POLL #1

Do you have a FORMAL definition for Risk Based Decision Making (RBDM) in your PQS?

- ❑ No, we do not have it defined formally
- ❑ Yes, we have a definition
- ❑ Not sure / Don't know

ISPE Expert Xchange Series

Risk-Based Decision Making: Advancing the Integration of QRM & KM

Tuesday, 18 January 2022 | 1000 – 1300 ET

Speakers

Marty Lipa
Merck

Valerie Mulholland
GMP Services Ltd

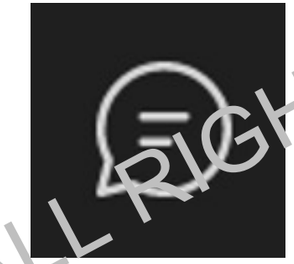
Dr Kevin O'Donnell
HPRA

Prof Anne Greene
Director, PRST, TU Dublin

Pharmaceutical REGULATORY SCIENCE Team

Getting Connected

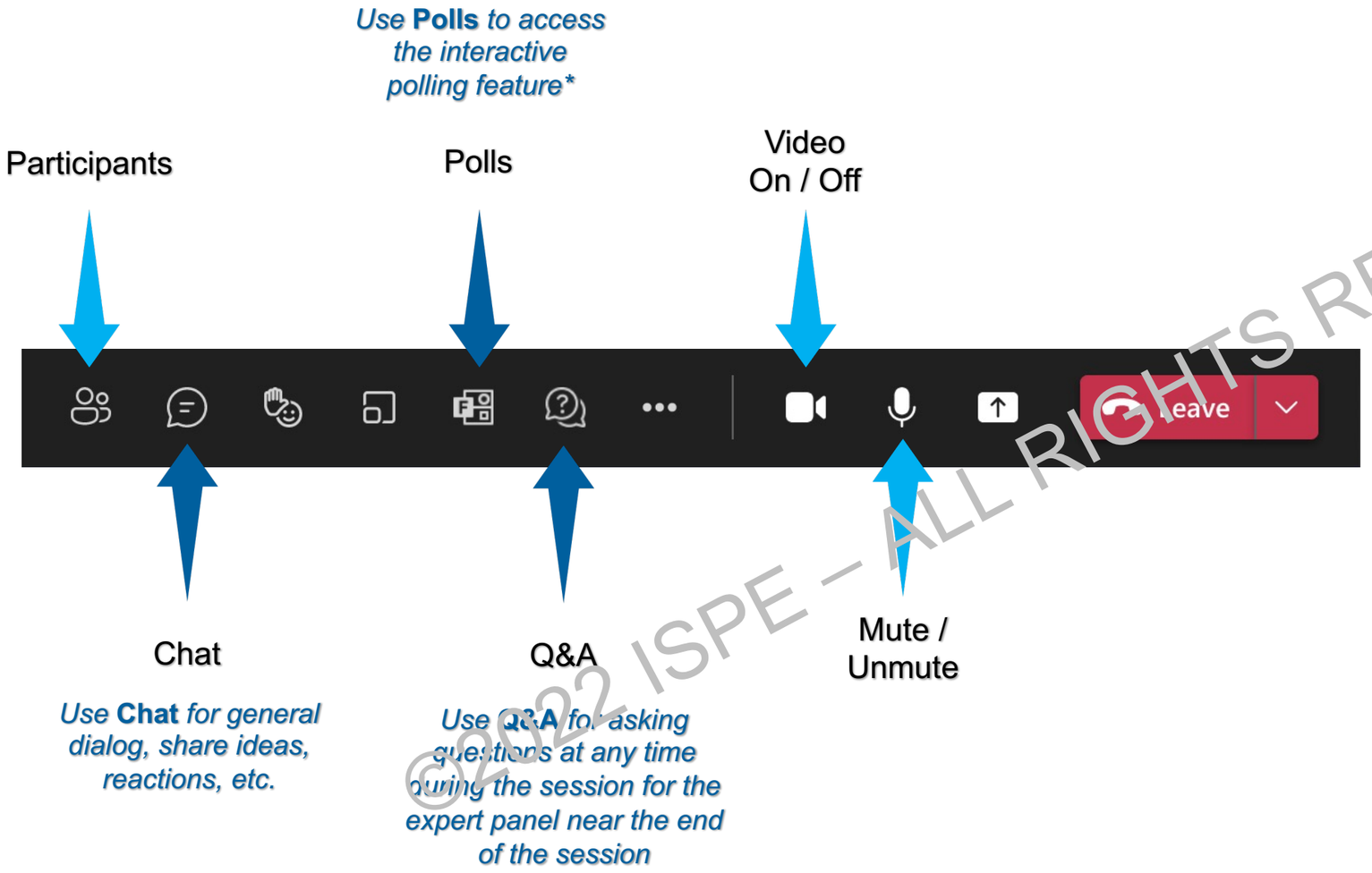
Please remember to keep yourself on mute unless speaking to avoid any audio feedback issues



Please use the chat feature to communicate any technical difficulties (do not use the Q&A)

If you are experiencing low bandwidth/connection issues, it is recommended that you turn off your camera

Tips for Effective Collaboration



*Polls once launched should also be visible in your chat, but may be truncated or difficult to view

Many of you will be familiar with Teams and its common features.

We will be using additional features you may not be as familiar with today, including

- Polls
- Q&A

Additional tips if you are having trouble:

- Having trouble with sound? Select *Call Me* under *More Actions* ···
- Use a hard-wired connection instead of Wi-Fi
- Disconnect and reconnect

POLL #1 - RESULTS

Do you have a <u>FORMAL</u> definition for Risk Based Decision Making (RBDM) in your PQS?

- ❑ No, we do not have it defined formally
- ❑ Yes, we have a definition
- ❑ Not sure / Don't know

Pharmaceutical
REGULATORY SCIENCE
Team

The Technological University Dublin
Pharmaceutical Regulatory Science Team (PRST)
was founded in 2005 in response to the drive for a paradigm shift
towards more science and risk-based approaches to ensure pharmaceutical product quality.

PRST actively engages with global industry and regulators to **address the challenges and opportunities of implementing Science and Risk based decision making and manufacturing approaches**.

PRST research emphasis is on the development of **patient-focused strategies, frameworks, models and tools** to enable those involved in the manufacture of drug products to meet the evolving international regulatory expectations **ensuring the availability of high-quality medicinal products**.

Anne Greene
Professor &
Director, PRST

TU Dublin

Learn more at http://prst.ie

Speakers

Marty Lipa
Executive Director - KM
Merck / MSD

PRST Researcher

Marty (Martin) Lipa has over 28 years of biopharmaceutical industry experience and 12 years of experience in Knowledge Management (KM). Lipa recently completed his PhD at TU Dublin in Pharmaceutical and Regulatory Science with a focus on enabling ICH Q10 through improved KM and its interdependency with QRM.

Valerie Mulholland
CEO
GMP Services Ltd

PRST Researcher

Valerie Mulholland is the CEO of GMP Services Ltd and is a GMP/Quality Consultant in Europe. She is a practitioner in the area of Quality Risk Management and is researching the topic of Risk-Based Decision Making for a PhD dissertation with the Pharmaceutical Regulatory Science Team (PRST) in TU Dublin.

Kevin O'Donnell
Market Compliance Manager

HPRA

Kevin O'Donnell is Market Compliance Manager at the Health Products Regulatory Authority, in Dublin, Ireland. He has been with the HPRA/IMB since 2001 and is a Senior GMP Inspector. He is also responsible for a number of compliance-related programmes at the HPRA. He obtained his PhD in the field of Quality Risk Management (QRM) in 2008. He is currently Chair of the PIC/S Expert Circle on QRM and is Rapporteur for the ongoing revision of ICH Q9.

Learning Objectives

1. Introducing and advancing the *Risk-Knowledge Infinity Cycle* (*RKI Cycle*) as a framework to unite QRM and KM, especially in the context of ICH Q9(R1)

2. An introduction to risk-based decision making (i.e., decisions based on science and evidence), and how the *RKI Cycle* can further enable risk-based decision making

3. Preliminary considerations & opportunities for where the *RKI Cycle* may be deployed to drive more informed decisions

4. An introduction to knowledge mapping as a technique to define inputs to QRM, and how this can inform requirements for KM

Agenda

1. Introduction & Welcome
2. General session: The emphasis on knowledge and knowledge management in the draft ICH Q9(R1) Guideline
3. General session: An Introduction to the RKI Cycle
4. General session: Risk-based decision making in the PQS
5. Workshop: Knowledge inputs into QRM (RKI Node 1)
6. Break ☺ (approx. 11:45 ET / 4:45 GMT +/-)
7. Reflections & Group Discussion: QRM knowledge outputs (RKI Node 4)
8. Q&A
9. Wrap Up

Perspectives on the role of KM in support of QRM

New insights from ICH Q9[R1]

Dr Kevin O'Donnell
HPRA &
Rapporteur, ICH Q9[R1]

The emphasis on knowledge and knowledge management in the draft ICH Q9(R1) Guideline

Kevin O'Donnell, PhD, Market Compliance Manager

January 18th, 2022

Knowledge informs decisions about Risk – this is a key concept in the draft ICH Q9(R1)

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Health Products Regulatory Authority

- **The current draft of ICH Q9(R1) makes many references to the use of knowledge and Knowledge Management in relation to QRM and Risk-based Decision Making**
- **e.g. Introduction:** In the development phase, quality risk management is part of building knowledge and understanding risk scenarios, so that appropriate risk control can be decided upon during technology transfer, for use during the commercial manufacturing phase. **In this context, knowledge is used to make informed risk-based decisions, trigger re-evaluations and stimulate continual improvements.**

The following are some of the key references to Knowledge and KM in the draft ICH Q9(R1) guideline

In the new text on Subjectivity in QRM… (Section 4.3 of the revised gudeline)

- While subjectivity cannot be completely eliminated from quality risk management activities, it may be controlled by addressing bias, the proper use of quality risk management tools and **maximising the use of relevant data and sources of knowledge** (see ICH Q10, Section II.E.1).

- **Decision makers should… assure** that a quality risk management process is defined, deployed and reviewed and **that adequate resources and knowledge are available.**

In the new text on Formality in QRM… (Section 5.1)

- The term "**uncertainty**" in quality risk management means lack of **knowledge about risks**. The level of uncertainty that is associated with the area being risk assessed informs how much formality may be required to manage potential risks. Systematic approaches for acquiring, analysing, storing and disseminating scientific information are **essential for generating knowledge**, **which in turn informs all quality risk management activities**. Uncertainty may be reduced via **effective knowledge management,** which enables accumulated and new information (both internal and external) to be used **to support risk-based decisions** throughout the lifecycle.
- Regardless of how much formality is applied, **the robust management of risk** is the goal of the process. This **should be based on evidence, science and knowledge**, where risk scores, ratings or assessments are supported by data or by an appropriate justification or rationale.

In the new Risk-based Decision Making text (Section 5.2)

- Approaches to risk-based decision-making are beneficial, **because they address uncertainty through the use of knowledge, facilitating informed decisions** by regulators and the pharmaceutical industry in a multitude of areas, including when allocating resources. They also help recognize where uncertainty remains, so that appropriate risk controls (including improved detectability) may be identified to enhance understanding of those variables and further reduce the level of uncertainty.
- **As all decision making relies on the use of knowledge, see ICH Q10 for guidance in relation to Knowledge Management**. It is important also to ensure the integrity of the data that are used for risk-based decision making.

In the new text on Product Availability Risks (Chapter 6)

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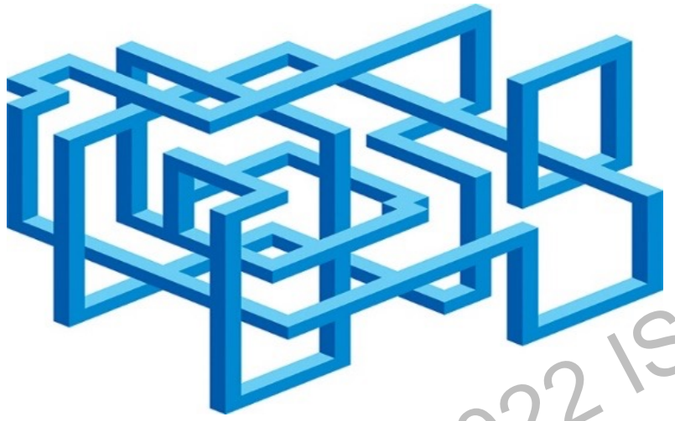
- **An effective pharmaceutical quality system** drives both supply chain robustness and sustainable GMP compliance. It also **uses quality risk management and knowledge management to provide an early warning system** that supports effective oversight and response to evolving quality/manufacturing risks from the pharmaceutical company or its external partners.
- **Approval and oversight of outsourced activities and material suppliers is informed by** risk assessments, **effective knowledge management,** and an effective monitoring strategy for supply chain partner performance.

