FLAWS TO QUALITY RISK MANAGEMENT

Compliance to ICH Q9 Quality Risk Management (QRM) became a mandatory requirement in the EU, when it was adopted into EU GMP Chapter 1. Companies were expected to identify and understand their risks, and ensure the appropriate technical and organizational controls are in place to minimize the potential impact on patients.

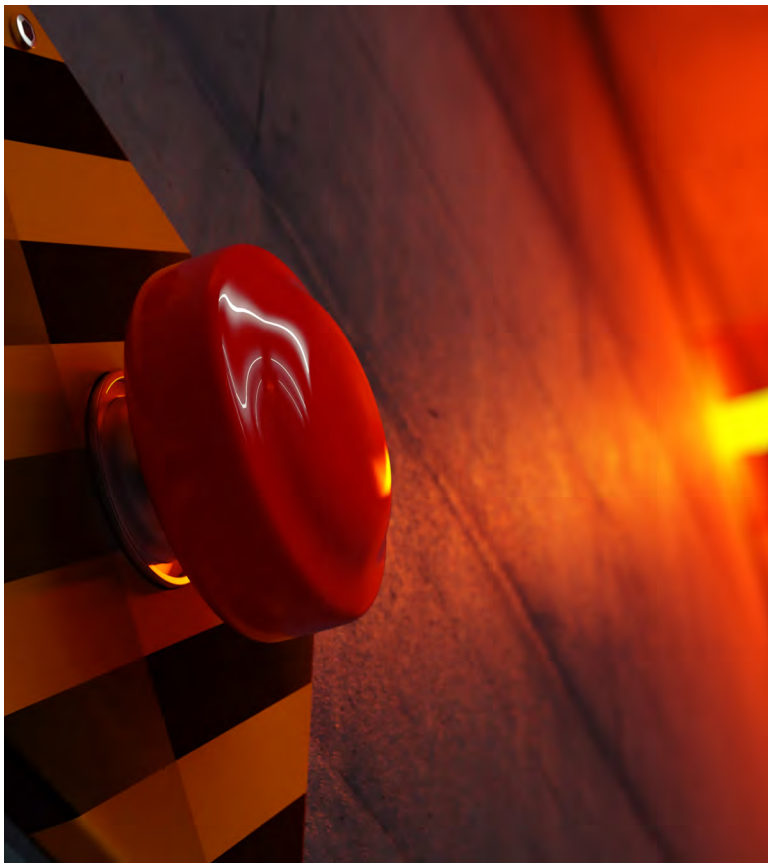
Most companies introduced a formal risk management process, yet very few actually changed the way they operate, thus failing to become more proactive in addressing problems.

QRM has been raised as a topic regularly at MHRA GMP symposia, yet at the recent GDP Symposium in Glasgow, Alan Bentley (Senior GDP Inspector), described risk-based activities as "something that goes spectacularly wrong at times." What's going wrong?

A QRM system depends on:

- Formalized procedures
- Trained and competent personnel
- Specific written instructions for the actual activities being undertaken
- A strong methodology with clear criteria for scoring of risk
- A reporting process

NSF has experience of companies that have conducted hundreds of risk assessments but failed to do anything at all with the output. It has been filed and forgotten rather than being used to steer the assessors to consider actions to reduce or eliminate risk and to balance benefits, risks and resources. There should be a clear and timely communication and escalation route for risk assessments within the company. Just because data is there, in a shared drive, it does not mean it has been communicated. We may have formed



our message and transmitted it but there needs to be someone to receive it and make sense of it. Risk assessments have become a source of bureaucratic inaction.

Weak methodologies can be behind some spectacular failures. Some systems appear to be deliberately designed to ensure that no action would ever be required! You could never score high enough numbers to warrant action, which is obviously of no use to anyone.

In 2013, WHO issued the draft document, Deviation Handling and Quality Risk Management, relating to deviations and QRM for the manufacture of prequalified vaccines for supply to United Nations agencies. The scoring system is worth considering as it ensures that potentially serious issues cannot be ignored.

