

Quality by Design (QbD) Implementation Guide for Individual Clinical Trials

# Overview

This tool helps study teams plan their implementation of Quality by Design (QbD) for an individual clinical trial. It can serve as a guide to key elements of QbD that will often be important to incorporate in trial planning and execution, and can also support ongoing self-evaluation and continuous improvement. Each organization and each study team should carefully tailor this Implementation Guide to best meet their unique needs—this tool is intended as a framework for critical thought, not a ‘recipe’ that can be followed for all trials and all situations. For detailed considerations, see [How To Use This Tool](#_How_To_Use) at the end of this document.

# Implementation Guide

|  | | **Implementation Planning and Tracking**  ***(Starting at Draft Study Concept Stage)*** | | | **After-Action Review**  ***(During Study Closeout)*** | |
| --- | --- | --- | --- | --- | --- | --- |
| **Factor** | **Component** | **Intend to Implement?**  **(yes / no)** | **Implemented?**  **(yes / no)** | **Notes** | **How Effective Was Implementation?**  **(Needs Improvement, Successful, Optimal, N/A)** | **Scoring Rationale /**  **Opportunities for Improvement** |
| **[Awareness & Supports](#AwarenessSupportsDefinition" \o "Includes the extent to which there is awareness of QbD across the organization, support for implementation of QbD principles at a leadership level, and the identification of a focal point or subject matter expert to drive implementation... )** | Engage organizational-level QbD ‘focal point’ or subject-matter expert to provide guidance and support (if applicable) |  |  |  |  |  |
|  | Ensure that all involved stakeholders [understand QbD concepts](https://www.ctti-clinicaltrials.org/our-work/quality/qbd-quality-by-design-toolkit/learn-about-qbd/) (to extent relevant), and also [set expectations](https://www.ctti-clinicaltrials.org/wp-content/uploads/2021/08/CTTI_QbD_Toolkit_Setting-Expectations.pdf) for how QbD will affect the study planning process |  |  |  |  |  |
|  | Identify mechanism for [documenting decisions](https://www.ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_QbD_Documentation_Tool.xlsx) about critical-to-quality factors, risks, and strategies for addressing risks (may be customized to needs of study) |  |  |  |  |  |
|  | Initiate QbD discussions early in study design (draft study concept stage; prior to developing full protocol) |  |  |  |  |  |
| **[Incentives](#IncentivesDefinition" \o "The ways in which management culture is reinforced. Incentives can be positive or negative; can target both behaviors and end results; and can function at individual and group levels. Includes the range of social and behavioral factors...)** | Highlight and address competing incentives and priorities (e.g., pressure to launch study as quickly as possible) early in study design |  |  |  |  |  |
|  | Develop plans to [recognize the study team](https://www.ctti-clinicaltrials.org/wp-content/uploads/2021/08/CTTI_QbD_Toolkit_Team_Recognition.pdf) for dedicating time to QbD-related efforts |  |  |  |  |  |
| **[Stakeholder Engagement](#StakeholderEngagementDefinition" \o "What quality means to each relevant internal and external stakeholder (e.g., the various internal sponsor roles, CROs and other service providers, patients and patient groups, investigators and site personnel, regulatory agencies and...)** | Identify the broad range of internal and external stakeholders to engage in study design ([see suggestions here](https://www.ctti-clinicaltrials.org/wp-content/uploads/2021/08/CTTI_QbD_Toolkit_Perspectives_Champions.pdf)) |  |  |  |  |  |
|  | Engage identified internal stakeholders as equal partners from the earliest stages of study design |  |  |  |  |  |
|  | Engage identified patient representatives as equal partners from the earliest stages of study design |  |  |  |  |  |
|  | Engage identified CRO representatives and other operational partners from the earliest stages of study design (ideally in RFP stage) |  |  |  |  |  |
|  | Engage identified investigative site personnel from the earliest stages of study design |  |  |  |  |  |
|  | Engage regulators early in study design, if appropriate (e.g., when a study has novel features in elements considered critical to quality) |  |  |  |  |  |
| **[Critical-to-Quality Focus](#CTQFocusDefinition" \o "The process of planning a study—protocol design, as well as related planning for operational considerations not captured in the protocol—including the identification of critical-to-quality factors and risk mitigation strategies.)** | Identify and prioritize a manageable set of study-specific [critical-to-quality factors](https://www.ctti-clinicaltrials.org/our-work/quality/qbd-quality-by-design-toolkit/teach-others-about-qbd/qbd-principles-document/) (CTQs) |  |  |  |  |  |
|  | For each CTQ, identify potential risks of important errors that could significantly impact trial integrity and/or participant safety |  |  |  |  |  |
|  | For each important risk, identify and implement strategies to eliminate or reduce important risks proactively—by changing the trial design where possible, and otherwise by implementation of risk-based trial oversight, or a combination of design and oversight |  |  |  |  |  |
|  | Ensure the final study design is streamlined to be as simple as possible (e.g., complexity is proportionate to study objectives; all endpoints and assessments are directly tied to study objectives and/or patient safety) |  |  |  |  |  |
|  | Simplify and streamline the protocol and all supporting operational plans and documents |  |  |  |  |  |
| **[Handover from Study Design to Execution](#HandoverDefinition" \o "Ensuring that all stakeholders with responsibilities during study execution understand their role and its relationship to all other roles, as well as the critical-to-quality factors identified, risk-mitigation strategies, and controls. )** | Ensure all project team members understand rationale for CTQs, risks, and mitigation strategies, and how these relate to operational plans and priorities |  |  |  |  |  |
|  | Ensure that training for all operational partners (sites, vendors, etc.) highlights and is aligned with CTQs |  |  |  |  |  |
| **[Management of Risks to CTQs](#ManagementOfRisksDefinition" \o "Ensuring that quality management activities – including risk-informed quality management – follows directly and logically from decisions about critical-to-quality factors and associated risks that were identified during study planning. This includes...)** | Ensure that risk-informed quality management approach directly addresses CTQs |  |  |  |  |  |
|  | Establish processes to ensure CTQs and risk mitigation strategies are regularly evaluated and updated across the study lifecycle (e.g., via a [Plan-Do-Check-Act approach](https://www.ctti-clinicaltrials.org/wp-content/uploads/2021/08/CTTI_QbD_Toolkit_Measurement_for_Study_Teams.pdf)) |  |  |  |  |  |
| **[Lessons Learned](#LessonsLearnedDefinition" \o "Emphasizes the importance of systematically conducting study ‘post-mortem’ reviews to assess decisions made during study planning, capture learnings from all stakeholders, and, most importantly, incorporate lessons learned...)** | Early in study design, review lessons learned from prior studies and incorporate those into QbD discussions to help identify critical-to-quality factors and important risks |  |  |  |  |  |
|  | [Implement mechanisms](https://www.ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_QbD_Documentation_Tool.xlsx) for capturing important lessons about study quality (e.g., risks to be aware of, effectiveness of mitigation strategies) throughout study lifecycle |  |  |  |  |  |
| **Continuous Improvement** [**Metrics**](#MetricsDefinition) | [Identify process and outcome metrics](https://www.ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_QbD_Metrics_Framework.pdf) related to QbD implementation that will be captured, and establish associated data collection, analysis, and review plans |  |  |  |  |  |

