The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Quality Risk Management ICH Q9 Briefing Pack

Introduction

ICH Q9 together with ICH Q8 and Q10 is one of the ICH Q-topics that encourage further development science based and risk based approaches to quality. The intention of ICH Q9 is to focus the behaviours of industry and regulatory authorities on the two primary principles of Quality Risk Management, which are:

- The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient; and
- The level of effort, formality and documentation of the Quality Risk Management process should be commensurate with the level of risk.

To support the implementation of Quality Risk Management into daily operations for Regulators and Industry some members of the ICH Q9 Expert Working Group have prepared a set of slides, which are intended to be used for information purposes in industry, regulators and other facilitators such as consultants. When using these slides it should be remembered that:

- **One purpose is to provide general guidance and references for some of the primary tools as well examples that might be used in quality risk management by industry and regulators.**
- **The slides are provided for illustrative purposes and suggest possible interpretations of the ICH Q9 guideline. It must be remembered that the selection of particular risk management methodology / tools is completely dependent upon specific facts and circumstances related to the risk being managed.**
- **Many of the slides contain animations. Viewing the slides in PowerPoint as a slide show will help the reader to understand the context in which the particular slide was derived.**
- **The slides are not intended to create any new expectations beyond the current regulatory requirements.**
- **The slides include the authors' views on the theory and practice of Quality Risk Management and do not represent official guidance or policy for either regulators or industry.**
- **The slides are placed in the public domain and should not be copied or republished for purposes of financial gain.**

 **Briefing Pack**

Disclaimer:
The Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Quality Risk Management ICH Q9 Briefing Pack

On the ICH Q9 document slides are available on:

Executive summary for regulators and industry	HTML	PPT
Background	HTML	PPT
History	HTML	PPT
Content	HTML	PPT
Tools - overall notes	HTML	PPT
Basic Risk Management Facilitation Methods	HTML	PPT
Failure Mode Effects (Criticality) Analysis (FMEA & FMECA)	HTML	PPT
Fault Tree Analysis (FTA)	HTML	PPT
Hazard Analysis and Critical Control Points (HACCP)	HTML	PPT
Hazard Operability Analysis (HAZOP)	HTML	PPT
Preliminary Hazard Analysis (PHA)	HTML	PPT
Risk Ranking and Filtering	HTML	PPT
Supporting Statistical Tools	HTML	PPT
Combination of Tools	HTML	PPT
Application - overall notes	HTML	PPT
Integrated Quality Management	HTML	PPT
Regulatory Operations	HTML	PPT
Development	HTML	PPT
Facilities, Equipment and Utilities	HTML	PPT
Materials Management	HTML	PPT
Production	HTML	PPT
Laboratory Control and Stability Studies	HTML	PPT
Packaging and Labelling	HTML	PPT
Frequently Asked Questions (Q&A)	HTML	PPT

For creating paper copies of a manual with all slides see the Acrobat (pdf) version

- Executive summary, Background, History, Content and FAQ
- Tools / Applications

Disclaimer:
The Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Team recruited from the Members of the Expert Working Group:

Writers

Stephan Rönninger (Chair)	F. Hoffmann-La Roche Ltd
Gregg Claycamp	FDA
Peter Gough	formerly with Eli Lilly Inc.; David Begg Associates
Malcolm Holmes	Glaxosmithkline
Takayoshi Matsumura	Eisai Co. Ltd
Christine Mundkur	Barr Laboratories
Tetsuhito Takarada	Mochida Pharmaceutical Co. Ltd
Hideki Sasaki	Nippon Shinyaku Co. Ltd

Reviewers

Emer Cooke	EMEA
Diana Dowthwaite	Health Canada
Albinus D'Sa	FDA
Gregg Guyer	Merck& Co. Inc.
David Horowitz	FDA
Yukio Hiyama	MHLW
Georgia Keresty	Centocor
Sabine Kopp	WHO
Urs Kopp	Swissmedic
Jacques Morenas	Agence Française de Sécurité Sanitaire des Produits de Santé - AFSSAPS
Markus Müller	Swissmedic
Etienne Ouimette	Health Canada
Fred Razzaghi	Consumer Health Care Products Association

Also supported by EFPIA and JPMA ICH Q9 Topic Groups.

Quality Risk Management ICH Q9

Executive summary
for competent authorities and industry

Disclaimer: *This presentation includes the author's views on quality risk management theory and practice. The presentation does not represent official guidance or policy of authorities or industry.*

The situation today

The situation today for both regulators and industry

> Increasing external requirements
> Increasing efforts and costs
> Growing complexity and scope of risks

Empowerment & Flexibility is needed

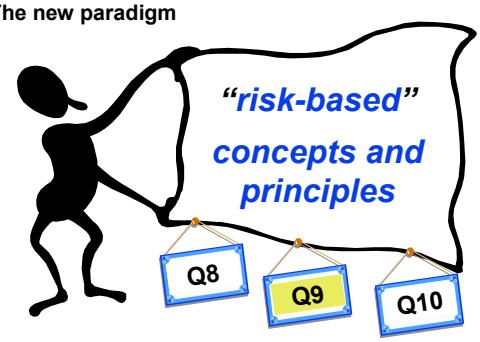
> Master complexity and streamline decision making
> Proactive disclosure build trust and understanding
> Improve communication through sharing best practice and science based knowledge
> Convert data into knowledge

New Regulatory Paradigm

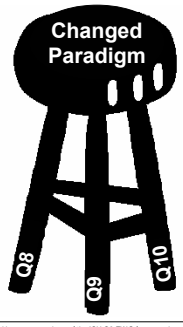
- **ICH Regulators:**
  - > **FDA: New paradigm with the 21st Century GMP initiative**
  - > **EMEA: Revised EU directives**
  - > **MHLW: Revised Japanese law (rPAL)**
- **EU & Japan became involved at ICH GMP Workshop in July 2003: 5 year vision agreed:**

  "Develop a harmonised pharmaceutical quality system applicable across the life cycle of the product emphasizing an integrated approach to quality risk management and science"
- **Consequent ICH Expert Working Groups (EWG):**
  - > **ICH Q8, on Pharmaceutical Development, doc. approved 2005**
  - > **ICH Q9, on Quality Risk Management, doc. approved 2005**
  - > **ICH Q10, on Quality Systems, topic accepted 2005**

The new paradigm



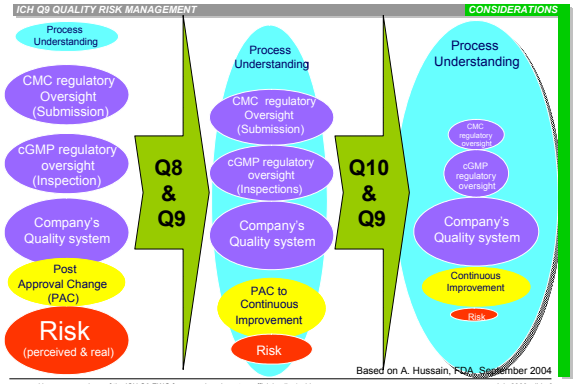
Incremental steps



Pharmaceutical Development (Q8)
Past: Data transfer / Variable output
Present: Knowledge transfer / Science based / Consistent output

Quality Risk Management (Q9)
Past: Used, however poorly defined
Present: Opportunity to use structured process thinking

Pharmaceutical Quality Systems (Q10)
Past: GMP checklist
Future: Quality Systems across product life cycle



Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Executive summary

ICH Q9 QUALITY RISK MANAGEMENT

The Desired State driven by ICH Q9

- Manage risk to patient, based on science:
  - > Product, process and facility
  - > Robustness of Quality System
  - > Relevant controls to assess & mitigate risk
- Level of oversight required commensurate with the level of risk to patient for:
  - > Marketing authorisation applications
  - > Post-approval change review
  - > GMP inspections

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance July 2006, slide 7

Executive summary

ICH Q9 QUALITY RISK MANAGEMENT

The Desired State

- Barriers to continuous improvement reduced or removed
  - > Improved manufacturing efficiency
  - > Sustained or improved product quality
- Specifications based on parameters that truly impact product quality
- Common understanding and language on risk
- Both, industry and competent authorities focus on areas of greatest risk and understanding of residual risks

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance July 2006, slide 8

Executive summary

ICH Q9 QUALITY RISK MANAGEMENT

Pharmaceutical industry and quality risk management

- Pharmaceuticals have lagged behind related industries in adopting structured risk management in the quality area; e.g.
  - > Medical devices have ISO 14971
  - > Food industry uses HACCP
- We are using quality risk management but
  - > Implementation is patchy
  - > It is often not fully integrated with rest of the Quality System

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance July 2006, slide 9

Executive summary

ICH Q9 QUALITY RISK MANAGEMENT

Advantages of quality risk management as technique

- Improves decision making
  - > Identifies what gives most benefit to the patient
- Is scientific & data-driven
  - > Reduces subjectivity
- Ranks risk - allows prioritization
  - > Better use of resources
- Means of building in Quality
- Improves transparency - inside organisation and builds trust with competent authorities
  - > Enables regulatory flexibility
- Benefits apply throughout product lifecycle

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance July 2006, slide 10

Executive summary

ICH Q9 QUALITY RISK MANAGEMENT

Why did we need ICH Q9?

