Q8 (R1) - Annex to Q8 Pharmaceutical Development

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Topics to be Discussed

- Where it all began
- Background on Q8 (Parent Guideline)
- Q8(R1) Issues and Challenges
- Structure of Q8(R1)
- Definitions
- Minimal and Enhanced Approaches to Pharmaceutical Development
- Next steps

Where did it all begin?

Structure of Q8

Q8 was envisaged as a 2 part guideline

- Part 1
- Core document
- Baseline expectations
- Optional information
- Regulatory Flexibility

Step 4: Nov 2005

- Part 2
- Annexes relating to specific dosage forms (as Q6a)
- References to use of risk management
- Focus on guiding towards Desired State

Started in May 2006

Q8: Pharmaceutical Development

- Parent guideline
  - Introduced the general principles of pharmaceutical development
    - Components of the drug product
    - Formulation development
    - Manufacturing development
  - Introduced new concepts
    - Minimal versus enhanced
    - Design space
    - Real time release (testing)

Q8 Timeline

- Adopted as ICH topic October 2003
- Step 4 - Chicago November 2005
- Implementation underway but everyone is learning!
- Continued straight into development of Q8R

Q8(R1) - Timeline

- Per ICH steering committee in May 2007, focus of guideline was revised to elaborate the principles of Quality by Design
- Step 2 draft guideline signed on November 1, 2007 in Yokohama
- **Step 4 signed on November 12, 2008 in Brussels**

Challenges for Expert Working Group

Balancing what to define vs. what is out of scope

Define

- Principles
- What – high level
- Illustrative examples

Out of scope

- How
- Application to drug substance & analytical methods
- Specific examples
- Regional implementation

Key issues addressed by EWG

- ✓ Approaches to pharmaceutical development?
- ✓ What should be included in a Design Space
- ✓ Critical quality attribute
- ✓ Critical process parameter
- ? Critical
- ✓ How a Design Space might be described in a dossier (including some illustrative examples)
- ✓ Control Strategy
- ✓ Lifecycle
- ✓ Location of Information in the dossier

Definitions for CQA & CPP

Critical Quality Attribute

- A physical, chemical, biological or microbiological property or characteristic that should be within an appropriate limit, range, or distribution to ensure the ***desired product quality***.

Critical Process Parameter

- A process parameter whose variability has an impact on a critical quality attribute and therefore should be monitored or controlled to ensure to process produces the ***desired quality***.

Other Definitions

- Control Strategy: Adopted the definition from Q10
- Quality by Design: A systematic approach to development that begins with predefined objectives and emphasises product and process understanding and process control, based on sound science and risk management
- Quality (Q8): The suitability of either a drug substance or drug product for its intended use. This term includes such attributes as the identity, strength, and purity *(from Q6A)*

Elements of a control strategy can include:

- Control of input material attributes
- Product Specifications
- Controls for unit operations that have an impact on downstream processing or end-product quality
- In-process or real-time release testing in lieu of end-product testing
- A monitoring program for verifying multivariate prediction models

Scope & Structure of Q8(R1)

- Chapter 1: Approaches to Phamaceutical Development (minimum & enhanced)
- Chapter 2: Elements of Pharmaceutical Development
  - Quality Target Product Profile
  - Critical Quality Attributes
  - Risk Assessment: Linking Material Attributes and Process Parameters to CQAs

Scope & Structure of Q8(R1)

- Chapter 2: Elements of Pharmaceutical Development (cont.)
  - Design Space
    - Selection of variables
    - Describing design space in a submission
    - Unit operation design space(s)
    - Relationship of design space to scale and equipment
    - Design space versus proven acceptable ranges
    - Design space and edge of failure

Scope & Structure of Q8(R1)

- Chapter 2: Elements of Pharmaceutical Development (cont.)
  - Control strategy
  - Product lifecycle management and continual improvement

Scope & Structure of Q8(R1)

- Chapter 3: Submission of Pharmaceutical Development & Related Information in CTD
  - Quality Risk Management and Product & Process Development
  - Design Space
  - Control Strategy
  - Drug Substance Related Information
- Glossary (ten terms defined)
- Appendices (one table & ten figures)

Q8(R1) – Minimal Approach to Pharmaceutical Development

- Quality Target Product Profile
- Identification of potential critical quality attributes of the drug product
- Determining the critical quality attributes of the components of the drug product
- Selecting an appropriate manufacturing process
- Determining a control strategy

Q8(R1) – Enhanced Approach (QbD) to Pharmaceutical Development

- Systematic evaluation, understanding
  - Use of prior knowledge, risk assessment
  - Functional relationship between material attributes and process parameters to product critical attributes
- Establishment of design space, real time release testing
- As a consequence facilitates continual improvement and innovation (ICH Q10)

- What are the next steps?
- How do we transition to the new quality paradigm?
- What are the hurdles and opportunities?

