



## Q&A on ICH Q7 – Good Manufacturing Practice Questions and Answers Document

March 2017

International Council for Harmonisation of Technical Requirements  
for Pharmaceuticals for Human Use



### ICH Q7 - Questions & Answers Document

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## Outline

- Background and Objectives
- Development process
- Scope/ Content
- Regulatory implementation
- Key message
- Summary

## Importance of the ICH Q7 Guideline

- First internationally harmonized Good Manufacturing Practice (GMP) guidance developed jointly by industry and regulators under the ICH umbrella
- Finalized November 2000 and adopted by most major Health Authorities including WHO
- Establishes one global GMP guideline for Active Pharmaceuticals Ingredients (APIs)
- Intended to facilitate API inspections
- Important to international cooperative regulation of API manufacturing

## Why an ICH Q7 Q&A Document?

- ICH Q7 was published in 2000
  - API manufacturing technology and practices have evolved since then
  - Good Distribution Practice (GDP) for API was included in ICH Q7
- API supply chains are global and complex
- Currently, many different health authorities regulate and/or inspect API manufacturers
- Regulators continue to find significant GMP deficiencies during API inspections

## ICH procedure

- ICH recommends a Q&A document when clarification is needed to aid interpretation of ICH guidelines
- Concept Paper is endorsed by ICH Steering Committee
- Implementation Working Group (IWG) is formed
- Q&As are based on issues for clarification raised by stakeholders as summarized in the Concept Paper

## Agreed Scope

- **ICH Q7 Q&A – is a ‘what to do’ document**
  - Desired Product: One harmonized Q&A document
  - Address/clarify issues raised in Concept Paper, including:
    - Distribution of APIs (GDP)
    - Agents, Traders, Distributors responsibilities
    - Contractor/supplier management (outsourcing)
    - Quality management systems (QMS) practices including the impact of Q8/Q11, Q9, Q10
    - Manufacturing APIs for use in clinical trials
    - Applicability of Q7 to biologicals/biotech & relationship to Q5D
  - Address one issue at a time
    - Clear, concise answers
    - Reference Q7 sections or other ICH documents, as appropriate

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## Discrimination criteria

- **ICH Q7 Q&A document does **NOT**:**
  - Explain ‘How to do’
  - Simply restate text already available in ICH Q7
  - Enlarge the scope of ICH Q7
  - Address questions that are too narrow or specific to be of widespread interest or importance
  - Establish new requirements
  - Address issues specific to a region or jurisdiction
  - Address issues that are outdated or otherwise irrelevant

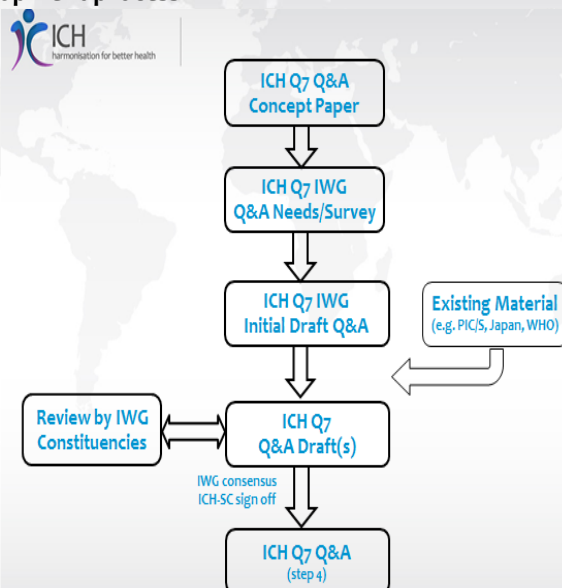
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## Work Plan & Deliverables

- **Questions were obtained from various sources**
  - Including existing Q&As from the PIC/S API Expert Circle, PDA/ Regulatory training 2002
  - Survey of constituencies for issues needing clarification conducted by the ICH Q7 IWG Feb.- Mar. 2013
- **The ICH Q7 - IWG**
  - Evaluated about 200 questions and suggested answers
  - Consolidated, drafted, revised Q&As as needed
  - 5 face-to-face meetings and several regional and worldwide teleconferences
  - Consensus on 55 Q&As achieved on April 20, 2015

