ICH Reform and Future Direction: US FDA Perspective

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Why Regulatory Harmonization Matters
(to Industry as well as Regulators)

- Evolution to globally based operations and global markets
- Need to meet regulatory requirements for each nation and region for planned marketing
- Specific requirements developed within each jurisdiction often differ--
  - Leading to potentially extensive duplication of effort that
  - Contributing to increased costs and delays in getting new drugs to patients
- Industry sponsors often best positioned to identify key areas of disharmony leading to duplicative effort

ICH (*International Council on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use*)

- Unique harmonization project involving the regulators and research-based industries
- Begun in 1990 involving US, EU and JP
- 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**
- Accomplish through the development and implementation of harmonized Guidelines and standards

5-Step Process for Guideline Development

5 ***Step 5:*** **Implementation** by ICH Regulatory Members

4 ***Step 4:*** Regulatory Members of the final document. Assembly **adopt** the final document

3 **Step 3:** Public consultation by ICH Regulatory Members and ICH Secretariat. All **comments** are considered by the EWG. **Finalized once concensus is reached** in EWG.

2 ***Step 2*** **a)**Assembly invited to **endorse** technical document. **b)** ICH Regulatory Members invited to endorse the **draft** Guideline.

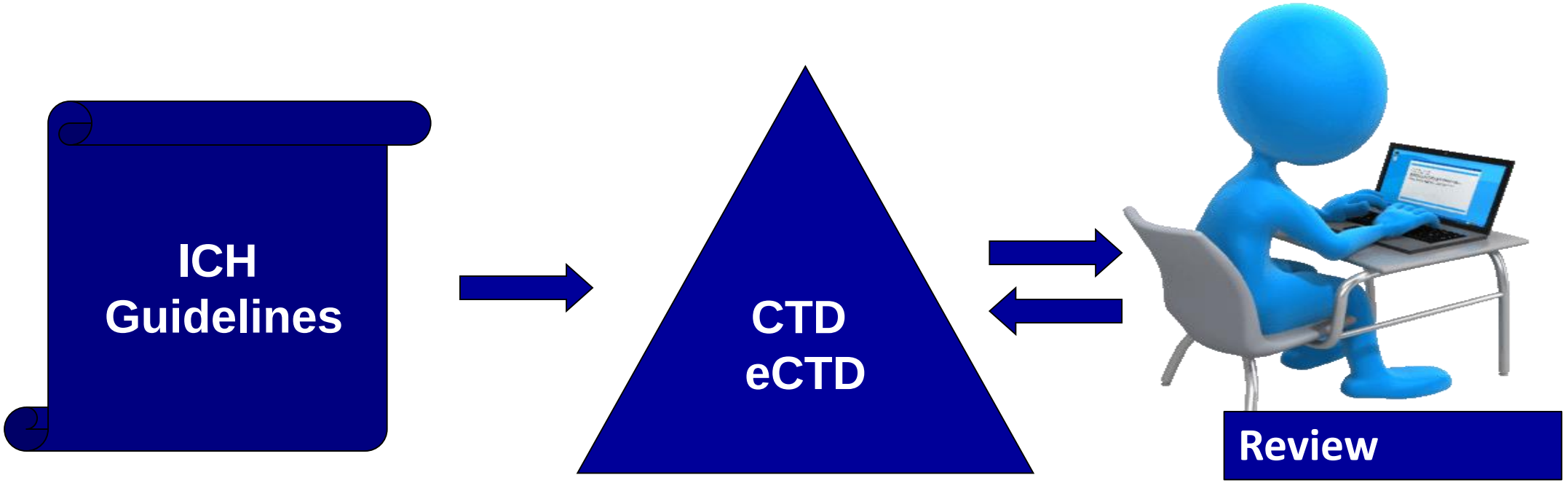
1 ***Step 1:*** Expert Work Group (EWG) works to prepare a **consensus draft** of the technical document.

Keys to ICH Success

- Involves expertise from both regulatory agencies and regulated industry
- Science-based, consensus driven
- Clear and effectively managed process
- Close collaboration of parties with comparable regulatory and technical capability
- Commitment of regulators to implement products of harmonization
- Common global platform and tools
- Robust processes and governance

Example of ICH Success

CTD/eCTD (Common Technical Document)



CTD brings together all Quality, Safety and Efficacy information in a common, harmonized format, accepted by regulators in all ICH regions.

It has revolutionized regulatory review processes for regulators and industry.

