Developing an Optimized Risk Assessment Portfolio

The Quality Risk Management Master Plan

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- Senior Consultant
  - Design and implementation of QRM programs
  - Creation and implementation of risk management training
  - Developing custom risk-based strategies
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  - Foundations of Risk
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Disclaimer

The content about to be presented has been accepted in article format and is pending publication.
Agenda

• Background for QRM / Risk Management Plans
• Strategic Objectives of the QRM Program
• Living vs Ad Hoc Risk Assessments—what should be included in the QRM Master Plan and Risk Assessment Portfolio?
• Example Strategies for Optimized Risk Assessment Portfolio
  • Example for an optimized risk portfolio for a less mature organization
  • Example for mature organization adapting to Annex 1 revision / CCS
• Contents of the QRM Master Plan
Lookback to the early 2000s
ICH Q9 - the OG

- Our industry’s QRM journey was in its infancy
- We began performing risk assessments – **lots** of risk assessments
  - Often with no attention on holistic strategy
- Many of those assessments were performed with no preparation or planning activities.
- We had no focus on:
  - What risk assessments were needed
  - When?
  - Why?
  - How?

"[following the initiation of the company’s QRM program], we performed more than 100,000 full FMEA analyses worldwide in the first year."

-December 2009 quote from Roche’s Wallace Torres in *The Gold Sheet*
What did we learn BOTH from the initial attempts at risk assessment strategy and our ideas on early 2000s fashion?

We can do better

Enter – the Quality Risk Management Plan
How did we get here?

• Historic lack of emphasis on QRM planning has led to:
  • Industry-wide struggle with the building and administration of the QRM program
  • Creation of myriad of risk assessments with no holistic vision
  • Siloed approach to QRM application and risk assessment performance

The lesson in this? We need to learn from our mistakes.
The Inspiration for QRM Strategy and Planning

ISO 14971 - Medical Device Risk Management Plans

- Requires medical device developers and manufacturers to define a plan for risk management activities throughout the product lifecycle.
- The standard states “a risk management plan is required because:
  - An organized approach is essential for good risk management
  - The plan provides a roadmap for risk management
  - The plan encourages objectivity and helps prevent essential elements from being forgotten
What did these plans look like?

Risk Management Plan:

- Roles and Responsibilities
- Scope (regarding product lifecycle)
- Governance Structure
- Processes
- Risk and Residual Risk Criteria
- Use of Production and Post-Production information (review)
- Milestones
- Activity Plan (schedule)
- Tools to be used
Translating the Risk Management Plan to ICH Q9 (R1)

- Revision from ICH Q9 to Q9 (R1) highlights application of thoughtful and objective decision-making throughout the QRM lifecycle
- Plan would demonstrate current state of QRM program as well as future plan for it.
- Risk Initiation step of the QRM lifecycle is the vehicle for strategy

1. Outline of Strategic goals for QRM Program
2. Outline Strategic Plan for Risk Assessment Portfolio
3. Detailed Plan on how firm intends to reach both Program and Portfolio goals
Strategic Objectives for QRM Program

- **Hire and Develop QRM Experts to enable QRM program**
  - QRM Lead
  - Facilitators

- **Integrate QRM Principles and Practices into Quality and Operational Systems**

- **Define and Create Portfolio of Living Risk Assessments**

- **Select and Validate QRM Software and / or Tools**

- **Establish a Risk Register**

- **Author QRM Policy, Procedures, Work Instructions**

- **Design and Implement Role Based Training**
  - Leadership / Decision makers
  - Facilitators
  - System / Process Owners
  - Subject Matter Experts
  - Quality

Focus for remainder of presentation
What goes in the Risk Assessment Portfolio?

- ICHQ9 (R1) clarified two important concepts:
  - Risk-Based Decision Making
    - Use of QRM principles for consistent decision making
    - Not necessarily using likelihood and severity
  - QRM formality and lifecycle stage
    - Some risk assessments don’t require the complete QRM lifecycle
    - Some risk assessments should live within the quality system that evoked them
    - Living vs. Ad Hoc risk assessments
Living Risk Assessments

- Represents the core of the QRM portfolio
- Objective is to
  - understand the risks
  - control risks to an acceptable level
  - review the risks in light of changing conditions to evaluate relevance of risks and controls
- Generally, more formal in nature
  - Process, product, or system assessment
- Intended to show the current state of a facility or process and how it will change over time
Ad-Hoc Risk Assessments

• A risk assessment that may be conducted to facilitate a decision **without continuing** to:
  • risk reduction
  • risk acceptance
  • risk review

• Generally, less formal in nature

• Risk assessments that **support a single decision point in time** (risk-based decision making)

• Often inputs into other living risk assessments

• Alleviates burden on the QRM program
  • Focuses energy and resources on the applicable portions of the lifecycle where needed

- Determining the impact of a deviation on product lots
- Evaluating Audit frequencies
- Assessing Impact of Product Complaints
- Assessing Proposed Change Controls
- Determining PM or Calibration schedules
So what would it look like if we proactively designed an optimized living risk assessment portfolio for cGMP operations?