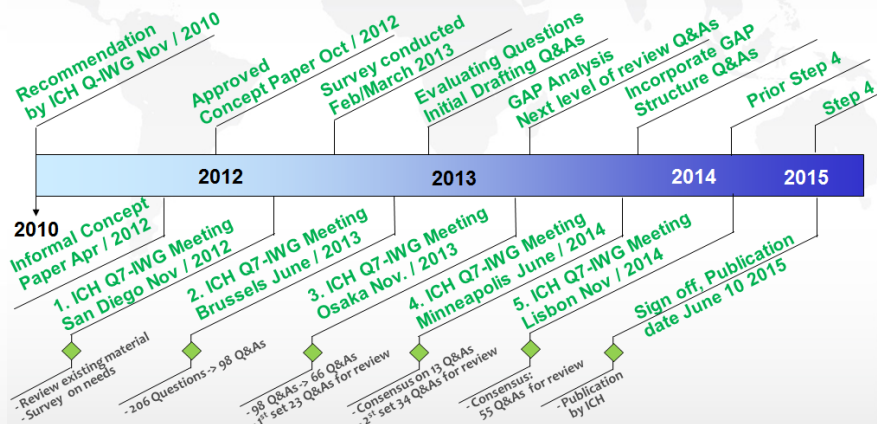
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## ICH Q7 Q&A Development Process: From Concept Paper to Final Step 4 Document



DRAFT

## Development Timeline



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## Step 4 – Adoption of Q7 Q&A Document

- **The Step 4 ICH harmonised document was posted to ICH website ([www.ich.org](http://www.ich.org)) on 10 June 2015**
  - Total of 55 Q&As
    - Questions cover all sections of ICH Q7 except Section 9 (Packaging and Identification Labelling of APIs/ Intermediates)
    - ICH Q7 sections with the most Q&As were:
      - Quality Management
      - Materials Management
      - Process Equipment
      - Laboratory Controls
    - Q&As include references to other ICH guidelines, including to Q8, Q9, Q10 and Q11 which were established after Q7 was finalised in 2000.

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## 55 Q&As by Section

ICH Section	Q&As	ICH Section	Q&As
1 – INTRODUCTION	2	11 – LABORATORY CONTROLS	5
2 – QUALITY MANAGEMENT	6	12 – VALIDATION	4
3 – PERSONNEL	2	13 – CHANGE CONTROL	1
4 – BUILDINGS & FACILITIES	2	14 – REJECTION & REUSE OF MATERIALS	3
5 – PROCESS EQUIPMENT	5	15 – COMPLAINTS & RECALLS	2
6 – DOCUMENTATION & RECORDS	3	16 – CONTRACT MANUFACTURERS	3
7 – MATERIALS MANAGEMENT	6	17 – AGENTS . . . RELABELLERS	4
8 – PRODUCTION & IN-PROCESS CONTROLS	2	18 – APIs MANUFACTURED BY CELL CULTURE/FERMENTATION	2
9 – PACKAGING & ID LABELLING OF APIs & INTERMEDIATES	0	19 – APIs FOR CLINICAL TRIALS	1
10 – STORAGE & DISTRIBUTION	1	20 – GLOSSARY	1

## Clarification of Uncertainties

### Examples of issues addressed in Q&A document:

#### 1. Introduction - Scope

- Manufacturing steps before the defined 'API starting material'
- Manufacturing steps for the addition of substance(s) to an API (e.g. to stabilize the API)

#### 2. Quality Management

- Responsibility and independence of quality unit(s) and performing sampling and API release testing
- Frequency of a product quality review and trend analysis

## Clarification of Uncertainties

### 3. Personnel

- Periodical assessment of training
- Delegation of tasks and/or responsibility to a consultant

### 4. Buildings and Facilities - Containment

- The use of Quality Risk Management to prevent cross-contamination (e.g dedicated production areas)

### 5. Process Equipment - Cleaning

- 'Visually clean' and visual examination
- Acceptance criteria for residues in dedicated equipment and confirmation of time limits in cleaning validation

## Clarification of Uncertainties

### 6. Documentation and Records

- Clarifying the meaning of 'completely distributed'
- Sequential batch numbering system and issuance of batch production records

### 7. Materials Management

- 'Grouping of containers' and 'identity tests'
- Qualification of suppliers of materials, 'full analysis' on batches of raw materials and on-site audits
- Expiry date and retest date of a raw material



## Clarification of Uncertainties

### 8. Production and In-Process Controls

- Yield ranges and 'appropriate specifications prior to blending'

### 9. Packaging and Identification Labelling of APIs and Intermediates

- *No question*

### 10. Storage and Distribution

- Transfer under quarantine to another unit under the company's control

## Clarification of Uncertainties

### 11. Laboratory Controls

- Impurities for APIs (extracted from herbal or animal tissue origin)
- Change in API test methods for ongoing stability studies
- Extending an API retest date
- 'Completely distributed' as it relates to reserve/retention samples
- Packaging system for reserve/retention samples

### 12. Validation

- Retrospective and Lifecycle approach to validation
- Expanding the range of a process parameters
- Process validation and change in the source of an API starting material

## Clarification of Uncertainties

### 13. Change Control

- Notification of drug manufacturers (customers) about relevant API manufacturing changes

### 14. Rejection and Reuse of Materials

- Storage of rejected materials
- Reprocessing or reworking of an expired API
- Recovery of material from mother liquor

