ICH Q7 - API

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Regulatory Knowledge, Practically Applied.

ICH Q7

ICH Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients (November 2000)

Adopted or referenced by:

- PIC/S in 2007 - Guide to GMP PE009 Part II
- FDA Notice in 2001 - Vol. 66 No. 186 p. 49028-9

Joint PDA/PICS initiative to assess the status of Q7 since 2012.

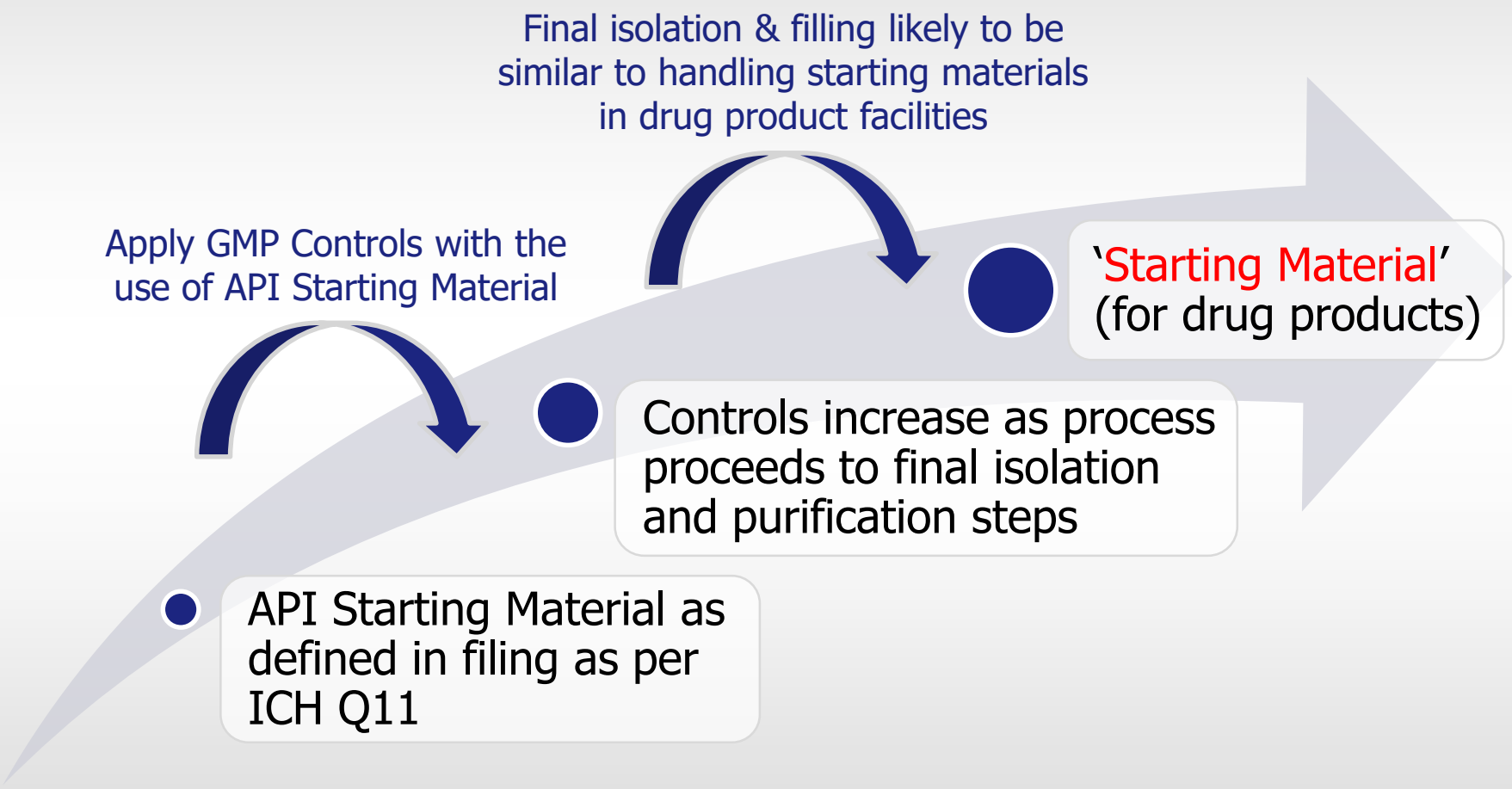
- International training rolled out in 2014.
- ICH Question & Answer – June 2015 clarification