See the definition of Risk-based Decision Making (Chapter 7)

Risk-based Decision Making:

An approach or process **that considers knowledge about risks** relevant to the decision and whether risks are at an acceptable level.

In the new Annex II.9 on the application of QRM to Supply Chain Control



- With regard to product availability risks related to quality/manufacturing issues, **lifecycle oversight of the supply chain includes maintaining current knowledge of quality/manufacturing hazards and prioritizing efforts to manage such risks**. Understanding hazards to quality/manufacturing is critical to maintaining supply predictability. When risks are well understood and minimized, a higher confidence in product availability can be attained.

Reflecting on Risk & Knowledge

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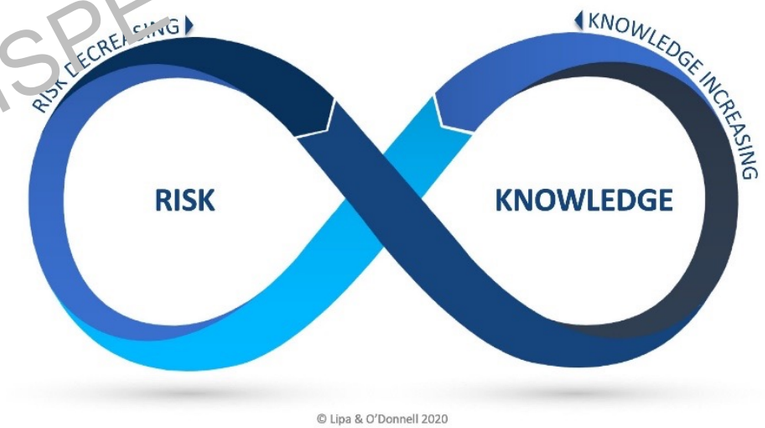
It is useful to note that, in the published ICH Informational Presentation on the revision, there is this statement:

> ***"The cross-references to ICH Q10 [in relation to KM] serve to highlight the importance of using available sources of knowledge… and Knowledge Management in general during QRM activities."***



An Introduction to the *RKI Cycle*

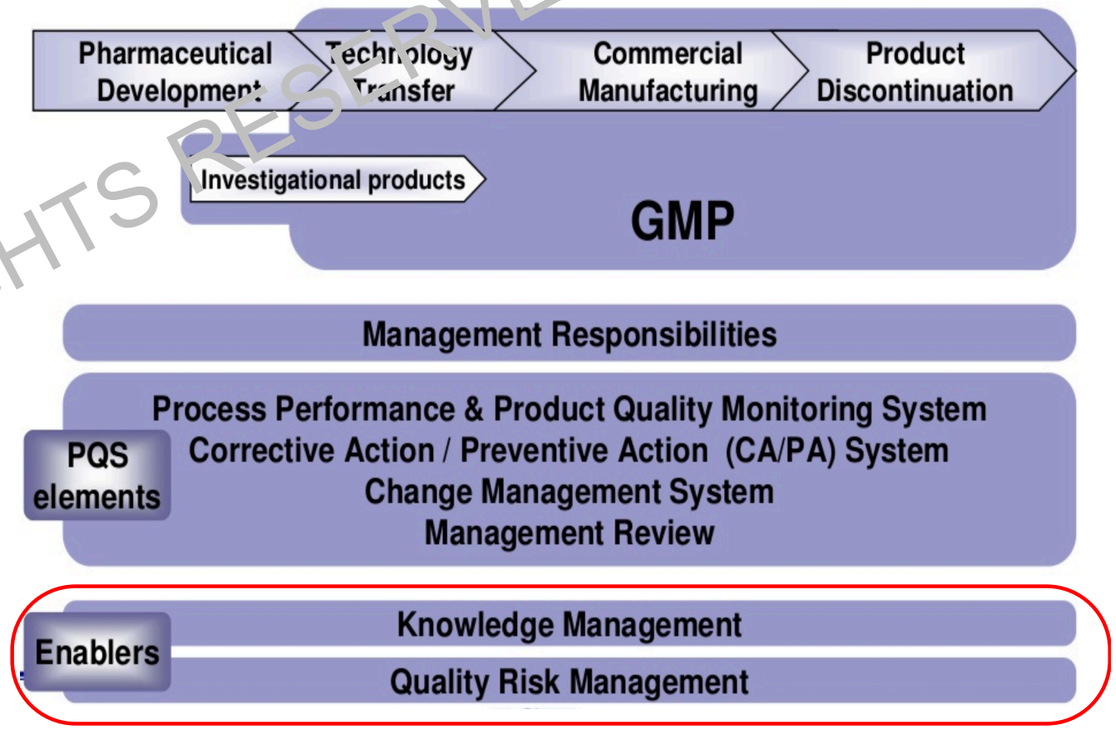
Re-thinking the connection between QRM and KM

Marty Lipa
Merck

Back to Basics

The purpose of QRM is to:
manage risk across the product lifecycle by
applying the best scientific knowledge
available to the organization
in order to
reduce risk to the patient

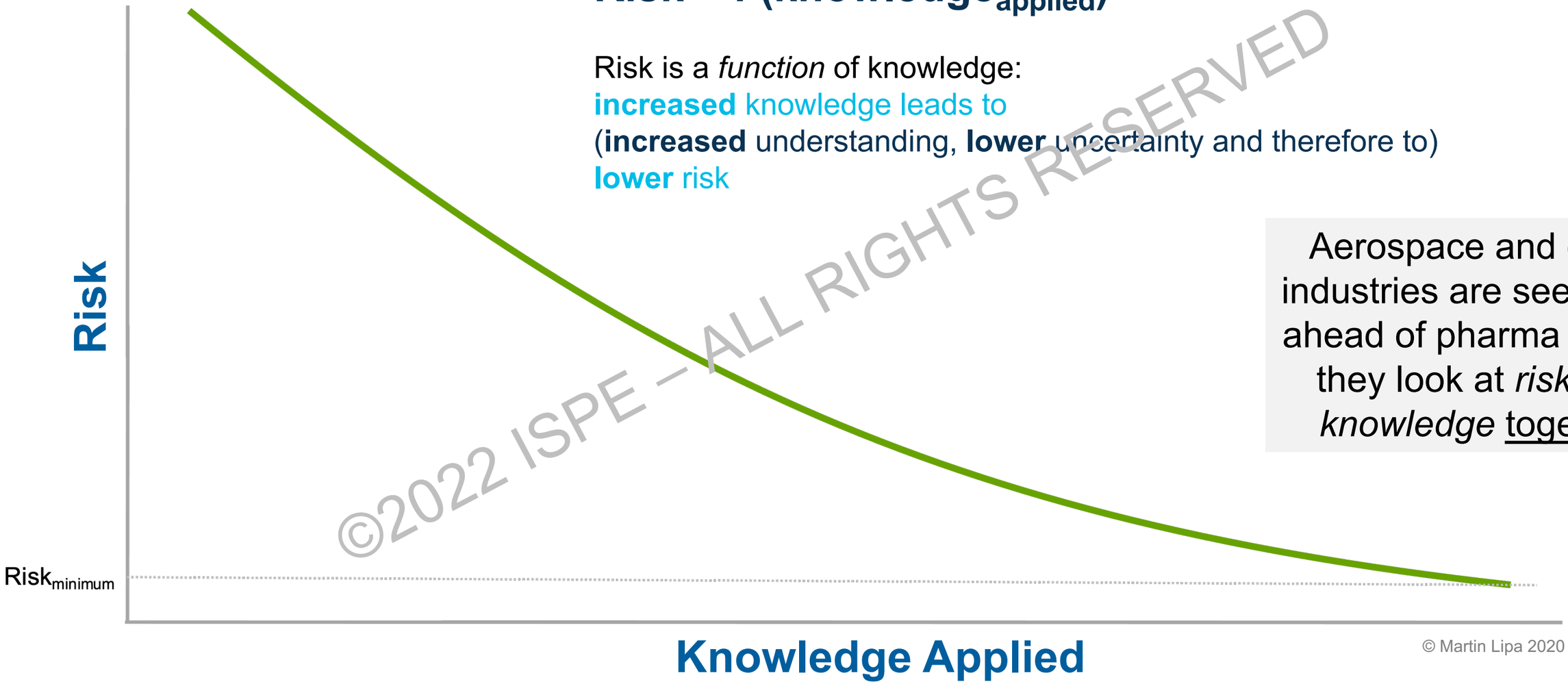
The purpose of KM is to:
deliver the **best available knowledge**
to the **right person**
at the **right time**
in order to
make the **right decision** and/or
give the **right advice**



Risk Varies Inversely with Knowledge *Application*

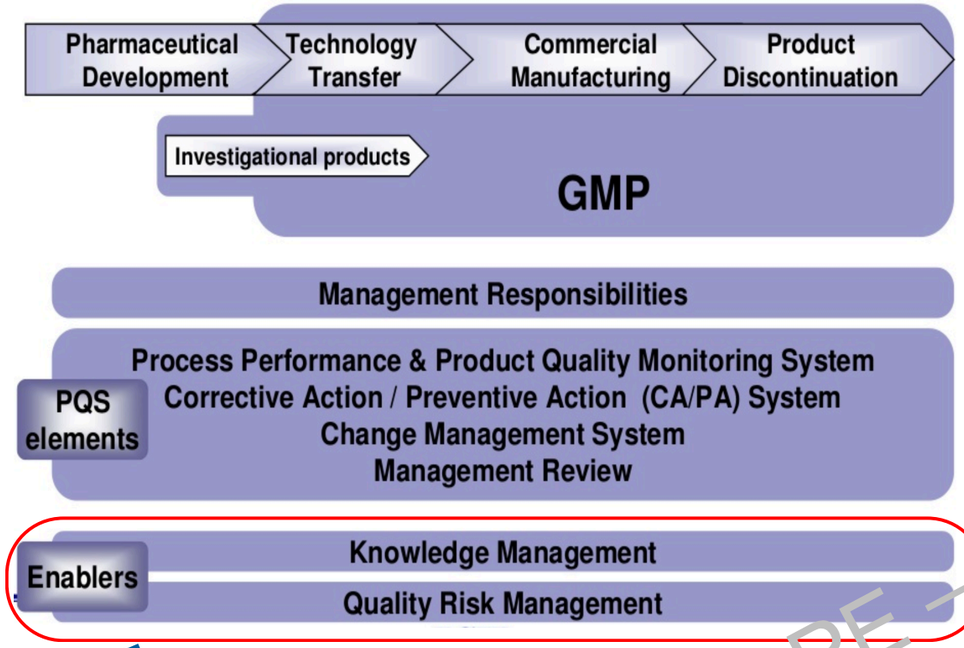
Risk = f (knowledge$_{applied}$)

Risk is a *function* of knowledge:
increased knowledge leads to
(**increased** understanding, **lower** uncertainty and therefore to)
lower risk