Queen Mary 2

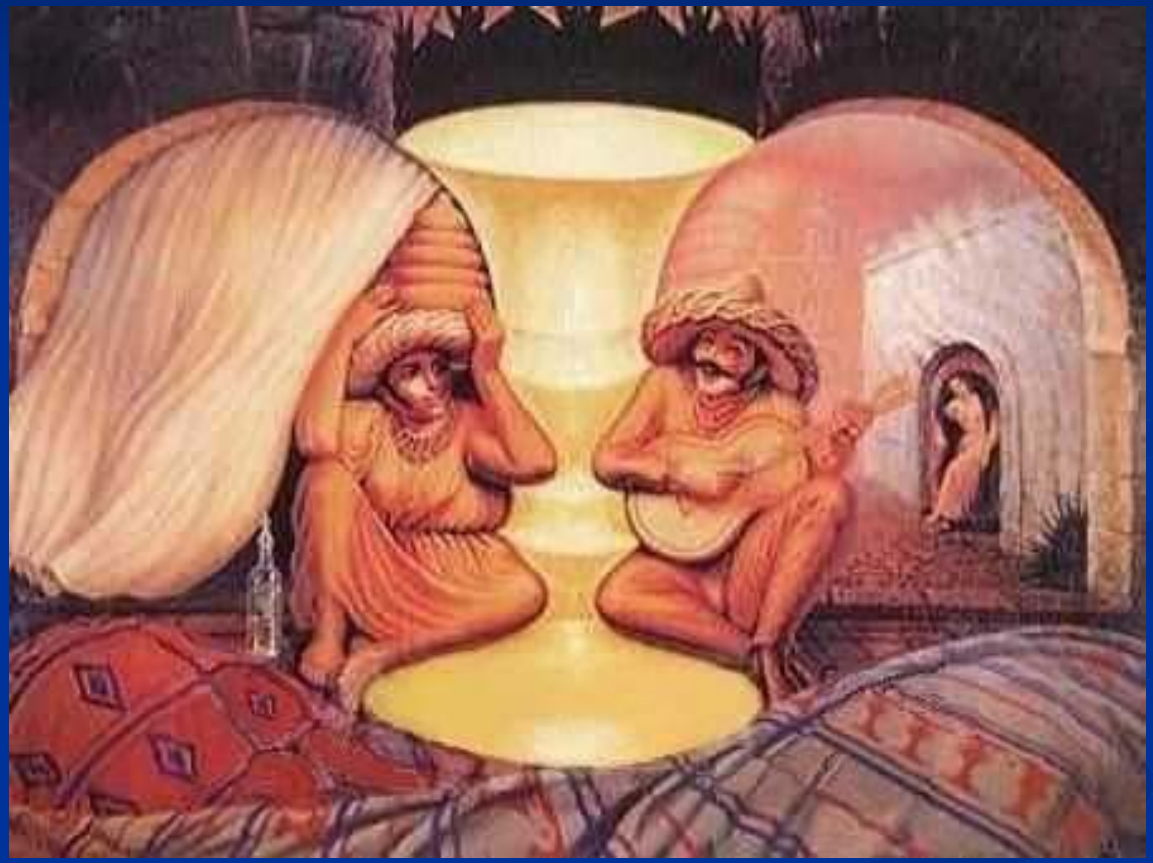
Length: 345 meters / 1132 feet Beam: 40 meters / 135 feet
Gross Tonnage: 150,000 gross tons
Passengers: 2620 Crew: 1253
Power: 157,000 horsepower Propulsion: Four pods
Strength: Extra thick steel hull for strength and stability for Transatlantic Crossings.

QM2 is more than twice as long as the Washington Monument is tall (550 ft.)
QM2 is 147 feet longer than the Eiffel Tower is tall (984 ft.)
QM2 is only 117 feet shorter than the Empire State Building is tall (1248 ft.)
QM2's whistle is audible for 10 miles.

… takes 5 miles before it stops
… takes ? miles to turn it around

Hurdles?

What opportunities do you see?



Frame of Reference