The Importance of International Harmonization

Brian Hasselbalch
Deputy Director
Office of Policy for Pharmaceutical Quality
CDER | US FDA

Pharmaceutical Quality Symposium 2021

Innovations in a Changing World – October 26-27, 2021

Overview

What are we doing to harmonize internationally?

What difference has it made?

Overview: What are we doing?

- ICH: International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

- PIC/S: Pharmaceutical Inspection Co-operation Scheme
- MRA: Mutual Recognition Agreement
- ICMRA: International Coalition of Medicines Regulatory Authorities
- WHO: World Health Organization
- Bilateral/multilateral

Overview: What are we doing?

ICH

- Q12, *Lifecycle Management*, being implemented!

- Q13, *Continuous Manufacturing*, in public consultation phase
- Q14/Q2, *Analytical Procedure Development/rev. Analytical Validation*, in development/drafting phase

- M4Q, *eCTD* revision, in 'design' phase

- Quality Discussion Group: completed recommendations

Overview: What are we doing?

PIC/S

- 54 member countries; US FDA accepted in January 2011

  PIC/S aims at harmonising inspection procedures worldwide by developing common standards in the field of GMP and by providing training opportunities to Inspectors. It also aims at facilitating co-operation and networking between competent authorities… thus increasing mutual confidence….

- "Distant assessment (inspection)"[remote evaluations]

Overview: What are we doing?

MRA

- Legal foundation: FDC Act section 809
- Implementing MRAs with EU and UK
  - Surveillance inspection reliance, including **third country**
  - Pre-approval/pre-licensing: pending further discussion
- Next?

Overview: What are we doing?

ICMRA

Is a voluntary, executive-level, strategic coordinating, advocacy and leadership entity of regulatory authorities… [36 members/associate members]

- Recent Q developments:
  - ICMRA statement in June 2021 *Global Pharmaceutical Quality Knowledge Management: Enhancing Regulatory Reliance and Agility*
  - Machine Learning / Artificial Intelligence
  - Reflections paper in development on remote evaluations in lieu of or in addition to inspections

Overview: What are we doing?

WHO

- Collaborate on technical guidelines
- Evaluate pharmacopeial monographs of interest to US market
- Share information about emerging issues; collaborate on response

Overview: What are we doing?

Bilateral/Multilateral

- EMA: collaboration on product applications for medically necessary drugs
- APEC: Joint training
- PAHO/APEC: Collaborate on guidelines
- Many: Share information about emerging issues

Summary of Arrangements

Strategic direction

- ICMRA, ICH

Standards of quality:

- ICH, WHO, National Authorities

Inspection/enforcement oversight:

- PIC/S, MRA

Poll Question…

Poll Question #1

What other areas should FDA harmonize?

A. Enforcement outcomes

B. Routine application assessments

C. Sampling/testing drugs

D. Application-specific facility inspection/evaluation

What difference has it made?

A Regulator's View on the Benefits of International Harmonization and Cooperation

Nitrosamine Response: A Regulator's View…

1. Risk identification: MRA, PIC/S
2. Policy: ICH
3. Assessment & inspection: MRA, PIC/S
4. Methods development & testing: ICH, MRA
5. Risk mitigation: ICH, MRA, PIC/S, WHO, Industry

Challenge Question #1

What statute authorizes FDA to engage in a Mutual Recognition Agreement about inspections:

A. None; matter solely at FDA discretion

B. Section 809 of the PHS Act

C. Section 809 of the FDC Act

D. 21 CFR 211, CGMP Regulations for Finished Pharmaceuticals

Challenge Question #2

Which of the following statements is NOT true?

A. As a member, FDA is legally obligated to enforce PIC/S CGMP guidelines

B. ICH and ICMRA provide strategic input over pharmaceutical programs and policies

C. MRAs allow FDA to share inspection-related information with partnering national regulatory authorities.

D. PIC/S fosters harmonization of inspection conduct while ICH collaborations result in policies directly impacting industry and regulators.

Summary

- FDA is involved in many different types of arrangements with international counterparts
- Some are by/among regulators; others include industry
- All help FDA maintain an effective regulatory system that protects patients

Questions?

Brian Hasselbalch
Office of Policy for Pharmaceutical Quality

CDER | US FDA