- To ensure a common understanding of Quality Risk Management (QRM) among industry and competent authorities
- To facilitate moving to the "Desired State"
  - > To facilitate communication and transparency
  - > To move from 'fire fighting' to management of risk
- ICH Q9 explains
  - > A common language and process
  - > Potential methodologies for QRM
  - > Where QRM can add value

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance July 2006, slide 11

Executive summary

ICH Q9 QUALITY RISK MANAGEMENT

Quality Risk Management is NOT

- Hiding risks
- Justifying poor quality of product and / or processes
- Excusing industry's obligation to comply with regulatory requirements

HOWEVER

- It might bring about the revision or withdrawal of some non risk base guidance

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance July 2006, slide 12

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Executive summary

What does Senior Management need to do?

- Ensure organisation is aware of ICH Q9 and the opportunity it affords
  - > Appropriate education and training
- Encourage open, risk aware culture
  - > Establish & support "QRM leaders" across organisations
- Encourage integration of Quality Risk Management with existing Quality systems
  - > Do NOT set up as a separate department
  - > Coordinate implementation and resource allocation
  - > Prioritise; start small, learn as you go

Executive summary

Conclusions

- ICH Q9, together with "Pharmaceutical development" (ICH Q8) and "Quality systems" (ICH Q10), provides opportunity for a revised, optimised and, less restrictive regulatory paradigm
  - > Based on scientific knowledge
  - > Enable continuous improvement
  - > Greater transparency and efficiency
  - > Focusing on things that add value for patients
  - > Improved relationship between industry and competent authorities based on trust
- We must seize this opportunity

Executive summary

Keep always in mind the

Principles of Quality Risk Management

The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient

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

ICH Q9

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Quality Risk Management ICH Q9

Background

Disclaimer: *This presentation includes the authors views on quality risk management theory and practice. The presentation does not represent official guidance or policy of authorities or industry.*

Purpose of this part

- To provide information on the background of the ICH Q9 document
- Give an aid by providing some points of discussions on the understanding of the quality risk management concept

Agenda

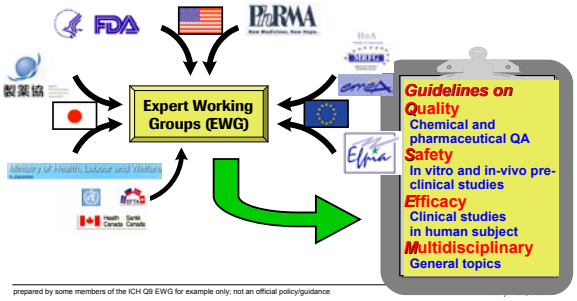
- The ICH process
- ICH Q9 and other ICH guidelines
- From "Risk" to "Quality Risk Management"
- Opportunities, Challenges and Benefit

Agenda

- The ICH process
- ICH Q9 and other ICH guidelines
- From "Risk" to "Quality Risk Management"
- Opportunities, Challenges and Benefit

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use

EWG's include observers and constituted from both authorities & industry



Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Background

ICH Q9 QUALITY RISK MANAGEMENT

Agenda

- The ICH process
- ICH Q9 and other ICH guidelines
- From "Risk" to "Quality Risk Management"
- Opportunities, Challenges and Benefit

Background

ICH Q9 QUALITY RISK MANAGEMENT

ICH Q-Documents

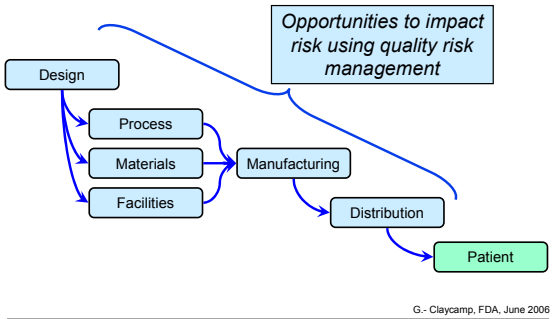
- Q1 Stability
- Q2 Analytical Validation
- Q3 Impurities
- Q4 Pharmacopoeias
- Q5 Quality of Biotechnological Products
- Q6 Specifications
- Q7 Good Manufacturing Practice
- Q8 Pharmaceutical Development
- Q9 Quality Risk Management
- Q10 Pharmaceutical Quality Systems

Different:
- not a recipe
- not a "SOP"
just a guidance

Background

ICH Q9 QUALITY RISK MANAGEMENT

ICH Q9 Link back to patient risk

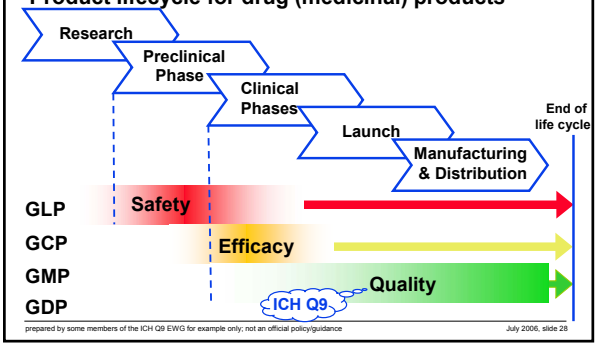


G.- Claycamp, FDA, June 2006

Background

ICH Q9 QUALITY RISK MANAGEMENT

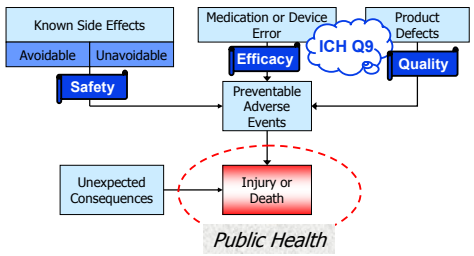
Risk Management across the Product lifecycle for drug (medicinal) products



Background

ICH Q9 QUALITY RISK MANAGEMENT CONSIDERATIONS

Managing the risk of drug (medicinal) product use



Source: basic model adapted from FDA (1999). *Managing the Risks from Medical Product Use.*

Background

ICH Q9 QUALITY RISK MANAGEMENT

New Regulatory Paradigm

- ICH Regulators:
  - > FDA: New paradigm with the 21st Century GMP initiative
  - > EMEA: Revised EU directives
  - > MHLW: Revised Japanese law (rPAL)
- EU & Japan became involved at ICH GMP Workshop in July 2003: 5 year vision agreed:

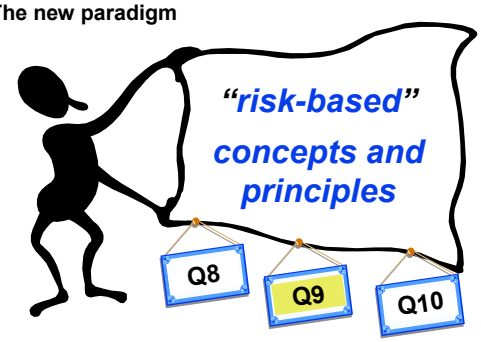
  "Develop a harmonised pharmaceutical quality system applicable across the life cycle of the product emphasizing an integrated approach to quality risk management and science"
- Consequent ICH Expert Working Groups (EWG):
  - > ICH Q8, on Pharmaceutical Development, doc. approved 2005
  - > ICH Q9, on Quality Risk Management, doc. approved 2005
  - > ICH Q10, on Quality Systems, topic accepted 2005

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Background

ICH Q9 QUALITY RISK MANAGEMENT

The new paradigm



prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 31

Background

ICH Q9 QUALITY RISK MANAGEMENT

Incremental steps

Pharmaceutical Development (Q8)

Past: Data transfer / Variable output

Present: Knowledge transfer / Science based / Consistent output

Quality Risk Management (Q9)

Past: Used, however poorly defined

Present: Opportunity to use structured process thinking

Pharmaceutical Quality Systems (Q10)

Past: GMP checklist

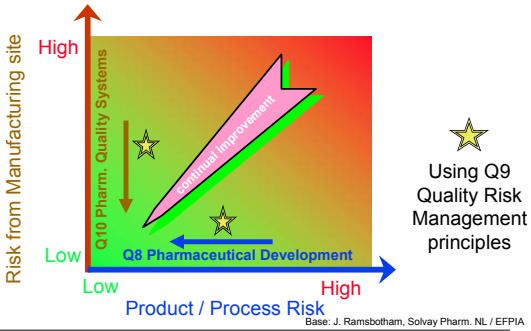
Future: Quality Systems across product life cycle

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 32

Background

ICH Q9 QUALITY RISK MANAGEMENT

How Q9 interacts with Q8 and Q10



Using Q9 Quality Risk Management principles

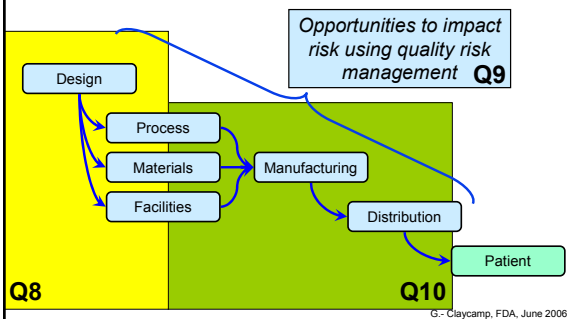
Base: J. Ramsbotham, Solvay Pharm. NL / EFPIA

