CTTI Recommendations: Identifying Qualified Investigators and Their Delegates to Conduct Sponsored Clinical Trials

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CTTI MISSION: To develop and drive adoption of practices that will increase the quality and efficiency of clinical trials

Clinical Trials Transformation Initiative. Identifying Qualified Investigators and Their Delegates to Conduct Sponsored Clinical Trials. Published November 2018. https://www.ctti-clinicaltrials.org/projects/investigator-qualification

OVERVIEW: Finding Value in Investigator Qualification

These recommendations are based on expert consensus and are intended to help sponsors, contract research organizations (CROs), and site teams better identify qualified investigators and their delegates to conduct clinical trials. This new approach to "qualification" goes beyond repetitive one-size-fits-all training to include individual experience and protocol-specific preparation. CTTI's recommendations address how to:

- Implement a more efficient and effective means of qualification,
- Determine whether a site team is a good fit for a particular protocol, and
- Improve the quality conduct of clinical trials.

The Challenge

The FDA regulations for clinical trials state that sponsors are responsible for "selecting investigators qualified by training and experience,"[a] and this requirement extends to delegated members of the site team (aka delegates).[b] However, the regulations do not provide guidelines for how to meet this requirement.

Although FDA regulations do not specify Good Clinical Practice (GCP) training, it is widely used as the industry standard for ensuring investigators are qualified. Therefore, sponsors generally require investigators and their delegates to complete GCP training before every clinical trial they conduct, regardless of their prior training and experience.

Takeaway: Sponsors, CROs, and site teams need a more efficient and effective means of identifying whether investigators and their delegates are qualified to conduct a particular protocol.

There is little evidence that completion of GCP training alone sufficiently qualifies investigators and their delegates to conduct quality clinical trials. In fact, the most common deficiencies noted during investigator inspections are directly related to GCP principles.[1] Furthermore, redundant training creates an unnecessary burden for site teams and limits the opportunity for more valuable, protocol-specific learning and preparation.

[a] Sponsors are responsible for selecting qualified investigators, per 21 CFR 312.50 and 312.53(a) for drugs and biologics and 21 CFR 812.40 and 812.43(a) for medical devices.
[b] References to "investigators and delegates" and "site teams" are used interchangeably throughout this document.

CTTI's Solution

To address this challenge, CTTI sought input from a multi-stakeholder team of experts to develop the following recommendations on how to identify qualified investigators and their delegates while simultaneously reducing inefficiencies in training and better preparing for the quality conduct of clinical trials.[c]

"Qualification" and "preparation" are often viewed as separate concepts. Here, we treat them as two sides of the same coin: If investigators and their delegates are appropriately prepared for a trial, then they are qualified to conduct it.

This shift will depend upon

1. Investigators and their delegates assuming greater control of their qualification, and
2. Sponsors and CROs being willing to accept documentation of relevant education and experience as evidence that investigators and their delegates are qualified

A NEW APPROACH TO IDENTIFYING QUALIFIED INVESTIGATORS AND THEIR DELEGATES

- A **move away from repetitive GCP training** as the one-size-fits-all approach to qualifying investigators and their delegates for the conduct of clinical trials
- A **step toward targeted and effective educational programming,** with less redundant and burdensome training
- A **shift in the perception of qualification activities** from "necessary but low value" to "an opportunity for improved quality and efficiency"
- **Recognition of previous training and experience** that supports the transfer of skills between studies
- **Identification of gaps in knowledge or skills** that are then addressed using innovative and constructive adult learning methods
- **Improved understanding of how to apply GCP principles** to the conduct of clinical trials

[c] Institutional review boards (IRBs) may also benefit from these recommendations in fulfilling their regulatory requirement to evaluate investigator qualifications, per 21 CFR 56.107(a).

To support the implementation of these expert-based recommendations, CTTI has developed a framework of characteristics to help sponsors, CROs, and site teams assess whether investigators and their delegates are qualified to conduct a particular trial. Freely adapt this framework as necessary to meet the unique needs of the site team and protocol under consideration. Site teams can also use this tool to evaluate their general preparedness for any trial.

ANTICIPATED IMPACT OF IMPLEMENTING THESE RECOMMENDATIONS

- A **culture of collaboration** between sponsors, CROs, and site teams in preparing investigators and their delegates to conduct clinical trials
- **Improved execution of study protocol** as sponsors and investigators are able to allocate more time to protocol-specific concerns
- **Fewer regulatory findings** related to GCP elements
- **Improved quality,** including better data, fewer queries and protocol deviations, and improved study participant safety
- **Improved efficiency,** including shorter recruitment timelines, improved study participant retention, and less time spent resolving discrepancies
- Ongoing support and communication through formalized **mentorship and knowledge-sharing platforms**

Successful clinical trials require a well-designed protocol and robust site-based research infrastructure in addition to well-qualified site teams. Therefore, we suggest you use these recommendations on qualifying site teams in conjunction with (1) CTTI's **Quality by Design recommendations** on protocol development and (2) CTTI's **Investigator Community recommendations** for a holistic approach to conducting quality clinical trials.

