ICH Q12: FDA Implementation

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CASSS CMC FORUM SUMMER 2021

Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.

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A quality product of any kind consistently meets the expectations of the user.

Drugs are no different.


Patients expect safe and effective medicine with every dose they take.

Pharmaceutical quality is

assuring *every* dose is safe and effective, free of contamination and defects.


It is what gives patients confidence in their *next* dose of medicine.

Q12 implementation **incentivizes robust product quality** by rewarding product and process knowledge, understanding, and quality oversight with lifecycle flexibility

Overview

- ICH Q12 status
- ICH Q12 Implementation Working Group activities
- FDA Implementation

ICH Q12 – Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

ICH Q12 Objectives

- Objectives* include:
  - …**Harmonize change management**…in a more transparent and efficient manner…across ICH regions
  - …Facilitate **risk-based regulatory oversight**…
  - Emphasize…**control strategy** as a key component of the…dossier
  - Support **continual improvement** and facilitate introduction of **innovation**
  - Enhance use of regulatory tools for **prospective change management**…enabling **strategic management of post-approval changes**…

*From the ICH Q12 concept paper

Scope

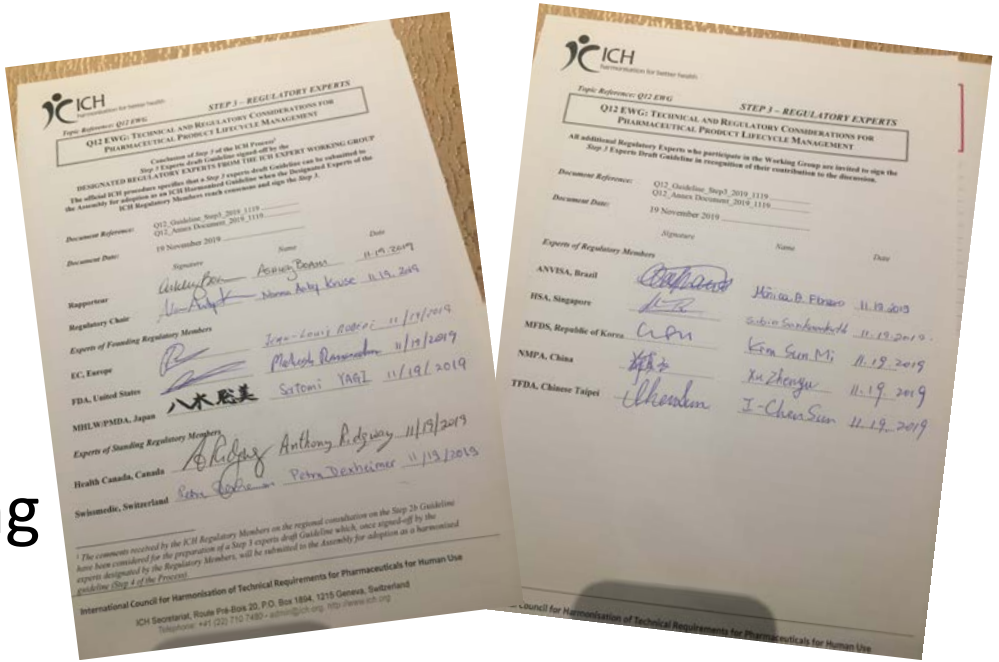
- Pharmaceutical drug substances and products (both chemical and biological) that require a marketing authorization
  - includes innovators, generics, biosimilars
- Drug-device combination products that meet the definition of a pharmaceutical or biological product
  - In the US, this includes CDER- and CBER-led drug-device and biologic-device combination products
- Does not include changes needed to comply with Pharmacopeial monographs

Tools in Q12

- Established Conditions
- Post-approval Change Management Protocols
- Product Lifecycle Management Document
- Structured Approaches for Frequent CMC Post-Approval Changes

ICH Q12 Status

- Step 4 reached in November 2019 (Singapore)
- Expert Working Group transitioned to Implementation Working Group



Implementation

- Implementation Working Group (IWG)
  - Concept paper approved in March 2020
  - IWG developing global training materials
  - ICH pilot with PIC/S to develop training materials for inspectorates
- Regions are beginning implementation
  - Regulatory Members of ICH are encouraged to provide publicly available information, preferably on their website, about the implementation of ICH Q12 in their region, especially with regard to regulatory considerations