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 33

Background

ICH Q9 QUALITY RISK MANAGEMENT

ICH Q9 Link back to patient risk



G.- Claycamp, FDA, June 2006

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 34

Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

A Vision of the future becomes fact

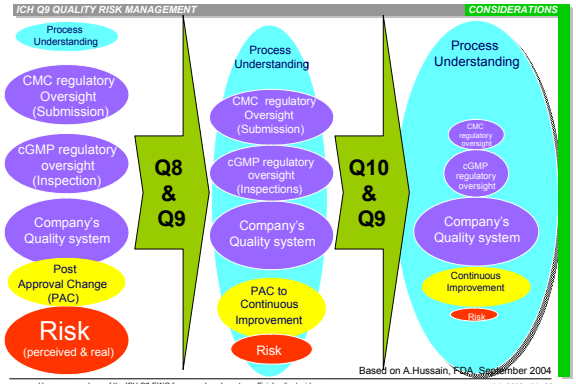
	Old Approach	New Approach	Remarks
Broad Concept	Quality decisions divorced from science and risk evaluation. Adherence to **filing commitments**.	Quality decisions and filing committments based on **Process Understanding** and **Risk Management**. Quality by Design.	**Design Space** concept introduced to integrate process knowledge with regulatory evaluation.
Quality	**Post-factum** sampling and quality testing. **Process Validation**.	Management of variability Process control focused on critical attributes. **Continuous Quality Verification**.	**Quality by design** definition applied. Measure critical process parameters to control output product quality.
Systems	Systems designed to inhibit changes & minimize business risks. **Discourages improvement & innovation**.	Changes managed within company's quality system. **Real time batch release** feasible.	Regulators and industry place higher **reliance / trust / understanding** on systems. Multidisciplinary evaluation and decision making.
Regulatory	**Compliance focus**. Changes require prior approval.	Regulatory scrutiny adjusted to level of Process Understanding. **Continuous improvement allowed within Design Space**.	Requires mechanisms to **communicate Process Understanding** data *("inspectable rather than reviewable")*.

Based on EFPIA, PAT Topic Group, 2005

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 35

Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS



Based on A.Hussain, FDA, September 2004

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 36

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Background

ICH Q9 QUALITY RISK MANAGEMENT

Agenda

- The ICH process
- ICH Q9 and other ICH guidelines
- From "Risk" to "Quality Risk Management"
- Opportunities, Challenges and Benefit

Background

ICH Q9 QUALITY RISK MANAGEMENT

ICH Q9
Quality Risk Management

What does it mean?
What is it worth?
Where does it lead?

Background

ICH Q9 QUALITY RISK MANAGEMENT CONSIDERATIONS

Managing risk is a behavior

"The investigation of risks is at once a scientific activity and an expression of culture"

Kasperson, Renn, Slovic et al. (1988)

Background

ICH Q9 QUALITY RISK MANAGEMENT CONSIDERATIONS

Risk Management as a discipline provides multiple benefits

- **Understand and influence the factors (hazards) which impact regulators and industry business**
- **Create awareness and a culture**
  - > Supports an effective pro-active behaviour
  - > Open factual dialogue
  - > Make decisions traceable and consistent
- **Provide assurance**
  - > Risks are adequately managed
  - > Compliance to external and internal requirements
- **Recognise risks at a desired level**
  - > Zero risk not possible

Background

ICH Q9 QUALITY RISK MANAGEMENT

The Hurdles

Increasing external requirements for best practice, transparency and compliance
- Public / Community
- Governments
- Regulators
- Patients
- Investors / Creditors

?

Growing complexity and scope of risks
- Globalisation "Multinational"
- Multi-factor approaches
- Regulatory expectations
- Acceptance of risk and uncertainty

Increasing efforts and costs for sustainability
- Documentation
- Projects
- Systems
- Interfaces

Based on D. Geller, Roche

Background

ICH Q9 QUALITY RISK MANAGEMENT

Empowerment & Flexibility

An appropriate integrated approach helps to meet requirements more efficiently

Proactive disclosure build trust and understanding

Quality Risk Management

Improve communication through sharing best practice and science based knowledge

Master complexity
Convert data into knowledge
e.g. by using methodology and tools

Based on D. Geller, Roche

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

Different meaning of risk

- **Individual**
  - > Risk is a cognitive and emotional response to expected loss
- **Technicians**
  - > Risk is usually based on the expected value of the conditional probability of the event occurring multiplied by the consequences of the event given that it has occurred
- **ICH Q9**
  - > Combination of the probability of occurrence of harm and the severity of that harm

Based on G. Claycamp, FDA, September 2005

Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

Different meaning of risk

- **Organizations might use many different meanings of risk**
  - > Depending on the type of risk management program
- **In general, "probability" and "severity" must be considered**
  - > In a given program definitions will fine-tune the concepts so that a risk management program can be created and applied
  - > Make the detail in the definition fit the objective of the program
- **Accept the different "realities" among the stakeholders**
  - > Harmonized guidance needs to focus concepts into useful terms for the purpose (e.g. protection of patient [Q9])

Based on G. Claycamp, FDA, September 2005

Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

Severity and *Probability* are simple concepts?

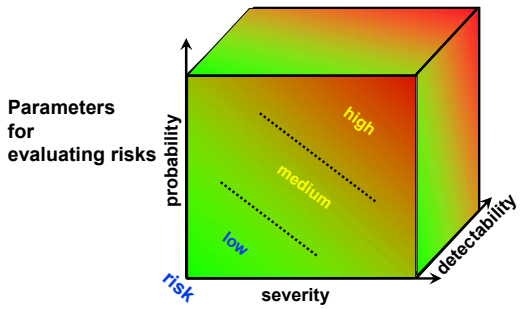
- **Which consequence is more severe?**
  - > 300 lives lost in single, fiery plane crash.
  - > 300 lives lost on US roads over a weekend.
  - > 300 lives *potentially* lost from cancer within the next 20 years
- **Which probability is probable?**
  What does a "30% chance of rain tomorrow" mean?
  - > 30% of the days like tomorrow will have at least a trace of rain.
  - > 30% of the area will have rain tomorrow.
  - > 30% of the time tomorrow, it will rain. **Gigerenzer, et. al (2005)**

G. Claycamp, FDA, September 2005

Background

ICH Q9 QUALITY RISK MANAGEMENT

The "risk-based approach"

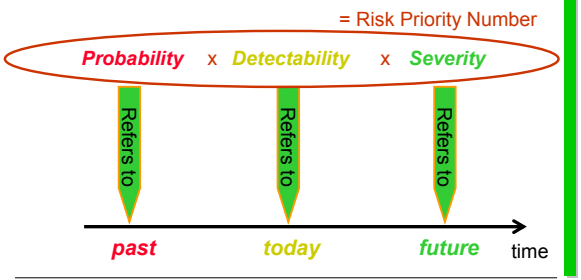


Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

Parameters for "calculating" risks

A picture of the life cycle



Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

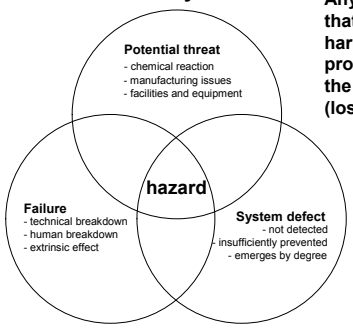
(Dis)Advantage calculated numbers & data

- **Numbers**
  - > Does the "Risk Priority Number" tell the truth?
- **Keep a robust data set for further evaluation!**
  - > Is the data set comparable?
  - > Are the data plain and concise?
  - > What about trending and use of statistics including extrapolation?
  - > What amount of data is enough?
    e.g. start with the existing data set

Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

Hazards in Quality



Anything that has the potential to harm patients, product quality or the business (loss, interruption, image)

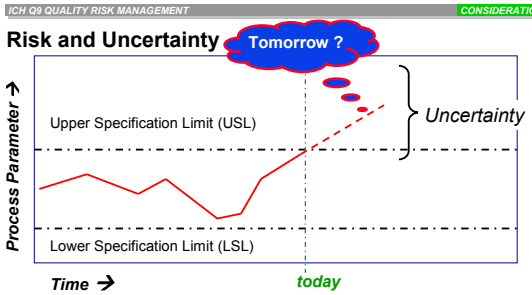
S. Rönninger, Roche, 2004

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 49

Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

Risk and Uncertainty



RISK: For a given severity of risk event, what are the chances (probability) of exceeding the USL in the next period of time?

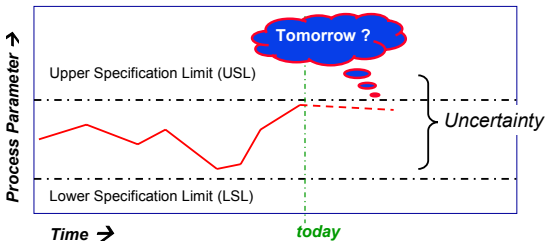
G. Claycamp, FDA, Sept. 2005

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 50

Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

Risk and Uncertainty
Different Risk Management Control?



RISK: Control options are scenarios for risk management. Note that this scenario shows the best estimate is below the USL.