CONTENTS AT-A-GLANCE

I. Quality Conduct by Design

Quality by design (QbD) principles[2] should be used to provide an effective, proactive framework for developing protocols that operate efficiently, adequately safeguard study participants, and produce credible and accurate information. Likewise, QbD can provide a practical, outcomes-focused approach to the identification of qualified investigators and their delegates.[d]

1. Expand qualification beyond GCP training

Completion of GCP training alone is insufficient to qualify investigators and their delegates for the quality conduct of clinical trials. Although the training covers principles that are critical to the credibility and accuracy of trial data and the protection of human subjects, repetitive didactic[e] presentation of GCP elements is unlikely to either:

A site team comprises many individuals with unique roles and learning needs who require different types of training in both content and delivery—it is not a single entity requiring the same training to become qualified.

- Adequately prepare an inexperienced member of a site team, or
- Add value to the practice of an experienced researcher.

CTTI's recommendations on **GCP Training for Investigators** describe how to optimize GCP training where members of the site team may still need education on applying GCP elements. However, those investigators and delegates who regularly demonstrate proficiency in applying GCP elements should be exempt from further GCP training requirements.

Recommendations for Sponsors and CROs

[d] This approach is also consistent with the renovations to the International Council for Harmonization (ICH) E6 guidelines on GCP that promote flexibility in managing risk during the conduct of clinical trials.

[e] Didactic learning describes instructor-led communication of theoretical knowledge.

- Move away from repetitive GCP training as the one-size-fits-all approach to qualifying investigators and their delegates for the conduct of clinical trials.
- Instead of repeating the standard one-size-fits-all training at the start of each study, develop educational programming that is tailored to your protocol and the members of your site team, as outlined in Section III, Improving Educational Programming.

Recognize the limits of GCP training as the first step to turning qualification from a "check-box-activity" to a valuable learning opportunity resulting in improved clinical trial quality.

Recommendations for Investigators and Their Delegates

- Recognize that completion of GCP training in isolation is insufficient to fully prepare for the quality conduct of a clinical trial.
- Evaluate your site team's preparedness to conduct clinical research before seeking selection as a trial site. To guide this assessment, CTTI has developed a framework of characteristics describing attributes that are within your control and can be modified through learning and training.

2. Identify the unique learning requirements of each trial

The knowledge, skills, and experience required for investigators and their delegates will vary with each trial. Different study phases, disease states, protocol designs, study participant populations, and clinical settings guide unique requirements.

Recommendations for Sponsors and CROs

- To support investigators in their assessment of their ability to conduct a given study protocol and identify any learning requirements, provide the completed or draft protocol to potential site teams at the beginning of the site selection process. Such transparency is crucial to establishing a collaborative approach to identifying qualified investigators and their delegates.
- Allow site teams to review and provide feedback on the protocol to help address potential feasibility issues or concerns up front. In addition, these site teams will better understand the protocol requirements once the study begins. This exchange of information is a critical part of the learning necessary for each new protocol and engages the site team in a way that didactic instruction does not.
- Complete thorough pre-study visits. CTTI has developed a framework of characteristics to help guide the assessment and selection of sites.

Recommendations for Investigators and Their Delegates

- To prepare for a specific trial:

- Request the full protocol—even if only in draft—as soon as you are contacted about a trial, and
- Assess whether you and your delegates are adequately qualified to conduct the trial. CTTI has developed a framework of characteristics to help guide this assessment.

- Discuss your assessment findings openly with the sponsor to close any gaps in preparedness. Such transparency and collaboration are necessary to ensure that the educational resources available through the sponsor are used in support of the site team's efforts to meet the specific needs of a given protocol.

3. Take a targeted approach to being qualified

A targeted, risk-based approach to being qualified involves (1) identifying potential high risks in protocol execution and (2) focusing targeted, applied learning solutions toward these high-risk areas. Risk analyses should not only consider potential challenges associated with a given protocol, but also reflect the most common deviations experienced by site teams on protocols similar in design or therapeutic area.

Recommendations for Sponsors and CROs

- Critically evaluate the skills, knowledge, and experience of site teams before (1) site selection and (2) formulation of learning requirements. CTTI has developed a framework of characteristics to help guide this evaluation.
- Discuss your evaluation of the site openly with investigators. Transparency surrounding your assessment of a site team's ability to satisfy the requirements of a particular protocol is critical for identifying educational needs and creating appropriate educational programming to ensure that investigators and their delegates are truly qualified.
- Consider reallocating resources to identifying qualified investigators and their delegates as needed. Investing time and effort toward site selection and preparation can preempt quality issues and avoid the need to invest additional resources to fix them.

Recommendations for Investigators and Their Delegates

- Consider your performance on past protocols to develop policies, procedures, or educational programming to improve the conduct of future studies. For example, reviewing common protocol deviations may allow you to create strategies to avoid such deficiencies. Analyses of recruitment and enrollment efforts may identify tactics that have worked, as well as areas that need improvement. Once addressed, you can focus on closing gaps that come up on a study-by-study basis. CTTI has developed a framework of characteristics to help guide this

assessment, and Appendix 1 provides an inventory of resources for training and learning.

