Opportunities for International Engagement:
Regulatory Cooperation, Convergence and Harmonization

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Presentation Overview

- FDA's engagement in global activities and current approach
- Review several key international harmonization and regulatory convergence initiatives, scope, goals and activities
- Learn what opportunities are available to regulators and industry across the globe

FDA's International Activities

- **Domestic/Internal US**: Intra-Center; Intra-Agency; USG Intergovernmental
- **International:** Bilateral Engagements
- **Multilateral Engagements**
  - Most efficient model - spares resources
  - Reduces duplication of efforts
  - Promotes global public health
  - Diversity- encourage international regulatory collaboration efforts across both developed and developing regulatory authorities
  - Promote implementation of internationally-developed guidelines and standards to reduce the burden of regulation

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

www.ich.org

ICH Overview

- **Regulators and industry:** international harmonization of technical guidelines to enhance public health
- Launched in 1990 by US, EU, & Japan. Has expanded global participation and engagement through recent reforms
- Well-defined objectives:
  - **To improve efficiency of new drug development and registration processes**
  - **To promote public health, prevent duplication of clinical trials in humans and minimize the use of animal testing without compromising safety and effectiveness**

HOW=> Developing harmonized, technical guidelines and standards that are implemented by regulatory authorities.

Major ICH Topic Areas

Safety

- Carcinogenicity studies
- Genotoxicity studies
- Toxicokinetics and Pharmacokinetics
- Duration of chronic toxicity testing
- Reproductive toxicology
- Safety pharmacology studies
- Immunotoxicology studies
- Nonclinical evaluation for anticancer pharmaceuticals
- Photosafety evaluation
- Nonclinical pediatric safety

Efficacy

- Clinical safety
- Clinical study reports
- Dose-response studies
- Good clinical practice
- Clinical trials
- Clinical evaluation by therapeutic category
- Clinical evaluation
- Pharmacogenomics

Quality

- Stability
- Analytical validation
- Impurities
- Pharmacopoeias
- Specifications
- Good manufacturing practice
- Pharmaceutical development
- Quality risk management
- Pharmaceutical quality system
- Development and manufacture of drug substances

Multidisciplinary

- MedDRA terminology
- Electronic standards
- Nonclinical safety studies
- CTD and eCTD
- Bioanalytical Method Validation
- Biopharmaceutics Classification System-based Biowaivers
- Data elements and standards for drug dictionaries
- Gene therapy
- Mutagenic impurities
- Drug Interaction Studies
- Bioequivalence for IR solid

ICH Members

Founding Regulatory Members

- EC, Europe
- FDA, US
- MHLW/PMDA, Japan

Founding Industry Members

- EFPIA
- PhRMA
- JPMA

Standing Regulatory Members

- Health Canada, Canada
- Swissmedic, Switzerland

Regulatory Members

- ANVISA, Brazil
- COFEPRIS, Mexico
- HSA, Singapore
- MFDS, Republic of Korea
- MHRA, UK
- NMPA, China
- SFDA, Saudi Arabia
- TFDA, Chinese Taipei
- TITCK, Turkey

Industry Members

- BIO
- Global Self-Care Federation
- IGBA

ICH Observers

Standing Observers

- IFPMA
- WHO

Regional Harmonization Initiatives

- APEC
- ASEAN
- EAC
- GHC
- PANDRH
- SADC

Legislative or Administrative Authorities

- AEC, Azerbaijan
- ANMAT, Argentina
- ANPP, Algeria
- CDSCO, India
- CECMED, Cuba
- CPED, Israel
- EDA, Egypt
- Indonesian FDA, Indonesia
- INVIMA, Colombia
- JFDA, Jordan

Int'l Pharmaceutical Industry Organizations

- APIC

Int'l Orgs regulated by or affected by ICH guidelines

- Bill & Melinda Gates Foundation
- CIOMS
- EDQM
- IPEC
- PIC/S
- USP

ICH Training

Guideline Training: ICH is working to ensure that high quality training is available based upon scientific and regulatory principles outlined in its guidelines.

Efforts include:

- Development of a Training Library on the ICH website
- Funding support for training programs organized by ICH regulatory members and observers.
- ICH Recognized Training Programs
- Online training materials development including some translations.

