ICH Q9
‘Quality Risk Management’
- an industry view

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Answers That Matter.

Contents

How did we get here?

- FDA 21st Century GMP Initiative
- ICH activity

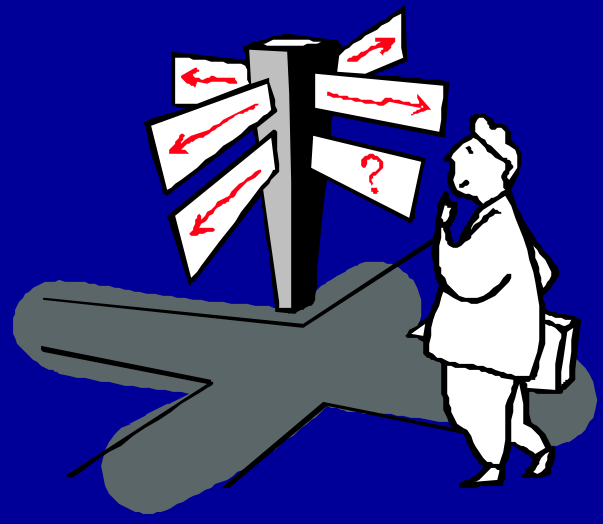
Introduction to risk management

Links between Q8, Q9 and Q10

Contents of Q9, Draft 4

Implications

Conclusion



FDA Pharmaceutical GMP Initiative

"seeks to **integrate quality systems and risk management** approaches into the existing programs and encourages adoption of modern and innovative manufacturing technology."

"intended to enhance the **integration of pre-approval review and cGMP programs** and achieve more consistent application across agency organization components."

"**use existing and emerging science and analysis** to ensure that limited resources are best targeted to address important quality issues, especially those associated with predictable or identifiable health risks."

Lester M. Crawford, FDA Deputy Commissioner, 21-August-2002

Flexible regulatory approach

Regulators evaluate category of risk, based on:

- Product, process and facility
- Controls to assess & mitigate risk
- Quality system implementation

Regulators determine ‘risk category’ and modify level of oversight accordingly for:

- Post-approval change review
- GMP inspections

Result:

- Removal of barriers to continuous improvement
- Efficient use of resources by industry & regulators

FDA announcement 27 Sep. 2004

A Challenge to Industry:

At the end of the cGMP Initiative the pharmaceutical community has arrived at a cross-road; one path goes towards the desired state and the other maintains the current state. The path towards the desired state is unfamiliar to many while the current state provides the comfort of predictability. The Agency hopes the pharmaceutical community will choose to move towards the desired state.

What Is Risk ?

RISK = **combination of probability of harm and severity of that harm**

Source: ISO Guide 51

Advantages of risk based GMP

Systematic, scientific & data-driven (reduces subjectivity)

Ranks risk - allows prioritization

Improves decision making

- Identifies what gives most benefit to the patient

Means of building in quality

Documented – improves communication

Pharmaceutical industry and risk management

Pharmaceuticals have lagged behind related industries in adopting formal risk management; e.g.

- Medical devices, ISO 14971
- Food, HACCP

We are using risk management but

- Implementation is patchy
- It is often not fully integrated with rest of the Quality System

Risk Management: Introduction

Risk Management is **NOT** about:

- making do with insufficient time, money, or people,
- providing an excuse not to do the right things,
- deciding what to do based on what might be observed during an inspection.

Risk Management does **NOT** provide an excuse to be out of compliance with applicable regulations.

Risk Management: Introduction

Risk Management **IS** about:

- knowing our processes (manufacturing and business),
- understanding what's truly important,
- not spending time on a low risk activity, process, event, or system BECAUSE IT JUST DOESN'T MATTER!
- focusing our money, time, energy, and people on the things that are really important; i.e.,
- focusing our efforts and resources on the things that provide quality assurance to our customers.

Risk Management: Introduction

If we do Risk Management properly, we should be able to:

- demonstrate that we understand what is important about our business;
- have a documented, approved rationale for our decisions;
- be proud to share these with regulatory agencies because they demonstrate our knowledge and logical thought processes.

