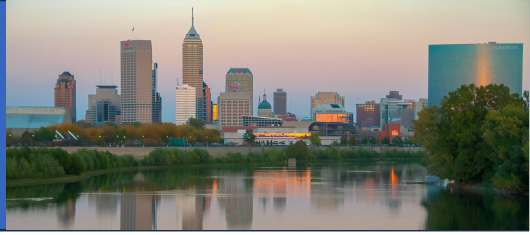
Sterility Assurance & Quality Risk Management Conference

PDA®
Parenteral Drug Association
Midwest Chapter

PDA Parenteral Drug Association Midwest Chapter

Sterility Assurance & Quality Risk Management Conference

October 25th & 26th



Developing an Optimized Risk Assessment Portfolio

The Quality Risk Management Master Plan

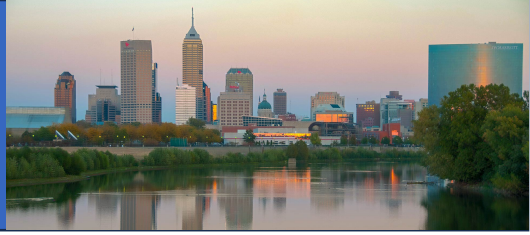
Tiffany Baker, MBA

Senior Consultant

ValSource, LLC

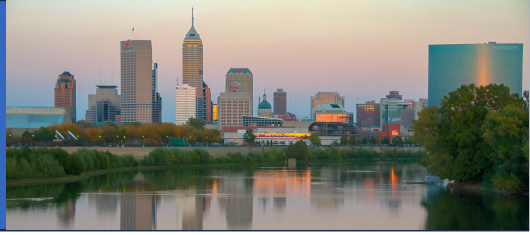
Tiffany Baker, MBA

- Senior Consultant VALSOURCE
  - Design and implementation of QRM programs
  - Creation and implementation of risk management training
  - Developing custom risk-based strategies
  - Risk facilitation
- Faculty at PDA Training Institute
  - Foundations of Risk
  - Practical Application of Quality Risk Assessment Tools
- Co-lead PDA Remote Audits and Inspection Task Force
- Member PDA Covid-19 Task Force
- Member of PDA QRM Interest Group
- Articles published on many QRM topics
- Bachelors of Science, Microbiology, University of Rhode Island
- Masters of Business Administration, Providence College



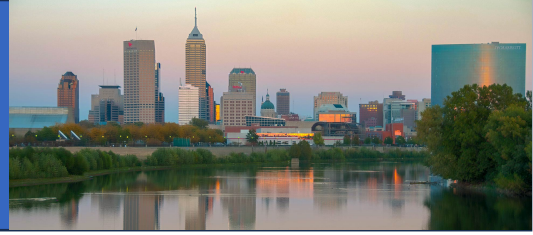
Disclaimer

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

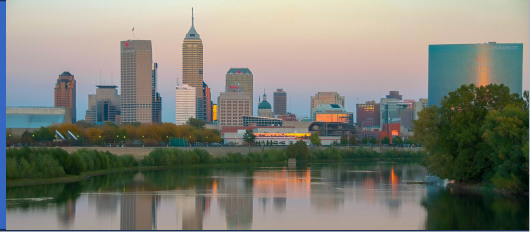


Agenda

- 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

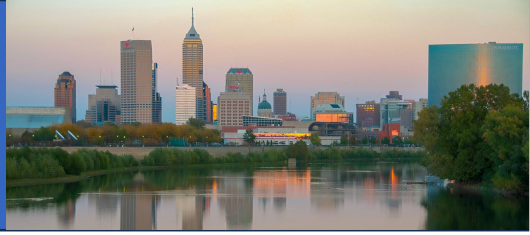


ICH Q9 - the OG

- 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."