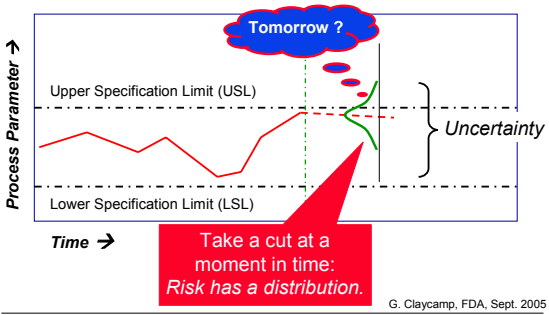
G. Claycamp, FDA, Sept. 2005

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 51

Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

Risk and Uncertainty
Is the Risk of Exceeding USL = Zero?



G. Claycamp, FDA, Sept. 2005

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 52

Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

Uncertainty and Quality Risk Management

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 53

Background

ICH Q9 QUALITY RISK MANAGEMENT

Definitions

Quality — Degree to which a set of inherent properties of a product, system or process fulfills requirements

Risk — combination of the probability of occurrence of harm and the severity of that harm

Management — Systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle

QRM

ICH Q9

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 54

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Background

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

Has QRM already been implemented?

Yes, however we need to firm-up and set the priorities in relation to risks

- **We need to know…**
  - > How good is our QRM compliance and decision making?
  - > To what extent QRM has to be implemented or formalised?
- **An then focus efforts and communicate in order to…**
  - > Avoid duplication of effort and to align initiatives
  - > Develop scope by using different viewpoints e.g. from management, internal and external customers

Background

ICH Q9 QUALITY RISK MANAGEMENT

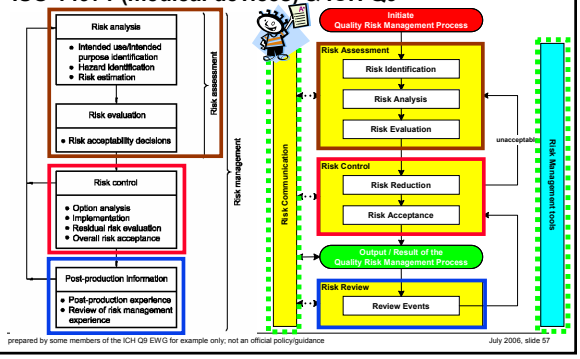
Risk Management Not a new concept

- **ISO/IEC Guide 73: 2002 - Risk Management - Vocabulary - Guidelines for use in Standards**
- **ISO/IEC Guide 51:1999 - Safety Aspects - Guideline for their inclusion in standards**
- **WHO Technical Report Series No 908, 2003 Annex 7 *Application of Hazard Analysis and Critical Control Point (HACCP) methodology to pharmaceuticals***
- **GAMP Good Practice Guide ISPE, 2005 *A risk-based approach to compliant electronic records and signatures***
- **ISO 14971:2000 - Application of Risk Management to Medical Devices**

Background

ICH Q9 QUALITY RISK MANAGEMENT

ISO 14971 (medical devices) & ICH Q9



Background

ICH Q9 QUALITY RISK MANAGEMENT

What is ICH Q9 about?

- **The ICH Q9 document:**
  - > Main body explains the "What?"
  - > Annex I give ideas on the "How?"
  - > Annex II give ideas on the "Where?"
- **It can be implemented by industry and regulators**
  - > Pharmaceutical development (ICH Q8) and Quality Systems (ICH Q10) will facilitate the "What?", "How?" and "Where?"
- ***"It helps prevent overly restrictive and unnecessary requirements being imposed by either industry or regulators"*** (ICH Q9)

Background

ICH Q9 QUALITY RISK MANAGEMENT

Why we have ICH Q9?

- **To show how it can be applied by regulators and industry to quality of pharmaceuticals (including API)**
  - > **We already do a lot of quality risk management activities without identifying them as such**
- **To enable manufacturing and regulatory flexibility**
- **Provides the "What?" "How?" and "Where?" for quality risk management**
  - > **Pharmaceutical development (ICH Q8) and Quality Systems (ICH Q10) will facilitate the "What?", "How?" and "Where?"**

Background

ICH Q9 QUALITY RISK MANAGEMENT

Quality Risk Management is NOT

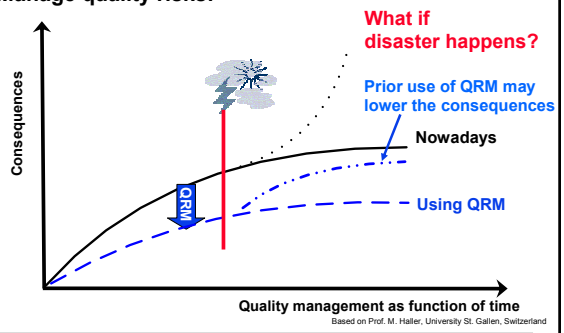
- **Hiding risks**
- **Writing half the truth (e.g. in an investigation report)**
- **A means of removing industry's obligation to comply with regulatory requirements**

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Background

ICH Q9 QUALITY RISK MANAGEMENT

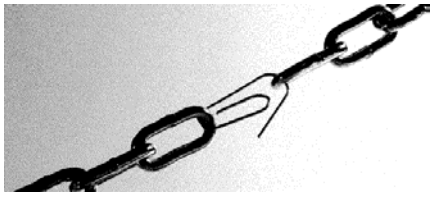
Manage quality risks!



Background

ICH Q9 QUALITY RISK MANAGEMENT

Implementing ICH Q9 means



The weakest chain will no longer be a problem

Background

ICH Q9 QUALITY RISK MANAGEMENT

Agenda

- The ICH process
- ICH Q9 and other ICH guidelines
- From "Risk" to "Quality Risk Management"
- Opportunities, Challenges and Benefit

Background

ICH Q9 QUALITY RISK MANAGEMENT

Integrate QRM during product life cycle

Background

ICH Q9 QUALITY RISK MANAGEMENT

Risk Management & Flexibility

- Definitions of "Compliance":
  - > Conformity in fulfilling official requirements
  - > The act or process of complying to a desire, demand, or proposal or to coercion
  - > A disposition to yield to others
  - > The ability of an object to yield elastically when a force is applied: flexibility
- Definition of "Flexibility":
  - > characterised by a ready capability to adapt to new, different, or changing requirements

Source: www.webster.com, 01. Nov.04

Background

ICH Q9 QUALITY RISK MANAGEMENT

QRM may help define acceptable quality levels

Use "science-based" and "risk-based" behavior

- Not every single detail can nor should be covered by
  - > Specifications (product quality)
  - > Documents (quality systems)
- Set priorities and allocate resources according to the potential for protection of patients

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Background

ICH Q9 QUALITY RISK MANAGEMENT

Opportunity for the Industry & Regulators

- Using the same guideline apply QRM to
  - > Industry (development, manufacture and distribution)
  - > Competent authorities (reviewer and inspectorate)
- Facilitates common approaches to quality risk management in our every day jobs
- Supports science-based decision making
- Focus resources based on risks to patients
- Avoids restrictive and unnecessary requirements
- Facilitates communication and transparency

Background

ICH Q9 QUALITY RISK MANAGEMENT

Conclusions for ICH Q9

- Over all: Positive Contribution to patient protection
  - > Further develops Quality Risk Management awareness, that is already part of industry and regulatory culture
- Ongoing change in behaviour
  - > Identifying risks can be positive
  - > A long list of identified risks that are assessed and controlled provides high quality capability
- Awareness of quality risks
  - > "Risk-based approach"
  - > A potential of risks remains - No "Zero" risk!

Background

ICH Q9 QUALITY RISK MANAGEMENT

Way Forward for Industry and Regulators

- Improve communication and transparency
- Adapt existing structures, organizations and systems
  - > Raise awareness of rationales for decision making
  - > Develop training on methods and tools, *as appropriate*
  - > Do not create new QRM organisations
  - > Do not create new requirements
- Adapt existing requirements using quality risk management behaviors

Background

ICH Q9 QUALITY RISK MANAGEMENT

Opportunities & Benefits

- Encourages transparency
  - > Create baseline for more science-based decisions
- Facilitates communication
  - > Matrix team approach
  - > An aid to convince the stakeholders with trust
- Encourages a preventive approach
  - > Proactive control of risks and uncertainty
  - > Benefit of knowledge transfer by team approach
- Changes behavior
  - > Better understanding of risk-based decisions
  - > Acceptance of residual risks

Background

ICH Q9 QUALITY RISK MANAGEMENT

Remember

- The use of Quality Risk Management is not mandatory

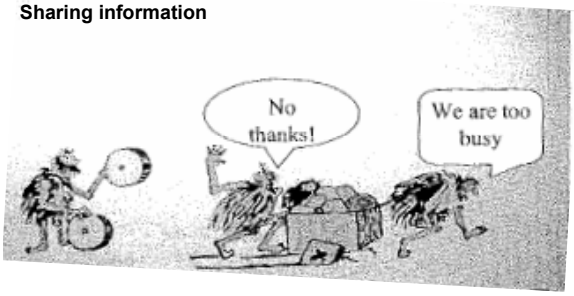
However, if you don't use it, you will not gain the benefits