IPRP

International Pharmaceutical Regulators Programme

www.iprp.global

IPRP

- Safe Harbor forum for global **regulators** to exchange information on issues of mutual interest and enable regulatory cooperation
- IPRP was established as a result of a consolidation of the International Pharmaceutical Regulators Forum (IPRF) and the International Generic Drug Regulators Programme (IGDRP) in 2013
- Meets biannually on borders of ICH meetings & interim tcons
- Recent Topics Discussed:
  - Regulatory Reliance
  - E-labelling for pharmaceuticals
  - ICH GL Implementation issues
  - Environmental Risk Assessments

IPRP Membership

- ANMAT, Argentina
- ANVISA, Brazil
- APEC
- ASEAN
- CECMED, Cuba
- COFEPRIS, Mexico
- CPED, Israel
- EAC
- EC/EMA, Europe
- FDA, United States
- GHC
- Health Canada, Canada
- HSA, Singapore
- Indonesian FDA, Indonesia
- INVIMA, Colombia
- Medsafe, New Zealand
- MFDS, Republic of Korea
- MHLW/PMDA, Japan
- MHRA, UK
- National Center, Kazakhstan
- NPRA, Malaysia
- NRA, Iran
- PAHO/PANDRH
- Roszdravnadzor, Russia
- SADC
- SAHPRA, South Africa
- SFDA, Saudi Arabia
- Swissmedic, Switzerland
- TFDA, Chinese Taipei
- TGA, Australia
- TITCK, Turkey
- EDQM (Observer)
- WHO (Observer)

IPRP Work Groups

- Bioequivalence for Generics
- Biosimilars
- Cell Therapy
- Gene Therapy
- Identification of Medicinal Products
- Nanomedicines
- Pharmacovigilance
- Quality

International Coalition of Medicines Regulatory Authorities

www.icmra.info

ICMRA

- Heads of Agency (HoA) leadership initiative
- Address current and emerging human medicine regulatory and safety challenges globally, strategically and in an ongoing, transparent, authoritative and institutional manner
- COVID-19 Focus: supporting strategic coordination and international cooperation among global medicine regulatory authorities:
  - to expedite and streamline the development, authorization and availability of COVID-19 treatments and vaccines worldwide
  - Increasing efficiency and effectiveness of regulatory processes and decision-making

ICMRA Members

- Australia: TGA)
- Brazil: (ANVISA)
- Canada: (HPFB-HC)
- China: (NMPA)
- European Union: (DG SANTE)
- European Union: (EMA)
- France: (ANSM)
- Germany: (PEI)
- Mexico: (COFEPRIS)
- India: (MoHFW)
- Ireland: (HPRA)
- Italy: (AIFA)
- Japan: (MHLW)
- Japan: (PMDA)
- Republic of Korea: (MFDS)
- The Netherlands: (CBG-MEB)
- New Zealand: (Medsafe)
- Nigeria: (NAFDAC)
- Singapore: (HSA)
- South Africa: (SAHPRA)
- Sweden: (MPA)
- Switzerland: Swissmedic
- UK: (MHRA)
- US: (FDA)

ICMRA Associate Members

- Argentina: ANMAT)
- Austria: (AGES)
- Colombia: (INVIMA)
- Cuba: (CECMED)
- Denmark: (DKMA)
- Ghana: Food and Drugs Authority
- Israel: (MOH)
- Poland: (URPL)
- Portugal: (INFARMED)
- Russia: (Roszdravnadzor)
- Saudi Arabia: (SFDA)
- Spain: (AEMPS)
- Ukraine: The State Expert Centre of the Ministry of Health of the Ukraine
- World Health Organization (WHO)

Current ICMRA Initiatives

- Communication
- Crisis Management
- Innovation
- Pharmacovigilance
  - Big Data
  - Increasing Adverse Event Reporting
  - Vaccines
- Supply Chain Integrity
- Antimicrobial Resistance (AMR)
- Reliance
- Pharmaceutical Quality Knowledge Management System (PQKMS)

Asia-Pacific Economic Cooperation

WWW.APEC.ORG

Regulatory Harmonization Steering Committee

Life Sciences Innovation Forum

APEC Member Economies

Australia
Brunei Darussalam
Canada
Chile
China
Hong Kong
Indonesia
Japan
Korea
Malaysia
Mexico
New Zealand
Papua New Guinea
Russia
Peru
Chinese Taipei
Philippines
United States
Singapore
Thailand
Vietnam