### 15. Complaints and Recalls

- Quality defects of released APIs versus complaint
- Return versus recall

## Clarification of Uncertainties

### 16. Contract Manufacturers (including Laboratories)

- Responsibilities
- Outsourced activities and subcontracting

### 17. Agents, Brokers, Traders, Distributors, Repackers, and Relabellers

- Clarifying the meaning of 'Agents, brokers, traders, distributors, repackers, or relabellers'
- Distributors as contract manufacturer for production steps
- Replacement of the original label
- Original manufacturer

## Clarification of Uncertainties

### 18. Specific Guidance for APIs Manufactured by Cell Culture/Fermentation

- Validation for viral removal/viral inactivation steps
- Applicability to classical fermentation and biotechnology

### 19. APIs for Use in Clinical Trials

- Equipment for pre-clinical and clinical materials

### 20. Glossary

- Terminology ‘deviation’ versus ‘non-conformance’

## ICH Q7 Q&A Document – Annex

Sections of ICH Q7	1: Introduction	2: Quality Management	3: Personnel	4: Buildings and Facilities	5: Process Equipment	6: Documentation and Records	7: Materials Management	8: Production and In-Process Controls	9: Packaging and Identification, Labeling of APIs and Intermediates	10: Storage and Distribution	11: Laboratory Controls	12: Validation	13: Change Control	14: Rejection and Re-use of Materials	15: Complaints and Recalls	16: Contract Manufacturers (including Laboratories)	17: Agents, Brokers, Traders, Distributors, Repackers, and Re-labelers	18: Specific Guidelines for APIs manufactured by Cell Culture/Fermentation	19: APIs for Use in Clinical Trials	20: Glossary	Other ICH Guidelines
<b>1. Introduction – Scope</b>																					
1	1.3																				Q11 Q5B Q5D
2	1.2																			20	
<b>2. Quality Management</b>																					
1		2.13																			
2		2.13									11.12					16.10				20	
3		2.22									11.10										
4		2.22	3.10			6.52					11.12										

Q&As are cross-referenced to Q7 sections & other ICH Guidelines

## ICH Guidelines referenced in Q7 Q&A

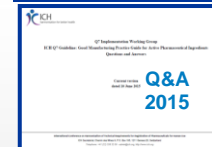
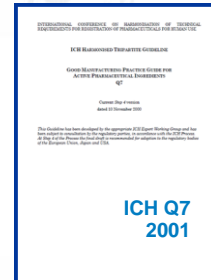
- ICH E2E Pharmacovigilance Planning, Nov. 2004
- ICH Q1A Stability Testing of New Drug Substances and Products, Feb. 2003
- ICH Q5A Quality of Biotechnological Products: Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin, Sept. 1999
- ICH Q5B Quality of Biotechnological Products: Analysis of the Construct in Cells Used for the Production of r-DNA Derived Protein Products, Nov. 2005
- ICH Q5D Quality of Biotechnological Products: Derivation and Characterization of Cell Substrates Used for Production of Biotechnological/Biological Products, Jul. 1997
- ICH Q6B Specifications: Test Procedures and Acceptance Criteria for Biotechnological/Biological Products, Mar. 1999
- **ICH Q7 Good Manufacturing Practice for APIs, Nov. 2000**
- ICH Q8(R2) Pharmaceutical Development, Aug. 2009; Part I: 'Pharmaceutical Development', Nov. 2006; Part II: 'Annex to Pharmaceutical Development', Nov. 2008.
- ICH Q9 Quality Risk Management, Nov. 2005; and the ICH Q9 Briefing pack
- ICH Q10 Pharmaceutical Quality Systems, Jun. 2008
- ICH Q11 Development and Manufacture of Drug Substances, May 2012

## Step 5–Regulatory Implementation

- Final step in the ICH harmonisation process
- Carried out using the same national/regional procedures as for other regional regulatory guidelines
- ICH harmonized guidelines are widely used, including in the European Union, Japan, USA, Canada, Switzerland, Australia, South Korea, Brazil and beyond
- ICH Q&A document may be posted on the official Websites of regulatory bodies that adopt them for use (e.g., EMA, MHLW/PMDA, FDA, Health Canada) as well as international organisations (e.g. PIC/S, WHO, ...)

## Key Message of the ICH Q7 Q&A

*The ICH Q7 document is intended to be read in its **entirety** regardless of the nature of the manufacturing activities being conducted to fully understand the linkages between certain sections and successfully implement appropriate GMPs at all stages of the API supply chain, including distribution.*



Read and implement existing guidelines

## Summary

- Experience gained with the implementation of the ICH Q7 Guideline since its finalisation in 2000 shows that uncertainties related to the interpretation of some sections exist.
- Technical issues with regard to GMP of APIs – also in context with new ICH Guidelines - are addressed in this Question and Answer document in order to:
  - Harmonize expectations during inspections,
  - Eliminate ambiguities and uncertainties
  - Harmonize the inspections of both small molecules and biotech APIs.