Risk Based Decision Making – using knowledge of risk throughout the lifecycle

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ICH Q9(R1): The Next Frontier

An audience with international thought leaders exploring how the effective use of knowledge can enhance QRM outcomes to benefit the patient

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Outline

Risk Based Decision Making – using knowledge of risk throughout the lifecycle

- Brief re-cap of ICH Q9R1 regarding Risk Based Decision Making
- Examples of different Risk Based decisions using knowledge from other QRM activities
- Learnings regarding setting up decision processes

ICH Q9R1 now describes risk based decision-making

Short re-cap of ICH Q9R1

Risk-Based Decision-Making:
An approach to, or a process of, making decisions that considers knowledge about risks relevant to the decision and whether risks are at an acceptable level.
ICH Q9R1

- Risk based decision-making is inherent in all Quality Risk Management activities
- Risk based decision-making requires use of knowledge, so management of knowledge is important throughout the lifecycle
- There can be varying degrees of structure with regard to approaches for risk-based decision-making – these are closely related to the level of formality applied

Different structured approaches to risk based decisions

Short re-cap of ICH Q9R1

- In general, higher levels of formality in QRM require higher levels of structure in relation to risk-based decision making
- There can be varying degrees of structure, and these should be considered in a continuum or spectrum
- The different approaches to risk-based decision-making are beneficial because they address uncertainty through the use of knowledge, facilitating informed decisions

Highly structured approaches

- Highly structured that can involve formal analysis of available options before decision
- In depth consideration of relevant factors
- Typicaly used for high importance and high uncertainty and/or complexity

Less structured approaches

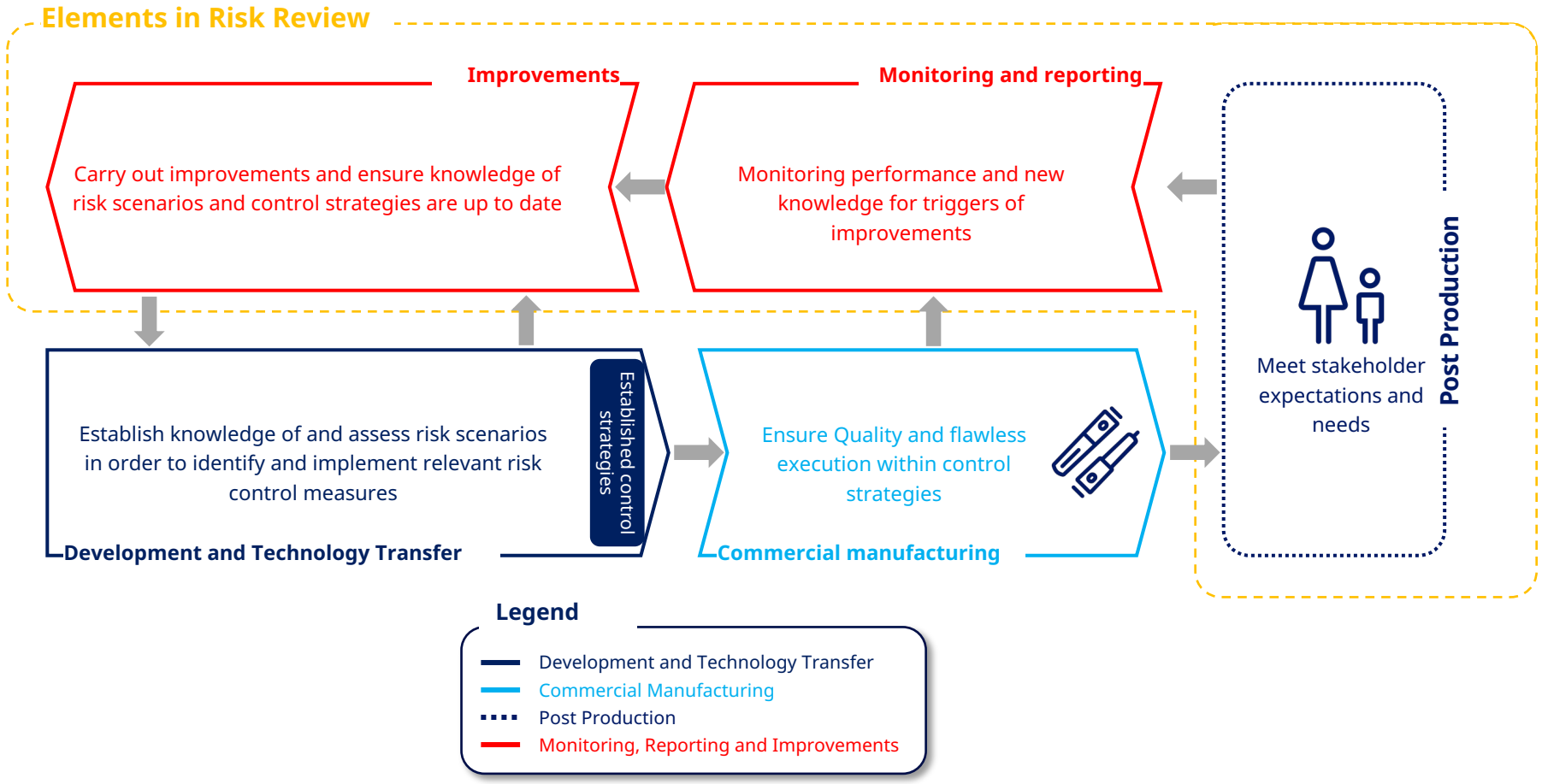
- Simpler approaches used to lead decisions
- Primarilly uses existing knowledge
- Typically used where uncertainty and complexity is lower

