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ICH Q9 (R1) Quality Risk Management Revision

By **Paul L. Pluta**

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Peer Reviewed

A revision to ICH Q9 Quality Risk Management (QRM) has been recently approved by the ICH Management Committee (1). ICH Q9 is a key document associated with change management and validation. The original ICH Q9 was issued more than 10 years ago. Relevant documents associated with the approved revision project are linked below.

This topic was endorsed by the ICH Assembly in November 2019. Two primary activities are addressed:

- Limited and specific adjustments to specific chapters and annexes in the current ICH Q9
- Specific training materials with examples to supplement current ICH Q9 and the proposed revisions.

Rapporteur for this project is Dr. Kevin O'Donnell (EC, Europe).
Regulatory Chair is Alex Viehmann, FDA.

The current ICH status is Step 1.

The following summarizes key points associated with the revision as expressed in ICH documents.

FINAL CONCEPT PAPER

The final concept paper was endorsed by the Management Committee on 11-13-2020 (2).

Type of Harmonization Action Proposed

The following harmonization actions are proposed:

1. Four areas of the current ICH Q9 will be addressed.
2. Training materials supplementing ICH Q9 and revisions will be developed. The concept paper specifically commented on the importance of training material and its roll out.

Statement of the Perceived Problem

The benefits envisioned by ICH Q9 have not yet been fully realized. Four areas for improvement are identified:

1. **High levels of subjectivity in risk assessments and in QRM outputs**. Highly subjective risk-scoring methods and assessments by stakeholders can lead to varying levels of QRM effectiveness. Revisions of specific sections and development of training materials with strategies and tools are planned.
2. **Product availability risks.** Emphasis on product quality issues affecting the supply chain predictability will be addressed. New sections on use of QRM in supply chain control, product availability discussion, and training materials

are planned.

3. **Lack of understanding as to what constitutes formality in QRM work**. Deeper understanding of formality to lead to more effective application and execution of QRM activities is needed. Confusion and uncertainty in interpretation of formality currently exists. Degrees of formality, factors for consideration, and related training are planned. *Understanding the Concept of Formality in Quality Risk Management by O'Donnell et al was recently published in JVT (3) and JGXP (4)*.
4. **Lack of clarity in risk-based decision-making.** Clarification of the meaning of good decision-making, use of QRM to improve decision-making, and how risk-based decisions are achieved is needed. Application of information from other industries is available. New sections and revisions with training are planned.

Other suggested points proposed by the ICH Quality Discussion Group include the following:

- Additional clarity on keeping risk assessment current based on lifecycle management is suggested. This concept ties in with ICH Q10 and ICH Q12.
- Risk Identification terminology should be changed to "Hazard Identification" for better relationship to patients and how hazards are perceived and assessed.

Background to the Proposal

When ICHQ9 was introduced in 2005, ICH Q10 was not yet issued. Integration of ICH Q9 and shifting to a proactive focus will enable continual improvement in quality systems.

Expert Working Group (EWG) and Resources

The EWG must address small molecules, new chemical entities, and biological products. Link to the EWG list document is provided.

Timing

The revised guideline and training materials are targeted for completion in June 2022 (ICH Step 4).

Annex 1: Anticipated Benefits of the Proposed Process Revision of IH Q9

Annex 1 of the concept paper discussed specific benefits from the revision and associated activities. Potential benefits identified are as follows:

- Less subjective risk assessments should lead to fewer quality defects that could present risks to patients. The foundational relevance of QRM will enable and accelerate implementation of Q8, Q10, Q11, and Q12.
- Increased emphasis on managing product availability related to manufacturing problems should help to address global supply chain issues.
- Additional clarity on concepts of formality may help ensure that the level of scientific and technical rigor in QRM is commensurate with the level of risk and should help with resource allocation.
- Additional guidance in the area of risk-based decision making should help improve decision quality especially in areas requiring rapid and robust decisions.

Other potential issues benefiting from the Q9 revision include digitization and emerging technologies in manufacturing processes.

FINAL BUSINESS PLAN

The final business plan was endorsed by the Management Committee on 10-26-2020 (5). This document provides more complete discussion and ICH thinking on topics described in the Final Concept Paper. Information and discussion provided in a Q&A format are as follows:

1. **The Issue and its Costs**
    1. What problem/issue is the proposed expected to tackle?
    2. What are the costs (social/health and financial) to our stakeholders associated with the current situation or associated with "non-action"?

2. **Planning**
    1. What are the main deliverables?
    2. What resources (financial and human) would be required?
    3. What is the timeframe of the project?
    4. What will be the key milestones?
    5. What special actions to advance the topic through ICH, e.g., stakeholder engagement or training, can be anticipated either in the development of the guideline or for its implementation?
3. **The Impacts of the Project**
    1. What are the likely benefits (social, health, and financial) to our key stakeholders of the fulfillment of the objective?
    2. What are the regulatory implications of the proposed work – is the topic feasible (implementable) from a regulatory standpoint?
    3. Will the guideline have implications for the submission of content in the CTD/eCTD? If so, how will the working group address submission of content in the dossier? Will a consult be requested with the ICH M8 Working Group??
4. **Post-Hoc Evaluation**
    1. How and when will the results of the work be evaluated?

Q9 EWG QUALITY RISK MANAGEMENT

Members of the Expert Working Group assembled for the ICH Q9 revision are listed below (6).

ANVISA, Brazil	Ms. Nathalie Dias Kuwabara
EC, Europe	Dr. Giampiero Lorenti, Mr. Andrei Spinei
EDQM	Dr. Cristina Baccarelli
EFPIA	Dr. Peer Schmidt, Michael Schousboe
FDA, United States	Mr. Rick Friedman, Mr. Alexey Khrenov
Global Self-Cate Federation	Ms. Jennifer Ahearn
IFPMA	Mr. Xuejian (Jerry) Xu, Mr. Seungmin Yu
IGBA	J. Paul McCall
JPMA	Hiroshi Fujie
MFDS, Republic of Korea	Ms. Miseop Choi
MHLW/PDMA, Japan	Aki Aoyama, Tomoaki Sakamoto
NMPA, China	Yi Cao
PhRMA	Stephen Mahoney, Dr. Timothy J.N. Watson
PIC/S	Dr. Karmin Saadat
Swissmedic, Switzerland	Mr. Markus Escandari
TFDA, Chinese Taipei	Ling-Fu Nieh

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