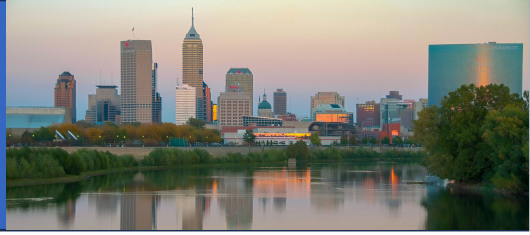
-December 2009 quote from Roche's Wallace Torres in *The Gold Sheet*



What did we learn BOTH from the initial attempts at risk assessment strategy and our ideas on early 2000s fashion?

We can do better

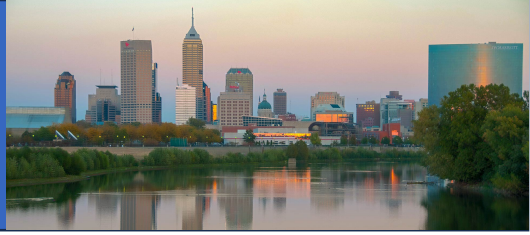
Enter – the Quality Risk Management Plan



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

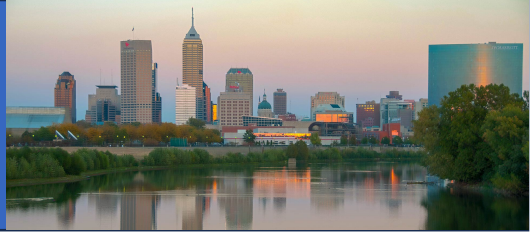
ISO 14971 - Medical Device Risk Management Plans

- 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

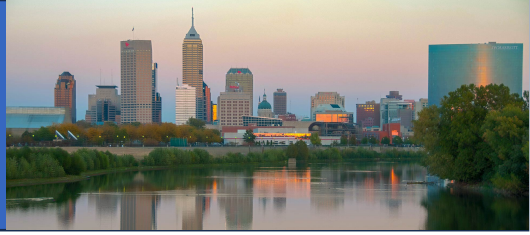
The plan encourages objectivity and helps prevent essential elements from being forgotten



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

Focus for remainder of presentation

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

Integrate QRM Principles and Practices into Quality and Operational Systems

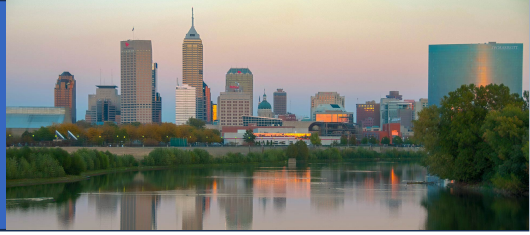
Define and Create Portfolio of Living Risk Assessments

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

Select and Validate QRM Software and / or Tools

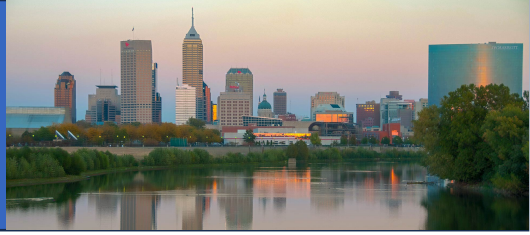
Establish a Risk Register

Author QRM Policy, Procedures, Work Instructions



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

Process Contamination Assessment

Manufacturing Process Assessment

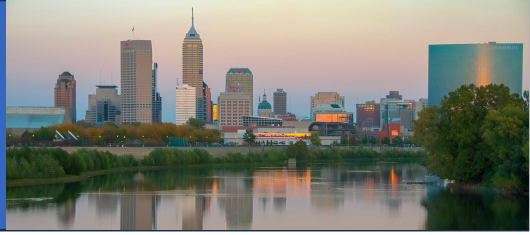
Transportation and Shipping Lane Assessment