Background

ICH Q9 QUALITY RISK MANAGEMENT

Change in behaviour

Sharing information



Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Background

ICH Q9 QUALITY RISK MANAGEMENT

Change in behaviour

From tick-box approach for compliance

towards

systematic risk-based thinking

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance July 2006, slide 73

Background

ICH Q9 QUALITY RISK MANAGEMENT

Change in behaviour

Doing things, that do not matter for the patient

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance July 2006, slide 74

Integration of QRM into existing systems and regulatory processes will take time, trust and communication

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Quality Risk Management ICH Q9

History

Disclaimer: *This presentation includes the authors views on quality risk management theory and practice. The presentation does not represent official guidance or policy of authorities or industry.*

Purpose of this part is to:

- Guide you through
  the history
  of the development of the ICH Q9 document
- Highlight some of the decisions and rationales for making them

The history of Q9 document

Osaka
November 2003

London
March 2004

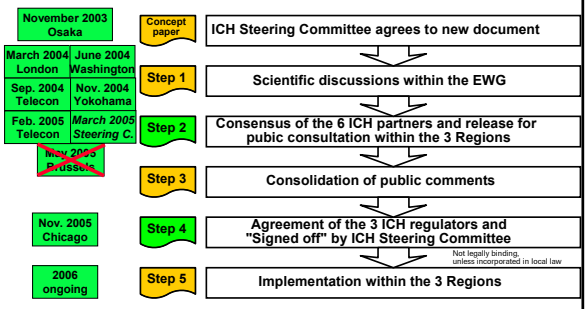
Washington
June 2004

Yokohama
November 2004

Draft for consultation
March 2005

Chicago
November 2005

ICH Q9 Milestones



ICH Concept paper Osaka, November 2003

- Technology focus
  - > Increase process capability
  - > Focus on critical control points
- Product
  - > Stabilise manufacturing steps (decrease variability)
  - > Guarantee shelf-life
- People
  - > Result in a superior performance of the Q-System
- Customer
  - > Reduce deviation
  - > Reduce market complaint rate
  - > Reduce technical related adverse events

Result of ICH Q9 EWG Meeting London, March 2004

- A draft table of contents, flow diagram, definitions were agreed
- Assignments to produce first drafts of the full text for each section of the draft table of contents were agreed
- Started the dialogue with the ICH Q8 EWG
- Regulatory flexibility
  - > The degree to which the final versions of both Q9 and Q8 could refer to 'regulatory relief' was a debate on principles.
  - > *Term changed to "regulatory flexibility" or "risk confidence".*

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

History

ICH Q9 QUALITY RISK MANAGEMENT

ICH Q9 Version 1

"Forget it"

expressed what the EWG was thinking
in terms of creating text on the agreed content

History

ICH Q9 QUALITY RISK MANAGEMENT

Result of ICH Q9 EWG Meeting Washington, June 2004

- Good agreement on overall content
  - > No major disagreements between parties
  - > Training and experience needed
- The first official draft (No 2) was issued
  - > All accept that wording is not perfect
- Reaching ICH Step 2 in November was still the target
  - > Highly dependent on the extent of comments received on draft

History

ICH Q9 QUALITY RISK MANAGEMENT

Result of ICH Q9 EWG Telecon September 2004

- Optional nature of ICH Q9 to be emphasized
- All EWG parties want to push ICH Q9 forward
  - > No support for delaying ICH Q9
- Appointments for redrafting in six groups
  - > Subgroup decide on details of Chapter 5 / 6 as annex or not
  - > One subgroup to deal with ICH Q8 relationships
- Case studies:
  - > Which ones are appropriate to use in ICH Q8, Q9 or Q10?
  - > Everybody should decide, whether the case studies should be included as an annex in the ICH Q9 document or used as training material - Decision to be made in Yokohama

History

ICH Q9 QUALITY RISK MANAGEMENT

Result of ICH Q9 EWG Meeting November 2004

- Milestone: Draft 4 issued as "pre-step 2" document
- Major concerns were addressed and resolved
- Primary principle: link back to the potential harm to the patient
- Integration of QRM into existing systems & regulatory processes will take time
- For more details:
  Peter Gough and Stephan Roenninger,
  ICH Q9 : Quality Risk Management - an update
  Regulatory Affairs Journal, *16*, **2005**, 91-93

History

ICH Q9 QUALITY RISK MANAGEMENT

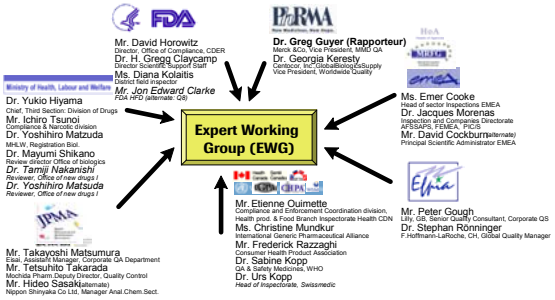
Result of ICH Q9 EWG Telecon February, 22 2005

- All EWG parties agreed
  to put Q9 forward to step 2
- Training slides will be provided
  - > Slides to be discussed after step 4
- Next meeting of the EWG:
  ICH Meeting, November 2005, Chicago

History

ICH Q9 QUALITY RISK MANAGEMENT

ICH Q9 Expert Working Group (EWG) as of ICH Step 2



Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

History

ICH Q9 QUALITY RISK MANAGEMENT

Result of ICH Q9 EWG Meeting
Chicago November, 6.-8. 2005

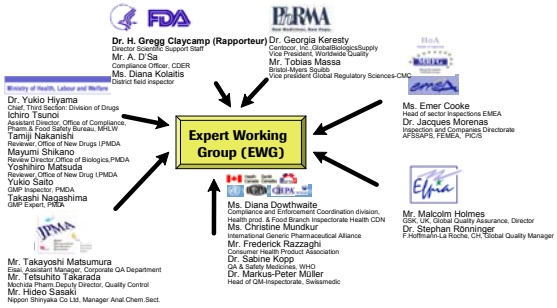
Points of discussion and changes to the step 2 document

- Separate the "How to do?" (annex) from the "What to do?" (text) and move the tools examples to the annex
- Modify original diagram in section 4
  - > Take an alternative proposal showing communication routes
- Move "continuous improvement" to Annex II.1 (see ICH Q10)
- Reduce complexity by combining and re-wording the individual sections
  - > "*formal*" and "*informal*" risk management referenced
  - > *"detectability"* as an element in several chapters

History

ICH Q9 QUALITY RISK MANAGEMENT

ICH Q9 Expert Working Group (EWG) as of ICH Step 4



History

ICH Q9 QUALITY RISK MANAGEMENT

Publication and implementation of ICH Q9

Legal position of ICH Q9

- **US / FDA:**
  - Guidance for Industry (June 2006)
  - By law, guidance documents are not enforceable or binding
    FDA will use the document internally in this spirit, as well
- **Japan / MHLW:**
  - Product GMP Guideline
    "Annex": ICH Guidelines
- **EU / EMEA:**
  EUDRALEX Volume 4 - Medicinal Products for Human and Veterinary Use : Good Manufacturing Practice
  - EU-GMP Vol. 4, Annex 20
  - Teams established to update chapters of EU-GMP, NfG etc.

History

ICH Q9 QUALITY RISK MANAGEMENT

European legal position of ICH Q9

Publication of the document in EU for comments:

- **"It should be borne in mind that this guideline does not introduce new requirements or expectations but should be considered a resource document that can be used together with existing quality-related guidelines when a risk-based approach is appropriate."**
- **"Therefore, as well as complementing GMP guidelines, the document should be seen as also complementing and supporting existing and future guidelines published by CHMP and CVMP concerning the quality of medicinal products."**

EU-Publication of Step 2 document

History

ICH Q9 QUALITY RISK MANAGEMENT

ICH Q9 Briefing Pack July 2006

Authors

- S. Rönninger, Roche (Chair)
- G. Claycamp, FDA
- P. Gough, former Lilly
- M. Holmes, GSK
- T. Matsumura, Eisai Co.
- H. Sasaki, Nippon Shinyaku
- T. Takarada, Mochida Pharm.

Reviewers

- E. Cooke, EMEA
- Y. Hiyama, MHLW
- D. Horowitz, FDA
- G. Keresty, Centocor
- U. Kopp, Swissmedic
- J. Morénas, AFSSAPS
- C. Mundkur, Barr Laboratories
- M.-P. Müller, Swissmedic
- F. Razzaghi, CHPA

Supported by EFPIA and JPMA ICH Q9 topic groups

History

ICH Q9 QUALITY RISK MANAGEMENT

ICH Q9 Briefing Pack

ICH EWG members published a set of slides with more details on possible implementations

> ICH homepage: www.ich.org -> Q S E M -> scroll down to ICH Q9

- **On the ICH Q9 Document**
  - > Background
  - > History
  - > Content
  - > Tools
  - > Applications
- **Additional features**
  - > Senior Management Training
  - > Frequently Asked Questions (Q&A)

Current direct link:
http://www.ich.org/cache/html/3157-272-1.html

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

History

Optional
but can benefit from its use!

