# Executive Summary: Use of Quality by Design in Clinical Trial Implementation Planning

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# Use of Quality by Design in Clinical Trial Implementation Planning

## Main Points

- Industry leaders in clinical trials research such as the United States Food and Drug Administration (U.S. FDA), International Council on Harmonisation (ICH), and the Clinical Trials Transformation Initiative (CTTI), recommend proactively identifying areas of risk to participant safety and data integrity in a trial's protocol before study implementation (CDER, 2024; ICH, 2021; Tenaerts et al., 2018).
- Quality by Design (QbD) provides principles to proactively identify and mitigate areas of risk, called Critical to Quality Factors (CTQFs), and mitigate these CTQFs in the study's implementation study plan (Bartakian, 2019; Tenaerts et al., 2018).
- A Doctor of Nursing Practice (DNP) project was implemented utilizing a clinical trial study start-up workbook, incorporating a proactive protocol risk assessment to assist research coordinators in organizing the detailed tasks required in the complex pre-enrollment activities.
- A post-pilot survey demonstrated that staff were open to the use of QbD concepts; however, mixed responses on the future use of the workbook tools.
- Survey results recommended more training on identifying CTQFs, mitigating these items into the implementation study plan, and having routine quality review meetings for individual study teams to identify and remediate any errors during the study lifecycle.

## Background and Purpose

Clinical trial research is a fundamental arm of medical science that takes laboratory discoveries and studies these concepts with human subjects in a controlled, clinical setting (Moradi et al., 2021). The safety of trial participants and the collection of accurate data to maintain study integrity are crucial to the success of a clinical trial. The DNP project site partner proposed a project to examine methods to integrate industry-recommended QbD principles into the everyday conduct of clinical trials (D. Stanton,

personal communication, May 16, 2024). Literature synthesis demonstrated that by applying current industry-recommended risk-based and proactive quality methodologies, such as QbD, clinical trial organizations can proactively detect, remediate, and prevent errors, ensuring participant safety and study integrity (CDER, 2024; ICH, 2021; Tenaerts et al., 2018). Furthermore, the literature suggests standardizing the trial start-up process and utilizing methods such as protocol dissection to critically appraise the study protocol as proactive measures to mitigate concerns about participant safety and study integrity (Agriesti & Smailes, 2018; Pelazza et al., 2024; Scarola, 2020).

**Methodology**

The DNP project was implemented at a clinical trial service center within the School of Medicine of an academic health system, located in central North Carolina, with the primary population targeted to include trials in their start-up phase. A Quality Improvement Team, utilizing the FOCUS-PDSA model, was formed and considered evidence from the literature (Abuzied et al., 2023). Based on evidence from the literature, the team developed a comprehensive study start-up workbook that covered pre-enrollment activities through study implementation, and it was implemented in collaboration with a single research unit. However, delays in study start-ups during the implementation timeframe limited the full use of the tool. The team then utilized an additional PDSA cycle to develop a scaled-down tool focusing primarily on protocol dissection and the study plan to allow for more streamlined implementation in other studies nearing enrollment. This scaled-back tool was accompanied by a narrated slide presentation to orient staff, covering QbD concepts, critical thinking, protocol dissection, and case studies. This tool was initiated in three other research units, with seven additional staff trained. The project was implemented on January 13, 2025, and completed on April 25, 2025.

Outcome measures included decreased protocol deviations and a post-pilot survey designed to gather staff opinions on the overall use of the tools, as well as to solicit general comments and direct questions to gather further details on the use of the QbD tools in conducting clinical trial studies.

**Results**

Due to start-up delays beyond the project site's control, only partial implementation of the tools occurred, and data from the post-pilot survey was collected. A 17-question Likert-style post-pilot survey, which included open-ended questions for general comments, suggestions, barriers, and ideas for future education, was circulated via email to eight participating staff members, with anonymous returns. Four post-pilot surveys were returned, representing a 50% return rate. Refer to the Appendix for a graphical representation of the survey data. The survey results showed an overall improvement in knowledge gained of QbD concepts during the pilot, with a one-point increase from 3.25 to 4.25 out of a 5-point scale. Survey results also demonstrated clear instructions on use and positive feedback on the orientation video. Overall, staff were satisfied with the application of QbD concepts in trial implementation planning.

The two survey findings that were least favorable in terms of outcomes were the tool's usefulness in time management and its potential for future use. While survey data indicated some staff were open to future use of QbD tools, others remained unsure. Additional clarity was obtained from the general comments and included suggestions for formatting the tool as a spreadsheet with tabs and milestones rather than a multiple-page document, and a preference for "a detailed study plan with QbD incorporated". Other comments included a need for more guidance on how to identify CTQFs and develop comprehensive study plans.

