

Integration of QRM in Quality Management Systems

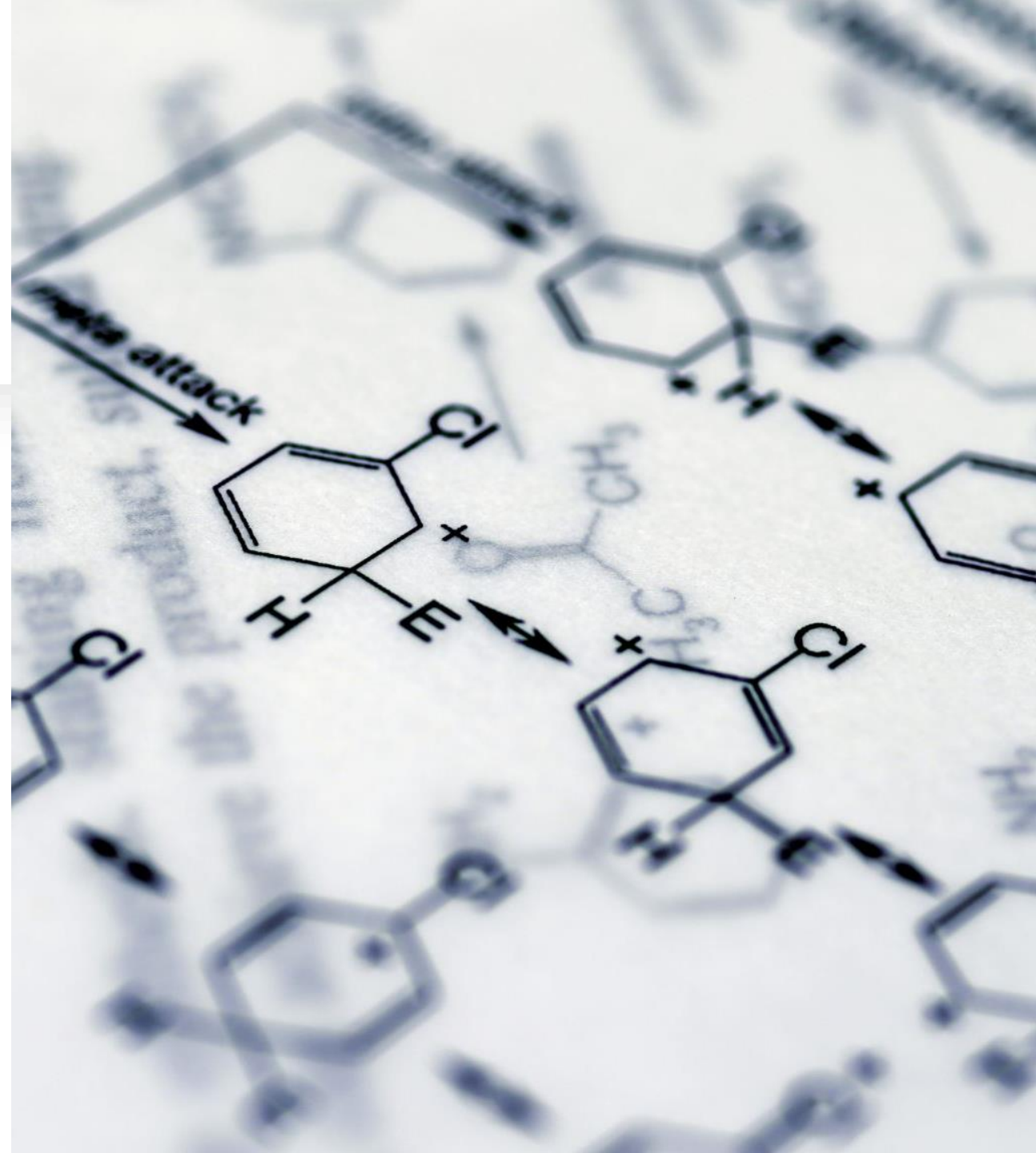
Quality Management System Applications of Risk-Based Decision-Making Approaches

Welcome

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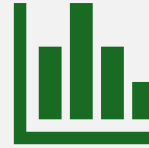
Work: 25+ years in the pharmaceutical
industry in the areas of Laboratory, Quality
Assurance, Auditing and External
Manufacturing. I have been at MSD for 9
years, currently in the manufacturing
division maintaining the Quality Risk
Management topic global standards.