Risk Management: Introduction

We have to do our Risk management properly.

Poor Risk Management will not impress regulators.

At best, they will think we do not know what's really important.

- If we don't know what's trivial, how can we know what's important?
- If everything is critical, nothing is critical.

Ultimately, it is about credibility.

A rational approach has to begin with the question "What is the impact on the patient?"

ICH

It was agreed that the FDA's 21st Century GMP initiative should form basis for discussions at the

International **C**onference on **H**armonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (**ICH**)

International Conference on Harmonisation (ICH)

Merging of regulatory authorities & industry

Not legal binding, unless incorporated in local law

Quality
chemical and pharmaceutical QA

Safety
in vitro and in-vivo pre-clinical studies

Efficacy
clinical studies in human subject

Multidisciplinary
general topics

Timeline of Key Events 2002 - 2004

Aug. 2002	FDA launch 21st century GMP initiative
Jul. 2003	ICH GMP Workshop
Sep. 2003	ICH Q8 ‘Pharmaceutical Development’ EWG established
Nov. 2003	ICH Q9 ‘Risk Management’ EWG established
Jun. 2004	ICH Q10 ‘Quality Management’ agreed “in principle”
Sep. 2004	FDA announcements on implementation
Nov. 2004	ICH EWG meetings

ICH GMP related activities - current status

Q8 – Pharmaceutical Development

- Part 1 reached step 2 in Nov. ‘04

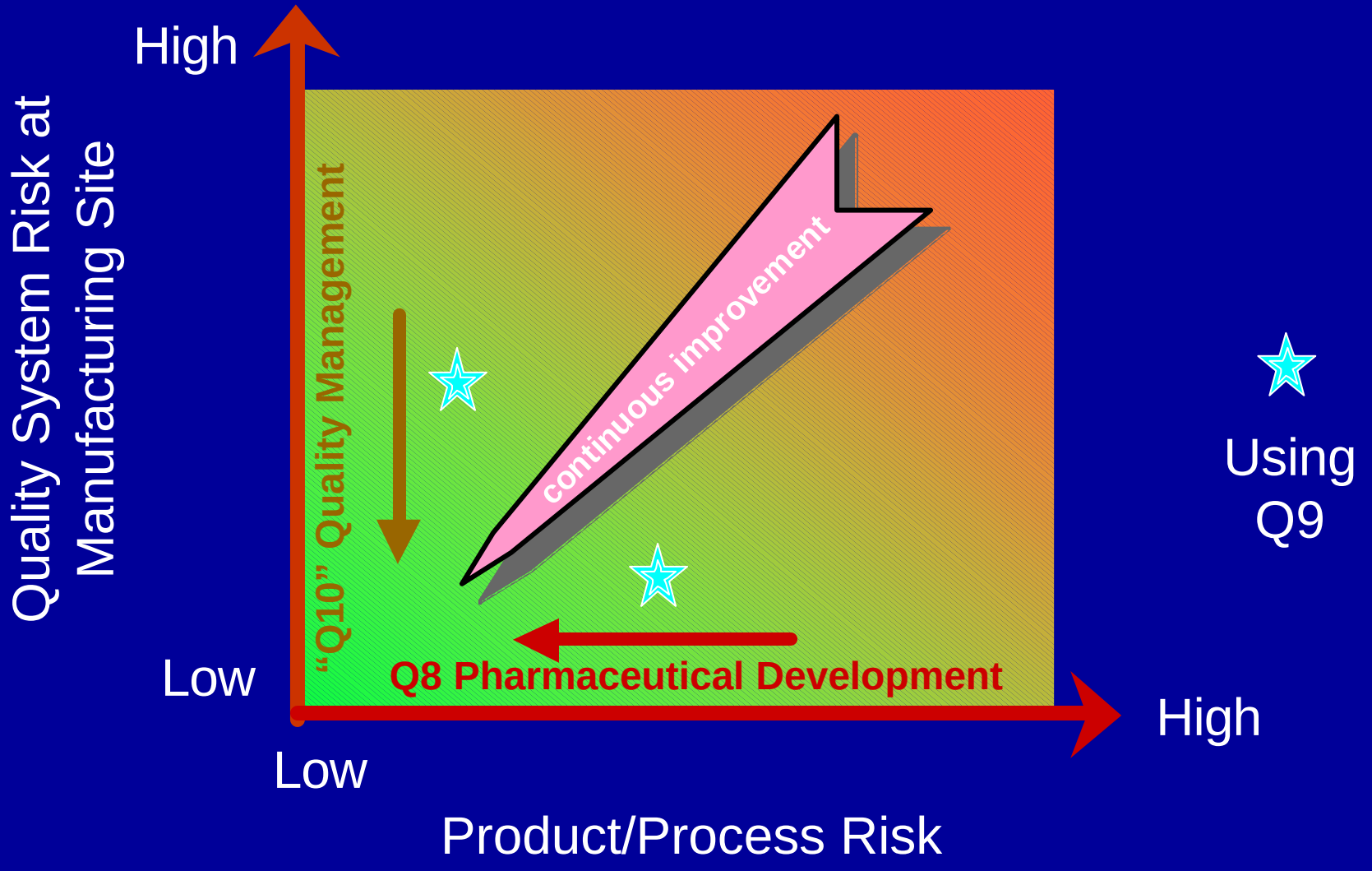
Q9 – Quality Risk Management

- At Step 1, draft 4 produced Nov. ‘04
- Likely to reach step 2 in March 2005

Q10 – Quality Management

- Agreed ‘in principle’
- Waiting for Q9 to reach Step 2 before starting

Links between ICH Q8, 9 & 10



Base: J. Ramsbotham, Solvay Pharm. NL / EFPIA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ICH Q9 Expert Working Group

ICH Q9 – Draft 4 Table of contents

1. Introduction
2. Scope
3. Principles of Quality Risk Management (QRM)
4. General Quality Risk Management Process
5. Risk Management Tools
6. Integration of QRM process into industry & regulatory operations
7. Glossary
8. References

Annex I: Potential opportunities for conducting QRM

1. Introduction

2. Scope

This guideline provides a framework that **may be** applied to all aspects of pharmaceutical quality, including development, manufacturing, distribution, inspection and submission/review processes throughout the lifecycle of drug substances and drug products, biological and biotechnological products, and the use of raw materials, solvents, excipients, packaging and labeling materials.