- A mature QRM program could set a strategy to ensure holistic assessment across an organization or site
  - Platform approaches could be leveraged for similar technologies, manufacturing platforms, or device types
  - Would be mindful of regulatory expectations across the risk assessment portfolio
  - Would support control strategies with a low number of focused assessments

We could avoid hundreds of disconnected risk assessment efforts!
Example 1 - optimized living risk assessment portfolio for a less mature (or new) organization
<table>
<thead>
<tr>
<th>Example Focus of risk assessment</th>
<th>May includes components of</th>
<th>Would deliver knowledge related to...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manufacturing process</td>
<td>• Manufacturing equipment</td>
<td>• Design and content of master batch production records</td>
</tr>
<tr>
<td></td>
<td>• Automation</td>
<td>• Process and operational control strategies</td>
</tr>
<tr>
<td></td>
<td>• Equipment cleaning and sterilization</td>
<td>• Contamination and cross-contamination control strategies</td>
</tr>
<tr>
<td></td>
<td>• Performance of Process</td>
<td>• Process monitoring strategies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Product sampling and testing plans</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Cleaning process design and validation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Computer systems design and validation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Maintenance and calibration plans</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Inspection plans and acceptance levels</td>
</tr>
<tr>
<td>Facility</td>
<td>• HVAC systems</td>
<td>• Contamination and cross-contamination control strategies</td>
</tr>
<tr>
<td></td>
<td>• Critical utilities (e.g. water, steam, and process gases)</td>
<td>• Cleanroom capabilities and classification</td>
</tr>
<tr>
<td></td>
<td>• Facility flows (e.g. personnel, product, waste)</td>
<td>• Environmental monitoring plans</td>
</tr>
<tr>
<td></td>
<td>• Facility and equipment layout and accessibility</td>
<td>• Critical utilities monitoring plans</td>
</tr>
</tbody>
</table>
What if you already have an established risk portfolio of risk assessments?

• It is common to utilize a QRM Master Plan to close a gap
  • New regulatory requirement is effective
  • Expansion of a product line
  • New facility build or expansion
  • Technology Transfer to a CMO
  • Introduction of new product
Example 2 – some companies need to align with EU Annex 1 requirements

- QRM Master Plan can be limited to developing living risk assessments to support the Contamination Control Strategy (CCS)
  - Note: different risk questions or risk tools should be distinct, different risk assessments!
  - None of these should be an FMEA

Classifying interventions into the Critical Zone (ISO 5 / Grade A)
Assessing hazards with all manufacturing and support processes
Assessing all hazards associated with classified areas of the facility and collocated clean utility distribution system (drops)
<table>
<thead>
<tr>
<th>Risk Assessment Focus</th>
<th>Risk Question(s</th>
<th>QRM Tool</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interventions into the ISO 5/Grade A Zone</td>
<td>What is the relative criticality of anticipated interventions into the ISO 5/Grade A zone? Can the risk associated with the interventions be reduced?</td>
<td>Intervention Risk Evaluation Method (IREM)</td>
</tr>
<tr>
<td>Aseptic manufacturing and support processes</td>
<td>What are the contamination-related hazards associated with the aseptic manufacturing and support processes, from parts preparation through vial capping? What is the risk associated with each hazard and is further reduction warranted? What are the critical control points associated with the process?</td>
<td>Process Hazard Analysis and Critical Control Points (HACCP)</td>
</tr>
<tr>
<td>Classified areas of the facility and related clean utility drop points from the distribution system</td>
<td>What are the contamination-related hazards associated with the classified areas of the facility and related clean utilities? What is the risk associated with each hazard and is further reduction warranted? What are the critical control points associated with the facility and clean utility distribution systems?</td>
<td>Facility Hazard Analysis and Critical Control Points (HACCP)</td>
</tr>
</tbody>
</table>
Contents of the QRM Master Plan

What should it look like?

What should be included?
Purpose

• Should describe the goal and intent of the plan
• Goals will differ by organizational maturity

Less Mature

- Develop QRM process, governance, infrastructure, training
- Perform first risk assessments in living portfolio

More Mature

- Expand QRM program into additional aspects of the quality system
- Perform risk assessments on new topics and regulatory requirements (ex. CCS)
## Scope

- **Should describe boundaries of the QRM Master Plan**
  - Use exclusionary language for explicit out of scope areas

- **The recommended timeline for the QRM Master Plan is 1-3 years**
  - Enables both short term “quick wins” AND longer-term strategic items

<table>
<thead>
<tr>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site(s) or buildings where QRM Master Plan applies</td>
<td>Products, product lines, or systems to which the plan applies</td>
</tr>
<tr>
<td>Product lifecycle phases to which the plan applies (e.g., development through phase 1, commercial only)</td>
<td>Types of risks covered by the plan (e.g., contamination related risks)</td>
</tr>
<tr>
<td>Quality System Elements to be included in this plan (e.g., change control, deviation management, etc.)</td>
<td>Timeframe covered in the plan</td>
</tr>
</tbody>
</table>
Roles and Responsibilities

• Include all those working or interacting with the QRM Plan

• Many firms find RACI matrices helpful for this task
  • R - responsible
  • A - accountable
  • C - consulted
  • I - informed