Purpose of ICH Q9 (R1)



PROACTIVE AND SYSTEMATIC
PROCESS FOR IDENTIFYING AND
MANAGING RISKS



ORGANIZATION OF DATA TO
DECIDE ON WHAT RISKS ARE
PRIORITIZED BY THE COMPANY



PROVIDES EXAMPLE OF
PRACTICAL TOOLS AND
APPLICATION FOR THE DIFFERENT
QUALITY ASPECTS IN PQS



PREDICT POTENTIAL RISKS TO
AVOID ITS REALIZATION USING
SCIENCE-BACKED DATA



AIM: IMPROVE PRODUCT QUALITY
AND ENSURE PATIENT SAFETY

Summary of Revisions

Managing And Minimizing Subjectivity

- Level Setting Perceptions
- Well-designed Risk Scoring Scales
- Improved Risk Questions
- Surfacing Assumptions And Controlling Bias

Product Availability Risks From Quality / Manufacturing Issues

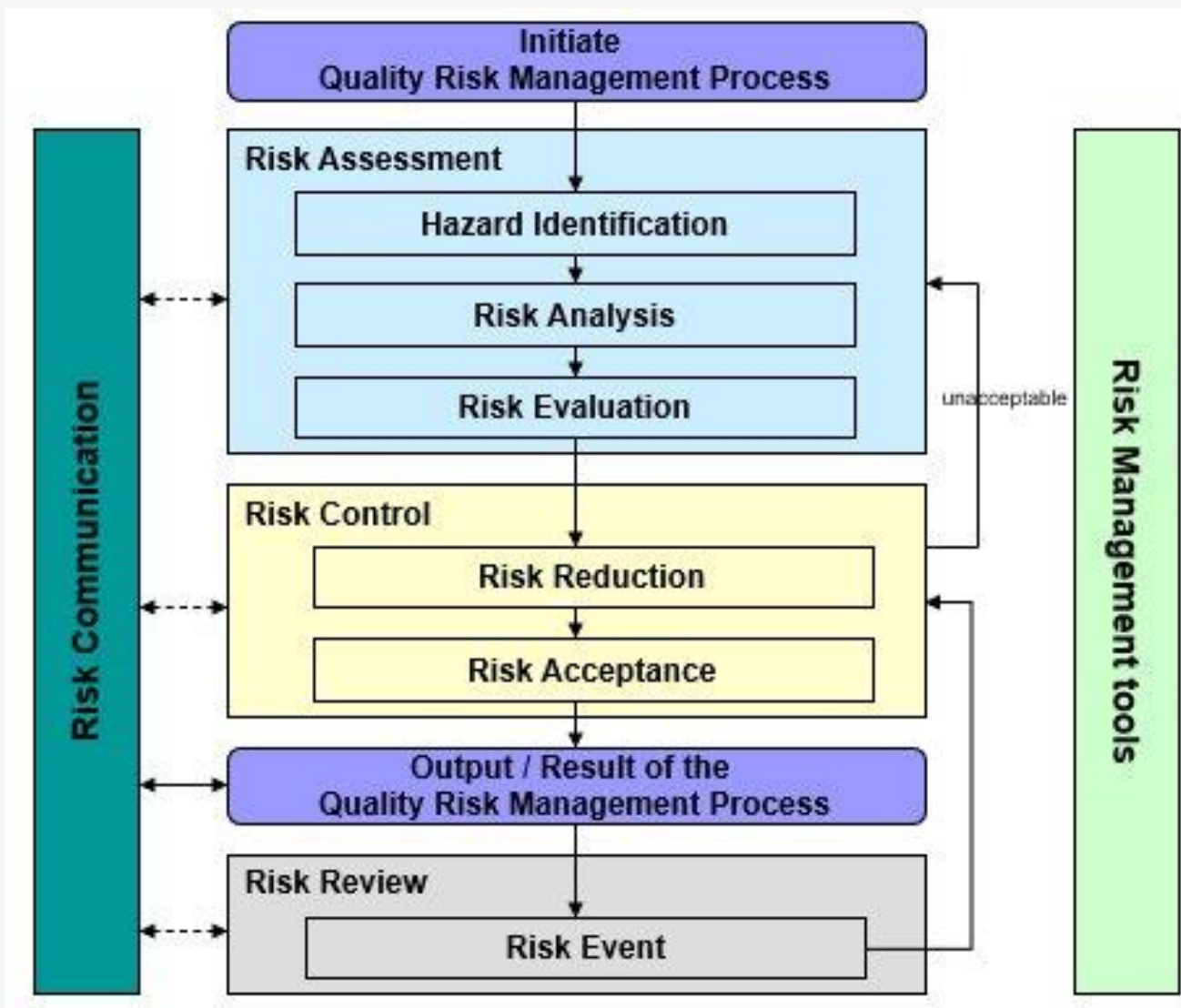
- Monitor And Investigate Departures From States Of Control
- Modernization
- Maintenance And Automation Of Facilities And Equipment
- Initial Qualification And Continual Oversight Of Outsourced Activities And Supplies