Sampling of Major Topic Areas Addressed by ICH Guidelines

Safety

- Carcinogenicity studies
- Genotoxicity studies
- Toxicokinetics and Pharmacokinetics
- Toxicity testing
- Reproductive toxicology
- Biotechnology products
- Pharmacology studies
- Immunotoxicology studies
- Nonclinical evaluation for anticancer pharmaceuticals
- Photosafety evaluation

Efficacy

- Clinical safety
- Clinical study reports
- Dose-response studies
- Ethnic factors
- Good clinical practice
- Clinical trials
- Clinical evaluation by therapeutic cat.
- Clinical evaluation
- Pharmacogenomics
- Multi-regional clinical trials

Quality

- Stability
- Analytical validation
- Impurities
- Pharmacopoeias
- Quality of biotechnology products
- 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
- Data elements and standards for drug dictionaries
- Gene therapy
- Genotoxic impurities

Scope now expanded beyond developed regions and beyond new drugs

- ICH Guidelines can benefit all drug regulatory entities and jurisdictions located in both **developing** and **developed** regions
- International generic drug industry perspective:
  - All but one of the ICH Guidelines are relevant to the regulatory requirements for their industry
  - ICH is currently developing 3 guidelines that are of particular interest for the generic industry:
    - M9 Biopharmaceutics Classification System-based Biowaivers
    - M10 Bioanalytical Method Validation
    - Q12 Lifecycle Management

ICH Reform - Establishment of Non-Profit Association

Major Goals

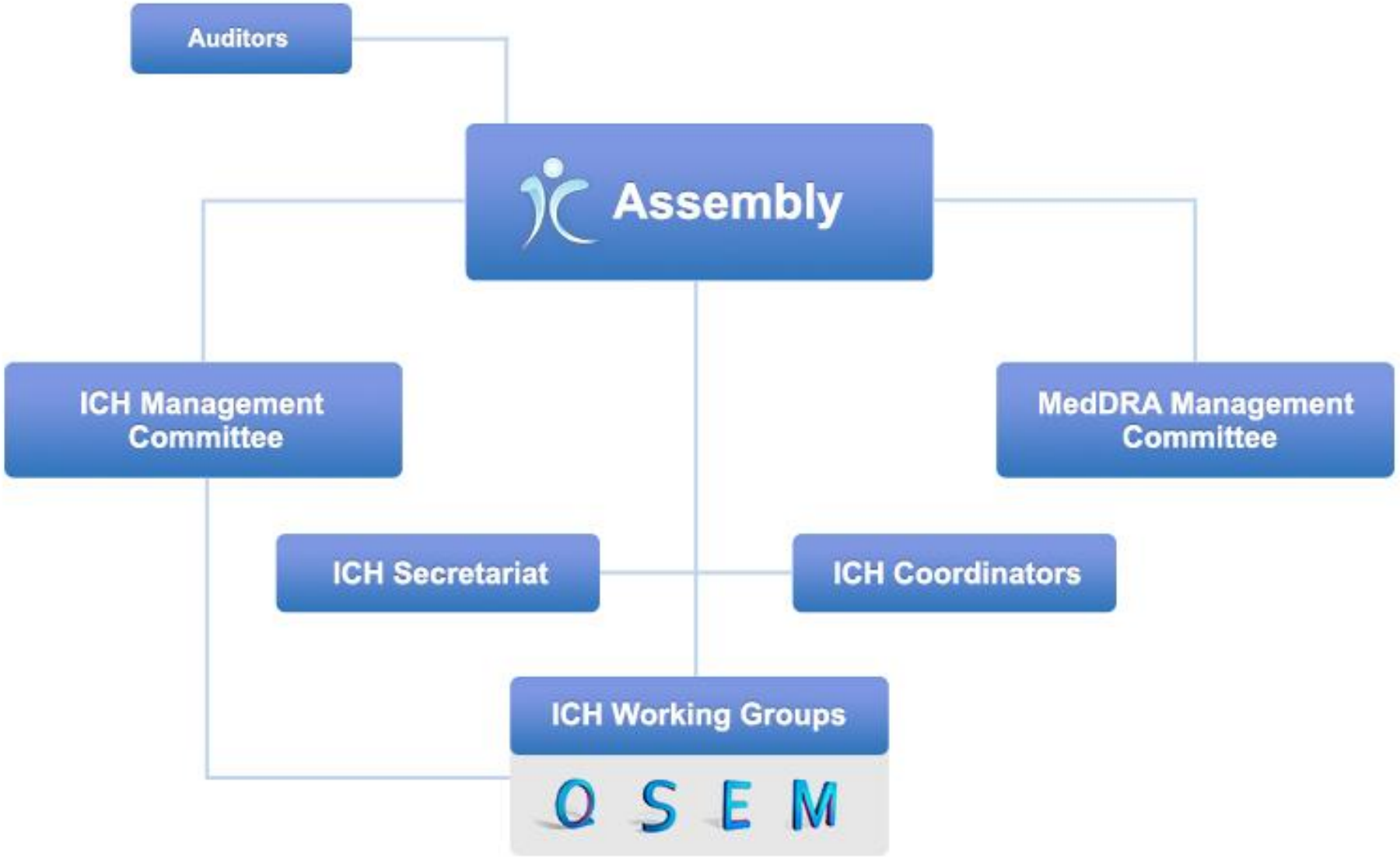
- More involvement from regulators around the world and wider inclusion of global industry sectors affected by ICH harmonization
- Focus global pharmaceutical regulatory harmonization work in one venue

