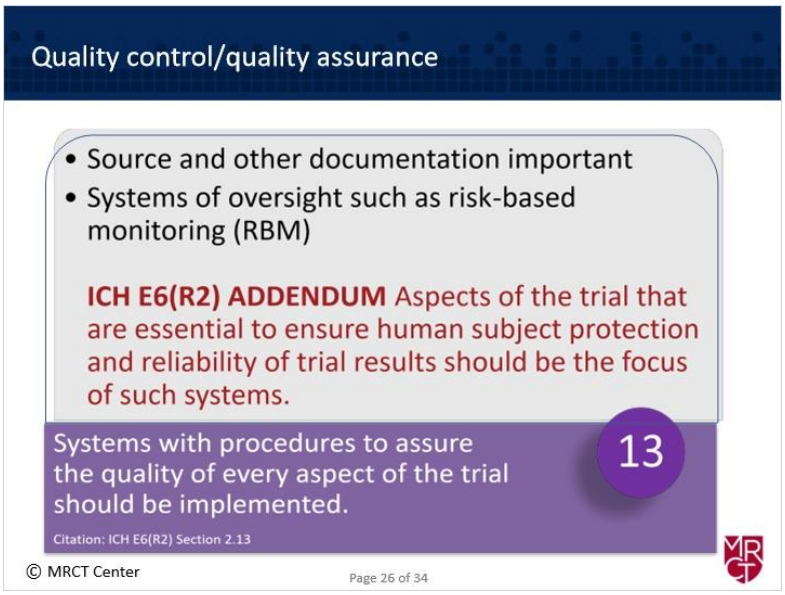


Notes:

Lastly, Principle 13 addresses quality control and quality assurance.	最后，第 13 条原则涉及质量控制和质量保证。

1.26 Quality control/quality assurance

质量控制/质量保证



Notes:

It dictates that systems should be implemented that support and assure the quality of every aspect of the trial, factoring in source and other study documentation, and putting appropriate systems of oversight into place. A second GCP addendum is added to this section, clarifying that oversight systems should focus on those aspects of a clinical trial that are essential to ensure human subject protection and reliability of trial results. This addendum addresses the concept of risk-based monitoring (or RBM) that suggests that the level of oversight may be apportioned to the level of risk either to participant safety or to data integrity. We will discuss RBM extensively later in this course.	该原则规定应实施支持和保证试验各方面质量的系统，包括源文件和其他研究文件，并建立适当的监督系统。本节增加了第二个 GCP 附录，阐明了监督系统应重点关注在确保受试者的保护和试验结果的可靠性这些至关重要的方面。 该附录涉及基于风险的监查（或称 RBM）的概念，表明监督的程度可与受试者安全或数据完整性的风险程度相适应。我们将在后面深入讨论 RBM。

1.27 Distributed Responsibilities: Understand their Roles

职责分配：理解各自的角色

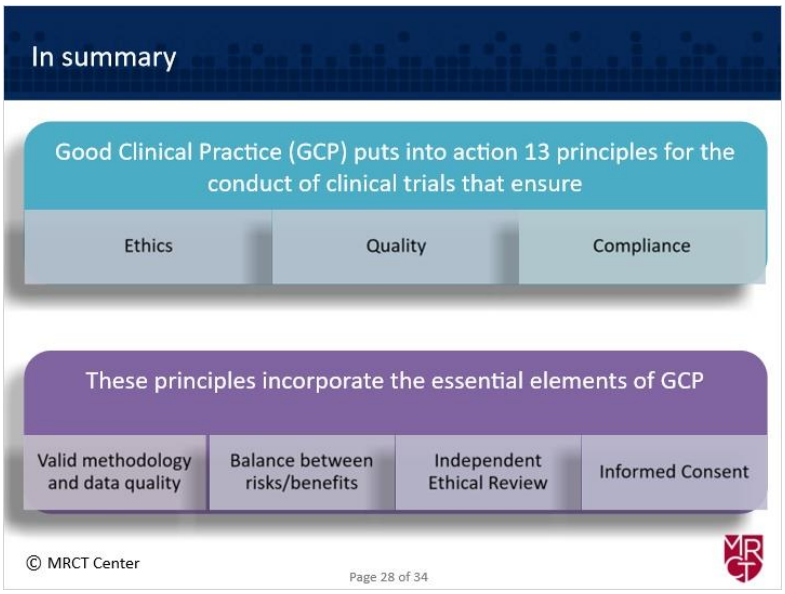
Notes:

There are many different stakeholders involved in designing, conducting, and reporting a trial. Each are responsible for the clinical trial, although their roles and responsibilities differ. Regulators should know and understand the many roles, including - Sponsors - Clinical investigators and the study team which can include - Research nurses - Clinical research coordinators - Clinical research associates	在设计、实施和报告一项试验时，有许多不同的利益相关者参与。尽管他们的角色和职责不同，每个人都对临床试验负责。监管人员应该知道并理解这些角色，包括：申办者、临床研究者和研究团队，可以包括：参与研究的护士、临床研究协调员、临床研究助理。
There are also the roles of - Study pharmacists - IRB/IEC - Contract Research Organizations - Medical monitors	此外，还有以下角色：参与研究的药剂师、机构审查委员会/独立伦理委员会（IRB/IEC）、合同研究机构、医学监查员、数据录入员和数据管理员、监管机构、研究受试者、以及其他人员。

