Overview of Changes:
ICH Q9 (R1) Quality Risk Management

Stephen Mahoney, JD, MS
Executive Director | Gilead Sciences, Inc.
PhRMA Topic Leader, ICH Q9 (R1)

SBIA: Joint US FDA - Health Canada ICH Public Meeting
February 22, 2024

DISCLAIMER

The views and opinions expressed in this presentation and on the following slides are those of the presenter in collaboration with the ICH Q9(R1) Implementation Working Group and not necessarily those of Gilead Sciences, Inc.

Overview

- Describe purpose of revised ICH Q9 guideline
- Highlight ICH Revision Milestones
- Discuss Revision Topics and Training

Purpose of the Revised ICH Q9 Guideline

There were several areas identified for improvement, including

1. High levels of **subjectivity** in risk assessments and in QRM outputs
2. Failing to adequately manage supply and **product availability** risks
3. Lack of understanding as to what constitutes **formality** in QRM work
4. Lack of clarity on **risk-based decision-making**
5. Terminology Change: Risk Identification → **Hazard Identification**
6. Lack of clarity on **risk review**

The revised guideline is supported by the development of official ICH Q9(R1) training materials

The ICH Q9 (R1) Revision

Key Milestones

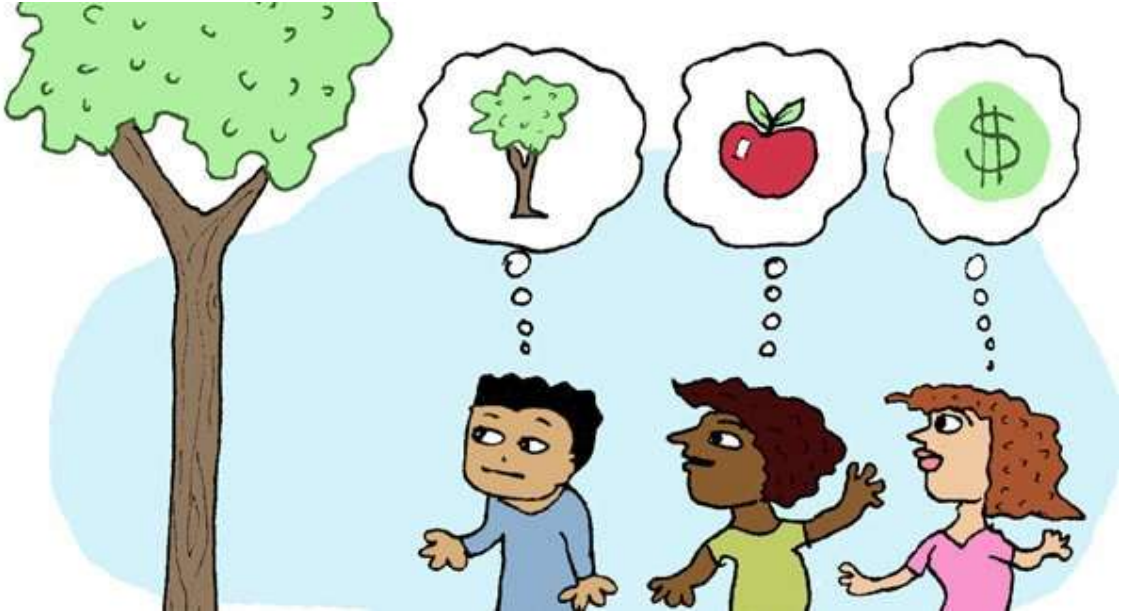
- November 2019: ICH decided to proceed with the proposal made by the European Commission / EMA / HPRA for a targeted revision
- June 2020: Informal ICH Working Group established to prepare for the revision
- November 2020: ICH Concept Paper and Business Plan agreed and published
- December 2020: The Expert Working Group (EWG) for ICH Q9(R1) was convened
- December 2021: Public Consultation on Draft Revised Guideline (Step 3)
- January 2023: Finalization & publication of the revised guideline (Step 4)
- May 2023: United States publishes final revised guidance (Step 5)
- June 2024: Finalization of supportive training materials

ICH Q9 (R1): Quality Risk Management
Revision Topics

1. Subjectivity
2. Product Availability
3. Formality
4. Risk-Based Decision Making
5. Hazard Identification
6. Risk Review

ICH Q9 (R1): Quality Risk Management

Topic 1: Subjectivity



ICH Q9 (R1): Quality Risk Management

Topic 1: Subjectivity

- **High levels of subjectivity in risk assessments are problematic**
  - May directly impact the effectiveness of the risk management activities and the decisions made.
- **Many causes for subjectivity, including:**
  - Differences in how hazards, risks and harms are perceived by different stakeholders (e.g., bias),
  - Inadequately defined risk questions, and
  - The risk scoring methods that some risk assessment tools use.
- **Eliminate subjectivity?**
  - No, but subjectivity may be controlled using well recognized strategies, including addressing bias and behavioral factors.

The revision of ICH Q9 and its associated training materials are addressing the above (and other) points.

ICH Q9 (R1): Quality Risk Management

Topic 2: Product Availability Risks

Did the original ICH Q9 address product availability?

- Yes, ICH Q9 already addressed product availability risks. The definition of harm included damage “from a loss of product quality or availability.”

Why the increased emphasis?

- Addressing such product availability risks more clearly and with more focus was important, given the extent of globalization of medicines supply chains.

The interests of patients are served by risk-based drug shortage prevention and mitigation activities that help to proactively manage supply chain complexities and ensure availability of needed drug (medicinal) products.