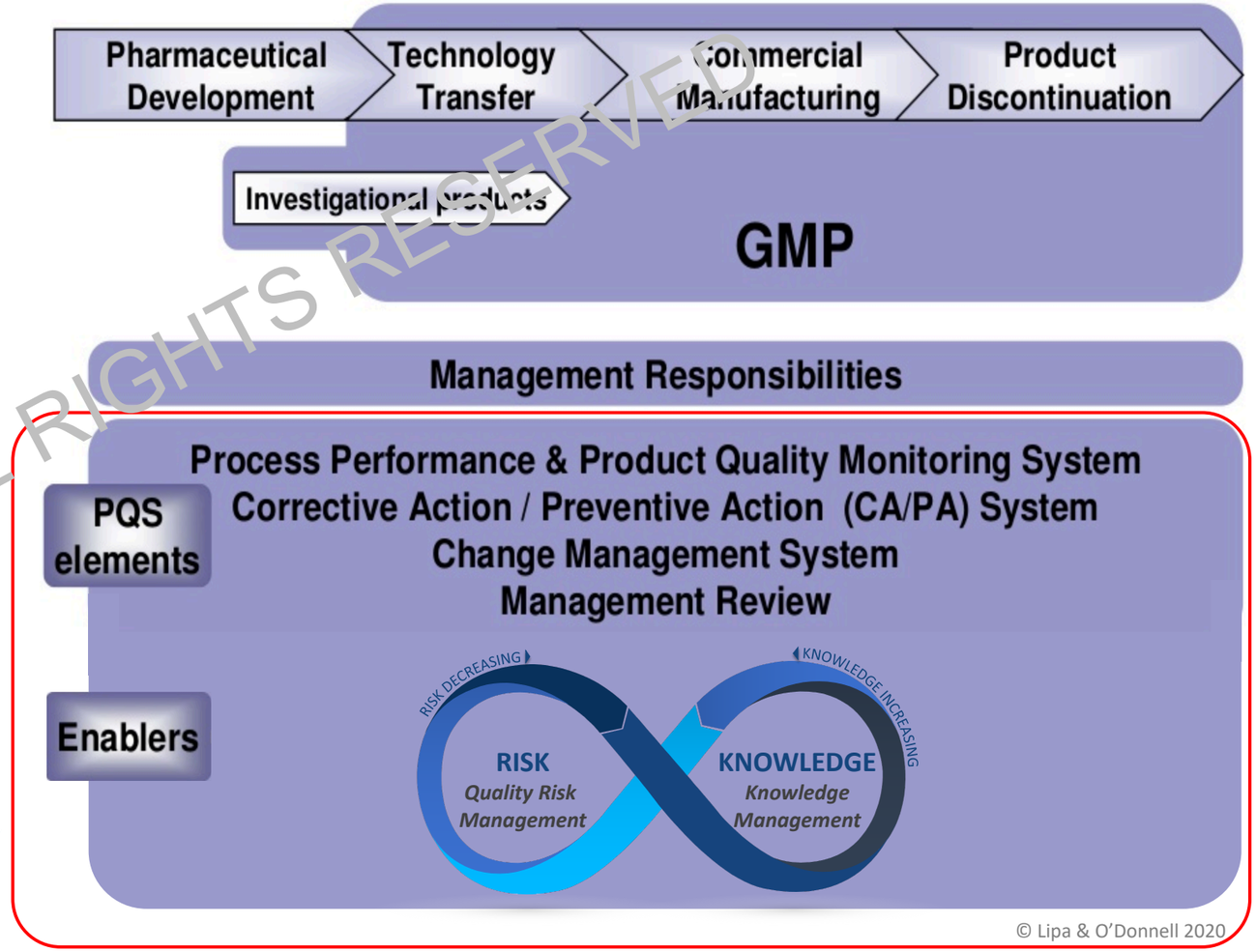
Aerospace and other industries are seemingly ahead of pharma in how they look at *risk* and *knowledge* together

Let's Look at the PQS Foundation Differently…



So why this…?

And not this…?



Risk-Knowledge Infinity Cycle (RKI Cycle) Framework

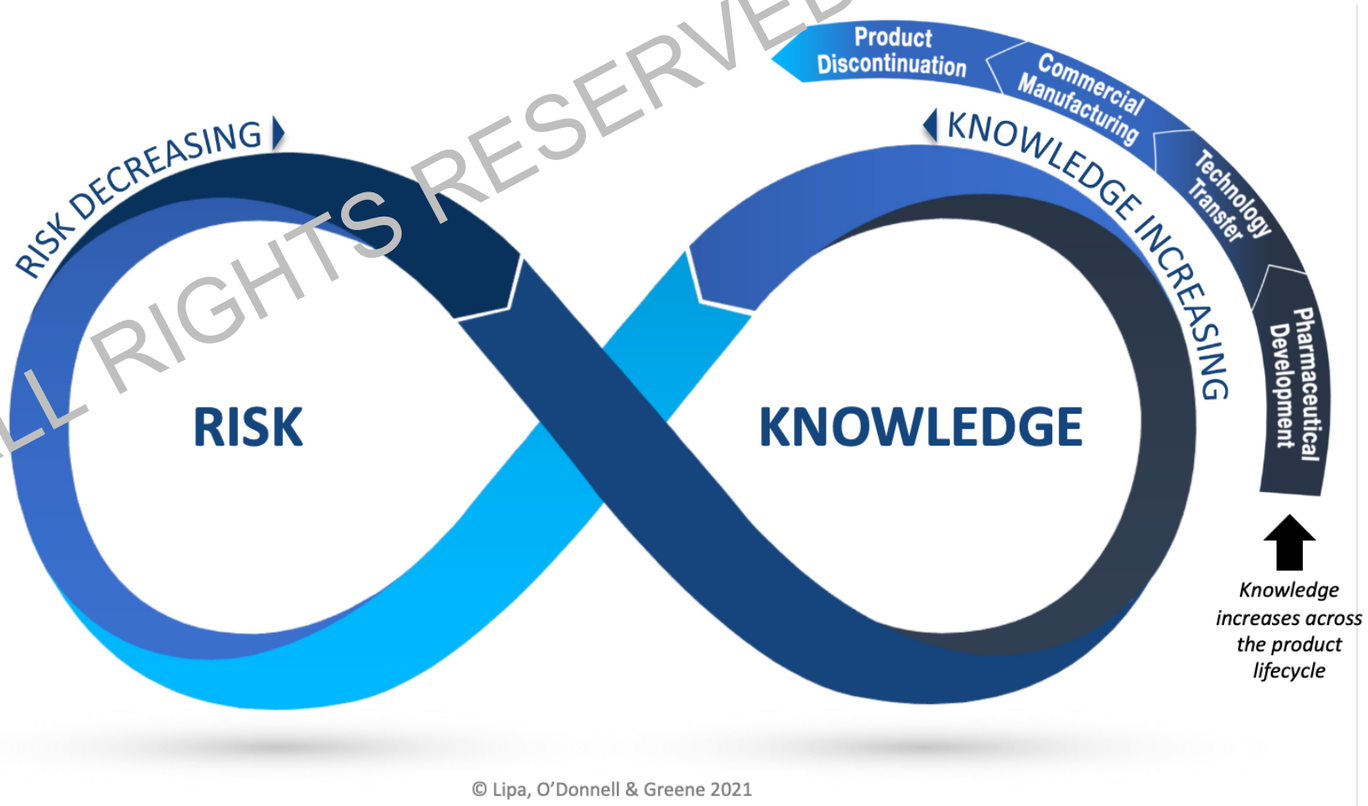
Key Concepts

- Knowledge is **both an input to and an output** from risk management
- Knowledge has an **inverse** relationship with risk
- **Concept of *flow***; knowledge flows effortlessly and on demand to inform risk, and risk informs new knowledge

- The cycle is **continuous and perpetual**; knowledge is always evolving and should be continually applied to inform risk

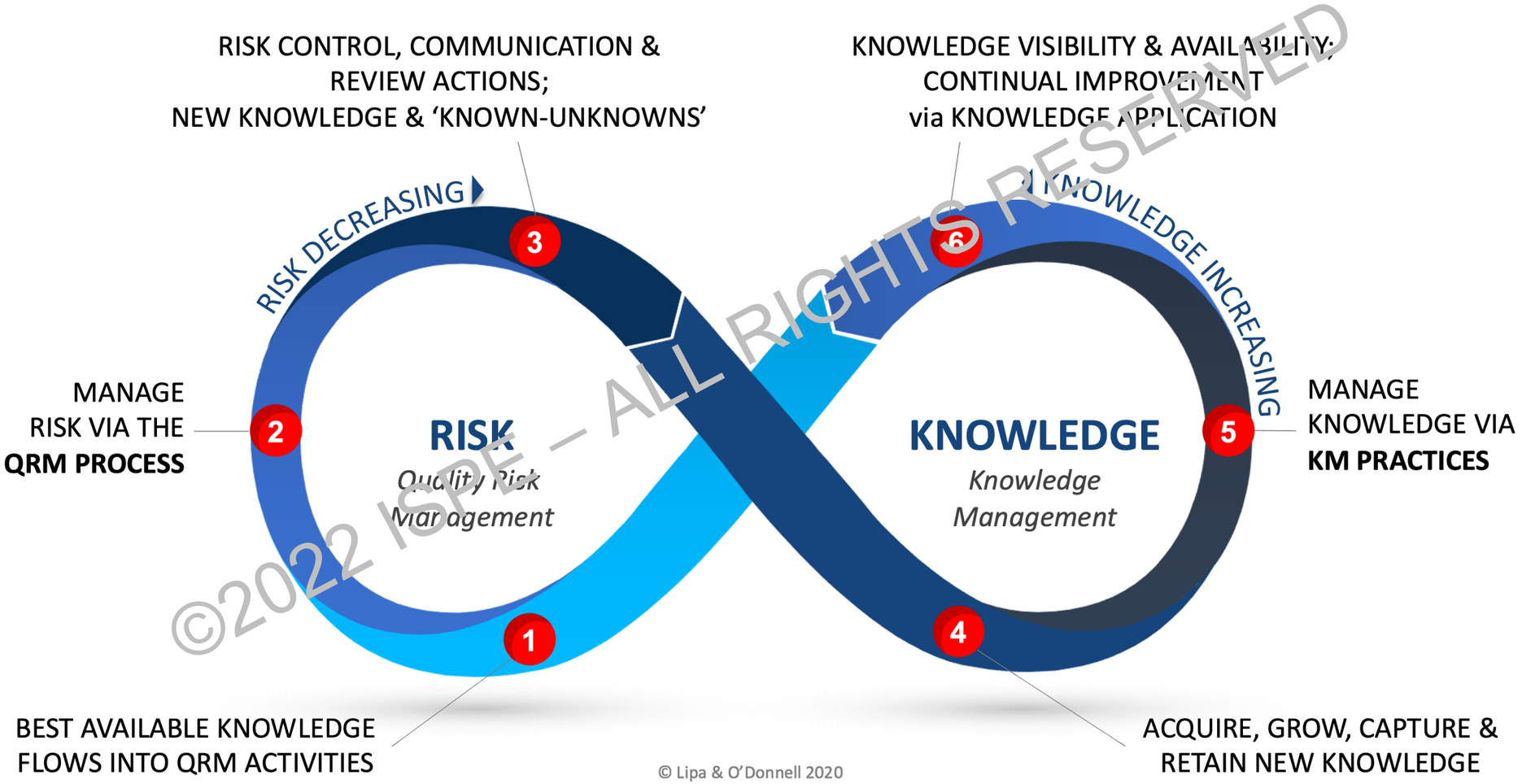
The *RKI Cycle* Applies across the Product Lifecycle

- Early in the product lifecycle when less is known about a product, **risk is higher**
- Over time **knowledge increases** through activities such as:
  - Application of prior knowledge, development activities
  - Manufacturing experience
  - Risk review
  - Investigations
  - Process changes
  - Innovations (etc.)
- This **knowledge** can (and should) be **applied** to **reduce risk**

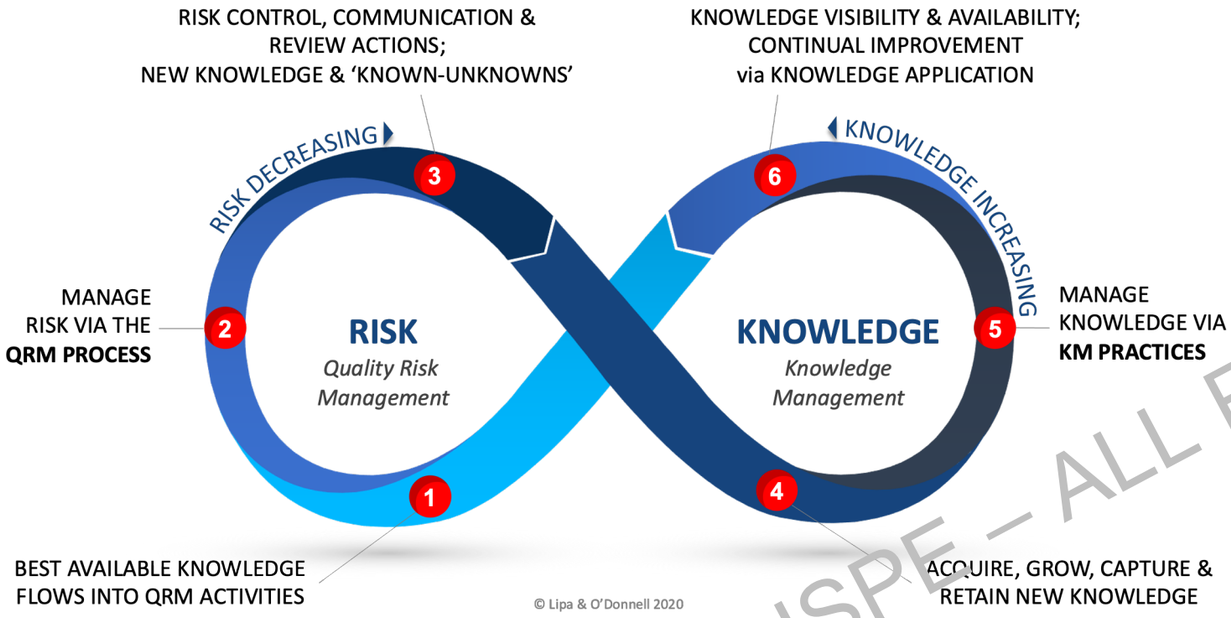


The *RKI Cycle* applied to ICH Q10

Applying a ‘systems thinking’ lens to the PQS co-enablers



The Opportunity of Meaningful QRM-KM Connectivity



90% agree deploying such a framework will improve QRM-KM integration

(10% unsure | 0% disagree)