Facility External Contamination Assessment

Multi-product Cross Contamination Assessment

Raw Material Assessment

Clinical Process Development Assessment



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

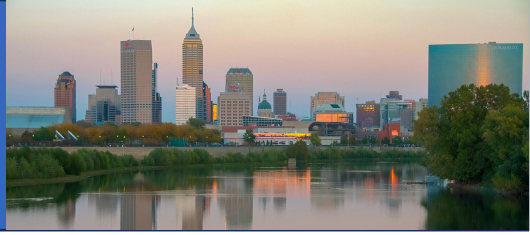
Evaluating Audit frequencies

Assessing Impact of Product Complaints

Determining the impact of a deviation on product lots

Assessing Proposed Change Controls

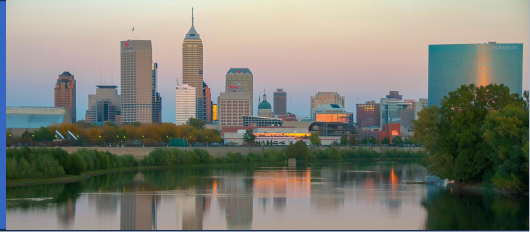
Determining PM or Calibration schedules



So what would it look like if we proactively designed an optimized living risk assessment portfolio for cGMP operations?

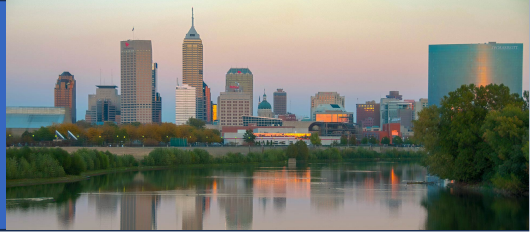
- A mature QRM program could set a strategy to ensure holistic assessment across an organization or site
  - Platform approaches could be leveraged for similar technologies, manufacturing platforms, or device types
  - Would be mindful of regulatory expectations across the risk assessment portfolio
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

We could avoid hundreds of disconnected risk assessment efforts!

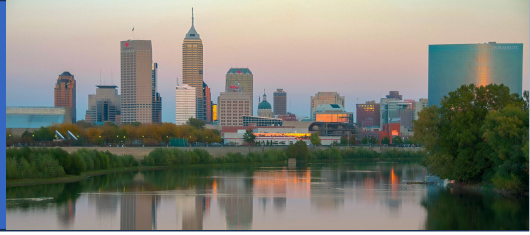


Example 1 - optimized living risk assessment portfolio for a less mature (or new) organization

- Manufacturing Process
- Starting Materials and Components
- Product Shipping
- Facility
- Analytical Methods

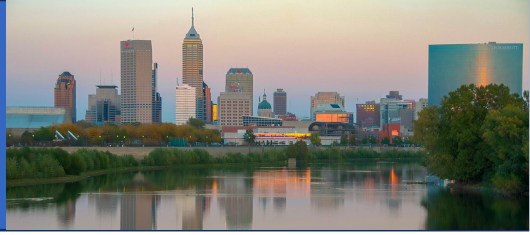


Example Focus of risk assessment	May includes components of	Would deliver knowledge related to…
Manufacturing process	• Manufacturing equipment • Automation • Equipment cleaning and sterilization • Performance of Process	• Design and content of master batch production records • Process and operational control strategies • Contamination and cross-contamination control strategies • Process monitoring strategies • Product sampling and testing plans • Cleaning process design and validation • Computer systems design and validation • Maintenance and calibration plans • Inspection plans and acceptance levels
Facility	• HVAC systems • Critical utilities (e.g. water, steam, and process gases) • Facility flows (e.g. personnel, product, waste) • Facility and equipment layout and accessibility	• Contamination and cross-contamination control strategies • Cleanroom capabilities and classification • Environmental monitoring plans • Critical utilities monitoring plans



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



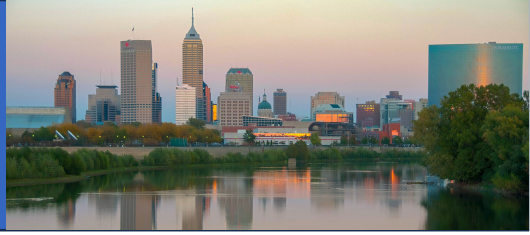
Example 2 – some companies need to align with EU Annex 1 requirements