Content

Quality Risk Management ICH Q9

Content

Disclaimer: *This presentation includes the authors views on quality risk management theory and practice. The presentation does not represent official guidance or policy of authorities or industry.*

Content

Purpose of this part

- To guide through the content of the ICH Q9 document
- Provide some considerations, possible interpretations and where appropriate examples

Content

ICH Q9: Quality Risk Management (QRM)

- Document is available on the ICH Webpage

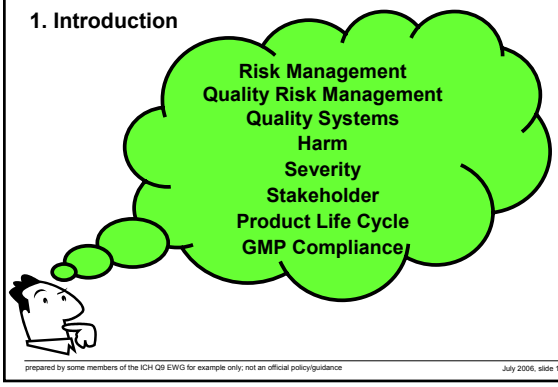
Content

Table of contents

1. Introduction
2. Scope
3. Principles of Quality Risk Management
4. General Quality Risk Management Process
5. Risk Management Methodology
   Annex I: Risk Management Methods and Tools
6. Integration of QRM process into Industry and Regulatory operations
   Annex II: Potential Applications for QRM
7. Definitions
8. References

Content

1. Introduction



Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Content

ICH Q9 QUALITY RISK MANAGEMENT

2. Scope

This guideline provides
principles & examples of tools
of quality risk management that can be applied to
different aspects of pharmaceutical quality.
These aspects include development, manufacturing, distribution, and the inspection and submission/review processes throughout the lifecycle
of drug substances, drug (medicinal) products, biological and biotechnological products

ICH Q9

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 103

Content

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

2. Scope

- Drug substances,
- Drug (medicinal) products,
- Biological and biotechnological products

Including the selection and use of

> Raw materials
> Solvents
> Excipients
> Packaging and labelling materials
> Components

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 104

Content

ICH Q9 QUALITY RISK MANAGEMENT

3. Principles of Quality Risk Management

Two primary principles:

The evaluation of the risk to quality should be based on scientific knowledge and ultimately link to the protection of the patient

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

ICH Q9

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 105

Content

ICH Q9 QUALITY RISK MANAGEMENT

4. General Quality Risk Management Process

Systematic processes
designed to
coordinate, facilitate and improve
science-based decision making
with respect to risk to quality

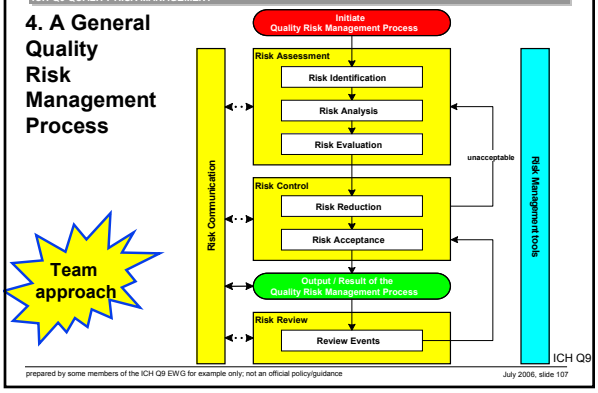
ICH Q9

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 106

Content

ICH Q9 QUALITY RISK MANAGEMENT

4. A General Quality Risk Management Process



ICH Q9

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 107

Content

ICH Q9 QUALITY RISK MANAGEMENT

4. General Quality Risk Management Process

Decision makers:
Person(s)
with competence and authority
to make a decision

- Ensuring that
  ongoing Quality Risk Management processes operate
- Coordinating
  quality risk management process
  across various functions and departments
- Supporting
  the team approach

Management responsibility

ICH Q9

prepared by some members of the ICH Q9 EWG for example only; not an official policy/guidance — July 2006, slide 108

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Content

4. General Quality Risk Management Process

Team approach

- Usually, but not always, undertaken by interdisciplinary teams from areas appropriate to the risk being considered e.g.
  - > Quality unit
  - > Development
  - > Engineering / Statistics
  - > Regulatory affairs
  - > Production operations
  - > Business, Sales and Marketing
  - > Legal
  - > Medical / Clinical
  - > &… Individuals knowledgeable of the QRM processes

Content

4. General Quality Risk Management Process

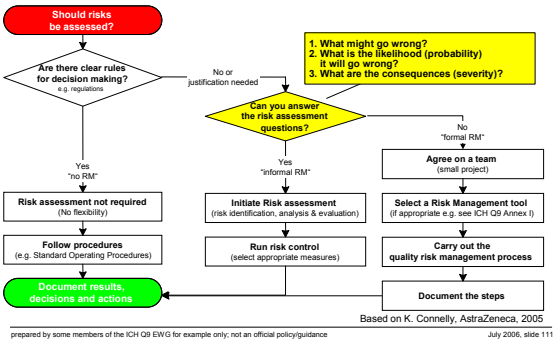
When to initiate and plan a QRM Process

- First define the question which should be answered (e.g. a problem and/or risk question)
  - > including pertinent assumptions identifying the potential for risk
- Then assemble background information and/ or data on the potential hazard, harm or human health impact relevant to the risk
  - > Identify a leader and necessary resources
  - > Specify a timeline, deliverables and appropriate level of decision making for the QRM process

ICH Q9

Content

When to apply Quality Risk Management?



Based on K. Connelly, AstraZeneca, 2005

Content

4. General Quality Risk Management Process

Risk Assessment

3 fundamental questions

- *Risk Identification*
  What might go wrong?
- *Risk Analysis*
  What is the likelihood (probability) it will go wrong?
- *Risk Evaluation*
  What are the consequences (severity)?

Note: People often use terms "Risk analysis", "Risk assessment" and "Risk management" interchangeably which is incorrect!

ICH Q9

Content

4. General Quality Risk Management Process

Risk Assessment: Risk Identification

"What might go wrong?"

- A systematic use of information to identify hazards referring to the risk question or problem
  - > historical data
  - > theoretical analysis
  - > informed opinions
  - > concerns of stakeholders

ICH Q9

Content

4. General Quality Risk Management Process

Risk Assessment: Risk Analysis

"What is the likelihood it will go wrong?"

- The estimation of the risk associated with the identified hazards.
- A qualitative or quantitative process of linking the likelihood of occurrence and severity of harm
- Consider detectability if applicable (used in some tools)

ICH Q9

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Content

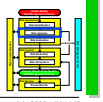
4. General Quality Risk Management Process

Risk Assessment: Risk Analysis

Often data driven

Keep in mind:
Statistical approach may or may not be used

- **Maintain a robust data set!**
- **Start with the more extensive data set and reduce it**
- **Trend and use statistics (e.g. extrapolation)**
- **Comparing between different sets requires compatible data**
- **Data must be reliable**
- **Data must be accessible**



Content

4. General Quality Risk Management Process

Risk Assessment: Risk Evaluation

"What is the risk?"

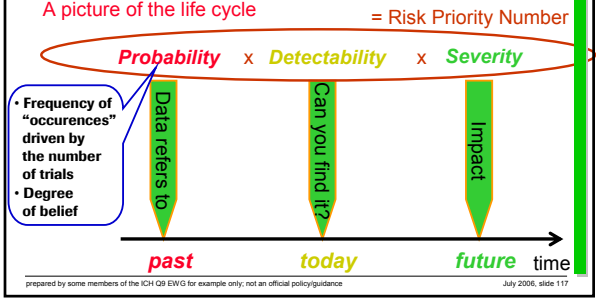
- **Compare the identified and analysed risk against given risk criteria**
- **Consider the strength of evidence for all three of the fundamental questions**
  - > What might go wrong?
  - > What is the likelihood (probability) it will go wrong?
  - > What are the consequences (severity)?

Content

4. General Quality Risk Management Process

Risk Assessment: Risk Evaluation

A picture of the life cycle



Content

4. General Quality Risk Management Process

Risk Control: Decision-making activity

- **Is the risk above an acceptable level?**
- **What can be done to reduce or eliminate risks?**
- **What is the appropriate balance between benefits, risks and resources?**
- **Are new risks introduced as a result of the identified risks being controlled?**

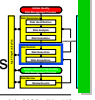
ICH Q9

Content

4. General Quality Risk Management Process

Risk Control: Residual Risk

- **The residual risk consists of e.g.**
  - > Hazards that have been assessed and risks that have been accepted
  - > Hazards which have been identified but the risks have not been correctly assessed
  - > Hazards that have not yet been identified
  - > Hazards which are not yet linked to the patient risk
- **Is the risk reduced to an acceptable level?**
  - > Fulfil all legal and internal obligations
  - > Consider current scientific knowledge & techniques



Content

4. General Quality Risk Management Process

Risk Control: Risk Reduction

- **Mitigation or avoidance of quality risk**
- **Elimination of risks, where appropriate**
- **Focus actions on severity and/or probability of harm; don't forget detectability**
- **It might be appropriate to revisit the risk assessment during the life cycle for new risks or increased significance of existing risks**

ICH Q9

Content

ICH Q9 QUALITY RISK MANAGEMENT

4. General Quality Risk Management Process

Risk Control: Risk Acceptance

- Decision to
  - > Accept the residual risk
  - > Passively accept non specified residual risks
- May require support by (senior) management
  - > Applies to both industry and competent authorities
- Will always be made on a case-by-case basis

Content

ICH Q9 QUALITY RISK MANAGEMENT CONSIDERATIONS

4. General Quality Risk Management Process

Risk Control: Risk Acceptance

- Discuss the appropriate balance between benefits, risks, and resources
- Focus on the patients' interests and good science/data
- Risk acceptance is not
  - > Inappropriately interpreting data and information
  - > Hiding risks from management / competent authorities

Content

ICH Q9 QUALITY RISK MANAGEMENT

What is an "acceptable risk"?