Rule based approaches

- SOPs, policies or rules in place to guide decisions into predetermined outcomes
- No new risk assessment is needed – uses previously obtained understanding of risk
- Typically used for quick response when uncertainty and/or complexity is low

QRM supports decisions across the QMS

A lifecycle view to QRM and knowledge



Transport Risk management model

Example of risk based decision

- The model was created to help evaluate risk and acceptability of specific individual transports of products in planning
- The model was created using existing understanding of risk scenarios related to transport of each product, and an understanding of how complexity and existing mitigations would impact.

Risk(RPN) =

Severity
- Product type
- Climate zone

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Occurrence
- Transport complexity
- Thermo equipment
- Qualification/Validation

*

Detectability
- Degree of temperature logging

High: Mitigate to reduce risk

Medium: Monitor the risk

Low: Acceptable – no action

Warehouse validation setup

Example of risk based decision

The model was created to help decide the following when defining the validation strategy:

- Effort used for temperature distribution testing
- Amount of load and use pattern testing
- Need for seasonal variation testing
- Monitoring setup in normal operation

Input parameters

Goods stored (Impact)

- Sensitivity of goods stored to temperature outside specified tempeature before impact
- Goods type (Product Impact)

Facility construction and use (Probability)

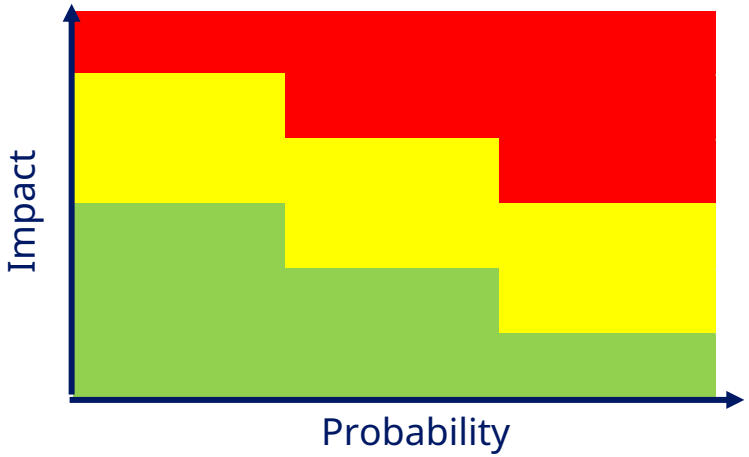
- Is a variation in temperature expected across the room (considering the design)
- Expected effect of typical load and use patterns
- Expected effect of seasonal variation