- 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

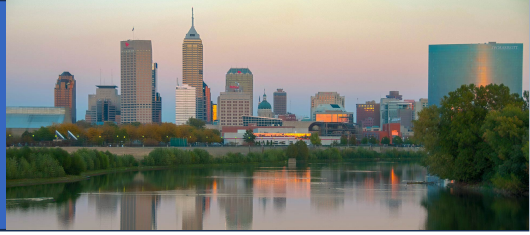
Classifying interventions into the Critical Zone (ISO 5 / Grade A)

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)



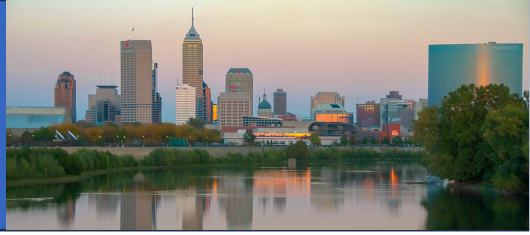
Risk Assessment Focus	Risk Question(s)	QRM Tool
Interventions into the ISO 5/Grade A Zone	What is the relative criticality of anticipated interventions into the ISO 5/Grade A zone? Can the risk associated with the interventions be reduced?	Intervention Risk Evaluation Method (IREM)
Aseptic manufacturing and support processes	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?	Process Hazard Analysis and Critical Control Points (HACCP)
Classified areas of the facility and related clean utility drop points from the distribution system	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?	Facility Hazard Analysis and Critical Control Points (HACCP)



Contents of the QRM Master Plan

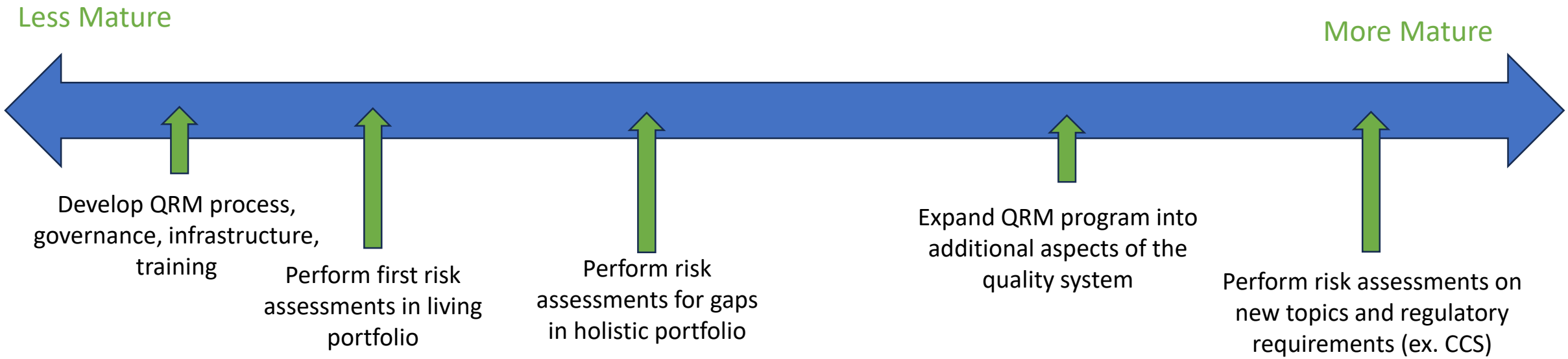
What should it look like?

What should be included?



Purpose

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



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

Site(s) or buildings where QRM Master Plan applies

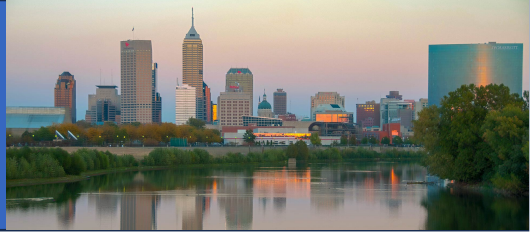
Products, product lines, or systems to which the plan applies

Product lifecycle phases to which the plan applies (e.g., development through phase 1, commercial only)

Types of risks covered by the plan (e.g., contamination related risks)

