JOB AID
ICH E6 (R2) Addendum
Quality Management Overview

This job aid highlights key points of the ICH E 6 Addendum on Quality Management. The resource for this information is the "Integrated Addendum to ICH E6 (R1): Guideline for Good Clinical Practice E6(R2.)"

Goal of Addendum to ICH E6 (R2)

The goal of the addendum to ICH E6 (R1) is "…to encourage implementation of improved and more efficient approaches to clinical trial design, conduct, oversight, recording and reporting while continuing to ensure human subject protection and reliability of trial results."

Reasons for revision of ICH E6

ICH E6 was revised for the following reasons:

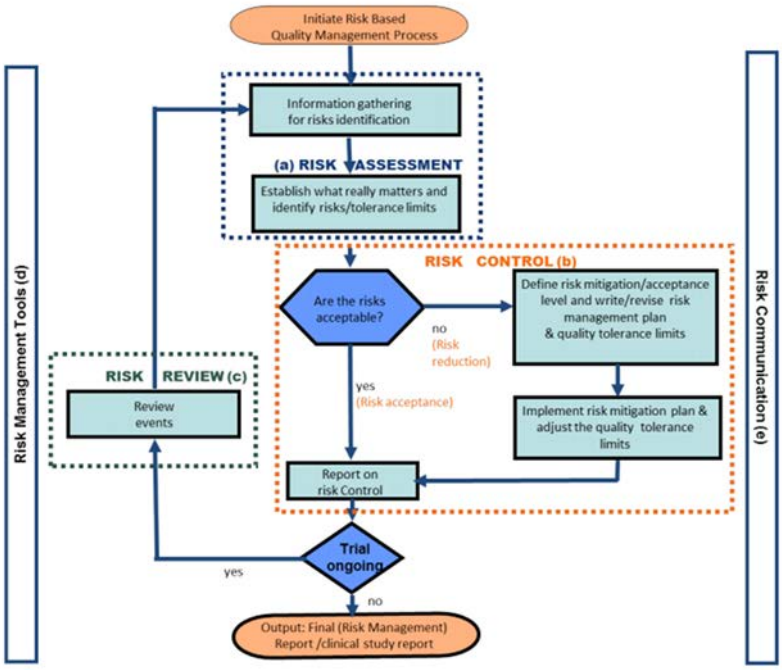
- Increase in Scale, Complexity & Cost
- Evolution of Technology & Risk Management Processes
- Increase in Electronic Data Collection
- Increase Clinical Trial Quality & Efficiency

Sponsor Responsibilities

This table provides a high-level overview of sponsor responsibilities and some examples of how they can apply their tasks per the ICH E 6(R2) guidelines.

Sponsor Focus/Tasks	Example
Implement a system to manage quality throughout all stages of the trial process	Design, conduct, record, evaluate, report, and archive
Focus on trial activities essential to ensuring human subject protection (HSP) and the reliability of trial results	HSP & data reliability
Utilize a risk-based approach	Method of quality is proportionate to inherent risks of the trial
Create operational feasibility (design efficient clinical trial protocols, tools and procedures for data collection and processing).	▪ Avoid complex forms and processes ▪ KISS principle

Quality Management System (QMS) Risked-Base Approach for Clinical Trials



Source: "European Medicines Agency (EMA) Reflection paper on risk based management in clinical trials" (November 18, 2013)

The ICH E6 (R2) QMS risk-based approach includes the following:

- Critical Process & Data Identification
  Identify your risks critical to human subject protection and data integrity. With a new protocol your company would review it and begin to ask if there any special safety concerns with this indication. For example, is the inclusion exclusion criteria vague? Are there specialized tests, equipment, procedures or other processes required? Consider timing- will there be competing trials?

- Identification of The Risk
  Identify risks to clinical trial process and data. Risks should be considered at both the system level and clinical trial level. For example, at the system level, review standard operating procedures and computerized systems. At the clinical trial level review trial design and data collection.

- Evaluate the Risk
  This involves probability, impact and detectability. Identify risks, against existing risk controls by considering the likelihood of errors occurring, the extent to which such errors would be detectable, and the impact of errors on human subject protections and reliability of trial results.

- Control the Risk
  Decide which risks to reduce through mitigation and which to accept as is. This decision is made as a team with the key players involved in the problem and the decision is documented.

- Communicate the Risk
  Communicate the risk and initial assessment that was documented in a formalized manner. This process should be used going forward as well. Every time there is a change it should be communicated in a formalized manner to ensure another risk review is performed so that nothing is missed. For example, if a protocol amendment occurred changing a detail within the IP preparation this would be critical. The review and communication also critical.

- Periodic Review of Risks (Not A One Time Process)
  Periodically a review of the risk controls should be performed to ensure nothing has changed. This should be done with all the key team members and document its outcome. Communicate this outcome as well to all necessary parties.

- Reporting Risks
  Any deviations, major noncompliance or other quality tolerance limit issues should be reported and have a predefined process aligned with the QMS. These incidents will move through the QMS and into the associated risk review and trigger another risk review based on the deviation etc. At that point the cycle would start again with the analysis, communication, documentation, etc. The risk review process should become yet another standard QMS process.