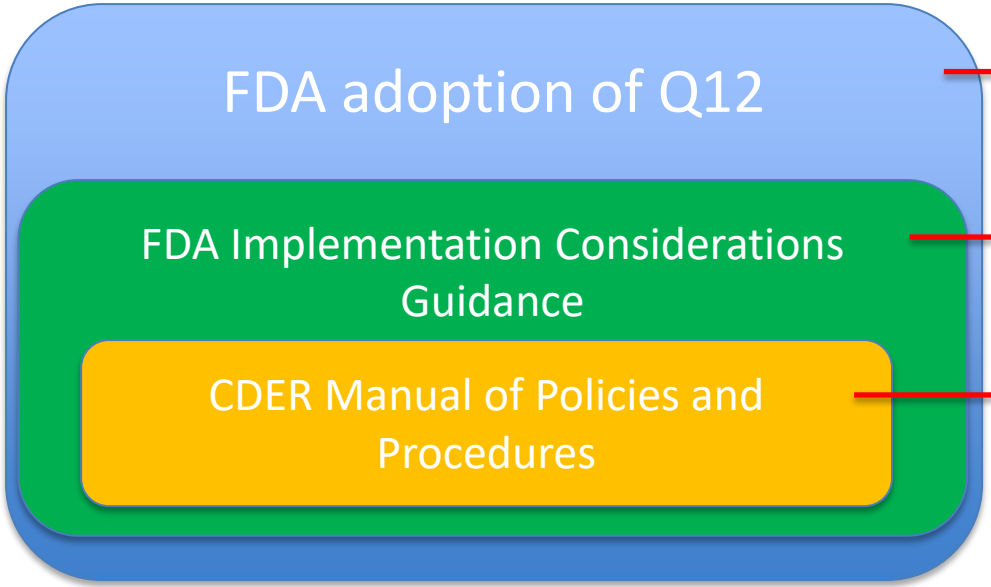
Q12 IWG

Training materials

- For ICH and non-ICH regions
- Modules addressing each section of guideline
  - Slides for 8 modules posted on ICH website in June 2021
- Case studies with additional examples and narrative text, including:

ECs for API	ECs for vaccine product	ECs for analytical method	PACMP
PQS	Drug-device combination		PLCM

ICH Q12 – FDA Implementation



Replaces FDA 2015 draft guidance: Established Conditions

How to use Q12 tools in the FDA system

More specific internal procedures

- Significant, multi-phase, training executed from 2018-present
- EC pilot informed FDA guidance and MAPP

FDA draft guidance: ICH Q12 Implementation Considerations for FDA-Regulated Products

- Clarifies how ICH Q12 tools can be implemented for CDER and CBER regulated products

- Submission of ECs
  - Clarity in the cover letter and 3.2.R on whether use of Q12 tools is proposed for the application is **critical**
  - **PLCM** should be submitted to 3.2.R and clearly identify relevant tools
  - ECs can be proposed for **entire** CMC section or a **subset** of CMC sections

FDA draft guidance: ICH Q12 Implementation Considerations for FDA-Regulated Products

- Identification and justification of ECs
  - A description of the applicant's risk assessment process, the criticality assessment conducted, and the supporting information for each should be provided
  - Scientific justification for proposed ECs and reporting categories (RC) in relevant module 3 eCTD sections
    - Elements not proposed as ECs that are normally considered ECs should be justified
    - Not necessary to justify elements that are not normally considered ECs
    - If RCs that differ from US regulation / guidance are not proposed, sponsor should provide a clear statement that RC will follow regulation / guidance

FDA draft guidance: ICH Q12 Implementation Considerations for FDA-Regulated Products

- Identification and justification of ECs
  - Drug master files
    - ECs are proposed for the application product, within the application file
    - ECs proposed in an application can leverage information in a drug master file; the sponsor refers to the specific location for the EC justification
    - Relationship between sponsor and DMF holder needs to account for EC identification and maintenance (e.g. changes to ECs and corresponding DMF updates)
  - Combination products
    - ECs for the device constituent part can be proposed considering primary characteristics and the combination product as a whole

FDA draft guidance: ICH Q12 Implementation Considerations for FDA-Regulated Products

- Maintenance:
  - In annual report, include a copy of all analytical procedures that have been modified through the PQS only (intended to be for **information only;** typically not subject to review unless there were changes to ECs)
- PLCM
  - Submit to 3.2.R in tabular format; updated PLCM with each supplement or annual report where ECs are change
  - Indicate the manufacturing sites (preferably by facility establishment identifier (FEI) number) where an EC will be implemented
- PQS
  - When introducing a new manufacturing site, the applicant should reassess the relevant ECs considering the capability of the new site's PQS
  - Justification for proposed changes to ECs as a result should be included in the application

Summary

- ICH Q12 includes tools and enablers to facilitate innovation and continual improvement
- Implementation is underway at FDA and with other regulators
- ICH Q12 IWG developing training materials to support global implementation

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