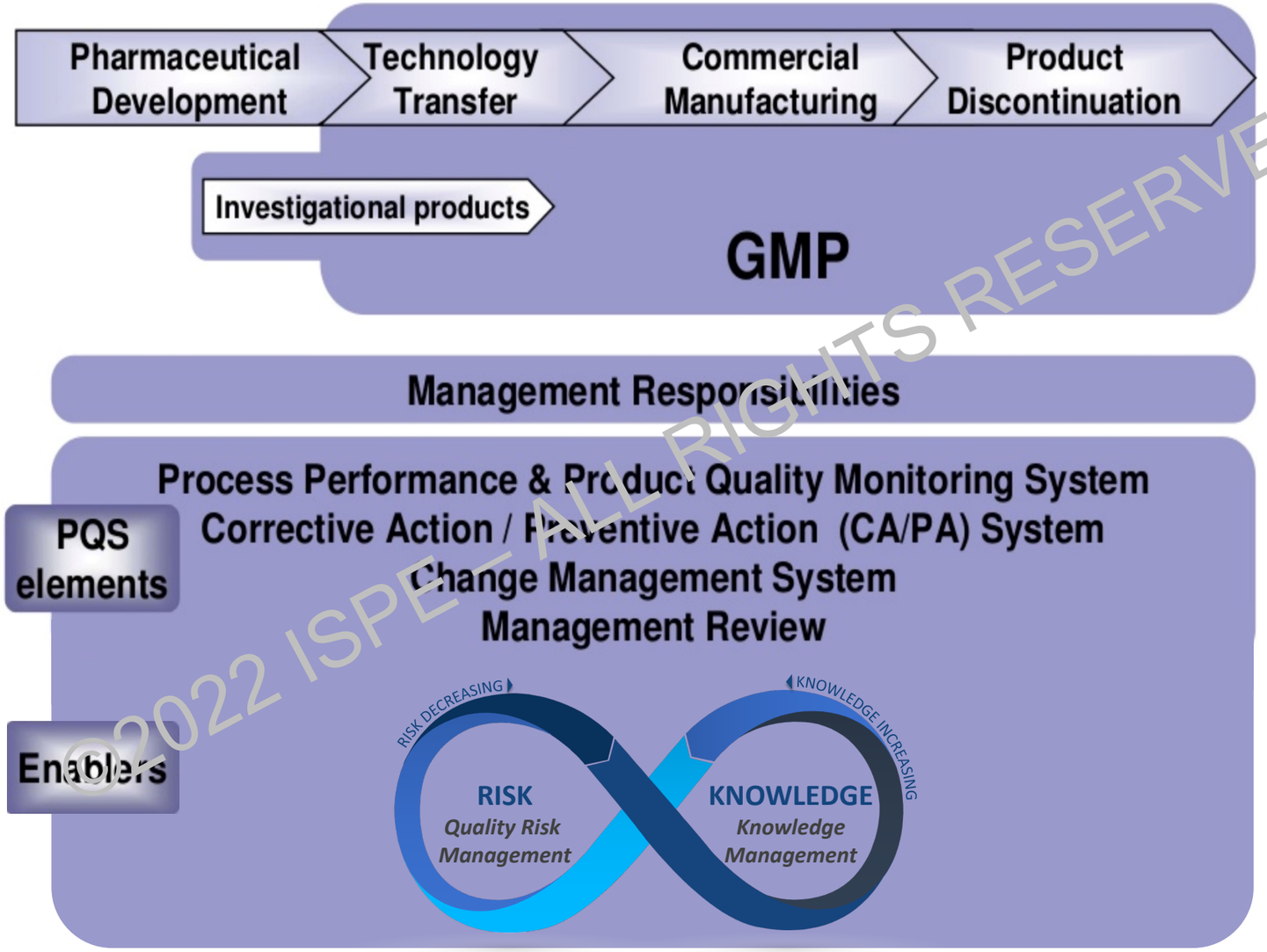
Top anticipated benefits

1. More **data driven risk assessments**
2. Better **risk-based decisions**
3. Increased ability to **leverage prior knowledge**

Top rated actions

1. Establish practices / procedures to **operationalize integration** of QRM & KM
2. Define type of **knowledge created by QRM** and how this should be managed
3. Develop ways where **KM is a formal input in all risk assessments**

A Re-imagined PQS Foundation



Effective Risk-Based Decision Making in the PQS

The Next Horizon in QRM

Valerie Mulholland
GMP Services Ltd

RBDM

Its Complex!

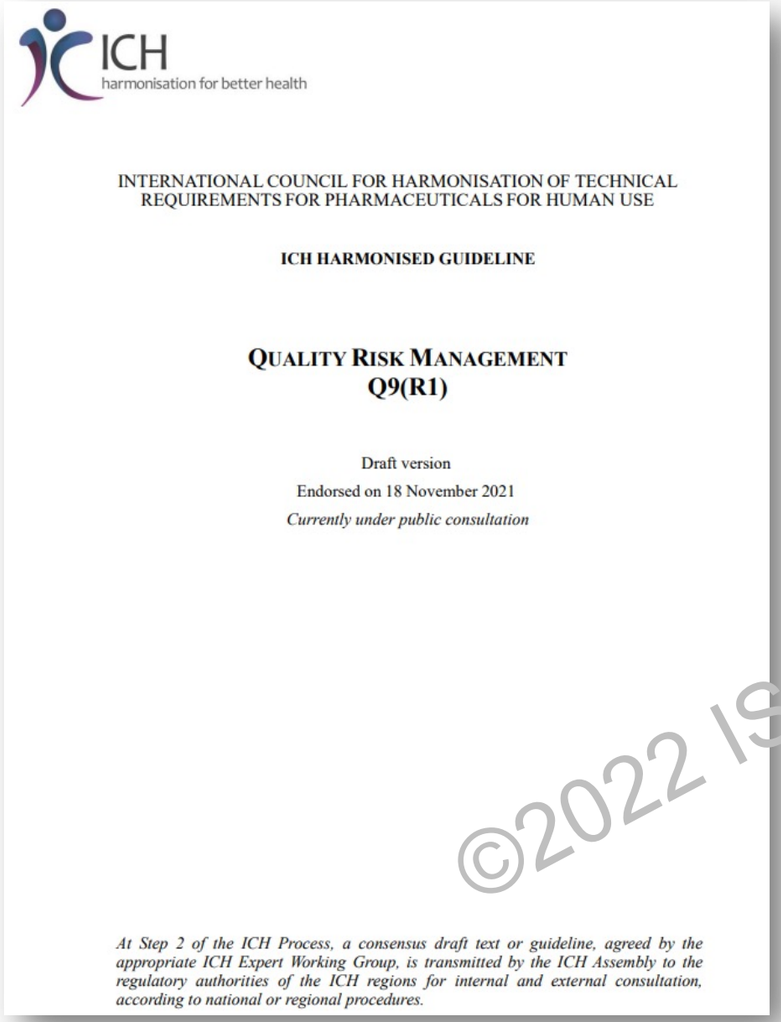
LACK OF CLARITY ON RISK-BASED DECISION-MAKING:

While there are references in ICH Q9 to decision-making,
there is a lack of clarity on what good risk-based decision making actually means,
how QRM may improve decision-making,
or how risk-based decisions might be achieved.

There is a breadth of peer-reviewed research in this area,
but the level of visibility (and uptake) of that research within the pharmaceutical industry may be improved

ICH Q9 (R1) Concept Paper – Nov 2020

RBDM – ICH Q9 (R1)



ICH
harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

QUALITY RISK MANAGEMENT
Q9(R1)

Draft version
Endorsed on 18 November 2021
Currently under public consultation

At Step 2 of the ICH Process, a consensus draft text or guideline, agreed by the appropriate ICH Expert Working Group, is transmitted by the ICH Assembly to the regulatory authorities of the ICH regions for internal and external consultation, according to national or regional procedures.

Risk Based Decision Making

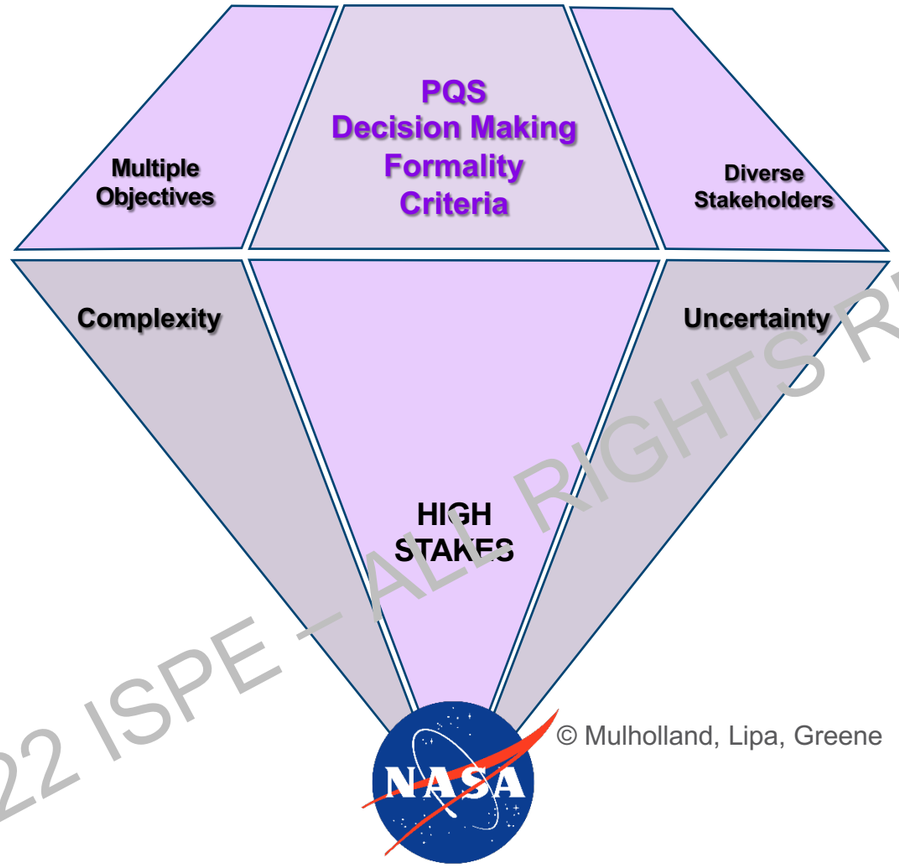
An approach or process that considers
knowledge about risks
relevant to the decision &
whether risks are at an acceptable level

IMPORTANCE

INFORMAL…..LOW HIGH

Potential to impact a CQA? CPP? High Severity?
Supply?
Outside our own PQS?

RBDM – Applying Formality



© Mulholland, Lipa, Greene

DECISION TRAIL

Mulholland, Valerie and Greene, Anne (2020)
"Quality Risk Management: Seeking the Diamonds: Making the Case for Improved Formality in QRM Decision-making,"
Level 3: Vol. 15: Iss. 2, Article 18. doi:https://doi.org/10.21427/yfw0-hy89
Available at: https://arrow.tudublin.ie/level3/vol15/iss2/18

RBDM – ICH Q9(R1)

Effective risk-based decision-making begins with determining the level of **effort, formality, and documentation** that should be applied during the quality risk management process.

Low Complexity
Low Uncertainty

Simpler Methods

- ✓ Voting
- ✓ Weighted Scoring
- ✓ Decision Trees
- ✓ Influence Diagrams
- ✓ Human Factor Analysis
- ✓ Risk / Benefit Analysis

NOT DESCRIBED IN ICH Q9 (R1)

RBDM – ICH Q9(R1)

Effective risk-based decision-making begins with determining the level of **effort, formality, and documentation** that should be applied during the quality risk management process.

NOT DESCRIBED IN ICH Q9 (R1)

- ✓ Multicriteria Decision-Making Tools
- ✓ Fuzzy Logic
- ✓ Cumulative Risk Assessments
- ✓ Transition Tools
- ✓ Monte Carlo Simulations
- ✓ Adaptive Modeling

High Complexity
High Uncertainty

Complex Methods

POLL # 2

Do you have FORMAL procedures or tools to support Risk Based Decision Making in your PQS?

