Formal vs. Informal Quality Risk Management – A neglected concept

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Why talk about formality in QRM?

- QRM is an area of active research at **HPRA**, in collaboration with the DIT’s **Pharmaceutical Regulatory Science Team** (PRST) and **Regulatory Science Ireland** (RSI)

- **McGee Pharma International** (MPI) is also heavily involved in QRM as part of its consulting activities with the industry

  - **We are collectively working to promote more effective and science-based risk assessment and QRM activities**

  - **Formality in QRM is at the core of ICH Q9, but this area has received little research attention to date**... and is probably not well understood

  - **A better understanding of formality in QRM may prove beneficial for the industry and regulators alike**
ICH Q9…. Remember this?
Formality in QRM - ICH Q9

Introduction

• It is neither always appropriate nor always necessary to use a *formal* risk assessment process (using recognised tools and/or internal procedures, e.g. SOPs). The use of *informal* risk management processes (using empirical tools and/or internal procedures) can also be considered acceptable.

3. Principles of QRM

• The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient; and

• The level of effort, *formality* and documentation of the quality risk management process should be commensurate with the level of risk.

4.4. Risk control

• Risk acceptance can be a *formal* decision to accept the residual risk or it can be a passive decision in which residual risks are not specified.
ICH Q9 cont’d

5. Risk Management Methodology

• Traditionally, risks to quality have been assessed in a variety of informal ways (empirical and/or internal procedures) based on, e.g., compilation of observations, trends and other information.

• Such approaches continue to provide useful information that might support topics such as handling of complaints, quality defects, deviations and allocation of resources.

• Additionally, the pharmaceutical industry and regulators can assess and manage risk using recognised risk management tools and/or internal procedures (e.g. SOPs)

• Below is a non-exhaustive list of some of these tools:
  – Basic Risk Management Facilitation Methods (flowcharts, check sheets, etc.)
  – FMEA, FMECA, FTA, HACCP, HAZOP, PHA, Risk Ranking and Filtering, Supporting Statistical Tools
ICH Q9 cont’d

5. Risk Management Methodology

• The degree of rigor and *formality* of QRM should reflect available knowledge and be commensurate with the complexity and/or criticality of the issue to be addressed
But what does formal vs. informal QRM actually mean in practice?

How can different degrees of formality be applied and still manage risks effectively?

Will the regulators accept informal QRM?
Other questions worth studying...

• **When is it appropriate** to apply informal QRM in a GMP setting?
• **What tools**, if any, would be considered as informal?
• What are the **benefits** of using informal approaches over formal ones?
• Can informal QRM be used to support **qualification and validation**?
• How would a company **document** its informal QRM activities?
• In Oct 2015, **Annex 15** strengthened the requirements for risk-based validation, stating states: “**The way in which risk assessments are used to support validation activities should be clearly documented**”.
  – Can a company use **informal** risk assessment to **comply** with this Annex 15 requirement, or must it always use a more formal approach?
Today’s Workshop

We will explore some of these questions and gauge the level of interest in doing further work in this area.
Workshop Activity 1 – QRM & Level of Formality (20 mins)

1. What do you see as the difference between Risk Assessment and Quality Risk Management?

2. Write down 5 words or phrases that you would apply to **Formal** QRM and to **Informal** QRM
Workshop Activity 1 contd (20 mins)

3. In terms of formality, complete these sentences….
   - *Risk Assessment is highly formalised when*....
   - *Informal Risk Assessment is when*....
   - *QRM is highly formalised when*....
   - *Informal QRM is when*....

4. **True or False:** *I would generally consider formal QRM to be superior to informal QRM*
Workshop Activity 2 (20mins)

Consider the following ICH slide on when to use formal vs. informal QRM

- What is its key message about formal vs. informal?
- Does this reflect your own thinking?
- Is this an approach you currently have in your own quality system?
Slide from the ICH Q9 Toolbox...

Should risks be assessed?

- Are there clear rules for decision making? (e.g., regulations)
  - No or justification needed
    - Can you answer the risk assessment questions?
      - Yes "informal RM"
        - Initiate Risk assessment (risk identification, analysis & evaluation)
          - Run risk control (select appropriate measures)
            - Select a Risk Management tool (if appropriate e.g. see ICH Q9 Annex I)
              - Carry out the quality risk management process
                - Document the steps
        - No "formal RM"
          - Agree on a team (small project)
            - Document results, decisions and actions
    - No RM
      - Risk assessment not required (No flexibility)
        - Follow procedures (e.g., Standard Operating Procedures)
Workshop Activity 3 (20mins)

What kind of QRM approach (None, Informal or Formal) might be best applied to these two situations?

- A change control to install a PAT analyser (for moisture determination) in a granulate drying process

- A deviation involving a broken metal mesh screen in an API process

Outline the approach you will use and justify it.
What risks are you trying to manage?
Do you have key questions to ask before you make a decision?
Open Discussion…

• **What do you think** about the topic of formality in QRM?
• Does it merit **further study and research**?
• Is there a need for **guidance** in the GMPs about it?
• Are you **interested** in PDA engaging on this topic further?
• What **next steps** would be useful?