Regulatory Harmonization Steering Committee (RHSC)

- **Mission**: facilitate regulatory cooperation among medical product regulatory authorities, build human capacity in regulatory science among medical product regulatory staff, and promote political will for convergence among regulatory policymakers in APEC
- **Scope**: Pharmaceutical Products & Medical Devices
- **Members**:
  - -Regulators from APEC Economies
  - -Industry coalitions: Research-based Pharmaceuticals
    Medical Devices
    Generic Pharmaceutical
    Biotechnological Products
    Advanced Therapies
  - -CoE Coalition of Training Partners

Focused Workstreams:
Priority Work Areas (PWAs)
(Champion Regulatory Authorities)

- Multi Regional Clinical Trails and Good Clinical Practices Inspections (Japan, Thailand)
- Pharmacovigilance (Korea)
- Biotherapeutics (US)
- Advanced Therapies (Singapore, US,)
- Good Registration Management (Chinese Taipei, Japan)
- Medical Devices (Japan, Korea, US)
- Global Supply Chain Integrity (US)

Current APEC Regulatory Training Centers of Excellence (CoEs)

- **Peking University** (MRCT/GCP and Pharmacovigilance)
- **Sichuan University** (Medical Devices)
- **PMDA** (Pharmacovigilance and Medical Devices)
- **PMDA w/NCC** (MRCT/GCP)
- **Kobe University** (Biotherapeutic Products)
- **KIDS, Korea** (Pharmacovigilance)
- **NIDS, Korea** (Medical Devices)
- **KoNECT, Korea** (MRCT/GCP)
- **Taylor's University, Malaysia** (Supply Chain)
- **Duke-NUS Singapore** (MRCT/GCP, Advanced Therapies, Biotherapeutics, Devices)
- **Thai FDA** (GRM)
- **TFDA** (Medical Devices)
- **TFDA with RAPS Taiwan Chapter** (GRM)
- **Northeastern University** (Biotherapeutics, Advanced Therapies, Medical Devices)
- **University of Tennessee HSC** (Supply Chain)
- **USP** (Supply Chain and Advanced Therapy Products)
- **MRCT Center of Brigham and Women's Hospital and Harvard** (MRCT/GCP)
- **University of Southern California** (Medical Devices)
- **Soonchunhyang University, Korea** (Medical Devices)

The Pharmaceutical Inspection Co-operation Scheme

www.picscheme.org

PIC/S

- The Pharmaceutical Inspection Co-operation Scheme (PIC/S): non-binding, informal cooperative arrangement between Regulatory Authorities in GMPs of human or vet medicinal products
- Open to any Authority having a comparable GMP inspection system.
- Goal: **harmonizing inspection procedures** worldwide by developing common GMP standards and training
- Facilitates **cooperation and networking** between competent authorities, regional and international organizations

PIC/S Participating Authorities

-Argentina
-Austria
-Brazil
-Chinese Taipei
-Cyprus
-Czech Rep (vet)
-Estonia
-France
-Greece
-Iceland
-Iran
-Israel
-Italy (vet)
-Australia
-Belgium
-Canada
-Croatia
-Czech Republic
-Denmark
-Finland
-Germany
-Hong Kong
-Indonesia
-Ireland
-Italy
-Korea
-Israel
-Japan (MHLW/PMDA)
-Latvia
-Lithuania
-Malta
-Netherlands
-Norway
-Portugal
-Singapore
-Slovenia
-Spain
-Thailand
-Ukraine
-Italy
-US
-Lichtenstein
-Malaysia
-Mexico
-New Zealand
-Poland
-Romania
-Slovak Republic
-South Africa
-Sweden
-Turkey
-UK

PIC/S Activities

- Expert Circles
  - API
  - Good Distribution Practices
  - Human Blood, Tissues, Cells & ATMPs
  - Quality Risk Management
  - Control of Cross-Contamination in Shared Facilities
  - Working group on Good Clinical and Good Pharmaceutical Practices
  - Working Group on Computerized Systems
  - Veterinary Medicinal Products
- PIC/S Inspectorates' Academy (PIA): web-based educational center aimed at harmonizing and standardizing GMP training at an international level

