



Workshop on Quality Risk Management: Understanding What Matters

Agenda of the Workshop held January 29-30, 2014

DoubleTree by Hilton Bethesda, Bethesda, Maryland

CTTI MISSION: To identify and promote practices that will increase the quality and efficiency of clinical trials

WORKSHOP OBJECTIVES:

- Develop understanding of risk-based Quality by Design for clinical trials, from general principles, real-world examples, and hypothetical case studies
- Gain confidence in the application of such concepts to clinical trials
- Identify obstacles to the adoption of this approach
- Identify opportunities for dissemination of these principles and practices to a broad array of stakeholders.

DAY 1 – JANUARY 29, 2014

8:30 am WELCOMING REMARKS

8:30 Introduction to the Clinical Trials Transformation Initiative
Pamela Tenaerts (CTTI)

8:40 Opening Remarks
Christy Foreman (FDA/CDRH)

8:50 am SESSION I: LANDSCAPE, RATIONALE AND PRINCIPLES

Facilitator: Martin Landray (Oxford)

Objectives:

- *Review the current landscape of medical device development and approval*
- *Discuss the principles and review the key drivers for quality (including the outcomes of previous CTTI activities)*
- *Review US regulatory and European perspectives on methods to ensure quality in clinical trials*

8:50 Quality Risk Assessment and Quality by Design in Clinical Research
Martin Landray (Oxford)

9:05 How US Regulatory Requirements Contribute to Study Quality
James Saviola (FDA/CDRH)

9:20 European Perspective on Quality
Angeles Alonso Garcia (EMA)

9:40 Current Issues in Device Development and Approval – Industry Perspective
Ted Lystig (Medtronic)

10:00 Current Issues in Device Development and Approval – Academic Perspective
Laura Mauri (Brigham and Women's Hospital)

10:20 Payor Perspective on Quality
Louis Jacques (CMS)

10:40 Discussion

11:00 am BREAK

11:15 am SESSION II: REAL-WORLD EXAMPLES

Facilitator: Roxana Mehran (Mount Sinai)

Objectives:

- *Review examples of clinical trials that have incorporated risk-based QbD approaches*
- *Discuss the advantages and the challenges of adopting this approach*

- 11:15 Example 1: CoreValve U.S Pivotal Trial
Ted Lystig (Medtronic)
- 11:30 Example 2: TASTE: Thrombus Aspiration During ST-Segment Elevation Myocardial Infarction. A Multicenter, Prospective, Registry Based Randomized Clinical Trial
Roxana Mehran (Mount Sinai)
- 11:45 Example 3: SAFE-PCI: The Study of Access Site for Enhancement of Percutaneous Coronary Intervention for Women
Sunil Rao (Duke)
- 12:00 Discussion
- 12:15 pm LUNCH (PROVIDED)**
- 1:00 pm SESSION III: PROVIDING GUIDANCE**
Facilitator: Ann Meeker-O'Connell (Janssen)
Objective:
- *Review and discuss the Principles Document, and suggest further improvements 1*
- 1:00 Principles Document Review
Ann Meeker-O'Connell (Janssen)
- 2:00 pm SESSION IV: BUILDING QUALITY IN TO A CLINICAL TRIAL (CASE STUDIES – Part I)**
Facilitator: Jean Mulinde (FDA/CDER)
Objectives:
- *Working in groups, participants will apply the Quality by Design principles to their hypothetical protocol outline, taking into account the concerns of key stakeholders.*
 - *Characterize the applicability of the Quality by Design factors as high, medium, or low.*
 - *Select the top 5 factors that are critical to the success and quality of the trial protocol and why they are important.*
 - *Develop 3 priority recommendations to assure a successful and efficient trial.*
- 2:00 Introduction to the Working Group Activities
Jean Mulinde (FDA/CDER)
- 2:15 Workgroup activity: Review trial brief and develop risk assessment
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| Jasmine | Workgroup 1: Interventional cardiology |
| Juniper | Workgroup 2: Interventional cardiology |
| Lavendar | Workgroup 3: Surgery |
| Lilac | Workgroup 4: Surgery |
| Insight | Workgroup 5: Diagnostics |
| Wisdom | Workgroup 6: Diagnostics |

3:30 pm BREAK

4:00 pm SESSION V: BUILDING QUALITY IN TO A CLINICAL TRIAL (CASE STUDIES – Feedback)

Facilitator: Martin Landray (Oxford)

Objective:

- *Presentation and discussion of the approach to identifying “critical to quality” parameters taken by each workgroup*
- *Characterize the applicability of the Quality by Design factors as high, medium, or low.*

4:00 Workgroups that used the same case study report, review similarities and differences between the 2 groups

4:30 Workgroup Report Out by Case Study Groups (10 Minutes/Case Study)

- How were the top 5 factors selected?
- What are the expected challenges in adopting the principles?
- What are the likely obstacles to adopting the principles?

