ICH Q9 QRM – The guideline on Quality Risk Management

"Your best friend or your worst enemy?"

January 2020

www.stepwiseengineering.com

CLOSER TO EXCELLENCE

stepwise®

PHARMA & ENGINEERING

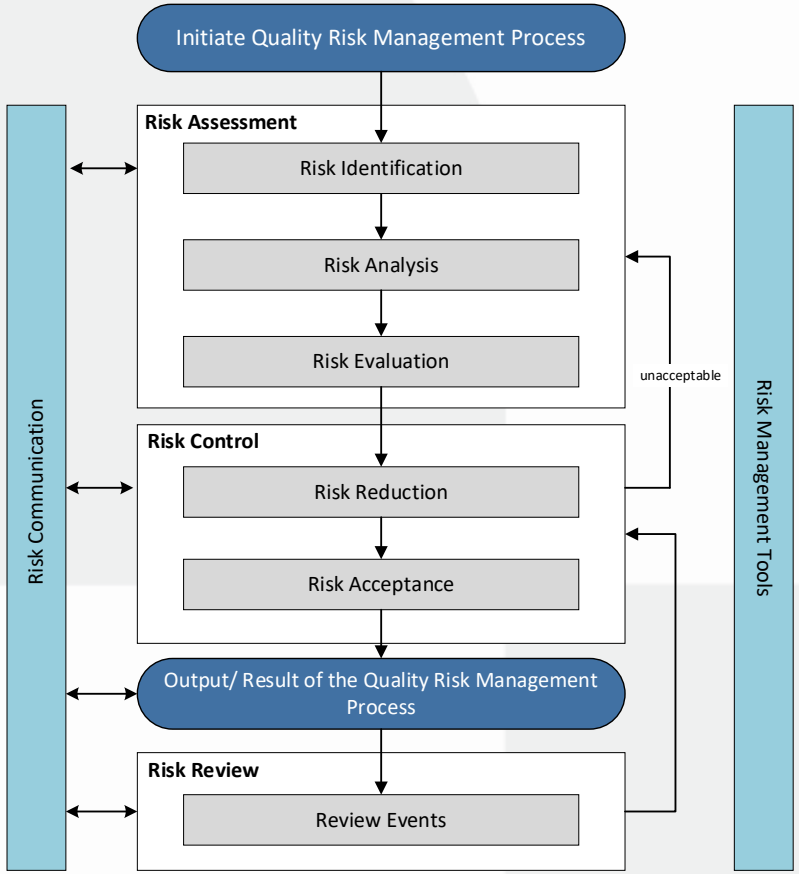
ICH Q9 Guideline

ICH Q9, Quality Risk Management was issue in June 2006.

"This guideline provides principles and examples of tools for quality risk management that can be applied to different aspects of pharmaceutical quality. These aspects include development, manufacturing, distribution, and the inspection and submission/review processes **throughout the lifecycle** of drug substances, drug (medicinal) products, biological and biotechnological products (including the use of raw materials, solvents, excipients, packaging and labeling materials in drug (medicinal) products, biological and biotechnological products).

Two primary principles of quality risk management are:

- The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the **protection of the patient**;
- The **level of effort**, formality and documentation of the quality risk management process should be **commensurate with the level of risk**."



You might expect, after 11 years, the industry would be fully on board with the practices recommended in this document, but we may not have come as far as one might think in the area of risk estimation.

Risk Assessment

After initiating a QRM process you should identify, analyze and evaluate your risks in order to answer the following questions:

- What might go wrong?
- What is the likelihood (probability) it will go wrong?
- What are the consequences (severity)?

Risk identification: Identification of the risks or potential sources of harm (hazards)

Risk analysis: Estimation of the risk associated with the identified hazards.

Risk evaluation: Compares the identified and analyzed risk against given risk criteria. Usually a "risk score" is used to estimate the risk according to his severity, occurrence and detection probabilities.

Risk Control

Risk control has in general 2 phases that might answer the following questions:

- Is the risk above an acceptable level?
- What can be done to reduce or eliminate risks?
- What is the appropriate balance among benefits, risks and resources?
- Are new risks introduced as a result of the identified risks being controlled?

Risk Reduction: focus on processes to mitigate or avoid quality risk when it exceeds a specified (acceptable) level. This phase includes an action plan to mitigate occurrence and detection probabilities.

Risk Acceptance: Reevaluation of the risk level and a final decision to accept risk level outcome.

All QRM system stands in the quality estimation criteria

Risk Criteria – Examples

ICH Q9 does not contemplate a standard risk criteria. This aspect is developed by each company. The scoring use systems varies from the basic score (3,2,1) to enhanced or more complex systems.