Actions

- The new ICH Association was officially established on October 23, 2015.
- The new ICH Association is a non-profit legal entity under Swiss Law with the aim to focus global pharmaceutical regulatory harmonization work in one venue

ICH Articles of Association:
http://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Organisational_changes/ICH_Articles_of_Association_Adopted_by_Founding_ICH_Members_October_23_2015_for_publication.pdf

ICH Governance



ICH Members

- All ICH Members have a voice and a vote in the Assembly on decisions related to:
  - Selection of new topics for harmonization (an annual process)
  - Approval of the annual and multi-annual strategic plan
  - Adoption, amendment, or withdrawal of ICH Guidelines
  - Approval or rejection of membership/observer admission
- ICH Members may also:
  - Nominate new topics for harmonization
  - Appoint experts to ICH EWGs in accordance with the Assembly Rules of Procedure

1 See ICH Articles of Association for more details at www.ich.org

ICH Members and Observers*

ICH Members	ICH Observers	
EC, Europe	IFPMA	GHC
FDA, US	WHO	PANDRH
MHLW/PMDA, Japan	CDSCO, India	SADC
EFPIA	CECMED, Cuba	APIC
JPMA	COFEPRIS, Mexico	BMGF
PhRMA	INVIMA, Columbia	CIOMS
Health Canada, Canada	MCC, South Africa	EDQM
Swissmedic, Switzerland	National Center, Kazakhstan	IPEC
ANVISA, Brazil	Roszdravnadzor, Russia	PIC/S
CFDA, China	TGA, Australia	USP
HSA, Singapore	APEC	TITCK, Turkey
MFDA, Republic of Korea	ASEAN	NPRA, Malaysia
TFDA, Chinese Taipei	EAC	
BIO		
IGBA		
WSMI		

*As of June 2018

Current Direction: "Strategic Portfolio" Approach

- Features of Approach:
  - Shift from mostly individual "one-off" topic proposals and planning to one that is more organized by theme
  - Develop **reflection paper(s)** *(aka white paper)* to further describe major revisions or development of guidelines in a specified area, where identified types of expertise are needed, and work would occur through a logical planned sequence of work packages (corresponding to discrete guideline work) over multiple years
  - Reflection paper(s) would undergo review and discussion and if favorably received, would then be integrated as a stream of work in the ICH multi-year future work plan
  - Per that plan, each discrete work package would later be further developed into a more specific topic proposal, concept paper, etc.

- This approach might eventually account for majority of topic work under way. Papers developed and endorsed to date: ●*GCP Renovation Paper* ●*Quality Reflection Paper*

FDA Reflection Paper *under development*

- Reflection Paper outlining a strategic approach for developing and enhancing ICH guidelines to support the harmonization of scientific and technical standards for **generic drugs**
- Proposed work would be targeted at scientific and technical standards for generic drugs—not harmonization of differing legal and regulatory requirements
- Harmonization of scientific and technical standards for generic drugs could improve public health:
  - May allow manufacturers to use the data submitted in support of a generic drug marketing application to meet other regions' regulatory requirements for approval
  - May increase size of markets and attract more competition from manufacturers, lower costs by increasing the number of market entrants, and expand patient access
- Areas for potential consideration:
  - Series of ICH guidelines on bioequivalence standards for simple dosage forms
  - Series of ICH guidelines on bioequivalence standards for complex dosage forms
  - Survey existing ICH Guidelines for updating as needed to incorporate recommendations for generic drugs

Thank you