Enabling Pharmaceutical Quality Management Through International Harmonization of Standards

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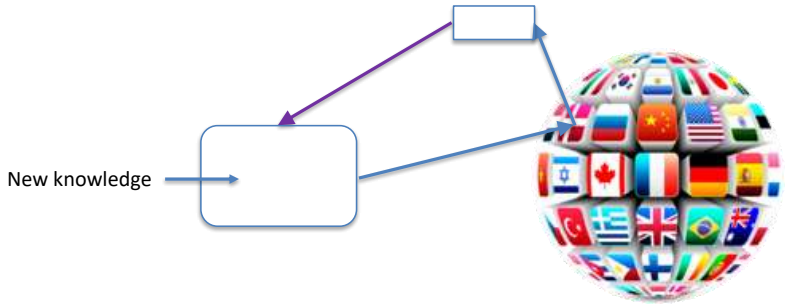
Effective Pharmaceutical Quality Management

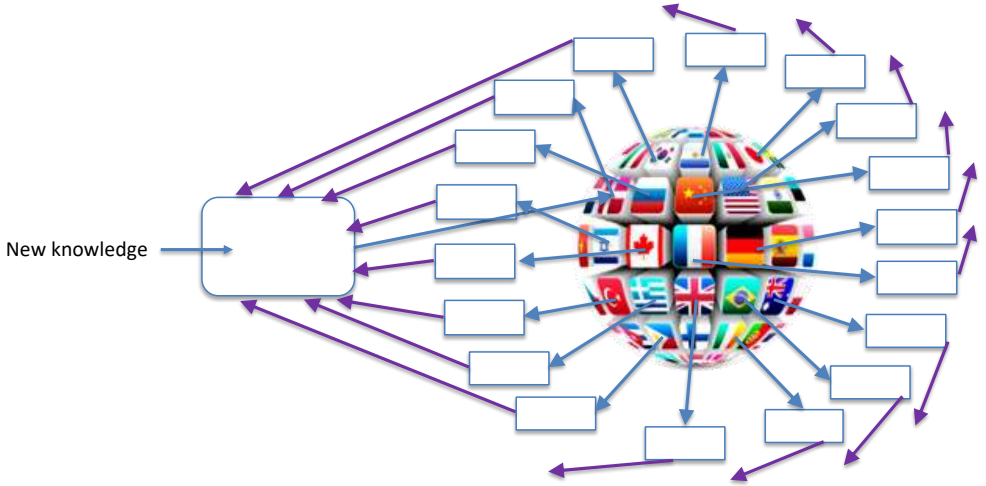
- Necessary to ensure against quality failures, supply disruptions, drug shortages
- Typically requires post approval changes (PACs) to regulatory filings
    - Facilities age, routine operations require updates to maintain cGMP compliance and state of control, regulatory requirements change, technology evolves, suppliers change, findings from regulatory agencies during inspections may require changes, and the company generates new knowledge about products and processes.

- Regulators want to encourage effective pharmaceutical quality management and enable firms to update and innovate
    - Apply knowledge gained during commercial operations to continually improve process and product

Regulatory complexity: Many PACs require separate prior approval by the regulatory authority where the product is marketed



"PAC visibility"
for a
Regulatory Agency



"PAC visibility"
for a
Pharma Company

Greater regulatory reliance could help reduce this sort of complexity

Some key enablers of reliance:

- ✓ Sufficient compatibility of regional laws and regulations to allow for **harmonization of regulatory requirements**
- ✓ Comparability of **basis for making regulatory assessments** and other aspects of other regulator's work product
- ✓ Regulatory **"work products"** (e.g., decisions and supporting assessments) **are readily accessible and understandable** by the other regulators
- ✓ **Regulators are reviewing same product quality dossier**, facilities, PAC-related submissions, etc.