Formality In QRM

- Extent Of Uncertainty, Complexity And Importance
- Efficiently Manage Resources
- Support Robustness Of The QRM Process

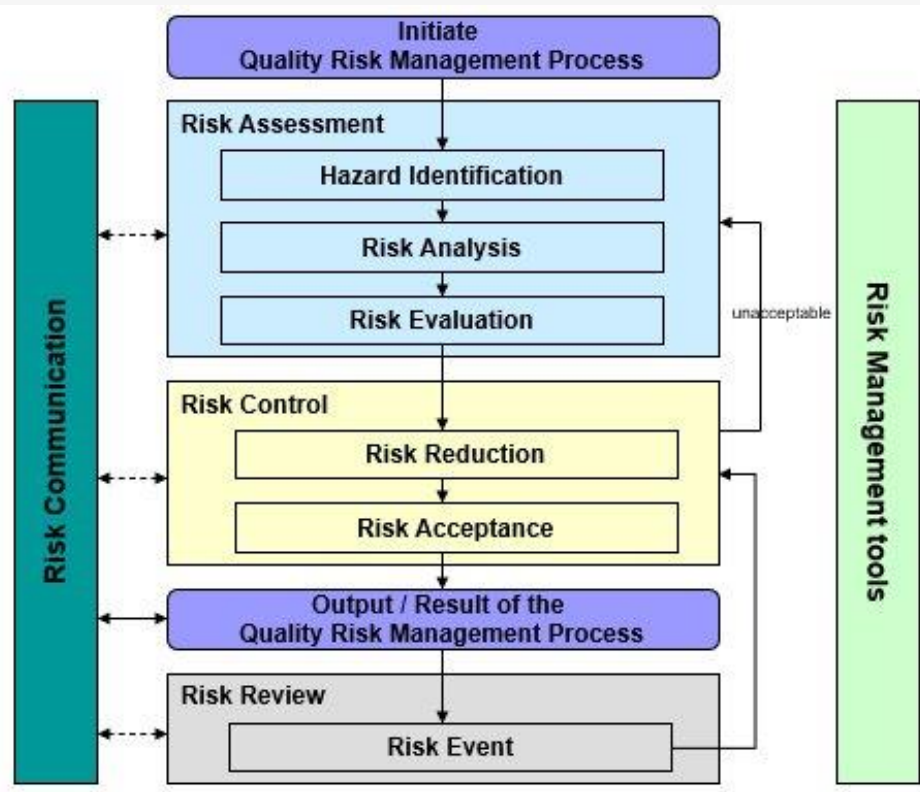
Risk-based Decision-making

- Bond Between QRM And Knowledge Management
- Uncertainties As A Driver For The Degree Of Structure
- Can Guide Level Of Effort, Formality And Documentation