LOW	HIGH
✓ Voting ✓ Weighted Scoring ✓ Decision Trees ✓ Influence Diagrams ✓ Human Factor Analysis ✓ Risk / Benefit Analysis	✓ Multicriteria Decision-Making Tools ✓ Fuzzy Logic ✓ Cumulative Risk Assessments ✓ Transition Tools ✓ Monte Carlo Simulations ✓ Adaptive Modeling

- ❑ No, we do not have formal tools for RBDM
- ❑ Yes, we have some formal tools, adequate for LOW complexity RBDM
- ❑ Yes, we have formal tools, adequate for HIGH complexity RBDM

RBDM – ICH Q9(R1)

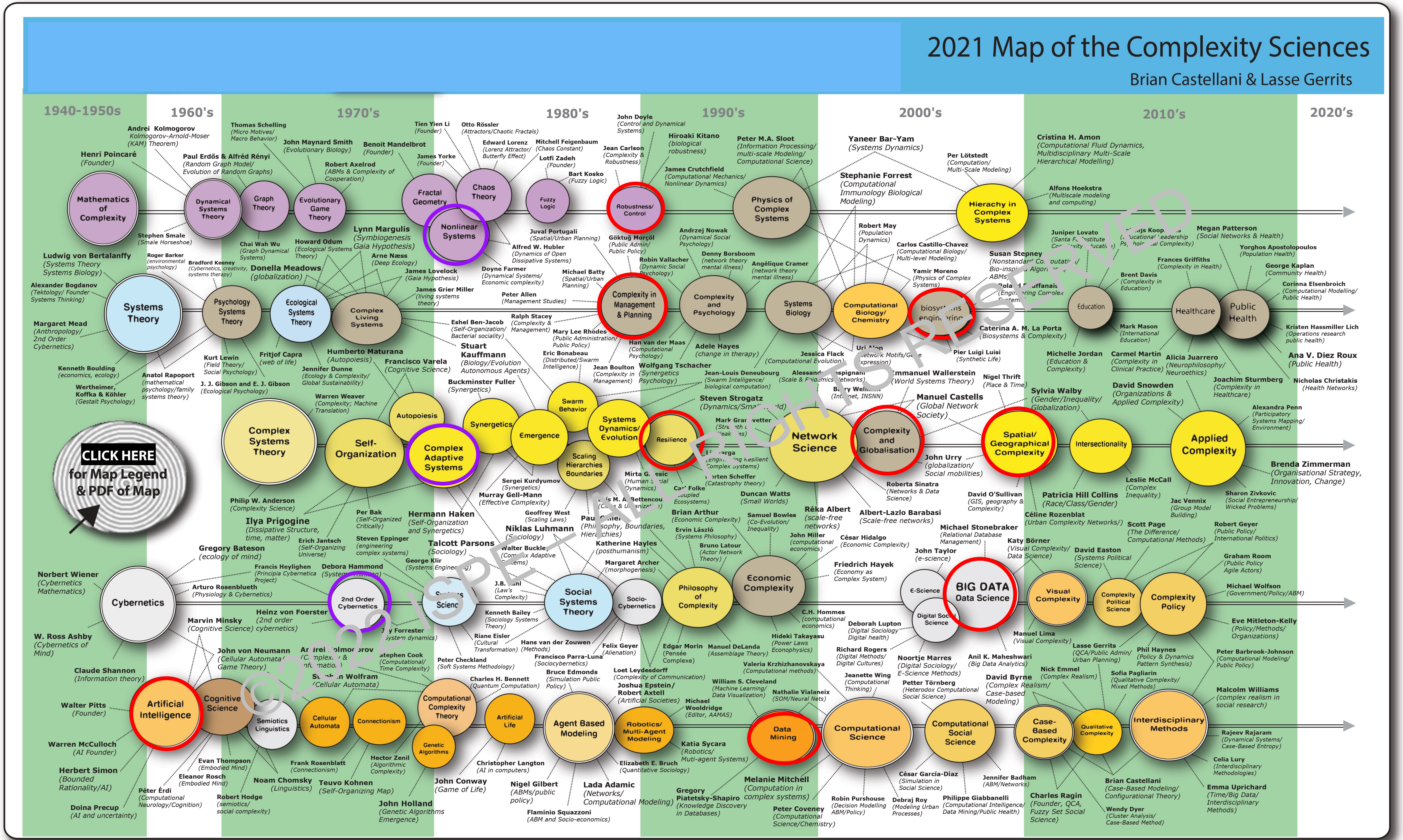
Effective risk-based decision-making begins with determining the level of **effort, formality, and documentation** that should be applied during the quality risk management process.

NOT DESCRIBED IN ICH Q9 (R1)

- ✓ Multicriteria Decision-Making Tools
- ✓ Fuzzy Logic
- ✓ Cumulative Risk Assessments
- ✓ Transition Tools
- ✓ Monte Carlo Simulations
- ✓ Adaptive Modeling

High Complexity
High Uncertainty

Complex Methods


2021 Map of the Complexity Sciences
Brian Castellani & Lasse Gerrits
1940-1950s
1960's
1970's
1980's
1990's
2000's
2010's
2020's
Mathematics of Complexity
Dynamical Systems Theory
Graph Theory
Evolutionary Game Theory
Fractal Geometry
Chaos Theory
Nonlinear Systems
Fuzzy Logic
Robustness/ Control
Physics of Complex Systems
Hierachy in Complex Systems
Systems Theory
Psychology Systems Theory
Ecological Systems Theory
Complex Living Systems
Complexity in Management & Planning
Complexity and Psychology
Systems Biology
Computational Biology/ Chemistry
Education
Healthcare
Public Health
Complex Systems Theory
Self-Organization
Autopoiesis
Complex Adaptive Systems
Synergetics
Emergence
Swarm Behavior
Systems Dynamics/ Evolution
Scaling Hierarchies Boundaries
Resilience
Network Science
Complexity and Globalisation
Spatial/ Geographical Complexity
Intersectionality
Applied Complexity
CLICK HERE for Map Legend & PDF of Map
Cybernetics
2nd Order Cybernetics
Social Systems Theory
Socio-Cybernetics
Philosophy of Complexity
Economic Complexity
E-Science
Digital Social Science
BIG DATA Data Science
Visual Complexity
Complexity Political Science
Complexity Policy
Artificial Intelligence
Cognitive Science
Semiotics Linguistics
Cellular Automata
Connectionism
Computational Complexity Theory
Genetic Algorithms
Artificial Life
Agent Based Modeling
Robotics/ Multi-Agent Modeling
Data Mining
Computational Science
Computational Social Science
Case-Based Complexity
Qualitative Complexity
Interdisciplinary Methods
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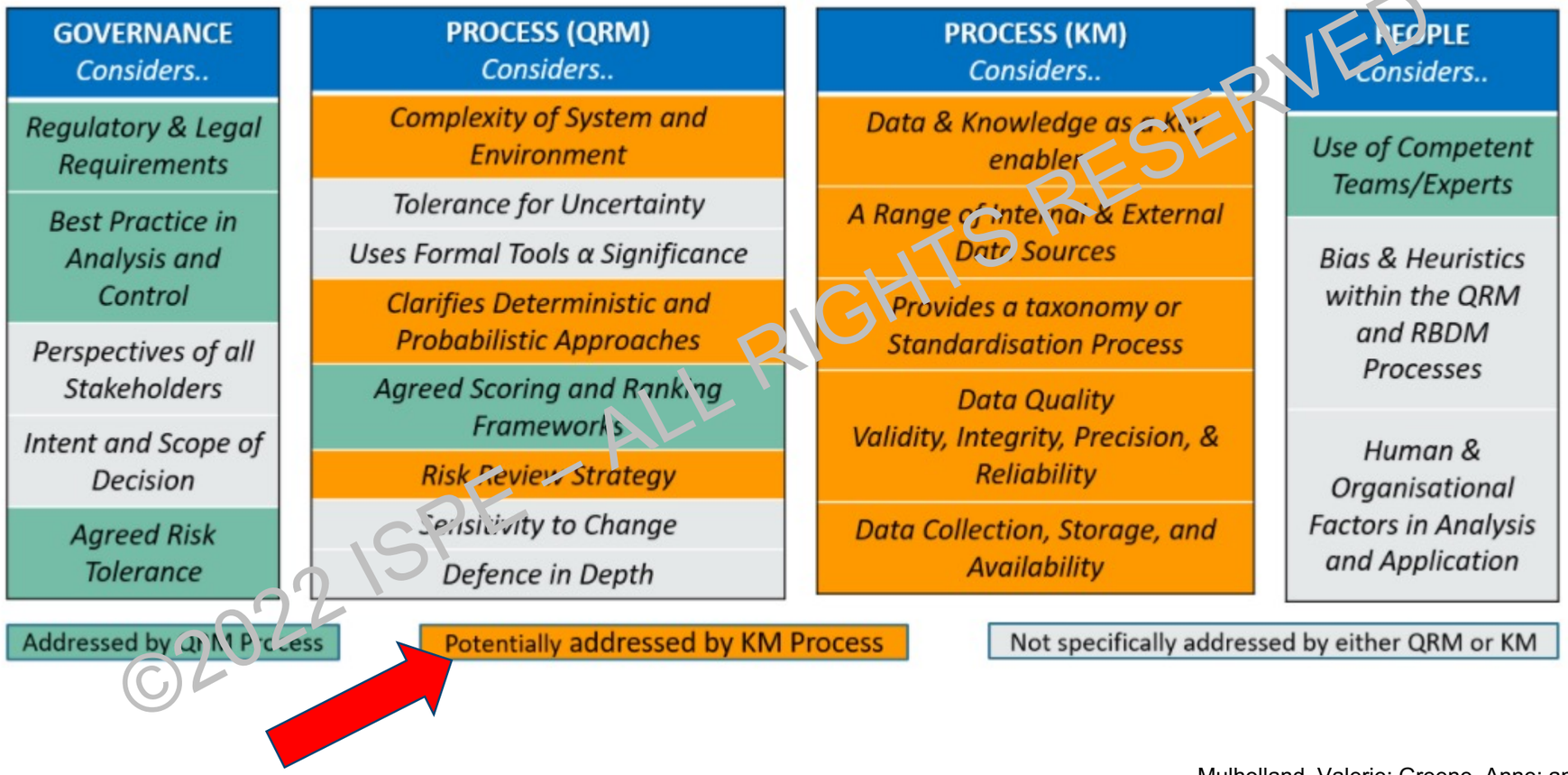
Explored these industry sectors…

Workplace Safety
Civil Aviation
Medicinal Products
Nuclear Energy
Aerospace
Project Management
Enterprise Energy
Defense
Finance
Medical Device
Blood Banking
Environment

And examined sector standards derived from…

ISO
SM ICG
HSE Health & Safety Executive
EUROPEAN MEDICINES AGENCY
Alliance of Blood Operators
Project Management Institute
UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
COSO
IAEA
NASA
HM TREASURY