• Responsibilities should directly correlate to the actions outlined in the plan
  • 1:1 correlation. Every activity should have a corresponding responsible party
## Example RACI Matrix for QRM Master Plan

<table>
<thead>
<tr>
<th>Activity</th>
<th>Leadership</th>
<th>Head of QRM</th>
<th>Facilitators</th>
<th>System/Process Owners</th>
<th>Subject Matter Experts</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete defined living risk assessments</td>
<td>I</td>
<td>C</td>
<td>R</td>
<td>A</td>
<td>R</td>
<td>C</td>
</tr>
<tr>
<td>Integrate QRM principles into quality system</td>
<td>C</td>
<td>A/R</td>
<td>N/A</td>
<td>R</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Establish risk register</td>
<td>I</td>
<td>A/R</td>
<td>N/A</td>
<td>R</td>
<td>C</td>
<td>I</td>
</tr>
<tr>
<td>Establish quality risk profile</td>
<td>I</td>
<td>A/R</td>
<td>N/A</td>
<td>R</td>
<td>C</td>
<td>C</td>
</tr>
</tbody>
</table>

R - responsible
A - accountable
C - consulted
I - informed
Activity List

• Discussion of objectives and activities to be completed as part of the plan
  • New assessments to be performed
  • Risk review on living assessments already in portfolio

• May be helpful to use risk-based prioritization tool to determine strategy and timelines

• Prioritization tool would rate all activities using the same criteria
  • Criticality of topic to be assessed
  • Complexity of the effort

“If we’re going to prioritize, we’re going to need some priorities.”
### QRM Activity Prioritization Tool

#### Example of Topic Criticality Ranking Criteria

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Critical</td>
<td>Topic directly impacts product quality and the health and safety of the patient.</td>
</tr>
<tr>
<td>Moderate</td>
<td>Topic indirectly impacts product quality and the health and safety of the patient.</td>
</tr>
<tr>
<td>Minor</td>
<td>Topic does not impact product quality or the health and safety of the patient.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Topic Criticality</th>
<th>Minor</th>
<th>Moderate</th>
<th>Critical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simple</td>
<td>Priority 7</td>
<td>Priority 4</td>
<td>Priority 1</td>
</tr>
<tr>
<td>Average</td>
<td>Priority 8</td>
<td>Priority 5</td>
<td>Priority 2</td>
</tr>
<tr>
<td>Complex</td>
<td>Priority 9</td>
<td>Priority 6</td>
<td>Priority 3</td>
</tr>
</tbody>
</table>

#### Example of Effort/Complexity Ranking Criteria

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complex</td>
<td>Significant resources and expertise required. (e.g., &gt;9 months required to implement, &gt; 4 department involvement required)</td>
</tr>
<tr>
<td>Average</td>
<td>A moderate number of resources and expertise required. (e.g., 3-9 months required to implement; 3-4 department involvement required)</td>
</tr>
<tr>
<td>Simple</td>
<td>Minimal resources and expertise required. (e.g., &lt;3 months required to implement; 1-2 department involvement required)</td>
</tr>
</tbody>
</table>
**Example Activity List**

<table>
<thead>
<tr>
<th>Activity</th>
<th>Resources required</th>
<th>Criticality</th>
<th>Complexity</th>
<th>Priority</th>
<th>Target completion date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete facility HACCP for contamination control</td>
<td>4 SMEs/departments needed</td>
<td>Critical</td>
<td>Average</td>
<td>2</td>
<td>Q1, Year 1</td>
</tr>
<tr>
<td>Complete process HACCP for fill/finish manufacturing</td>
<td>5 SMEs/departments needed</td>
<td>Critical</td>
<td>Complex</td>
<td>3</td>
<td>Q2, Year 1</td>
</tr>
<tr>
<td>Develop QRM approach to supplier management</td>
<td>1 SME/department needed</td>
<td>Moderate</td>
<td>Simple</td>
<td>4</td>
<td>Q3, Year 1</td>
</tr>
<tr>
<td>Complete IREM for fill/finish interventions</td>
<td>2 SMEs/departments needed</td>
<td>Critical</td>
<td>Simple</td>
<td>1</td>
<td>Q1, Year 1</td>
</tr>
<tr>
<td>Develop risk register</td>
<td>3 SMEs/departments needed</td>
<td>Minor</td>
<td>Average</td>
<td>8</td>
<td>Q4, Year 1</td>
</tr>
</tbody>
</table>
In Conclusion

• Now is the time to mature from our early 2000’s-and-beyond bad QRM habits

• Taking the time to step back and plan a holistic QRM strategy can help us avoid:
  • Having a program (and risk assessment portfolio) that exists in silos
  • Duplicated risk assessment efforts
  • And can make all the risk assessments that we perform both meaningful and value-add

• Understanding the difference between Living and Ad Hoc risk assessments can help streamline the risk assessment portfolio and apply the appropriate phases of the ICH Q9 (R1) lifecycle

• The QRM Master Plan can be implemented at any stage of organizational QRM maturity
  • To build a program in less mature organizations
  • To address gaps that exist in more mature programs
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  • Co-author for publication