Initiation

- Initiation of QRM activities include planning activities:
- Define risk question and objective for Product/Process/System to be assessed/evaluated
- Identify what is IN and OUT of scope
- Identify methodology, expected outcomes and rationale for tool selection
- Develop communication plan
- Gathering resources
- Identifying role assignments
- **The better the preparation, the better the end results will be!**
- **Communication is performed at any stage to inform decision-makers and stakeholders**
- **Tools provide structured techniques for assessing, and selection must appropriate for the risk question**

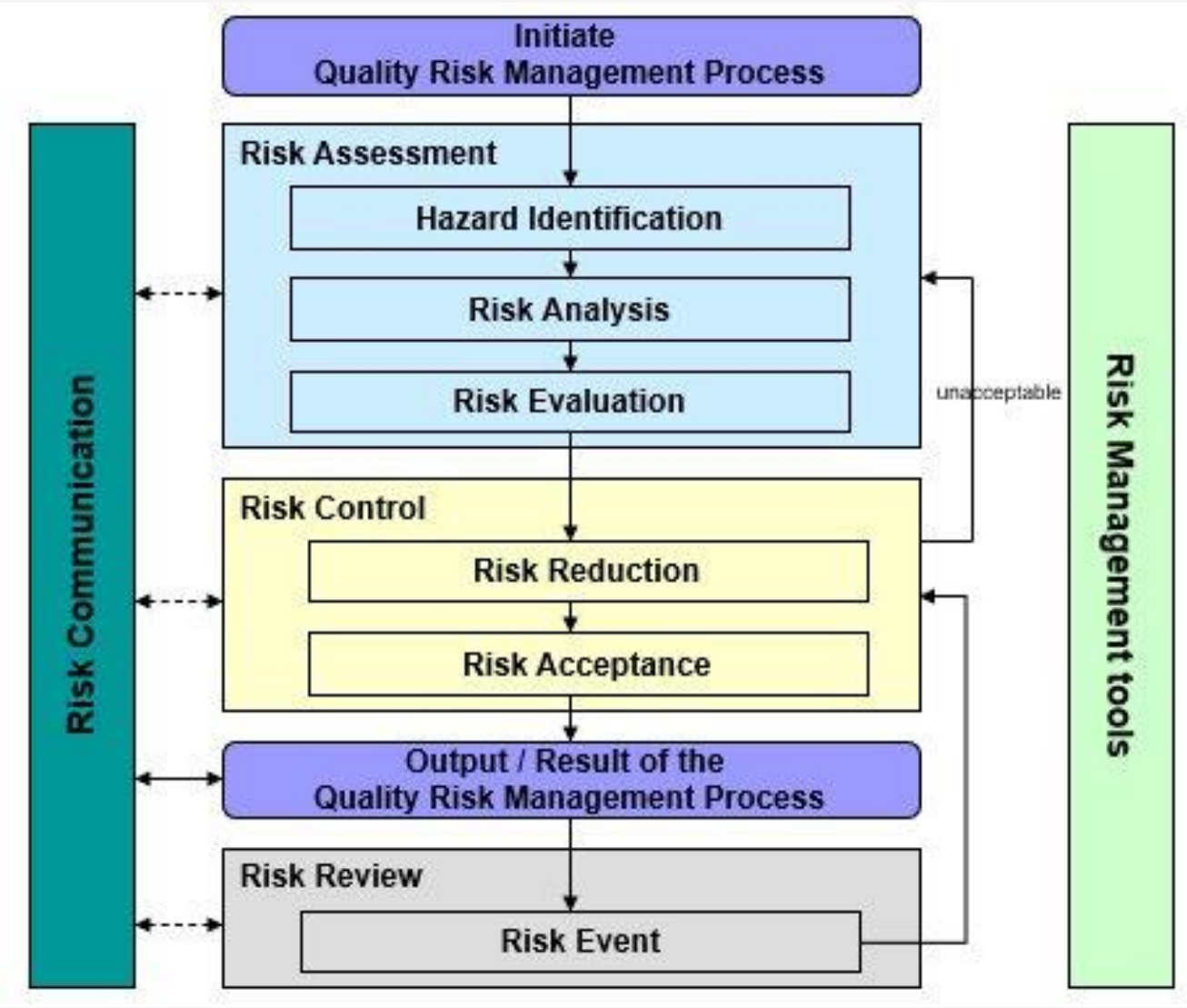


ICH Q9(R1) Quality Risk Management Process¹



Risk Assessment and Risk Control

- Risk assessment is comprised of:
 - Hazard identification - potential source of harm
 - Risk analysis – scoring or qualifying the severity and probability of occurrence
 - Risk evaluation – prioritizing/ranking risks
- Risk control is comprised of:
 - Risk reduction – level can be further reduced
 - Risk acceptance – level is acceptable and cannot be further reduced
- Risk control recommendations are provided by the QRM Team
- Risk control decisions are made by Decision Makers
- REMEMBER: Alleviating one risk can bring up other unintended risks.



ICH Q9(R1) Quality Risk Management Process¹

Output and Risk Review

- Risk Output
- Prioritized risks (medium and high levels)
- Risks that are accepted and mitigated
- Conclusion
- Risk Review
- Types of risk reviews:
 - Scheduled reviews
 - Event-based reviews.
- Monitoring of risks and updates should be based on knowledge management:
 - New risks identified,
 - Changes to existing risks, and
 - Changes to risk control mechanisms/decisions
 - New information