**QbD Implementation Guide vs. Maturity Model**

There is a direct correspondence between the Factors in this Implementation Guide and the Factors in CTTI’s [QbD Maturity Model](https://www.ctti-clinicaltrials.org/wp-content/uploads/2021/06/CTTI_QbD_Maturity_Model.docx)**.**

The tools can be used together:

* This Implementation Guide helps *individual study teams* ensure complete and effective QbD implementation.
* The Maturity Model is aimed at doing the same *for organizations*.

Reviewing recent trial-level self-evaluations completed in this Implementation Guide may also help inform organizational-level self-evaluations with the Maturity Model.

# How To Use This Tool

For optimal results, begin using this tool and planning QbD implementation as early as possible in study design—ideally at the draft study concept stage or earlier. The following steps are suggested:

**1. Determine who will use the tool**

This tool should be used by and accessible to the entire study team. However, consider designating one person within the study team who will take responsibility for customizing the tool based on team discussions, tracking decisions, and capturing lessons learned. The best person/role may vary.

**2. Customize the tool**

All elements of the tool should be reviewed and customized as QbD implementation is planned. Make sure to discuss:

* Specific components (rows) to combine and/or break out further, to match desired level of detail
* Additional QbD-related activities to implement and track (by adding rows to the table)
* Which QbD components will be implemented (using the ‘Intend to Implement’ column, or simply deleting rows)
* How implementation status will be tracked (‘yes/no’, as shown, or more-detailed approach)
* Self-evaluation approach, modifying the two right-most columns to match

**3. Implement and track status**

Of the QbD components shown in this tool, many would ideally be implemented or in progress by the draft study concept stage. All should be implemented by the time the final protocol is approved.

**4. Conduct self-evaluation**

At the end of the study, the study team can conduct a self-evaluation of QbD implementation as part of their ‘after-action review’. This tool suggests capturing a semi-quantitative ‘score’ (Needs Improvement, etc.), alongside more-detailed notes, as shown in the two right-most columns. A variety of alternative self-evaluation and/or scoring approaches can be used.

Most important is to ensure the study team identifies what worked well and what could be improved, and then disseminates lessons-learned within the organization and to operational partners in an appropriate way.