ICH Q9 (R1): Quality Risk Management

Topic 2: Product Availability Risks, cont'd

The revised guideline addresses:

(a) Quality/manufacturing issues, including non-compliance with Good Manufacturing Practice (GMP), are a significant cause of product availability issues (e.g., product shortages).

(b) Effective PQS uses QRM to provide an early warning system that supports effective oversight and response to evolving quality/manufacturing risks from the pharmaceutical company or its external partners.

(c) The level of formality applied to risk-based drug shortage prevention and mitigation activities may vary.

(d) Several Quality/manufacturing factors that may affect product availability, including: (1) Manufacturing Process Variation and State of Control, (2) Manufacturing Facilities and Equipment, and (3) Oversight of Outsourced Activities and Suppliers.

The revision of ICH Q9 and its associated training materials are addressing the above (and other) points.

ICH Q9 (R1): Quality Risk Management

Topic 3: Formality

ICH Q9 states: *"The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk."*

The revised version of Q9:

1. Seeks to clarify what "formality" in QRM means,
2. Discusses degrees of "formality" and the factors that might be considered,
3. Provides guidance on the characteristics of higher and lower levels of formality, and
4. Emphasizes that there is flexibility in how much formality may be applied in relation to QRM activities.

ICH Q9 (R1): Quality Risk Management

Topic 3: Formality, cont'd

Additional clarity on formality may:

- Help ensure that the extent of scientific and methodological rigor applied during QRM is commensurate with the level of risk, and
- Lead to resources for QRM being used more efficiently.

The revision of ICH Q9 and its associated training materials are addressing the above (and other) points.

ICH Q9 (R1): Quality Risk Management

Topic 4: Risk Based Decision Making

The Covid-19 pandemic illustrated the importance of effective risk-based decision making by regulators and industry in a myriad of areas.

ICH Q9 (R1): Quality Risk Management

Topic 4: Risk Based Decision Making

Where does Risk-based Decision Making Occur?

ICH Q9(R1) states that “Risk-based decision-making is inherent in all quality risk management activities; it provides an essential foundation for decision makers in an organization.”

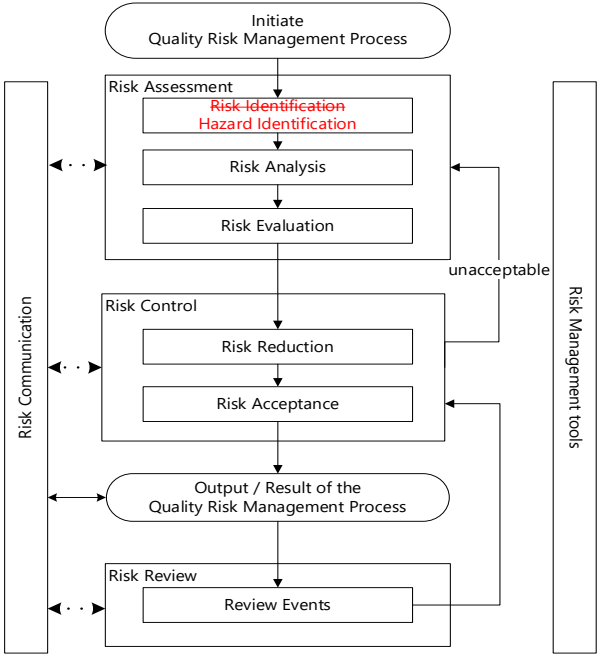
The guideline also indicates that the decisions made from quality risk management activities include those in relation to:

- what hazards exist,
- the risks associated with those hazards,
- the risk controls required,
- the acceptability of the residual risk after risk controls, and
- the communication and review of quality risk management activities and outputs.

Effective risk-based decision-making begins with determining the level of effort, formality and documentation that should be applied during the quality risk management process.

ICH Q9 (R1): Quality Risk Management

Topic 5: Hazard Identification



- The term “Risk Identification” has been changed in the revised guideline to “Hazard Identification”
- This was done to better reflect the guidance in ICH Q9 on Risk Assessment…
- *“Risk assessment consists of the **identification of hazards** and the analysis and evaluation of risks associated with exposure to those hazards…”*

This change aligns with the expectation to identify hazards relevant to patients when evaluating risks, and it may improve how hazards are perceived and assessed.

ICH Q9 (R1): Quality Risk Management

Topic 6: Risk Review

The ICH Q9 revision seeks to provide additional clarity on the expectations relating to keeping risk assessments current and the implementation of risk reviews.

- This takes lifecycle manufacturing performance and quality feedback into account.
- Risk Review ties in with the concept of continuous improvement as expressed in ICH Q10 and in the lifecycle management guidelines (e.g., ICH Q12).

This area was addressed by developing training materials on this topic only.

Summary

- Describe purpose of revised ICH Q9 guideline
- Highlight ICH Revision Milestones
- Discuss Revision Topics and Training
    1. Subjectivity
    2. Product Availability
    3. Formality
    4. Risk-Based Decision Making
    5. Hazard Identification
    6. Risk Review

Questions?

Stephen Mahoney, JD, MS
Gilead Sciences, Inc.
PhRMA Topic Leader, ICH Q9 (R1)

Resources

- ICH Quality Guidelines (and training materials)
- ICH Q9(R1) Guideline
- ICH Q9(R1) Final Concept Paper (November 12, 2020)
- ICH Q9(R1) Final Business Plan (October 26, 2020)
- ICH Q9(R1) Final Work Plan (February 24, 2023)
- ICH Working Group Presentation: Step 4 document (March 2023)
- FDA Guidance for Industry: Q9(R1) Quality Risk Management

Acknowledgements

- Members of the ICH Q9(R1) Expert Working Group (EWG)
- Members of the ICH Q9(R1) Implementation Working Group (IWG)