Practical Point of View

GMP processes are established / working

- Growth in scope and size of an organization can be marked with complexity
- Wealth of information can be better structured into defensible decisions

Reasons for adopting QRM

- Proactive risk management of future process
- Streamline/Improve current process
- Agile reaction to signals – trend, new information where issues may arise from
- Focus priorities on what would have greater impact

Internalizing QRM



1. Simplify, Optimize, Standardize, Digitize

- Implement ICH Q9 process steps
- Establish Procedure (elements include defined roles, scoring criteria, control decision matrix, decision trees for initiating assessments and risk reviews)
- Integrate QRM into PQS (change control, tech transfers, audits, validations, etc.)
- Digitize execution and output (digitized tools, reports, Risk Register, assessment log, etc.)



2. Adoption

- Sponsorship
- Leverage highly skilled facilitators (trained on tools, bias and time management, consistent execution)
- Demand engaged participation
- Scheduled formal risk communications/meetings



3. Institutionalize

- Efficiency gained from consistent practice of QRM Process steps and digital tools
- Invested participants with familiarity of the different tools, bias and time management, ICH Q9 process steps
- Adhoc or scheduled communications/meetings
- Metric tracking mitigation closures



4. Internalize

- Actions are strategic
- Active and Engaged Community (knowledge and experience sharing, best practices)
- Community garners interest and promotion from both experts and non-practitioners
- Offshoot teams are formed for common interests

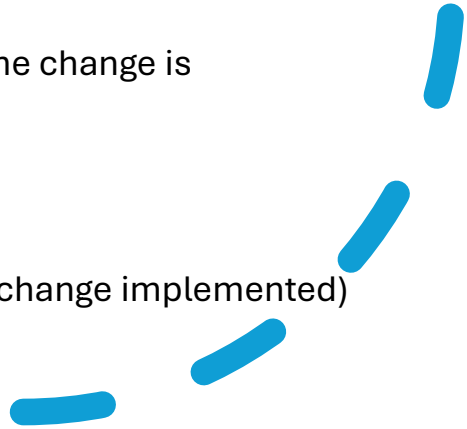
Risk-Based Decision- Making Applications in PQS