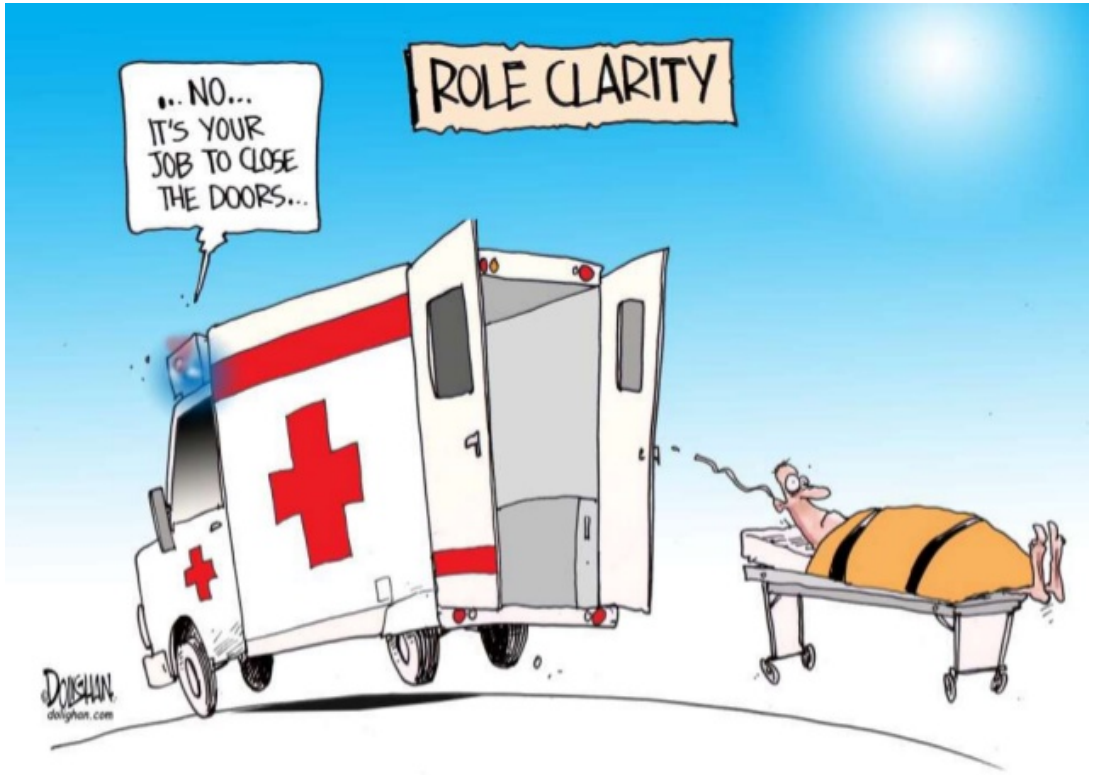
Quality System Elements to be included in this plan (e.g., change control, deviation management, etc.)

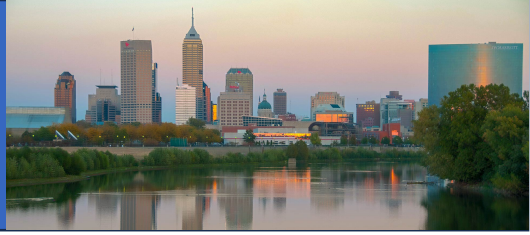
Timeframe covered in the plan



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

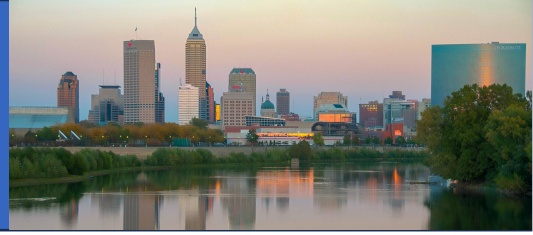




Example RACI Matrix for QRM Master Plan

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

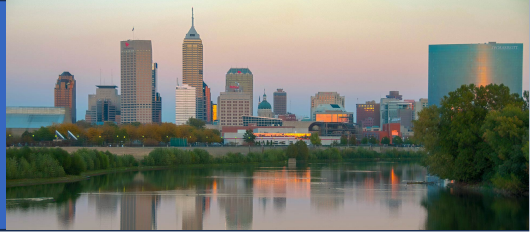
R - responsible
A - accountable
C - consulted
I - informed



