Workshop on Quality Risk Management: Making Clinical Trials Fit for Purpose

Executive Summary of Meeting held August 23-24, 2011

Project: Workshops on Quality by Design

Clinical Trials Transformation Initiative (CTTI)

February 2012

Workshop on Quality Risk Management: Making Clinical Trials Fit for Purpose[1]

A Clinical Trials Transformation Initiative (CTTI) Meeting

August 23–24, 2011, Bethesda, Maryland

EXECUTIVE SUMMARY

During an expert meeting held in October 2010 for the CTTI monitoring project, representatives from a broad cross-section of the clinical trial enterprise discussed clinical trial monitoring as one component of an overall quality framework. Panelists and participants agreed that broad adoption of an enlightened approach is needed to ensure trial quality and efficiency. Such an approach would apply risk management principles to clinical trials by prospectively identifying those aspects in a given trial that are critical to ensure the reliability of results and protection of participants. Those responsible for designing the trial would identify potential risks affecting those aspects and tailor protocol design and implementation to mitigate those risks. This approach borrows concepts and solutions from the pharmaceutical manufacturing sector, which has confronted challenges to product quality as the number of products, facilities, and processes have expanded nationally and globally. In the manufacturing sector, a holistic approach to quality management that incorporates risk management principles has been well described in ICH Q8 and ICH Q9— this approach is involves the concept of "quality-by-design" (QbD).[2,3,4]

1 Financial support for this meeting was provided by Grant # U19 FD003800 from the U.S. Food and Drug Administration (FDA). Volunteer time was provided by Pfizer, the European Medicines Agency, and FDA.

[2] International Conference on Harmonisation. Harmonised Tripartite Guideline: Pharmaceutical Development Q8(R2) Current Step 4 version (ICHQ8, August 2009). 2009. http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q8_R1/Step4/Q8_R2_Guideline.pdf. Accessed on 9-22-2011.

The August 2011 workshop was the first in a planned series intended to share among participants examples of how risk management and QbD principles can be applied to clinical trials and therapeutic development programs. Meeting participants included a broad array of stakeholders, with representatives from government agencies, industry (including pharmaceutical, biotech, and contract research organizations), academic institutions, patient advocacy, investigator groups, and other interested parties.

Workshop presentations addressed a range of subjects, beginning with an overview of risk management and QbD principles as they have been applied in the manufacturing sector and examples of how such principles could be adapted for use in clinical trial design and execution. Representatives from various regulatory bodies—including the Food and Drug Administration (United States), Pharmaceuticals and Medical Devices Agency (Japan), the European Medicines Agency, the Medicines and Healthcare products Regulatory Agency (United Kingdom), Agence Francaise de Securite Sanitaire des Produits de Sante (France), and Federal Institute for Drugs and Medical Devices (Germany)—stressed that regulators are supportive of risk-adapted approaches to quality, outlining steps taken by their agencies to better enable the use of QbD principles in clinical trial design and oversight. Case studies were then offered by a number of presenters from academia, industry, and contract research organizations, demonstrating their experience of applying the QbD approach to clinical trials and sharing lessons learned about enhanced efficiencies and potential obstacles. Time was also spent discussing how best to promote adoption of these new practices throughout the clinical research enterprise and how to communicate to the general public the necessity for and potential impact of this transformational

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[3] International Conference on Harmonisation. ICH Harmonised Tripartite Guideline: Quality Risk Management (ICHQ9). 2005. http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Quality/Q9/Step4/Q9_Guideline.pdf. Accessed on 9-22-2011.

[4] International Conference on Harmonisation. ICH Harmonized Tripartite Guidance: Q10 Pharmaceutical Quality Systems. 5-9-2007. http://www.fda.gov/downloads/RegulatoryInformation/Guidances/ucm128031.pdf. Accessed on 9-22-2011.

change.

With these discussions as a backdrop, the meeting participants then agreed upon a number of action items that should be undertaken to spur the shift to quality-by-design as the fundamental approach for ensuring reliable results and patient safety.

1. If quality is defined as the absence of errors that matter, the definition ultimately needs to be individualized for a specific trial. However, general principles about what really matters in clinical trials can and should be developed—i.e., what do we really need to get right to ensure reliability of results and patient protection? A glossary of QbD-related terms and a document containing case examples shared by research sponsors will supplement this effort.
2. An array of stakeholders will be engaged in a series of workshops to discuss and further develop these principles and their application. The workshops will provide a venue for the sharing of best practices and obstacles encountered so that participants may learn from the successes and failures of their peers.
3. A shift to a quality-by-design and risk management-based approach across the clinical research enterprise will be promoted via the series of workshops mentioned above, as well as by manuscripts to be published by CTTI and through presentations made at industry and medical meetings. Word-of-mouth will also be an important means of dissemination, with meeting participants acting as QbD "ambassadors" spreading the message about the initiative in appropriate venues and acting as QbD "champions" within their organizations.
4. Harmonization both within and across regulatory agencies should be also actively pursued to ensure uniformity of definitions and consistency of guidance.