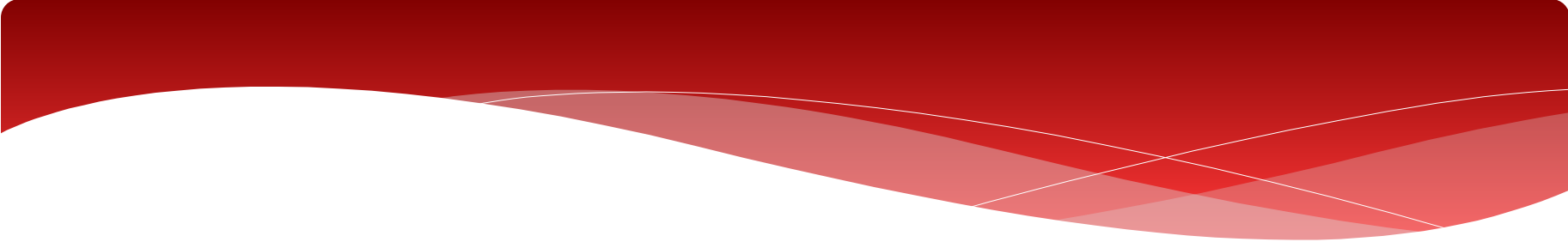




Regulatory Perspective: Enhancing Trial Quality

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Desired State for Clinical Development

“Maximally efficient, agile clinical development programs that reliably produce high quality data* and protect trial participants without extensive regulatory oversight”

*Data that are fit for purpose

- Janet Woodcock, MD CTTI Monitoring Workstream #3 Workshop



Another perspective

* *If everything is under control, you are moving too slow*

* Mario Andretti

-

Are we there yet?



Building Quality into Clinical Trials

- * Quality cannot be monitored, audited, or inspected in retrospectively
- * “The most important tool for ensuring human subject protection and high-quality data is a well-designed and articulated protocol.”

FDA Draft Clinical Monitoring Guidance (published 29 August 2011)

- * At the trial level, the protocol – or more appropriately the investigational plan -- is the blueprint for quality

Streamlining Trial Design

“You start out with a beautiful green tree that should be admired and then everybody in the family wants to put an ornament on it... and no one will take grandma’s ornament off the tree. So you end up with a protocol that is impossible to do and is very distracted from answering the question you originally had.”

- * Dr. Robert Califf, Mind the Gap seminar, “Innovative Approaches to Clinical Trials.”

Building Quality into the Scientific and Operational Design of Trials

- * Prospectively identify the aspects of a trial that are “critical to quality”
- * Identify important and likely risks to “critical to quality” aspects
- * Tailor the investigational plan and trial implementation to eliminate or reduce the impact of “errors that matter”



FDA Requirements – Clinical Trial Quality

- * Broad sponsor responsibilities for clinical trials under 21 CFR 312, including:
 - * selecting qualified investigators
 - * monitoring trial progress
 - * ensuring trial is conducted per investigational plan
 - * reviewing and analyzing accumulating evidence relating to the safety and effectiveness of drug

Where do
Quality by
Design and
Quality Risk
management
fit?



Additional Considerations

- * There is not one “right way” to implement QbD and QRM in clinical trials
- * Approaches must be
 - * sufficiently flexible and
 - * not unduly burdensome
- * Should not be “another layer” on existing practices

What is FDA Doing?

August 2011 Draft Monitoring Guidance

- * Makes clear that sponsors can use a variety of approaches to fulfill monitoring responsibilities
 - * “No single approach to monitoring is appropriate or necessary for every clinical trial”
- * Encourages sponsors to develop risk-based monitoring strategies and plans that are:
 - * Tailored to the risks of the trial
 - * Use a combination of monitoring activities
 - * Incorporate greater reliance on centralized monitoring practices

What is FDA doing?

- * Collaboration with other stakeholders to improve clinical trial efficiencies and promote best practices, e.g.
 - * Clinical Trial Transformation Initiative (CTTI)
 - * IOM Forum on Drug Discovery, Development and Translation
 - * OECD Working Group to Facilitate International Cooperation in Non-commercial Clinical Trials
 - * EMA – FDA Good Clinical Practices Initiative
- * Encouraging a proactive, risk-adapted approach to design, conduct, monitoring, data management and reporting of clinical trials, e.g.
 - * DIA Special Interest Area Community on QRM
 - * CDER Pilot Prospective Reviews – Quality Management and Monitoring Plans
 - * CTTI Quality – by –Design Project



Closing Thoughts

“Many ideas grow better when transplanted into another mind than the one where they sprang up.”

- *Oliver Wendell Holmes*



Thank you!

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