International Medical Device Regulators Forum (IMDRF)

www.imdrf.org

IMDRF Overview

- Launched 2012 as successor to the Global Harmonization Task Force (GHTF)
- Chair and secretariat rotate on annual basis, beginning with Australia (2012), EU (2013), US (2014), Japan (2015), Brazil (2016), Canada (2017), China (2018), Russia (2019), Singapore (2020), S. Korea (2021), Australia (2022)
- Decisions are made by consensus, not voting
- 2 in person meetings per year (March and September)
  - **Includes public stakeholder session which provides updates from MC members, IMDRF working groups, RHIs, industry associations, etc.**

World Health Organization

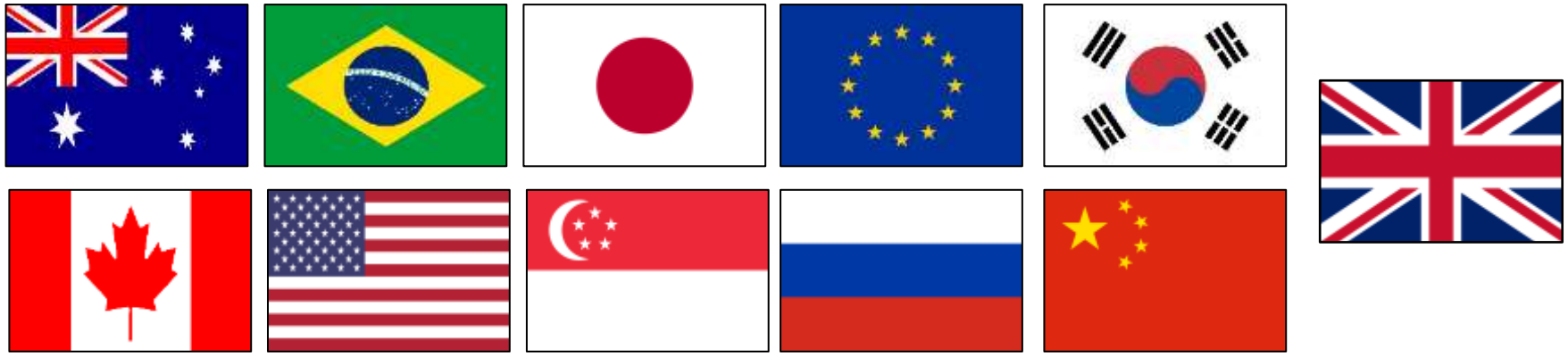
Official Observers

APEC
Asia-Pacific Economic Cooperation

Global Harmonization Working Party
GHWP Towards Medical Device Harmonization

Pan American Health Organization

Regional Harmonization Initiatives



Management Committee (MC) Members

IMDRF
International Medical Device Regulators Forum

IMDRF Mission and Goals

Mission

To strategically accelerate international medical device regulatory convergence to promote an efficient and effective regulatory model for medical devices that is responsive to emerging challenges in the sector while protecting and maximizing public health and safety.

Goals

- Accelerate international medical device regulatory harmonization and convergence building on the work of the Global Harmonization Task Force.
- Address common public health regulatory challenges to convergence due to the globalization of medical device production and the emergence of new technologies.
- Accelerate innovation by clear and practical regulatory expectations.
- Focus on premarket and postmarket requirements.

Current IMDRF Working Groups

IMDRF

International Medical Device Regulators Forum

1. Good Regulatory Review Practices (GRRP) (Chairs: US and Singapore)
2. Regulated Product Submission (RPS) (Chairs: US and Canada)
3. Cybersecurity (Chairs: US and Canada)
4. Personalized Medical Devices (Chair: Australia)
5. Artificial Intelligence (Chair: S. Korea)
6. Adverse Event Terminology (Chair: Japan)
7. IVD Clinical Evaluation (Chair: Russia)
8. Software as a Medical Device* (Chairs: US and Canada)

* WG approved in April 2022

Summary

- International regulatory cooperation has become an essential part of dealing effectively with the challenges of an increasingly complex and global environment
- Engaging in regulatory convergence and harmonization efforts can improve efficiencies of the medical product development process
- Working multilaterally has many benefits including sparing of resources, avoiding duplication of efforts and reaching more stakeholders in efforts to improve global public health

Thank you

www.fda.gov