(21) Characteristics of RBDM



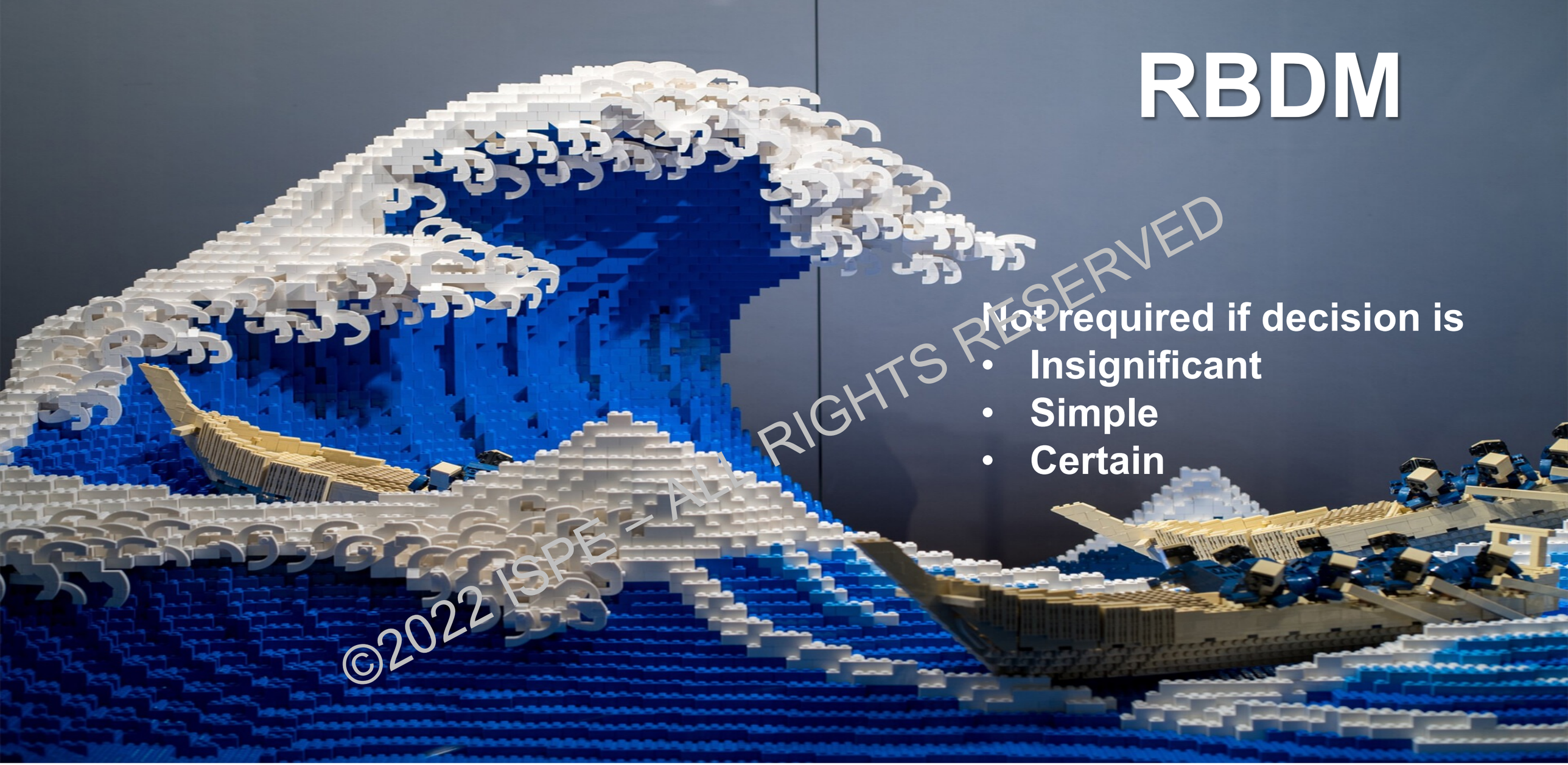
Mulholland, Valerie; Greene, Anne; and Lipa, Martin J. (2021)
"Steps Beyond Risk Assessment in QRM: RBDM, The next horizon,"
Level 3: Vol. 16: Iss. 1, Article 2.
Available at: https://arrow.tudublin.ie/level3/vol16/iss1/2

21 RBDM Characteristics

1	2	3	4	5	6	7
Intent & Scope of Decision is Clear	Meets all Legal Requirements	Satisfies all Stakeholders	Risk Tolerance is agreed	Uses agreed Ranking Scores	Based on high quality risk analysis	Considers Uncertainty
8	9	10	11 ★	12 ★	13 ★	14 ★
Considers Complexity	Deterministic v Probabilistic Approach	Uses Formal RA Tools	Uses Best available Knowledge	References both Internal & External Sources	Knowledge is Codified and Accessible	Knowledge is accurate and reliable
15	16	17	18	19	20	21
Competent Teams	Subjectivity is Controlled	Human Factors are Considered	Prefers Defence in Depth	Considers Risk Sensitivity	Applies Risk Review Strategy	Records Decision Trail

Addressed by QRM Process

Potentially Addressed by KM Process



RBDM

Not required if decision is

- **Insignificant**
- **Simple**
- **Certain**

KNOWLEDGE

- Dynamic / Many Influences
- Non-Linear
- Complex (High)
- Risk-Based Decision Making

- Rule-Based Decision Making
- Low → High

RBDM

Connecting Pharmaceutical Knowledge

ISPE®

Pharmaceutical REGULATORY SCIENCE Team

Effective RBDM – The Next Horizon

- QRM and KM are fundamental as enablers
- Decision Makers need to fully understand Complexity, ..and Uncertainty, when making IMPORTANT decisions with respect to Risk.
- Good RBDM may also depend on a number (21?) of further considerations (AKA characteristics) – but KM is key to 8/21

WORKSHOP: Exploring RKI Node 1

How could KM inform QRM for improved RBDM?

Workshop Intro: A Knowledge Map for QRM

Recall, an array of guidance including ICH Q8, Q9, Q10, WHO establish a **clear expectation that knowledge informs risk** and should be used together to inform decision making in order to protect the patient

At the outset of a QRM activity, one must be prepared to answer fundamental questions

1) What could go wrong?
2) How likely is it?
3) Will you be able to detect it?

And a categorical fourth question

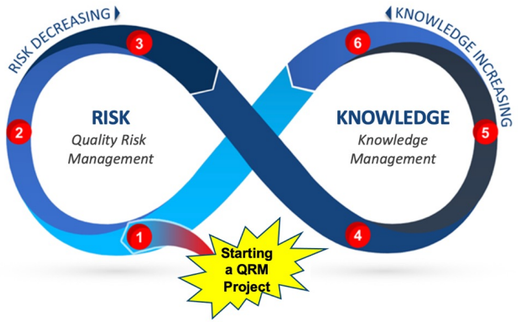
4) How sure are you? How sure do you need to be? Is the result suitable?

Workshop Intro: A Knowledge Map for QRM

How will you ensure you **apply the best knowledge, experience, know-how, expertise & prior knowledge** to perform an optimal risk assessment and support the best possible risk-based decision?

Ask yourself…

1) Is the most current knowledge visible, available and accessible on demand?
2) Is the knowledge of sufficient 'quality' for use?
3) What are you missing?



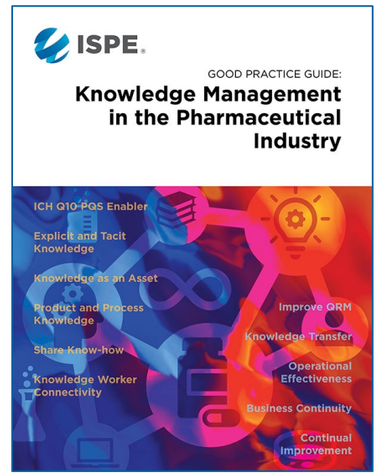
QRM questions:

1) What could go wrong?
2) How likely is it?
3) Will you be able to detect it?
4) How sure are you?
   How sure do you need to be?
   Is the result suitable?

Activity OR process step	What knowledge is needed?	Who has it? (Sources)	Who needs it? (Recipients)	Where is it?	What format is it in?	Gap (high, med, low)	Comments
A							
B							
C							

https://www.apqc.org/blog/great-process-improvement-begins-knowing-your-knowledge-gaps

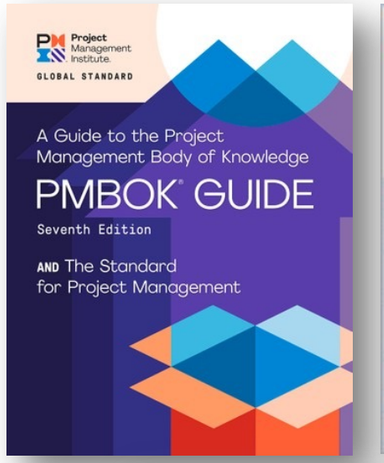
A **knowledge map** can help answer these questions!

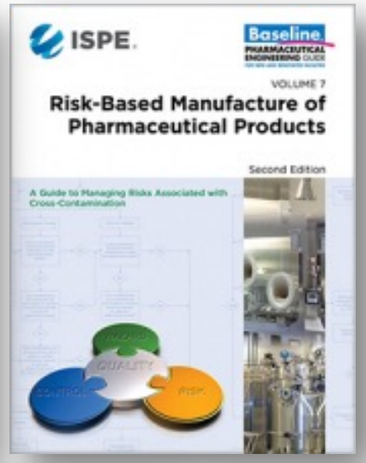


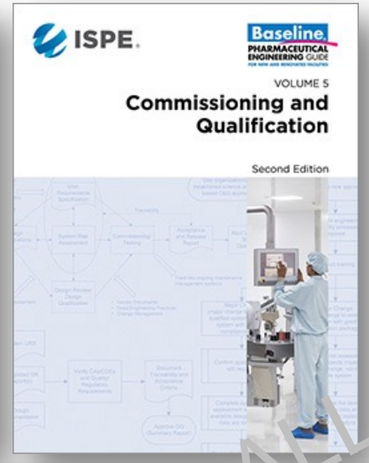
Also featured in **ISPE KM Good Practice Guide**

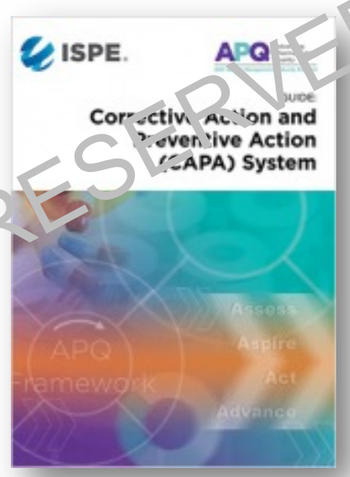
Sources of Knowledge for QRM: The Guidance!

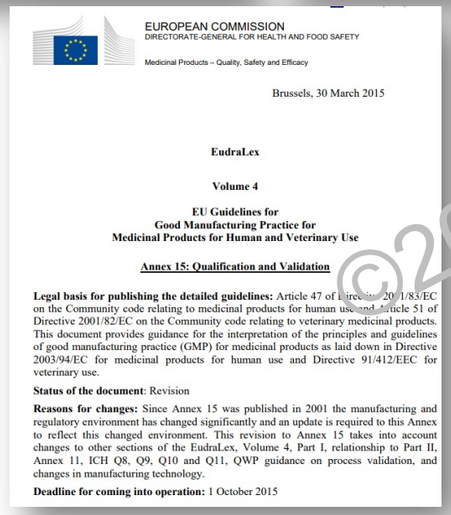
We explored several guidance documents that **detail** sources of information & knowledge that may inform the QRM process (and consequentially RBDM)

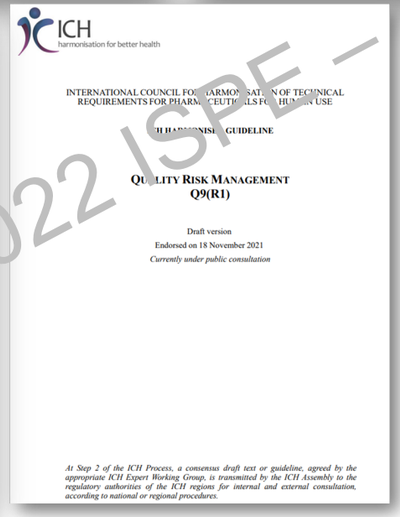


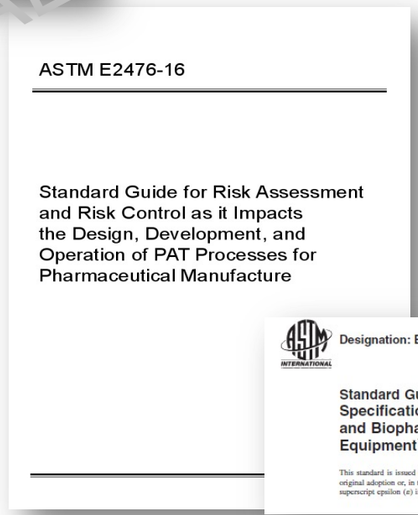


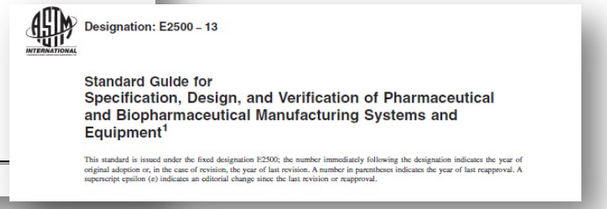












Perhaps there are more?

Bias to 'New' Processes & Technology

Sources of Knowledge for QRM: The Guidance!

Product Knowledge	Regulatory Requirements	PQS Knowledge	Project Capability	QRM Knowledge
• Lifecycle documents • Specifications/ Acceptance Criteria – Product • Specifications/ Acceptance Criteria – Materials • Design/ Validation Documents - Measurement & Analysis Systems • History of Product Issues (Product under analysis or related) • Supply Chain (Product & Materials) • Toxicology Data/ Acceptable Daily Exposure (ADE) Value • Information and/ or data on the potential hazard, harm or human health impact relevant to the risk assessment; • Degradation Pathways/ Stability Data	• Applicable Legislation, Laws, EHS, etc. • Guidance/Best Practice Documents • Pharmacopeial and Test Standards • Submitted/ Approved Regulatory Filings	• Change Management Strategy • PQS Procedures - Process under analysis • Quality Records • Maintenance Records • Validation Procedures and Policies • Supplier Management/Procurement P&Ps • CAPA Data - Complaints/ audits/ Deviations/ Trends • APR/Management Reviews • Business Strategy/Priority for Product	• Contracts/Scope/Turn-Over-Packages • C&Q Plans/Schedules • Capabilities & Resources • Laboratory Support Capabilities • Training Procedures and Policies • Good Engineering Practice • Roles & Responsibilities • EHS Documents -Safety Data • Conflicting Objectives/Requirements • KM Outputs (Legacy Requirements)	• Risk Management Knowledge • Risk Management Procedures and Policies • Defined Risk Question/Scope • Trained RM Practitioners/Facilitators • Specify a timeline, deliverables and appropriate level of decision making for the risk management process.