Example 1: (basic scoring (3,2,1) system)

Severity	(S)	Description	Occurance	(O)	Description	Detectability	(D)	Description	Evaluation Outcome
High	3	High potential to influence the quality or safety of the product; High impact on yield or production capability	High	3	> 10% of units from a batch (or expected to reach this level)	Low	3	Control system in place has a low probability of detecting the defect	**HIGH: SxOxD >12** (You must review your control system)
Moderate	2	May influence the quality or safety of the product; moderate impact on yield or production capability	Moderate	2	<10% of units per batch	Moderate	2	Control system in place may or may not detect the defect	**MODERATE: 6<SxOxD ≤12** (You must review your control system)
Low	1	No potential impact on product quality, yield or production capability	Extremely low	1	<1% of units per batch	High	1	Control system in place has a high probability detecting the defect	**LOW: SxOxD≤6** (No further control needed)

Risk Criteria – Examples

Example 2: (More complex system: WHO, "Deviation Handling and Quality Risk Management" relating to deviations and QRM for the manufacture of prequalified vaccines for supply to United Nations agencies)

Severity	(S)	Description	Occurance	(O)	Description	Detectability	(D)	Description	Evaluation Outcome
Critical	54	Serious GMP non-compliance;	High	8	Highly probable to occur	Extremely Low	8	Control system in place has a high probability of detecting the defect or its effects.	**HIGH: SxOxD >216** (You must review your control system)
High	6	Major GMP non-compliance;	Moderate	6	Probable to occur	Low	6	Control system in place has a low probability of detecting the defect	
Moderate	4	More than one minor GMP non-compliance;	Low	4	Improbable to occur	Moderate	4	Control system in place may or may not detect the defect	**MODERATE: 40<SxOxD <216** (You must review your control system)
Low	2	Minor GMP non-compliance;	Extremely low	2	Highly improbable to occur	High	2	Control system in place has a high probability detecting the effect	**LOW: SxOxD≤ 40** (No further control needed)

Risk Criteria – Examples

Hypothetical statement: A pharmaceutical company will produce over 1,000,000 units of a sterile product per year. Experience shows that an average of 2000 complaints are received per year related with incorrect sealing. Once this failure compromises the sterility of the product what can cause microbial contamination that will have serious impacts on patient health, a QRM process must be applied.

Lets see what would be the outcome of the two examples seen if we applied them:

Example 1:

Severity	Occurrence	Detectability
High (S)=3	Low (O)=1	Moderate (D)=2

Outcome: LOW RISK

No further control needed

Example 1: Not adequate risk criteria

This could cause the release of a potential dangerous product to the market

Example 2:

Severity	Occurrence	Detectability
Critical (S)=54	Moderate (O)=6	Moderate (D)=4

Outcome: HIGH RISK

You must review your control system

Example 2: This criteria is adequate for this statement

Conclusions

- "It is better to be safe than sorry", The aim of this guideline should be to know your risks and prevent them from happen instead of correcting them;
- You should have a **rigorous**, **well-structured** and **science based** Quality Risk Management System that assures compliance of your company products, processes and systems; Depending on the company complexity, one may implement a more simple system (example 1) as long as you guarantee that it will not result in the oversight of potentially high severity risks;
- You must not use QRM to miss qualify your risks;
- Despite of the risk criteria you should always have a **critical judgement**. If you find the risk estimation criteria underestimate the risk level itself, you should communicate and review the risk criteria;

Key Words of QRM:

- Risk Estimation Criteria
- Prevent
- Communicate
- **Review!**

References

1. European Medicines Agency (EMA), “ICH Guideline Q9 on quality risk management”, 2015.
2. European Commission, “EudraLex Volume 4 - Part 1: EU Guidelines for GMP for Medical Products for Human and Veterinary Use; Chapter 1 - Pharmaceutical Quality System,”, 2012.
3. WHO Expert Committee on Specifications for Pharmaceutical Preparations, “WHO guidelines on quality risk management. Annex 2,” *WHO Technical Report Series.*, no. No. 981, 2013.
4. WHO/ EMP/ HIS, “Deviation Handling and Quality Risk Management,” *World Health Organization*, 2013.
5. R. Carmichael, “Flaws to Quality Risk Management,” *NSF International*, 2020.
6. P. Gough, “A Beginner’s Guide to Quality Risk Management (QRM),” *NSF International*, 2017.

About Stepwise

Engineering Services tailored for Pharma industries

Stepwise's offers services differentiate from other engineering companies by being tailored for the highly GMP-regulated pharmaceutical and life sciences industries.

The entire pharmaceutical and life science industries manufacturing lifecycle is supported by us helping to set direction, assessing benefits of strategic investments and optimizing manufacturing and business processes.

We assist our customers from Research and Development (R&D) to Commercial manufacturing.

Our goal is to help our customers to achieve and maintain GMP manufacturing excellence and assist them in the route to market.

The Author:

Bruna Coelho
Junior Pharma Consultant

The Team:

Aldo Vidinha
CEO & Founder

Nuno Santos
Business Manager- Pharma

João Silva
Junior Pharma Consultant

WWW.STEPWISEENGINEERING.COM