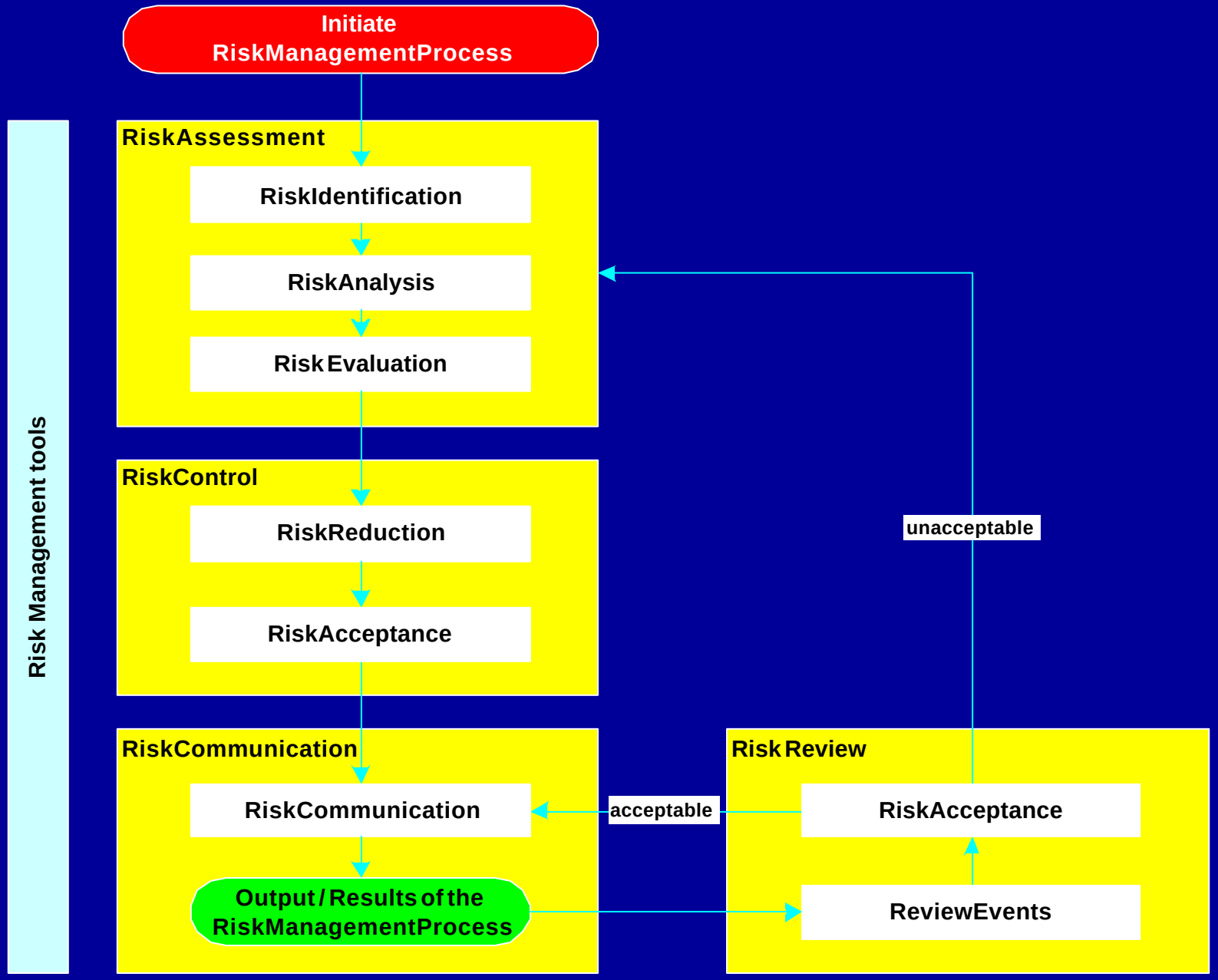
3. Principles of Quality Risk Management

Two primary principles:

1. The evaluation of the quality risk should ultimately link back to the potential harm to the patient.

2. The level of effort, formality and documentation of the quality risk management process should be commensurate with the level of risk.

4. Quality Risk Management Process



5. Risk Management Tools

- Failure Mode Effects Analysis (FMEA)
- Failure Mode Effects & Criticality Analysis (FMCEA)
- Fault tree analysis (FTA)
- Hazard Analysis of Critical Control Points (HACCP)
- Hazard Operability Analysis (HAZOP)
- Risk Ranking and Filtering
- Preliminary Hazard Analysis (PHA)
- Supporting statistical tools

For each tool:
Short description
Potential areas of use

Q9 – Implications

Companies can choose whether to use formal quality risk management

- If used it should enable regulators to adopt a more flexible approach to their oversight of a site

It will be acceptable to continue to use informal approaches to managing risk

Quality risk management is likely to become ‘best practice’ over time

Q9 – Implications

Significant risk management knowledge gap

- Both in industry and regulatory authorities
- ICH EWG plan to produce training guidance

Industry and regulatory authorities will need to initiate programs to

- Educate broadly on quality risk management
- Train a cadre of experts who can facilitate implementation of the risk management process

Conclusion

Quality Risk Management provides a useful process that enables both industry and regulators to focus on what is important for patients.

Integration of Quality Risk Management into existing systems and regulatory process will take time.

ICH Q8, Q9 & Q10 together will enable the pharmaceutical community to move towards the desired state for 21st century quality management.