- Data entry personnel and data managers - Regulatory authorities - Research participants - And others, as applicable We will discuss the roles and activities of many of these different stakeholders throughout this GCP course.	我们将在整个 GCP 课程中讨论这些不同利益相关者的角色和活动。

1.28 In summary

小结



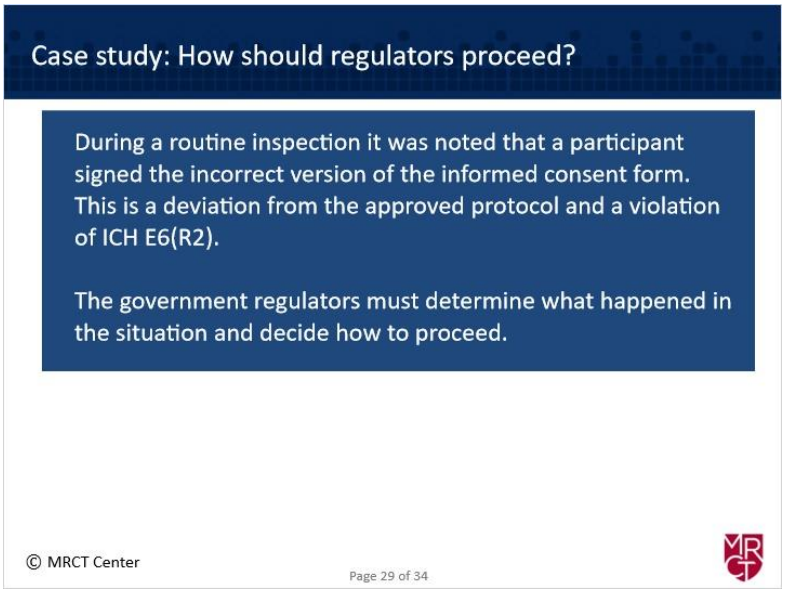
Notes:

In summary, good clinical practice puts into action 13 principles that 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	总之，药物临床试验质量管理规范将 13 项原则付诸行动，以确保临床试验的伦理、质量和合规性，整合了 GCP 的基本要素： • 有效的方法论和数据质量 • 风险与获益的平衡

• Independent ethical review • Informed consent	• 独立伦理审查 • 知情同意

1.29 Case study: How should regulators proceed?

案例分析：监管人员应如何实施监管？

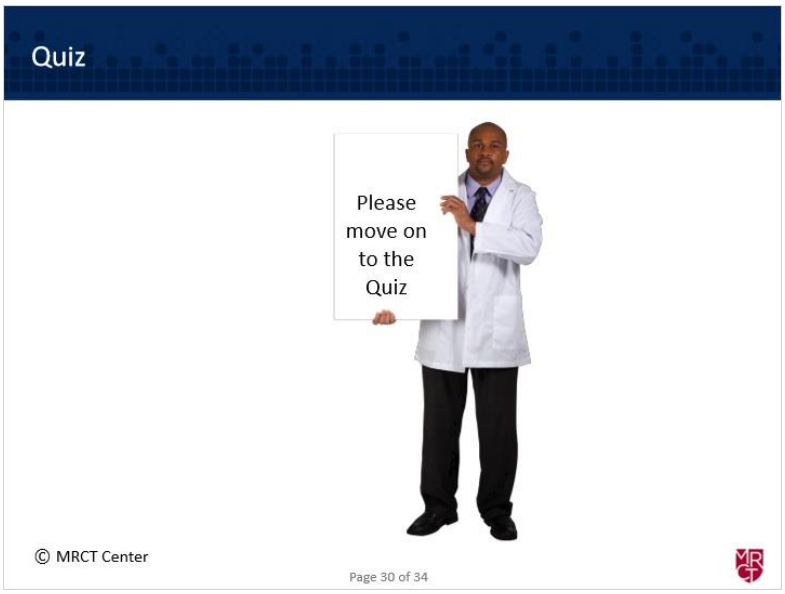


Notes:

Returning to the case study presented earlier in the module, let us consider how we might investigate this issue given the principles of GCP just presented.	回到本模块前面介绍的案例，让我们考虑一下，根据刚才介绍的 GCP 原则，我们可以如何调查这个问题。
In Section 2.3 it is noted that the rights, safety, and well-being of the trial subjects are the most important considerations.	第 2.3 节指出，受试者的权利、安全和福祉是最重要的考虑因素。
And in Section 2.9 it states that freely given informed consent must be obtained from	第 2.9 节指出，必须从每位受试者那里获得自由的知情同意——但为了使受试者给予知情同意，

every subject – but in order to give informed consent, the individual considering participation must be presented with the correct information. Signing the incorrect version of a consent form raises questions about the protection of subjects and the validity of the consent. So let's review how you might respond to the following questions.	必须向考虑参与的个人提供正确的信息。 签署错误版本的同意书会使人质疑对受试者的保护和知情同意的有效性。 让我们回顾一下你可以如何回答以下问题。

1.30 Quiz



Notes:

Please review and respond to the following questions at your own pace. When complete, please click Submit.