Process Knowledge

• Process User Requirements • Specifications/ Acceptance Criteria - Process • Design/ Validation Documents - Facility & Utilities • Design/ Validation Documents - Process and Equipment • Design/ Validation Documents - Process Controls • Design/ Validation Documents - Measurement & Analysis Systems • Design/ Validation Documents - Software Systems • Design/ Validation Documents - Cleaning • History of Problems with process/outputs	• Drawings • Calibration Requirements • QRM Documents from design/previous stages • System Integration Requirements • Equipment Manuals/ Technical Specifications • Materials of Construction • Process Capability/Performance Indices • Routes for Contamination/Cross Contamination • Cleaning Process Performance Capability • Training & Competence in Process • Prior Knowledge/Lessons Learnt - current or other locations

Case Study: Installation of an Autoclave (Parts Sterilization)

Product Knowledge	Regulatory Requirements	PQS Knowledge	Project Capability	QRM Knowledge
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Process Knowledge

• Process User Requirements • Specifications/ Acceptance Criteria - Process • Design/ Validation Documents - Facility & Utilities **Technical/Explicit** • Design/ Validation Documents - Process and Equipment • Design/ Validation Documents - Process Controls • Design/ Validation Documents - Measurement & Analysis Systems • Design/ Validation Documents - Software Systems • Design/ Validation Documents - Cleaning • History of Problems with process/outputs	• Drawings • Calibration Requirements • QRM Documents from design/previous stages • System Integration Requirements • Equipment Manuals/ Technical Specifications • Materials of Construction • Process Capability/Performance Indices • Routes for Contamination/Cross Contamination • Cleaning Process Performance Capability • Training & Competence in Process • Prior Knowledge/Lessons Learnt - current or other locations **Prior/ Tacit**

Case Study: Installation of an Autoclave (Parts Sterilization)

	Characteristic	Category	Chosen to illustrate…
1	Design/ Validation Documents - Facility & Utilities	Process Knowledge	Technical / Explicit
2	Prior Knowledge/Lessons Learnt - current or other locations	Process Knowledge	Prior / Tacit
3	Routes for Contamination/Cross Contamination	Process Knowledge	Explicit / Tacit
4	QRM documents from Product/Process Development	Product/ Process Knowledge	Explicit / Tacit
5	System Integration Requirement e.g. MES, EBR, BMS, etc	Process Knowledge	Planning
6	Applicable Regulations/Guidance	Regulatory Knowledge	Governance

Instructions – QRM Knowledge Map

Explicit Knowledge = Codified knowledge
[written down in a document, a video, an image, …]

Tacit Knowledge = Knowledge in people's heads
[know-how, know-why, know-who, experience, expertise, decision rationale, rules of thumb, thought models, …]

1. Simplified knowledge map template
   (1) Knowledge type (tacit or explicit)
   (2) Knowledge FLOW
   (3) Knowledge QUALITY

2. Today is about the process, not the data…
   - Ratings will be highly org specific
   - Portraying a common and established example
   - The discussion is about the thinking and the insights a Knowledge Map can provide

Attribute / Rating	*FLOW* of knowledge - **Available, accessable, on demand**? - Are **heroics** needed? - Can a **newcomer** figure it out quickly?	*QUALITY* of knowledge - **Reliable** (for intended use)? - Sufficient **Context & Rationale**? - Is it **Complete & Accurate**?
Excellent	Flows readily. You get what you need on demand, when and where needed. Processes are in place.	Meets all criteria as expected (no lacking context, rationale, etc.)
Marginal	Minor issues or inefficiency but can get what is needed without wasting much time or energy	Minor issues requiring simple clarification or explanation with no disruption
Poor	Significant barriers, waste, frustration, inconsistency (etc.) in finding what is needed on demand	Issues which require resources (time, people, etc.) to resolve or not optimally support QRA / RBDM

Rating rubric

3. In your ratings…
   - Consider the overall experience – not just *you* personally. Think: Can a newcomer figure it out?
   - Don't overlook tacit knowledge: Is a document alone *really* sufficient or do you need to talk to a human?
   - Use the most conservative rating if unsure (in alignment with QRM principles)
   - Be honest and candid, there is no right or wrong; use CHAT to share any comments

Knowledge Mapping Exercise

Survey on QRM Knowledge Mapping

Break Time!

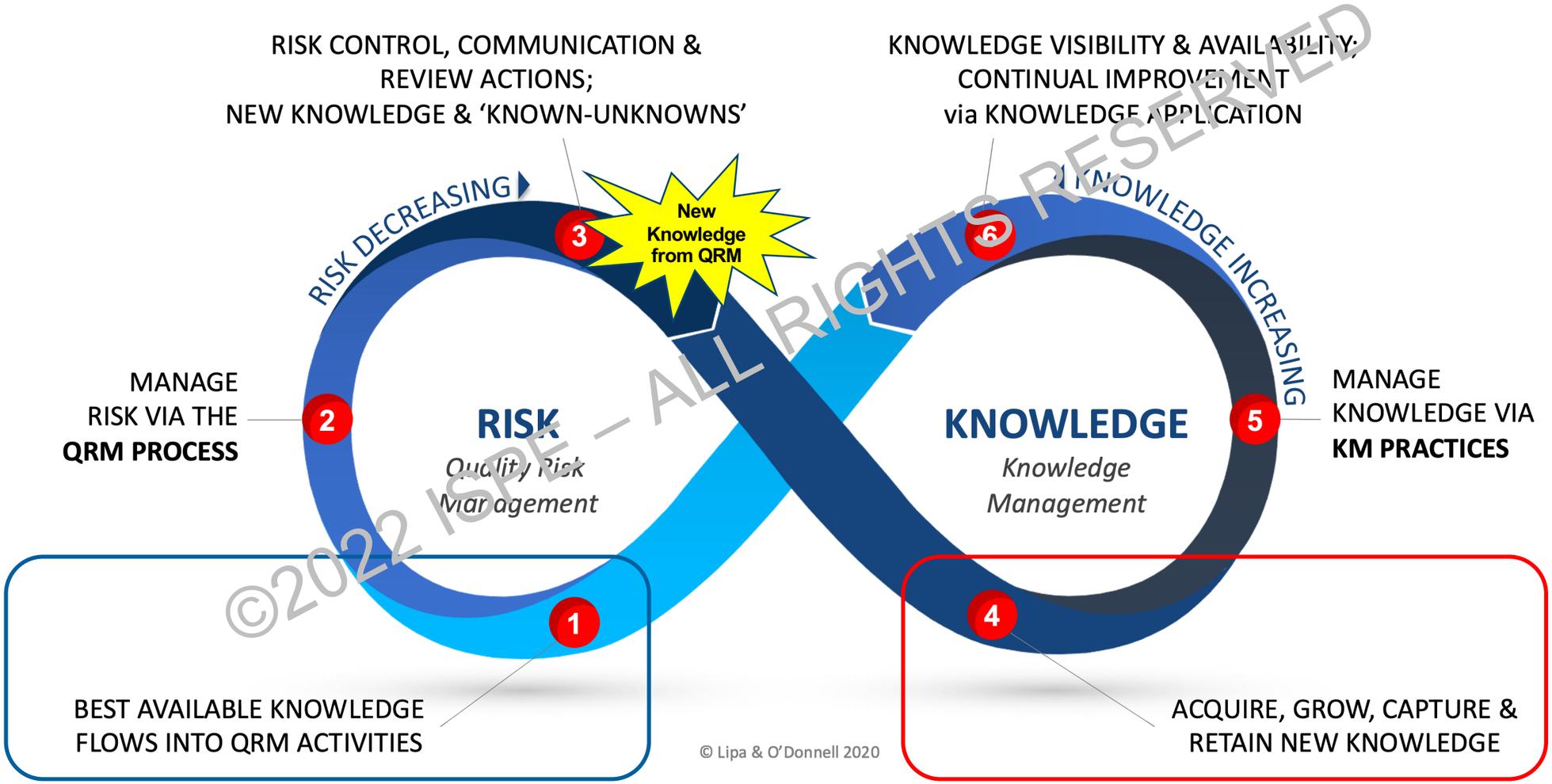
Please take a quick stretch and biobreak

Exploring RKI Node 4
New Knowledge from QRM

Reflection & Group Discussion

The *RKI Cycle* applied to ICH Q10

Applying a ‘systems thinking’ lens to the PQS co-enablers



Knowledge as an Output from QRM
Illustrative excerpts from regulatory guidance

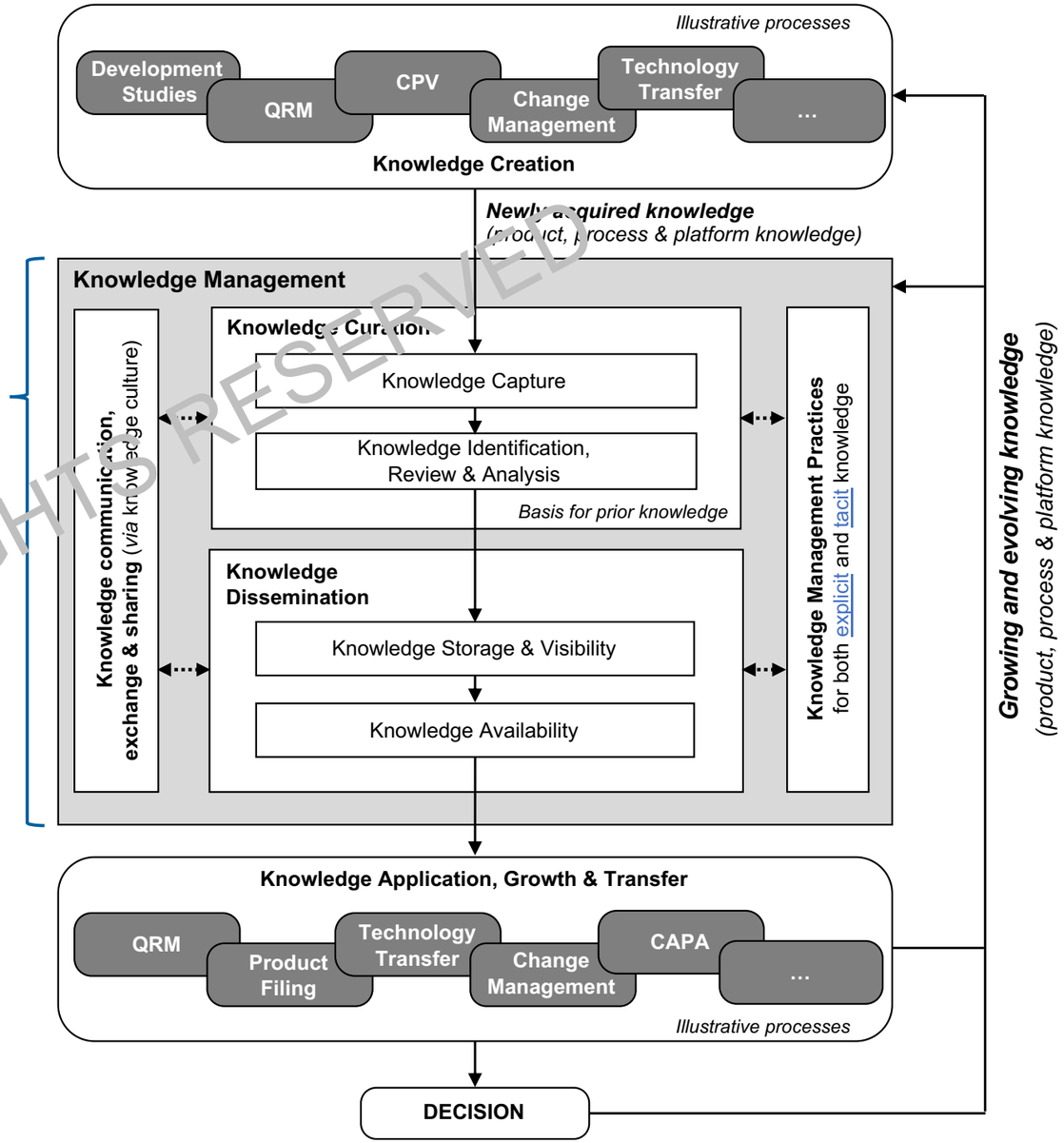
- ICH Q8(R2)
  - "[Pharmaceutical Development] provides an opportunity to present the **knowledge gained during application of** scientific approaches and **QRM**"
  - "Appropriate use of QRM principles can be helpful in prioritising the additional pharmaceutical development studies to collect such knowledge."
- WHO Guidelines on Quality Risk Management – Annex 2
  - "The QRM approach may be used to…facilitate the **transfer of process knowledge and product development history** to ease product progression throughout its life-cycle and to supplement already available knowledge about the product."
  - "Early in development, **the purpose of the QRM process may be to acquire sufficient product and process knowledge to assess risks** associated with [the process]"
  - A **crucial aspect of** product development and **QRM** is the maintenance of an **effective and secure knowledge management** and documentation system