Risk Control: Risk Acceptance
Who has to accept risk?

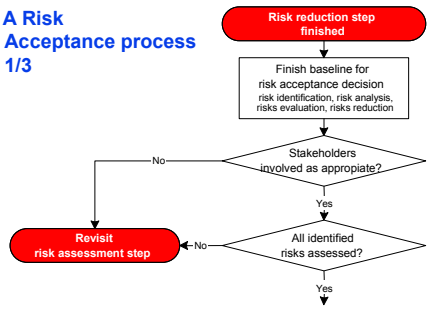
- Decision Maker(s)
  - > Person(s) with the competence and authority to make appropriate and timely quality risk management decisions
- Stakeholder
  - > Any individual, group or organization that can …be affected by a risk
  - > Decision makers might also be stakeholders
  - > The primary stakeholders are the patient, healthcare professional, regulatory authority, and industry (ICH Q9, definition)
  - > The secondary stakeholders are patient associations, public opinions, politicians

Content

ICH Q9 QUALITY RISK MANAGEMENT EXAMPLE

4. General Quality Risk Management Process

A Risk Acceptance process 1/3

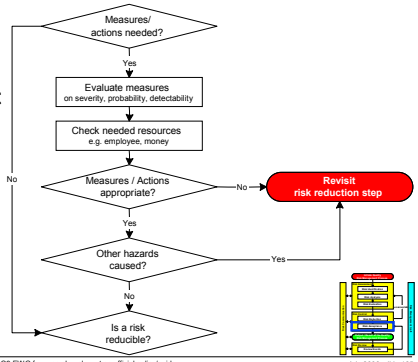


Content

ICH Q9 QUALITY RISK MANAGEMENT EXAMPLE

4. General Quality Risk Management Process

A Risk Acceptance process 2/3

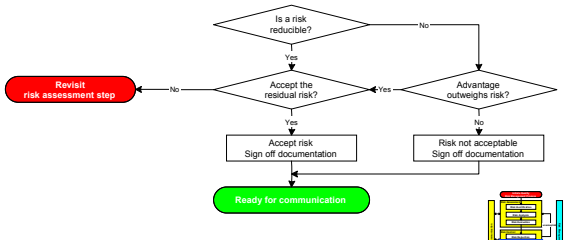


Content

ICH Q9 QUALITY RISK MANAGEMENT EXAMPLE

4. General Quality Risk Management Process

A Risk Acceptance process 3/3



Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Content

ICH Q9 QUALITY RISK MANAGEMENT

4. General Quality Risk Management Process

Risk Communication

- Bi-directional sharing of information about risk and risk management between the decision makers and others
- Communicate at any stage of the QRM process
- Communicate and document the output/result of the QRM process appropriately
- Communication need not be carried out for each and every individual risk acceptance
- Use existing channels as specified in regulations, guidance and SOP's

According to ICH Q9

Content

ICH Q9 QUALITY RISK MANAGEMENT CONSIDERATIONS

4. General Quality Risk Management Process

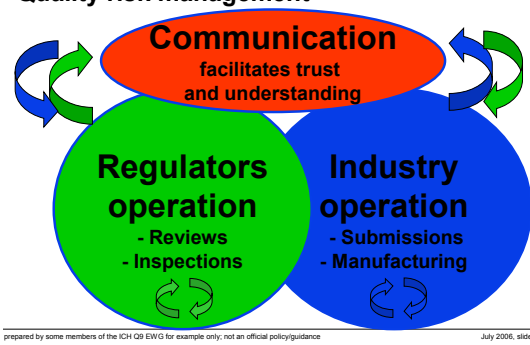
Risk Communication

- Exchange or sharing of information, as appropriate
- Sometimes formal sometimes informal
  - > Improve ways of thinking and communicating
- Increase transparency

Content

ICH Q9 QUALITY RISK MANAGEMENT CONSIDERATIONS

Quality risk management



Content

ICH Q9 QUALITY RISK MANAGEMENT

4. General Quality Risk Management Process

Risk review: Review Events

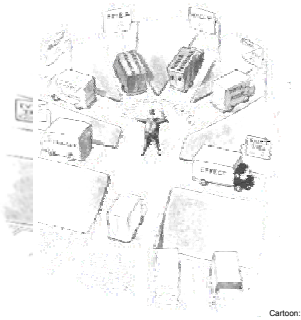
- Review the output / results of the QRM process
- Take into account new knowledge and experience
- Utilise for planned or unplanned events
- Implement a mechanism to review or monitor events
- Reconsideration of risk acceptance decisions, as appropriate

ICH Q9

Content

ICH Q9 QUALITY RISK MANAGEMENT

5. Risk Management Methodology



One method "all inclusive"?

Cartoon: © Zurich Insurance Inc.

Content

ICH Q9 QUALITY RISK MANAGEMENT CONSIDERATIONS

Expectations on methods and tools

- Supports science-based decisions
- A great variety are listed but other existing or new ones might also be used
- No single tool is appropriate for all cases
- Specific risks do not always require the same tool
- Using a tool the level of detail of an investigation will vary according to the risk from case to case
- Different companies, consultancies and competent authorities may promote use of different tools based on their culture and experiences

Content

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

Contributing items to manage quality risks

- **System Risk** (facility & people)
  - > e.g. interfaces, operators risk, environment, components such as equipment, IT, design elements
- **System Risk** (organisation)
  - > e.g. Quality systems, controls, measurements, documentation, regulatory compliance
- **Process Risk**
  - > e.g. process operations and quality parameters
- **Product Risk** (safety & efficacy)
  - > e.g. quality attributes: measured data according to specifications

Content

ICH Q9 QUALITY RISK MANAGEMENT

5. Risk Management Methodology

- Supports a scientific and practical approach to decision-making
- Accomplishing steps of the QRM process
  - > Provides documented, transparent and reproducible methods
  - > Assessing current knowledge
  - > Assessing probability, severity and sometimes detectability

ICH Q9

Content

ICH Q9 QUALITY RISK MANAGEMENT

5. Risk Management Methodology

- Adapt the tools for use in specific areas
- Combined use of tools may provide flexibility
- The degree of rigor and formality of QRM
  - > Should be commensurate with the complexity and / or criticality of the issue to be addressed and reflect available knowledge
- Informal ways
  - > empirical methods and / or internal procedures

ICH Q9

Content

ICH Q9 QUALITY RISK MANAGEMENT

Annex I: Risk Management Methods and Tools

- Provides a general overview of and references for some of the primary tools
- Might be used in QRM by industry and regulators
- This is not an exhaustive list
- No one tool or set of tools is applicable to every situation in which a QRM procedure is used
- For each of the tools
  - > Short description & reference
  - > Strength and weaknesses
  - > Purely illustrative examples

ICH Q9

Content

ICH Q9 QUALITY RISK MANAGEMENT — CONSIDERATIONS

Overview: Some tools and their key words

- **Failure Mode Effects Analysis (FMEA)**
  - > Break down large complex processes into manageable steps
- **Failure Mode, Effects and Criticality Analysis (FMECA)**
  - > FMEA & links severity, probability & detectability to criticality
- **Fault Tree Analysis (FTA)**
  - > Tree of failure modes combinations with logical operators
- **Hazard Analysis and Critical Control Points (HACCP)**
  - > Systematic, proactive, and preventive method on criticality
- **Hazard Operability Analysis (HAZOP)**
  - > Brainstorming technique
- **Preliminary Hazard Analysis (PHA)**
  - > Possibilities that the risk event happens
- **Risk ranking and filtering**
  - > Compare and prioritize risks with factors for each risk

Content

ICH Q9 QUALITY RISK MANAGEMENT

5. Risk Management Methodology

- Supporting statistical tools
  - > Acceptance Control Charts (see ISO 7966)
  - > Control Charts (for example)
    - **Control Charts with Arithmetic Average and Warning Limits (see ISO 7873)**
    - **Cumulative Sum Charts; "CuSum" (see ISO 7871)**
    - **Shewhart Control Charts (see ISO 8258)**
    - **Weighted Moving Average**
  - > Design of Experiments (DOE)
    - **Pareto Charts**
  - > Process Capability Analysis
  - > Histograms
  - > Use others that you are familiar with….

ICH Q9

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Content

5. Risk Management Methodology




Q9 does not provide "drivers licences"

Content

6. Integration into Industry and Regulatory Operations

- Foundation for "science-based" decisions
- Does not obviate industry's obligation to comply with regulatory requirements
- May affect the extent and level of direct regulatory oversight
- Degree of rigor and formality commensurate with the complexity and/or criticality of the issue
- Implement QRM principles when updating existing guidelines

ICH Q9

Content

Annex II: Potential Applications for QRM

This Annex is intended to identify potential uses of quality risk management principles and tools by industry and regulators.

However, the selection of particular risk management tools is completely dependent upon specific facts and circumstances.

These examples are provided for illustrative purposes and only suggest potential uses of quality risk management.