5:00 Day 1 Wrap-Up: Review of the Day’s Activity

Before leaving the room, participants must propose, in writing, each of the following:

- One suggestion for improvement of the Principles document.
- One aspect of identifying “critical to quality factors” that is challenging
- One component of the exercise that they will promote in their organization

6:00 pm RECEPTION

DAY 2 – JANUARY 30, 2014

8:30 am SESSION VI: BUILDING QUALITY IN TO CLINICAL TRIALS (CASE STUDIES – Part II)

Facilitator: Roxana Mehran (Mount Sinai)

Objectives:

- *Explore the role of risk management and monitoring in clinical trial design*
- *Take the one most important critical to quality parameter identified in Part I of the case study and address the following:*
 - *What proactive steps can be taken to avoid problems (mitigation plan)?*
 - *What ongoing checks can be performed to detect problems?*
 - *What type of error will trigger corrective actions?*
- *Promote continuous improvement. Consider:*
 - *What steps can be taken to ensure that corrective and preventive actions remain focused on CTQ aspects of a trial, are sustainable, and efficient? (Avoid the need to add additional*

- activity for the sake of adding activity and making more complex and the complexity leads to inability to implement and sustain)*
- *What steps can be taken to ensure the corrective action stays focused on addressing errors that matter?*
- *How will lessons learned be captured and communicated?*

8:30 Overview of Approaches to Quality by Design
Roxana Mehran (Mount Sinai)

8:50 Workgroup Activity: Designing Trial Operations & Monitoring Approaches

Jasmine	Workgroup 1: Interventional cardiology
Juniper	Workgroup 2: Interventional cardiology
Lavendar	Workgroup 3: Surgery
Lilac	Workgroup 4: Surgery
Insight	Workgroup 5: Diagnostics
Wisdom	Workgroup 6: Diagnostics

10:10 am BREAK

10:30 am SESSION II: REFLECTION AND IDENTIFICATION OF NEXT STEPS

Facilitator: John Alexander (Duke)

Objectives:

- *Review and reflection (what worked, what didn't):*
 - *Principles document*
 - *Working group approach*
 - *Disseminating training within organizations*
- *Identify need for further training materials and approaches – what are practical steps to take*
- *Identify external barriers to widespread adoption of the risk-based Quality by Design approach. Who needs to be convinced and how would this best be achieved?*

10:30 Workgroups that used the same case study report, review similarities and differences between the 2 groups

11:00 Workgroup Report out by case study groups (20 min per case study) and Interactive discussion/brainstorming (all attendees)

12:15 Closing remarks
Pamela Tenaerts (CTTI), Karen Smith (PDF)

12:30 pm ADJOURN

For more information, contact the QbD & QRM Project Manager Annemarie Forrest at Annemarie.Forrest@duke.edu or visit <http://www.ctti-clinicaltrials.org>.

Appendix A. Workshop Background

Current models for clinical trial design, implementation and oversight may have become outmoded and unsustainable in a global, complex clinical trial environment. In particular, existing oversight models, which generally rely on frequent, on-site monitoring visits by sponsor personnel, may not optimally address the most critical risks to trial integrity. A key conclusion of a Clinical Trials Transformation Initiative (CTTI) monitoring project was that clinical trial monitoring should be viewed as one component of an overall quality framework. Project participants, representing a broad cross-section of the clinical trials enterprise, agreed that widespread adoption of an enlightened “quality-by-design” approach to trial planning, conduct, and oversight is needed to ensure trial quality and efficiency. Such an approach would apply risk management principles to the design and execution of clinical trials.

Quality-by Design (QbD) emphasizes building quality into a process from the beginning and has been successfully applied in the manufacturing arena. Applied in clinical development, this approach would prospectively examine the design and objectives of trial and identify “critical to quality” factors (e.g. key data and trial processes such as randomization). Understanding what aspects of a trial are “critical to quality” is essential to subsequently identifying and managing important and likely risks to trial quality. These risks can be managed through modifying trial design, tailoring its implementation, and providing sensible, risk-based oversight.

Participants in an inaugural CTTI workshop on “Quality Risk Management: Making Clinical Trials Fit for Purpose” held in August 2011 explored principles of risk management and Quality-by-Design from other disciplines and examined how such principles could be adapted to enhance clinical trial design and execution. Participants generally agreed that these approaches have the potential to improve clinical trial efficiency while enabling sponsors and clinical investigators to meet their fundamental obligations to protect individuals who volunteer for research and to oversee their trials. In particular, these approaches reposition monitoring as one tool for ongoing evaluation and improvement. Focusing on critical aspects of a trial could also substantially reduce the burden of clinical trial conduct by relieving sponsors of a perceived obligation to mitigate every potential risk posed by a trial, especially for those activities that minimally affect data quality and human subject protection.

In September 2012, CTTI undertook a series of workshops on Quality by Design to evaluate one potential model for efficiently building quality into the scientific and operational design of trials. We are delighted to have you participate in this effort.

Appendix B. Workshop Participants

WORKSHOP CO-CHAIRS

Mark Behm (AstraZeneca)
Diane Dorman (NORD)
Martin Landray (Oxford University)
Ted Lystig (Medtronic)

Ann Meeker-O'Connell (Janssen)
Roxana Mehran (Mount Sinai)
Jean Mulinde (FDA/CDER)
Eric Richardson (FDA/CDRH)

WORKSHOP ATTENDEES

Our workshop participants include representatives from a broad cross-section of the clinical trial enterprise including regulators, government sponsors of clinical research, academia, industry, patient advocates, clinical investigators, and other interested parties. Participants are expected to be actively engaged in dialogue both days.

STAFF

Elena Benjamin (UMM)
Lee Cohen (TRS)
Matt Falloretta (TRS)
Annemarie Forrest (CTTI)
Cheri Janning (CTTI)

Leanne Madre (CTTI)
MariJo Mencini (CTTI)
Bray Patrick-Lake (CTTI)
Jordan Shipman (Louder Than 11)
Pamela Tenaerts (CTTI)