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

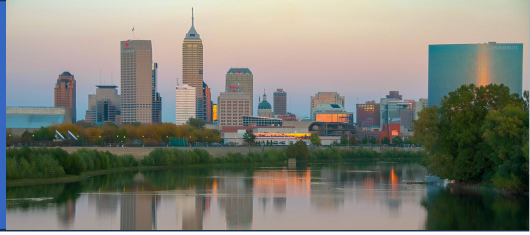
Example of Topic Criticality Ranking Criteria

Ranking	Criteria
Critical	Topic directly impacts product quality and the health and safety of the patient.
Moderate	Topic indirectly impacts product quality and the health and safety of the patient.
Minor	Topic does not impact product quality or the health and safety of the patient.

Example of Effort/Complexity Ranking Criteria

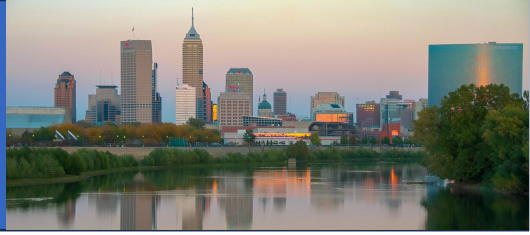
Ranking	Criteria
Complex	Significant resources and expertise required. (e.g., >9 months required to implement, > 4 department involvement required)
Average	A moderate number of resources and expertise required. (e.g., 3-9 months required to implement; 3-4 department involvement required)
Simple	Minimal resources and expertise required. (e.g., <3 months required to implement; 1-2 department involvement required)

Effort/Complexity	Topic Criticality: Minor	Topic Criticality: Moderate	Topic Criticality: Critical
Simple	Priority 7	Priority 4	Priority 1
Average	Priority 8	Priority 5	Priority 2
Complex	Priority 9	Priority 6	Priority 3