Spectrum of Risk-Based Decision-Making Approaches

- Highly structured with formal analysis of the available controls for the mitigation for decisions to be evaluated
- Less structured, simpler approach (risk-informed) to guide the level of controls to mitigate risk
- Rule-based decision making with standardized decisions for the controls to use.

Application for Change Control

Challenge: Change proposed may impact current validated parameters, decision to proceed or discontinue plans for the change are evaluated based on risk.

1. Evaluate if there is potential impact to product critical quality attribute, process parameters, material attributes, specification, detection controls.
 - Can be rule-based to determine if a prospective QRA is needed
 2. Risks to the prospective change are assessed.
 - A highly structured risk-based decision-making tool can be used to assess potential of change to negatively impact the product, process or system based on the importance of the risk.
 3. Change is implemented or withdrawn if risk is unacceptable
 - Can be rule-based matrix to conclude if the change can proceed as is (low risks) , requires further development/control (mitigation) or if the risk is unacceptable (high risk)
 - Risks are not added to the risk register until and unless the change is implemented
 4. Risk Review after change is implemented
 - Residual risks are added to the risk register
 - Can be a simple documentation update of the controls (change implemented)
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Application to Technical Transfers

Challenge: Knowledge transfer from a site to another site, from a development to commercialization, from internal to external of the company or vice versa

1. Identifying difference (gaps) between sending site and receiving site capabilities

- Can be risk-informed (less structure) approach for risk-based decision making
- Identifying gaps may be straightforward - can be a checklist depending on the type of transfer to identify the gaps
- Gaps are assessed by the organization accepting the new technology
- Gaps can be classified from low risk gaps or no gaps to high risk gaps depending on how closely the accepting site can adhere to the original parameters
- Prioritizing on the parameters to control reduces documentation and resource pull

2. Medium and high risk gaps are further assessed at the accepting site to identify mitigation controls (to achieve acceptable attributes and parameters)

- Can be highly structured risk-based decision making (uncertainty is still high)
- Use of formal tools to systematically identify hazards from the gaps

3. Risk Review

- Gap is reduced to an acceptable level or eliminated (risk-informed)
- Add further controls to reduce the gap (more formal risk-based decision making tool to further identify or control hazards)
- Evaluation of changes to validated parameters for equivalency or improvement (more formal tool)
- Evaluation of trends (investigations, assays, other tests and indicators) for signals of unintended consequences or drifts (statistical tools)
- Periodic evaluation for knowledge management



Application to Oversight of Contract Manufacturers/ External Suppliers

Challenge: External Quality Management Systems need to be initially scrutinized and continually monitored to be able to react to quality signals.

1. Identifying if capabilities in their Quality Management Systems are able to meet company requirements (due diligence, audits and inspections, initial qualification)
 - Can be a risk-informed tool comparing the capabilities (criticality of service or materials) between the company and the supplier/contractor
2. Periodic risk review of acceptable contractors/suppliers are further monitored that they are able to meet expectations (quality agreement parameters)
 - Can be a tool multi-decision risk based tool
 - A risk-informed tool is used to assess each key indicator for its level of risk according to the requirements of the company
 - A rule-based decision tool can be used to from each of the indicators above are tallied to reach a final risk ranking that decides on the level of oversight (frequency of audits and inspections, agreements, intentional supervision
 - Continual Improvement – decision to continually maintain relationship or to explore alternate sources

References

1. International Council on Harmonization. ICH Q9(R1) Quality Risk Management.

https://database.ich.org/sites/default/files/ICH_Q9%28R1%29_Guideline_Step4_2025_0115.pdf