Warehouse validation setup

Example of risk based decision

	Choose the scenario from the drop down menu that best fits your case			Rating	Rationale
Goods stored	How sensitive is the goods evaluated to be when stored in temperatures outside the specified range for the room?	Goods is known or estimated to be very stable outside room specification for more than a day (>24H)	L	H	Explain rationale for score here or attach enclosure
		Goods is known or estimated to be moderate stable outside room specification for less than a day but more than an hour (1H < t < 24H))	M		
		Goods is known or estimated to be unstable outside room specification for less than an hour (<1H) or Temperature sensitivity for goods outside room specification is unknown/unspecified or cannot be estimated	H		
	Goods type	Supporting materials: (e.g. equipment components, cleaning agents, plast components, plast granulla)	L	H	Explain rationale for score here or attach enclosure
		Product matrix materials: (e.g. Intermediate, API, excipients, raw materials)	H		

- The outcome is defined using a specific risk acceptability grid/model for each decision
- A tool was created to provide text outcomes for each decision based on the provided input variables



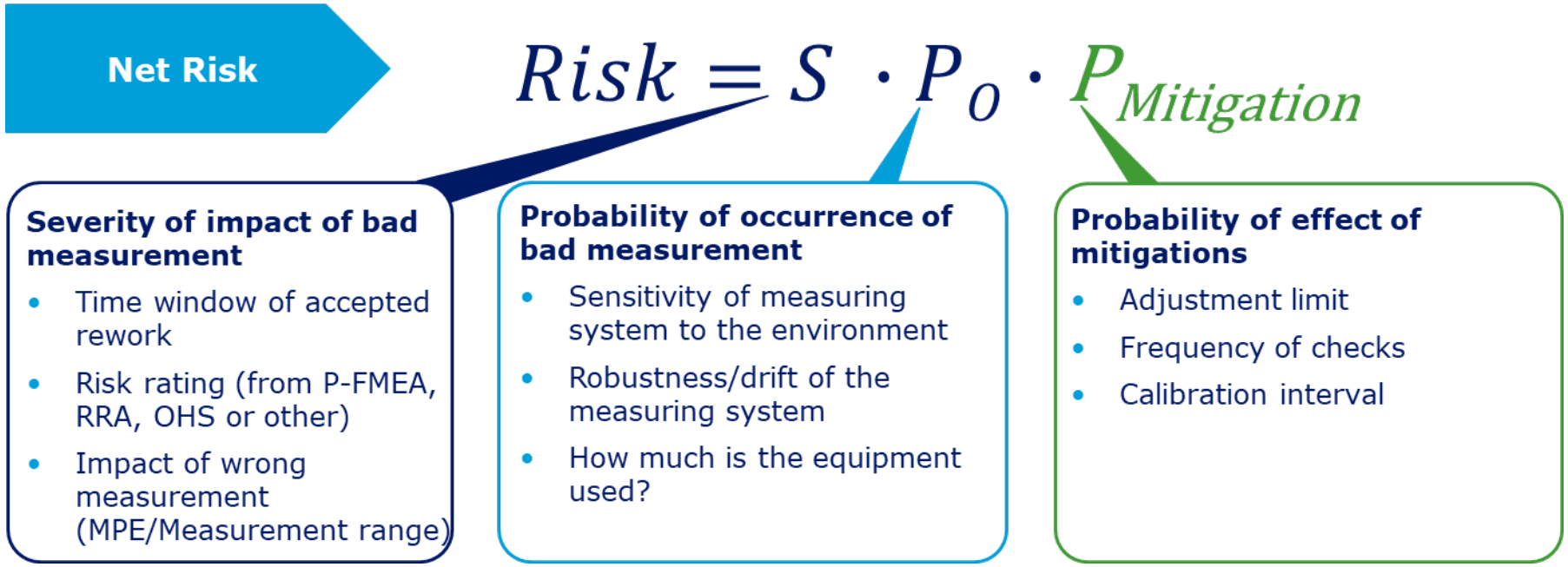
Effort used for temperature distribution testing

Low	No temperature mapping needed in empty state
Med	Temperature mapping with a few sensors to identify hot and cold spot for monitoring - could be done in connection with load and use test
High	Extensive temperature mapping with many sensors reflecting complexity of the room design

Defining calibration intervals

Example of risk based decision

- The model was created to help define acceptable combinations of calibration interval, adjustment limits and checks
- It builds on understanding of how measurements can stay within Maximum Permissable Error (MPE), and what drives impact and variation



Defining calibration intervals

Example of risk based decision

Chose the scenario that best fit your measuring equipment.