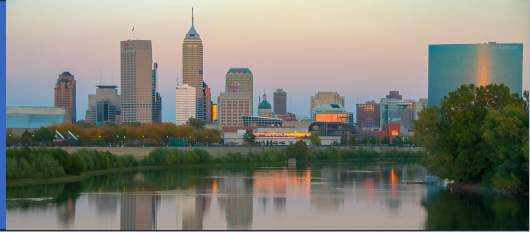
Example Activity List

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



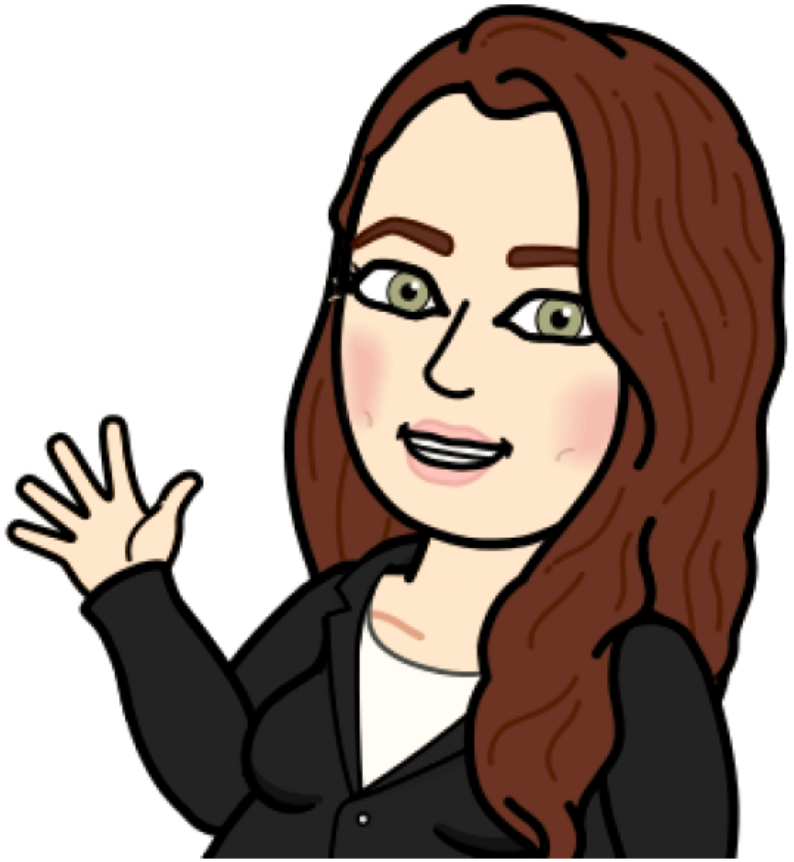
In Conclusion

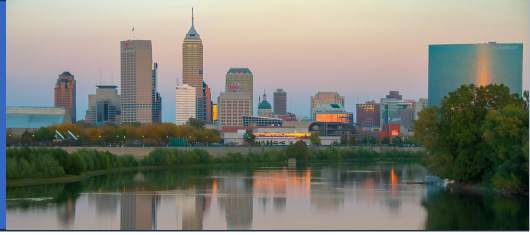
- Now is the time to mature from our early 2000's-and-beyond bad QRM habits
- Taking the time to step back and plan a holistic QRM strategy can help us avoid:
  - Having a program (and risk assessment portfolio) that exists in silos
  - Duplicated risk assessment efforts
  - And can make all the risk 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



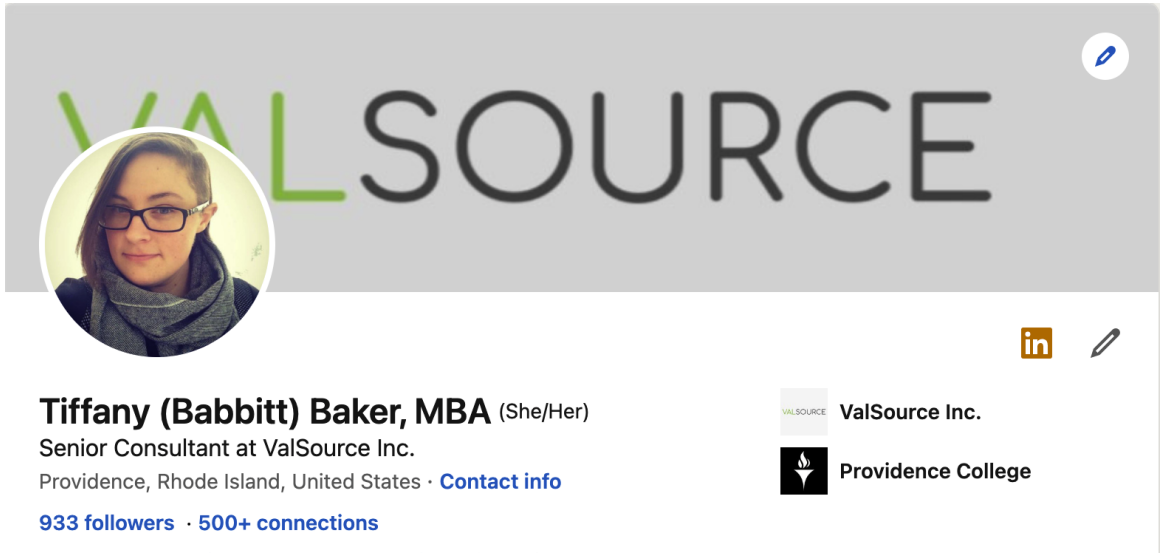
Acknowledgements

- Kelly Waldron, PhD
  - ValSource Business Unit Manager, Quality and Manufacturing Science Consulting
  - Co-author for publication





Contact Info



tbaker@valsource.com

401.256.7242

www.valsource.com