2014 ICH Q7 (API) PIC/S PDA Training

Main Discussion Points:

- Represents an update on the 2000 version by ICH Q7 EWG members, PDA & PIC/s joint initiative in 2012.
- Understanding of 'API Starting Material' as opposed to Starting Material
- Chapter 17: Agents, Brokers, Traders, Distributors, Repackers, and Relabellers (ABTDRR)
- Chapter 18: Cell Culture / Fermentation
- Chapter 19: API for Clinical Trials

2014 ICH Q7 (API) Training
API Starting Material



2014 ICH Q7 (API) Training
Chapter 18 Fermentation / Cell Culture

Type of Manufacturing	Application of this Guide to steps (shown in grey) used in this type of manufacturing				
Biotechnology: fermentation/ cell culture	Establishment of master cell bank and working cell bank	Maintenance of working cell bank	Cell culture and/or fermentation	Isolation and purification	Physical processing, and packaging
"Classical" Fermentation to produce an API	Establishment of cell bank	Maintenance of the cell bank	Introduction of the cells into fermentation	Isolation and purification	Physical processing, and packaging

Increasing GMP requirements

Increasing process control and risk based decisions

Certain GMP requirements applicable in early process steps (e.g. Documentation)

2014 ICH Q7 (API) Training
Chapter 18 Fermentation / Cell Culture

Key Messages

- Ch. 18 Should not be read as a standalone chapter
  - Addresses additional info for biotech manufacture
- In general cell culture processes require additional controls not needed for small molecules (e.g. virus control, tighter contamination control)

2014 ICH Q7 (API) Training
Chapter 18 Fermentation / Cell Culture

Key Messages

18.1 Bioburden

- Not contamination unless levels have been exceeded or defined objectionable materials have been detected (Risk based)

QRM: Levels of Protection

- Level A (Patient)
- Level B (Manufacturing using WCB)
- Level C (Employee & Environment)

Note: different level of control for classical fermentation versus biotech processes

2014 ICH Q7 (API) Training
Trends from API inspections

Key Messages

- Inspections of API facilities, conducted by PIC/S members, have recently been reporting critical deficiencies related to laboratory controls, records/investigations, quality systems, equipment cleaning/maintenance, and process validation.

Trends and observations related to inspections

Since the implementation of Q7, most API manufacturers appear to have a better understanding of GMP principles.

Firms are doing well:

- Quality systems
- Process understanding
- Seeking opportunities for optimization
- Robust change control systems
- Good laboratory controls and procedures to facilitate knowledge management

On the other hand:
Inspections also reveal that some API manufacturers continue to struggle with achieving sustainable compliance with GMP requirements.

Trends and observations related to inspections

Data integrity issues

PIC/S members and partners have also noted an increase in findings of data-integrity practices during inspections of API sites.

These deficiencies include:

- Recording data in logbooks, falsification of batch records and test results, pretesting samples and ignoring or not investigating out-of-specification results.
- Blending or mixing API batches that failed to meet the established released specifications with batches that met the required final specifications.
- Lacking the necessary controls in handling and managing critical data, and entering manufacturing activities on records before they had occurred.

Trends and observations related to inspections

Outsourced operations and the changing face of API manufacturing

With the increase in the outsourcing of APIs by sponsors/drug applicants/finished drug product owners/contract givers (party that purchases APIs), **there is more concern about how the roles and responsibilities of each party are established and managed**.

Trends and observations related to inspections

Inspector training

During **PIC/S' API Expert Circles**, inspectors are trained on new technology, quality trends, and critical deficiencies and how to detect problems.

Potential problems:

- The quality of the APIs produced
- The impact on the finished drug products
- Subsequent affects on the patients who consume these medicines

Trends and observations related to inspections

Conclusion

A **regulator's role** is to determine whether firms are operating in sustainable compliance with GMP for APIs, pursuant to ICH Q7.

- Inspections are limited by time and other resource constraints
- Therefore, regulators rely heavily on manufacturers to implement and maintain appropriate quality systems and processes to ensure that all APIs produced meets the required quality standards

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Thank you for your time.
Questions?

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