This Annex is not intended to create any new expectations beyond the current regulatory requirements.

ICH Q9 Introduction to Annex II

Content

Annex II: Potential Applications for QRM

Quality risk management as part of

- **Integrated quality management**
  - > Documentation
  - > Training and education
  - > Quality defects
  - > Auditing / Inspection
  - > Periodic review
  - > Change management / change control
  - > Continual improvement

Competent authorities

Industry

Content

Annex II: Potential opportunities for conducting quality risk management

Quality risk management as part of

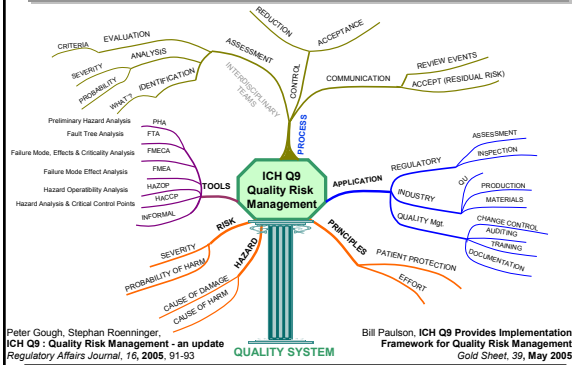
- **Regulatory operations**
  - > Inspection and assessment activities
- **Industry operations**
  - > Development
  - > Facilities, equipment and utilities
  - > Materials management
  - > Production
  - > Laboratory control and stability testing
  - > Packaging and labelling

Competent authorities

Industry

Competent authorities

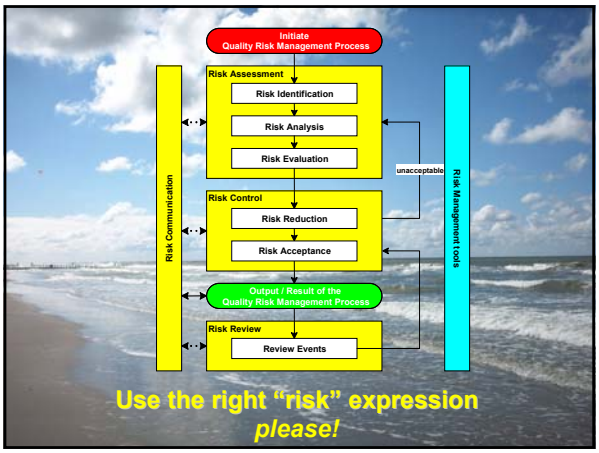
Content



Peter Gough, Stephan Roenninger, **ICH Q9 : Quality Risk Management - an update** *Regulatory Affairs Journal*, *16*, **2005**, 91-93

Bill Paulson, **ICH Q9 Provides Implementation Framework for Quality Risk Management** *Gold Sheet*, *39*, **May 2005**

Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.



Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

Quality Risk Management ICH Q9 Frequently Asked Questions (FAQ)

Disclaimer: *This presentation includes the authors views on quality risk management theory and practice. The presentation does not necessarily represent official guidance or policy of authorities or industry.*

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

Purpose of this part

- **To provide answers to questions that have been frequently asked of members of the ICH Q9 Expert Working Group.**

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

What makes Q9 different?

- **It provides principles and a framework for decision making**
  - > Q9 is a quality improvement methodology
- **It is a "guidance" not an "SOP"**
  - > Simple
  - > Flexible
  - > Not mandatory
- **It supports science-based decision making**
  - > Facilitates communication and transparency
  - > Supports build up trust
- **Q9 is for both industry and competent authorities (CA)**

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

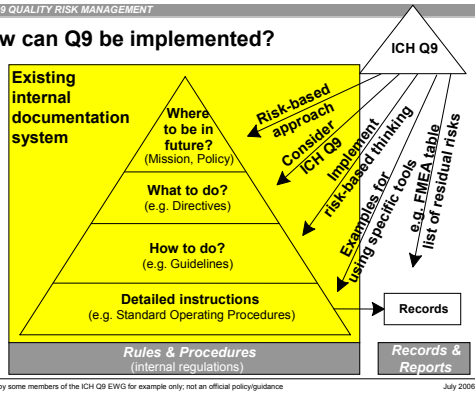
How can Q9 be implemented?

- **It can be implemented by industry and competent authorities (reviewers and inspectorates)**
- **The ICH Q9 document:**
  - > **Main body explains the "What?"**
  - > **Annex I give ideas on the "How?"**
  - > **Annex II give ideas on the "Where?"**
  - > **Pharmaceutical Development (ICH Q8) and Quality Systems (ICH Q10) will facilitate the use of Q9**
- **Do not set up a QRM department**
- **See following slide indicate some of the impacts that ICH Q9 can have on an existing documentation system.**

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

How can Q9 be implemented?



Disclaimer: The ICH Q9 briefing pack is offered as a supplementary explanation of the material in ICH Q9. It was prepared by some members of the ICH Q9 EWG for example only. It has not gone through any ICH formal process. It does not represent an official policy/guidance.

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

How to select the tool for my needs?

- The level of detail and quantification needed helps to determine the tool to use:
  - > Methodology
    e.g. formal or informal risk management process
  - > System risks
    e.g. risk ranking and filtering, FMEA
  - > Process risks
    e.g. FMEA, HACCP, process mapping, flow charts
  - > Product risks
    e.g. flow charts, decision trees, tables, check sheets

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

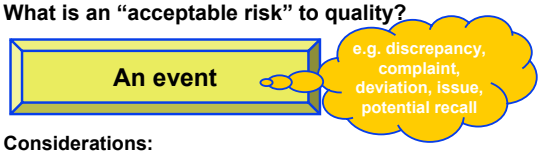
What is an "acceptable risk"?

- This has to be decided in the context of each specific risk management problem
- If you put in precise and definite data, you will receive a clear answer. This enables decision makers to make good and transparent decisions
- Accept residual risk, where further effort to reduce a risk is disproportional to the protection of the patient
- Always remember: The protection of the patient
- It's up to the organization whether they accept risks that meet the principles of QRM

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

What is an "acceptable risk" to quality?



Considerations:

- "Industrial risk" could be different from "political risk"
- Notion of "risk" could be not the same for industry and competent authority (CA)
- CA are often face to face with public opinion and politicians
- Compromise according to ICH Q9: "link back to the protection of the patient"

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

What is a residual risk?

- Residual risk addresses hazards that
  - > Have been assessed and risks that have been accepted
  - > Have been identified but the risks have not been correctly assessed
  - > Have not yet been identified
  - > Are not yet linked to the patient risk
- Is the risk transferred to an acceptable level?
  - > Consider current scientific knowledge & techniques
  - > Fulfil all legal and internal obligations

As hazards remain Zero risk is never possible

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

What is the content of the "output/result" box?

- The rationale and output have to be communicated after decision making
  - > The means and records of what is communicated will vary in individual circumstances
- Adequate documentation
  - > The choice from short summary to detailed report is case dependant
  - > It should contain the rationale and conclusions

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

When to stop a QRM process?

- When you decide, through a risk management process, that a certain residual risk is acceptable, you can close your QRM process for that particular risk
  - > You should communicate the outcomes on that QRM process, as appropriate, to stakeholders
- However, quality risk management process is continuous and the outputs/results may or may not need to be reviewed frequently during the life cycle
  - > The need to review or not should be decided based upon the level of accepted risk and other cumulative factors (e.g. process changes, events)

see section 4 of ICH Q9 document

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

How will Q9 be involved in the submission and review process?

Q9 supports presentation of scientific arguments:

- **For proposals in the submission**
- **For answering subsequent questions and proposals the reviewers may raise**
- **When linked with "Pharmaceutical development" (ICH Q8) it might avoid the need for such questions by reviewers**

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

Will ICH Q9 be applied by competent authorities as they develop / review regulations?

- **There have already references been made to the use of ICH Q9 principles in recent regulatory documents. This indicates the awareness and commitment to ICH Q9 in some competent authorities**
- **There are some existing and proposed regulations which do not recognise the use of ICH Q9 principles. It is the hope and expectation that this will be taken into account as the opportunity arises for revision or prior to publication**

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

How will Q9 activity be inspected/audited?

No structured Quality Risk Management in place

=

In theory

- **no observation**
- **No recommendation**

because using ICH Q9 is not mandatory

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

How will Q9 activity be inspected/audited?

- **However inspections/audits already focus on QRM activities e.g.**
  - **> How the problems have been solved?**
  - **> What corrective and preventive measures have been taken?**
- **Inspectors/Audits might review/inspect:**
  - **> Whether the quality risk management performed is integrated in the Quality System of the organization**
  - **> Traceability, transparency**
  - **> How was the decision made?**
  - **> Was a (risk) problem / question defined?**
  - **> Did the process performed answer this question?**
  - **> Were the appropriate functions allocated to all teams?**
  - **> Were the right documents recognized?**
  - **> Was the decision based on scientific knowledge?**

Frequently Asked Questions (FAQ)

ICH Q9 QUALITY RISK MANAGEMENT

How will Q9 outcomes be reviewed and inspected?

- **Competent authorities will check if the science used for the quality risk management process is acceptable**
- **Competent authorities may not accept the outcome of the risk management process if it is not satisfactory in terms of science**

  > Debate and seek agreement on science