**Strengths and Limitations**

The four returned surveys were completed in their entirety and anonymously; however, they only represented a 50% return rate for the targeted sampling of eight research staff. The returned surveys provided information for use in future iterations of studies regarding the implementation of QbD concepts, specifically focusing on the efficacy of using these tools in clinical trials at the investigative site. With a primary limitation being that the tools were never fully implemented due to

trial start-up delays, planning a study period to allow for full implementation of the QbD tools, while also considering a time allowance for monitoring visits to occur to track protocol deviations. Since the tools were not implemented to prove any effectiveness, any future use would require further validation of efficacy in trial risk mitigation.

**Implications**

Although only a partial implementation, the project demonstrated that utilizing proactive concepts of QbD shows potential as an effective tool for implementing clinical trial studies. Furthermore, utilizing QbD approaches, such as protocol dissection, can help identify areas of risk, leading to a robust implementation study plan tailored to each trial.

Recommendations for future iterations include conducting more robust projects to demonstrate the positive impact of QbD on trial safety and integrity, such as implementing a six- to twelve-month timeframe, allowing for the trial to be fully implemented and for monitoring visits to identify any protocol deviations. Furthermore, it is recommended to establish concrete methods for risk assessment to identify CTQFs in study protocols. Another strategy to consider is targeted learning on QbD concepts, including an emphasis on identifying CTQFs and the protocol dissection process. A recommendation from the post-pilot survey is to conduct a project studying the impact of a weekly quality review with individual study teams, and how these reviews assist in remediating errors or deviations more effectively. Finally, integrating QbD concepts into an organization's quality management plan further demonstrates QbD as a priority, aligning with industry-accepted standards.

**Conclusion**

Participant safety and study integrity are paramount to the success of clinical trials. QbD concepts are designed to provide a framework for proactively identifying CTQFs and formulating necessary mitigating steps in the trial study plan, to preserve participant safety and study integrity. Given the limited information in the literature on implementing QbD concepts at the investigative site

level, a continuation of this project over a longer timeframe has the potential to serve as a case study to share with other sites, to show any potential impact of QbD philosophies on the improvement of safety and integrity in clinical trials at the point of study implementation.

**References**

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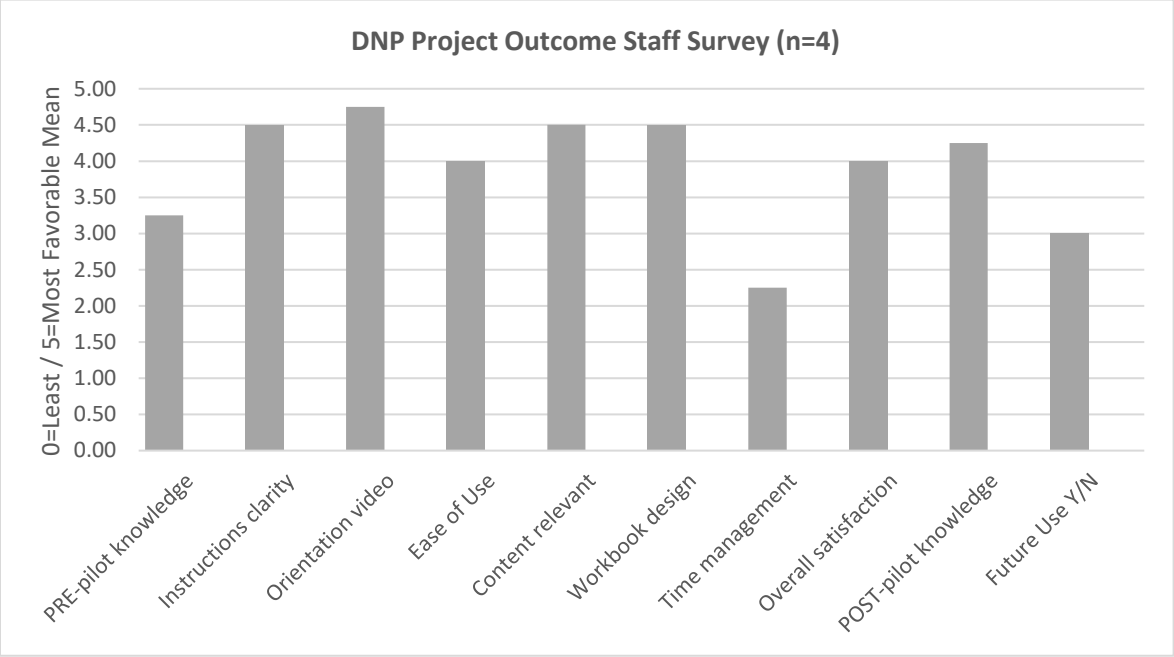
**Appendix**


DNP Project Outcome Staff Survey (n=4)
0=Least / 5=Most Favorable Mean
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
PRE-pilot knowledge
Instructions clarity
Orientation video
Ease of Use
Content relevant
Workbook design
Time management
Overall satisfaction
POST-pilot knowledge
Future Use Y/N