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SEVERITY SCORES (WHO):

SEVERITY	(S)	DESCRIPTION
Low	2	Minor GMP non-compliance; no possible impact on patient, yield or production capability
Moderate	4	More than one minor GMP non-compliance; possible impact on patient; moderate impact on yield or production capability
High	6	Major GMP non-compliance; probable impact on patient; high impact on yield or production capability
Critical	54	Serious GMP non-compliance; probable serious harm or death; critical impact on yield or production capability

OCCURRENCE SCORES (WHO):

OCCURRENCE	(O)	DESCRIPTION
Extremely low	2	Highly improbable to occur
Low	4	Improbable to occur
Moderate	6	Probable to occur
High	8	Highly probable to occur

DETECTABILITY SCORES (WHO):

DETECTABILITY	(D)	DESCRIPTION
High	2	Control system in place has a high probability of detecting the defect or its effects.
Moderate	4	Control system in place could detect the defect or its effects.
Low	6	Control system in place has a low probability of detecting the defect or its effects.
Non existent	8	There is no control system to detect the defect.

As with all FMEA systems, the risk prioritization number (RPN) is SxOxD, and risk is classified as:

High if > or equal to 216

Medium if >40 and <216

Low if ≤40

Let us consider an event where a complaint is received for a sterile liquid in a glass container, capped with a non-integral container closure. It is a repeat event (noted on 1,500 occasions in the last four years). Purely at the gut feel level it cannot be ignored. Using the WHO methodology, you could identify the scoring as:

Severity, critical (54), serious GMP non-compliance; probably serious harm or death; critical impact on yield or production capability.

Occurrence, moderate (6), probable to occur, may happen.

Detectability, moderate (4), control system in place could detect the defect or its effects.

So, the RPN would be 1,296 so easily classified as critical.

Using some basic scoring systems of risk (3, 2 or 1) could allow this issue not to be classified as high and an important opportunity to seek improvement could be missed.

Looking more closely:

SEVERITY – BASIC SCORES

1 Minor GxP non-compliance – no potential impact on product or patient, yield or production capability

2 Significant GxP non-compliance, potential impact on patient; moderate impact on yield or production capability

3 Serious GxP non-compliance. Probable serious harm or death, critical impact on yield or production capability

OCCURRENCE – BASIC SCORES

1 Improbable to occur. Rare event – <1% of units from a batch

2 Probable to occur. May happen – <10% of units from a batch

3 Highly probable to occur. Realistic chance/ expected to happen. > 10% of units from a batch

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DETECTABILITY – BASIC SCORES

1 Control system in place has a high probability of detecting the defect or its effects.

2 Control system in place could detect the defect or its effects.

3 There is no control system to detect the defect.

Severity should be very high (scoring 3), as it is a potentially leaking sterile product in the marketplace.

Occurrence – 1,500 over four years, 0.4% of our 375,000 units a year could score 1.

Detectability is not easy to see before shipping but there is a check in place so there is a system (scoring 2).

So, the RPN (SxOxD) could be just 6 which is unlikely to raise the required red flags that this example should warrant.

If your methodology could allow potentially critically flawed product to be ignored, it is time to consider your approach. FMEA may not achieve the desired outcome.

In conclusion it is time to **STOP** using ICH Q9 to obscure or downgrade issues, or to justify the indefensible or inaction. Please make 2020 the year you **STOP** using ICH Q9 to hide quality issues in your organization. Contact us at **pharmamail@nsf.org** with any questions.

ABOUT THE AUTHOR

Rachel Carmichael has over 20 years' experience of pharmaceutical manufacture, control and quality management including nearly 11 years as a GMDP Inspector for the UK Competent Authority, the MHRA. This includes serving as the lead inspector representative within the MHRA for the transition from the Medicines Act to the Human Medicines Regulation, SI 2012 1916.

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