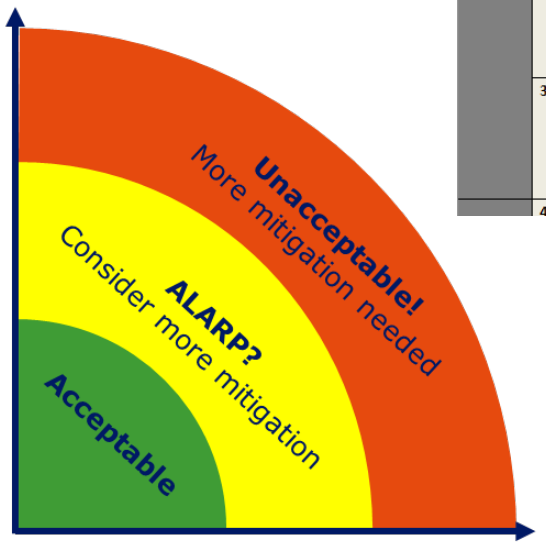
		Question	Low	Medium	High	Score
Impact	1	How long time can you risk to have an equipment which exceeds MPE (how long time are you willing to go back in your documentation if calibration fails)?	14-36 months	8-13 months	0-7 months	
			○ Low	○ Medium	◉ High	3
	2	What is the risk rating of the measurement or parameter in the related risk assessment (p-FMEA, RRA, FMECA or similar)?	Low Risk: No consequences or unlikely impact on product quality	Medium Risk: Potential impact on product quality	High Risk: Impact on product quality	
			○ Low	○ Medium	◉ High	3
		What is the environmental, health and safety rating?	Minor/Moderate	Major	Critical	
			○ Low	○ Medium	◉ High	3
	3	How much does MPE or uncertainty make of the range between lower and upper limit of the measurand ((MPE or U)/((Upper limit-Lower limit)))?	Less than 10%	10-30%	More than 30%	
			○ Low	○ Medium	◉ High	3
	4	Does the environment impact the	No	Yes, but mitigating activities are	Yes	

S_{Impact}

- Time window of accepted rework
- Risk rating from other risk assessments
- Impact of wrong measurement (MPE/Measurement range)

$P_{Occurrence}$

- Sensitivity of measuring system to the environment
- Robustness/drift of the measuring system
- How much is the equipment used?



$P_{Mitigations}$

- Adjustment limit
- Frequency of checks
- Calibration interval

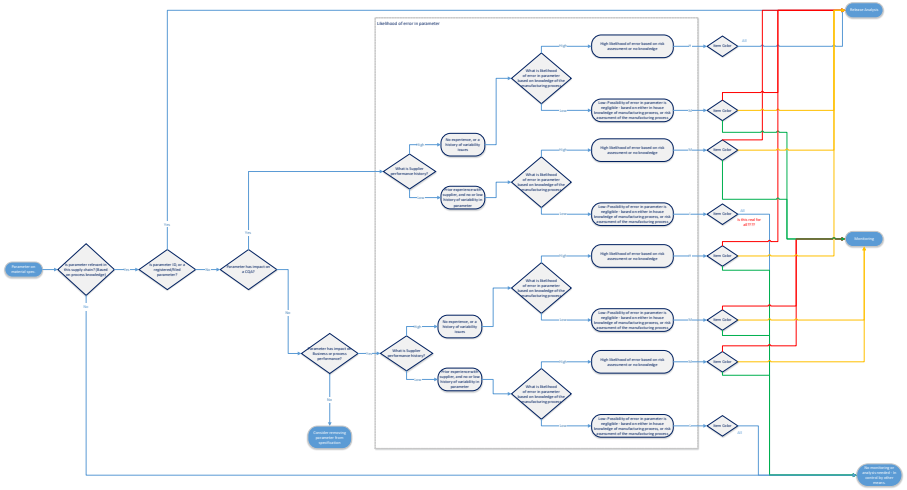
learnings regarding setting up decision processes

- **Scope and resolution:**
  Clarify what the decision is about, and what the expected outcomes should be

- **Teamwork!:**
  A good mix of QRM expertice, and business understanding

- **Variables:**
  Clarify what information is needed to take the decision – and what is expected to be known already

- **Business logic:**
  Use existing knowledge and understandning of risk scenarios, the uncertainty and complexity to establish variability and acceptability in the model



Questions?