- Share your findings with sponsors and CROs during the site selection process to guide effective preparation of the site team.

II. Improving Educational Offerings

1. Create educational programming with adult learners in mind, taking into account individual study roles

To ensure investigators and their delegates are qualified, educational programming should focus on the learning requirements of the specific trial and address the gaps in knowledge and skills identified in Section I, Quality Conduct by Design.

Active learning encompasses a broad range of unstructured/informal and structured/formal approaches to increasing knowledge and skills.

Training is one type of learning that imparts information through a structured, learner-centered approach with measurable outcomes.

Site-based learning activities may include:

- Mentoring programs,
- Job-shadowing programs,
- Virtual or in-person knowledge-sharing networks,[f] and
- Mock run-throughs of study participant visits and protocol procedures.

[f] A knowledge-sharing network is a collection of individuals and teams who come together across organizational, spatial, and disciplinary boundaries to create and share a body of knowledge.

These activities are based on established adult learning methods (see box at right). CTTI has compiled a compendium of existing mentoring programs and knowledge-sharing networks to illustrate how these activities are being implemented in practice (see Appendix 2).

Recommendations for Sponsors and CROs

What is adult learning?

- **Self-directed:** Empowers the learner to diagnose learning needs and formulate goals
- **Experience-based:** Leverages professional experience when introducing new material
- **Goal-oriented:** Times the delivery of information so that the learner may soon apply the skill during a trial
- **Relevant:** Emphasizes why practices are recommended or required
- **Practical:** Focuses on application of knowledge, concepts, and skills
- **Collaborative:** Creates a partnership between the learner and the instructor

Adapted from 'Malcolm Knowles' Adult Learning Theory

- Recognize the value in learning approaches that go beyond traditional training methods. Consider establishing knowledge-sharing networks for specific trials, which provide forums for information exchange and peer support (see Appendix 2).
- Accept documentation of (1) the completion of previous relevant training, and/or (2) the continued application of knowledge and skills during the conduct of clinical trials as evidence that investigators and their delegates are qualified (see CTTI's Quick Reference Guide to Documenting Qualification for Investigators and Their Delegates and the documentation template).
- Consider the previous application of required skills when tailoring protocol-specific educational programming to meet individual learning needs.
- Apply adult learning approaches when developing educational programming.
- Clearly define gaps in knowledge and skills as you consider the learning requirements for a study, and develop educational programming to address them. CTTI has developed a framework of characteristics to help identify learning goals.
- Create role- and protocol-specific education goals that communicate what is new, unique, and difficult about the study to assess and manage risk.
- Recognize that different members of the site team may benefit from different types of education and experience in pursuit of the same learning goal.

Recommendations for Investigators and Their Delegates

- Consider how to best meet your learning goals, including through approaches other than traditional training as described above. See Appendix 2 for specific examples.
- Seek out educational offerings that meet content-specific learning goals and suit individual learning styles. Time the completion of educational programming to coincide with conducting trial activities that require the knowledge and skills learned.
- Encourage more experienced members of the site team to participate in mentoring programs with less experienced members.
- Document learning activities, as well as the successful application of knowledge and skills pertinent to your role in conducting trials, to serve as a record demonstrating your qualification for the conduct of clinical trials. CTTI has developed a Quick Reference Guide to Documenting Qualification for Investigators and Their Delegates and a documentation template for recording this information.

REFERENCES

1. FDA: BIMO inspection metrics [Internet]. Silver Spring (MD): U.S. Food and Drug Administration; cited 2018 Aug 21. Available from: https://www.fda.gov/ScienceResearch/SpecialTopics/RunningClinicalTrialsucm261409.htm
2. CTTI: quality by design [Internet]. Durham (NC): Clinical Trials Transformation Initiative; cited 2018 Aug 21. Available from: https://www.ctti-clinicaltrials.org/projects/quality-design

ABOUT THE RECOMMENDATIONS

- These recommendations are based on results from CTTI's Investigator Qualification Project.
- CTTI's Executive Committee approved on Sept. 24, 2018.
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- All of CTTI's official recommendations are publicly available. Use of the recommendations is encouraged with appropriate citation.

ABOUT CTTI

Clinical Trials Transformation Initiative (CTTI), a public-private partnership co-founded by Duke University and the U.S. Food and Drug Administration, seeks to develop and drive adoption of practices that will increase the quality and efficiency of clinical trials. Comprised of more than 80 member organizations—representing academia, clinical investigators, government and regulatory agencies, industry, institutional review boards, patient advocacy groups, and other groups—CTTI is transforming the clinical trials landscape by developing evidence-based solutions to clinical research challenges. Many regulatory agencies and organizations have applied CTTI's nearly 20 existing recommendations, and associated resources, to make better clinical trials a reality. Learn more about CTTI projects, recommendations, and resources at www.ctti-clinicaltrials.org.