Knowledge Management Process Model

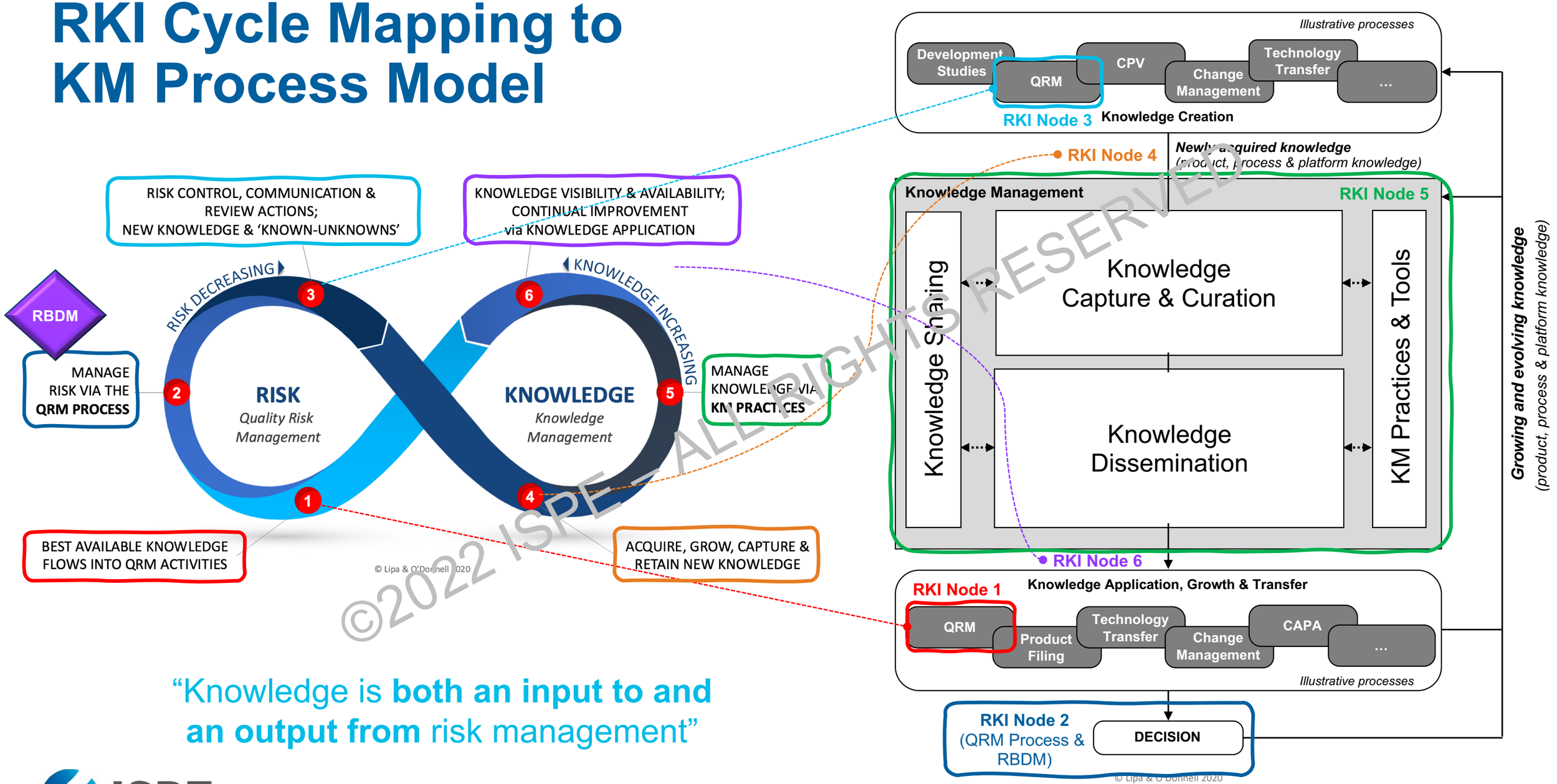
- A *proposed* model to enhance the practical understanding of KM
  - A practical definition of KM…

    Tools & practices to enable knowledge to flow to the right person, at the right time, to inform the best decision

- Encompasses ICH Q10 definition of KM & further <u>enhances</u> as follows:
  - **Knowledge must flow *and* be applied**
  - **KM practices** to for **both <u>explicit and tacit</u>** knowledge
  - **Knowledge communication, exchange and sharing**



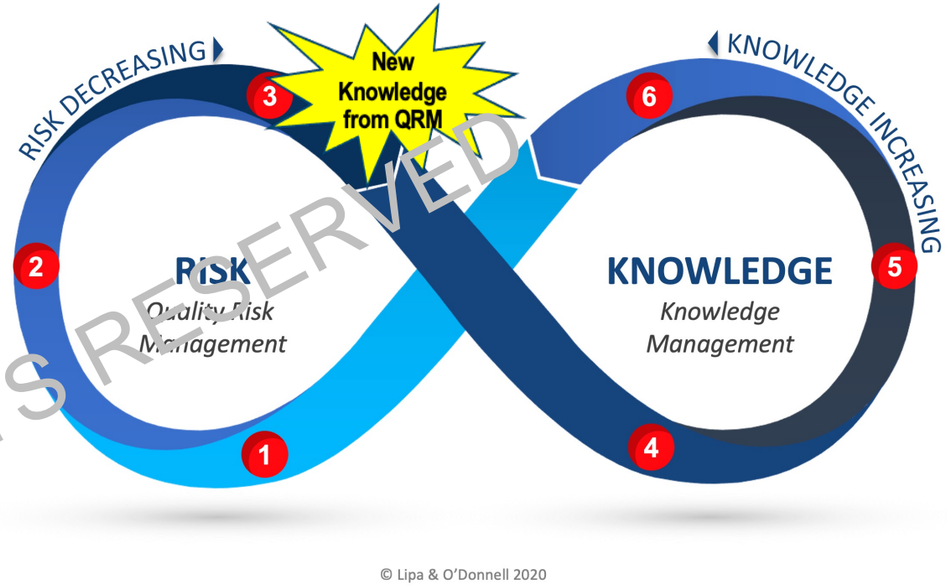
RKI Cycle Mapping to KM Process Model



"Knowledge is **both an input to and an output from** risk management"

QRM as a Critical Source of Knowledge

- QRM is a critical source of new knowledge
  - Directly, e.g., QRA outputs, decisions made, mitigations planned and their effectiveness, decision rationale, …
  - Indirectly, e.g., directing development efforts, triggering new studies
  - Through *Risk Communication & Risk Review*



- Ask yourself…
  - Do we recognize this new knowledge as an asset and have intentional processes in place to manage it?
  - Does this new knowledge wind up in a "silo"?
  - Is *tacit* knowledge captured and managed?
    - e.g., the *why* behind decisions, what was known at the time, alternatives & why rejected, …
  - How do these outputs become inputs for future QRA *and* to other processes?
    - A source of 'prior knowledge'?

Breakout Activity – Node 4

- We will break out into six (6) breakout groups of ~6-7 persons per room

- Breakout instructions:
  - Identify **timekeeper**, **scribe** & person to **report out**
    - Scribe: Please capture notes on a single PowerPoint slide, post this into the chat during the report out
  - Introductions: 5 minutes
  - Discussion: 10 minutes

Room	Room Name	Your Question to discuss
Room 1 Room 2	Knowledge from QRM	What knowledge is created during a QRM exercise? (*Tip:* consider both tacit & explicit)
Room 3 Room 4	Risk Review	What is the role of KM in risk review?
Room 5 Room 6	Risk Communication	What is the role of KM in risk communication?

Breakout Activity Report Out – Node 4

- Breakout report out instructions:
  - ~2-3 minutes per group, will go in pairs

Room	Room Name	Your Question to discuss
Room 1 Room 2	Knowledge from QRM	What knowledge is created during a QRM exercise? (*Tip:* consider both tacit & explicit)
Room 3 Room 4	Risk Review	What is the role of KM in risk review?
Room 5 Room 6	Risk Communication	What is the role of KM in risk communication?

Group Discussion | Q&A

Panelists

Marty Lipa
Merck

Valerie Mulholland
GMP Services Ltd

Dr Kevin O'Donnell
HPRA

Moderator

Prof Anne Greene
Director, PRST, TU Dublin

Takeaways

- The *RKI Cycle* is a framework that can help unite QRM and KM, enabling more effective QRM, RBDM and PQS effectiveness
- RBDM opportunity for improvement in our industry
- *Knowledge mapping* is a simple but powerful technique which can help one stop and think about knowledge needs for QRM (or any process) and can help identify gaps in knowledge affecting efficiency and effectiveness
- Highlights of this session will be captured in an upcoming *ISPE Pharmaceutical Engineering* article (anticipated Jul/Aug 2022 edition)
- To explore these concepts further, exchange ideas or share best practices, please reach out!
  - Marty Lipa @ martin.lipa@prst.ie
    - RKI Cycle, knowledge mapping, knowledge management
  - Valerie Mulholland @ valerie@gmp.ie
    - RBDM
- Additional resources available (next slide)

Thanks to ISPE for hosting this event!
Thanks to each of you for your engagement!

Resources & Additional Reading

- Managing Knowledge and Risk: A Literature Review on the Interdependency of QRM and KM as ICH Q10 Enablers
  - https://arrow.tudublin.ie/level3/vol15/iss2/3
- Knowledge as the Currency of Managing Risk: A Novel Framework to Unite Quality Risk Management and Knowledge Management
  - https://arrow.tudublin.ie/level3/vol15/iss2/4 (includes *RKI Cycle* and *KM Process Model*)
- Quality Risk Management: Seeking the Diamonds: Making the Case for Improved Formality in QRM Decision-making
  - https://arrow.tudublin.ie/level3/vol15/iss2/18
- Steps Beyond Risk Assessment in QRM: RBDM, The Next Horizon
  - https://arrow.tudublin.ie/level3/vol16/iss1/2
- APQC Resources on Knowledge Mapping
  - Great Process Improvement Begins With Knowing Your Knowledge Gaps – https://www.apqc.org/blog/great-process-improvement-begins-knowing-your-knowledge-gaps
  - 4-Step Guide to Knowledge Mapping – https://www.apqc.org/blog/4-step-guide-knowledge-mapping
- ISPE Good Practice Guide: Knowledge Management in the Pharmaceutical Industry
  - https://ispe.org/publications/guidance-documents/good-practice-guide-knowledge-management-pharmaceutical-industry
- Exploring the Risk-Knowledge Infinity Cycle across the Product Lifecycle (An *ISPE Case Study*)
  - https://ispe.org/sites/default/files/publications/papers/ISPE_Managing%20Knowledge%20across%20the%20Product%20Lifecycle_Case%20Studies.pdf

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Upcoming Webinars

Explore the NEW ISPE Knowledge Management Good Practice Guide
Wednesday, 26 January 2022
Complimentary

Call for papers! ISPE is currently seeking articles for a Pharmaceutical Engineering KM Focus issue. If you have KM topics to share or you would like to partner with one of the authors of the *ISPE Good Practice Guide on KM in the Pharmaceutical Industry* to develop a paper, please reach out to Paige Kane (paige.Kane@merck.com) or Susan Sandler (SSandler@ispe.org) by by **31-Jan-2022**. Articles are due by 01-Mar-2022.

Implementation of a Sound Cleaning & Disinfection Program as a part of Contamination Control Strategy
Wednesday, 9 February 2022
Extended Learning – Bundle & Save!

Cleaning Considerations during Design, Start-up, & Commissioning of Biopharmaceutical Equipment
Tuesday, 15 February 2022
Extended Learning – Bundle & Save!

On Demand Webinars Now Available!
Visit ISPE.org/webinars for the full calendar

Topic Ideas or Feedback?
Send to ispeak@ispe.org

Thank you!