ICH

- The **International Council for Harmonisation of Technical Requirements of Pharmaceuticals for Human Use (ICH)** is a unique harmonization organisation involving regulators *and* the pharmaceutical industry.
- Launched in 1990 by the US, EU, and Japan.
- 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
- Accomplished through **development of harmonized, technical guidelines and standards that are implemented by regulatory members.**

ICH Now Has 21 Members and 36 Observers

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
EDA, Egypt
HSA, Singapore
MFDS, Republic of Korea
NMPA, China
SFDA, Saudi Arabia
TFDA, Chinese Taipei
TITCK, Turkey

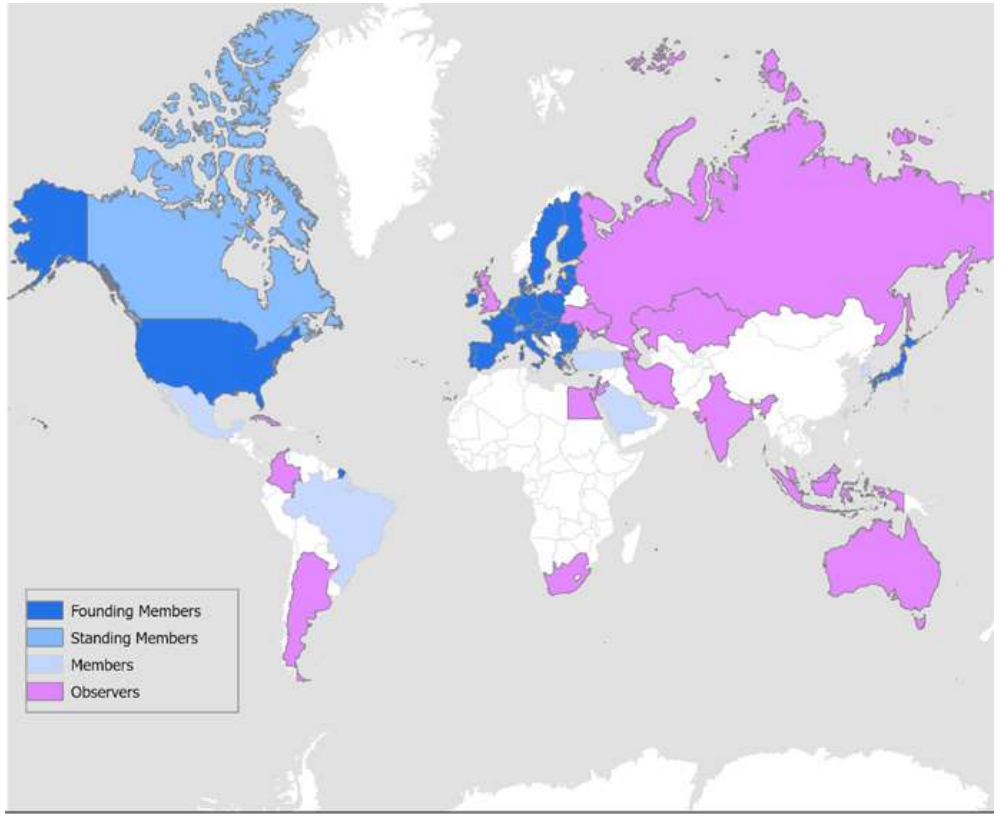
Industry Members
BIO
Global Self-Care Federation
IGBA

Observers

Standing Observers
IFPMA
WHO

Legislative or Administrative Authorities
AEC, Azerbaijan
ANMAT, Argentina
CDSCO, India
CECMED, Cuba
CPED, Israel
Indonesian FDA, Indonesia
INVIMA, Colombia
JFDA, Jordan
MHRA, UK
MMDA, Moldova
MOPH, Lebanon
NAFDAC, Nigeria
National Center, Kazakhstan
NPRA, Malaysia
NRA, Iran
Roszdravnadzor, Russia
SAHPRA, South Africa
SCDMTE, Armenia
SECMOH, Ukraine
TGA, Australia

Regional Harmonization Initiatives
APEC
ASEAN
EAC



Created on 29 April 2022 by FDA/OEM/GIS | Sources: FDA, Natural Earth, ESRI

ICH Products

As of November 2022

- 72 Guidelines on technical requirements on:
- Safety – 16 Guidelines
- Quality - 25 Guidelines
- Efficacy – 22 Guidelines
- Multidisciplinary - 9 Guidelines

- Electronic Standards for the Transfer of Regulatory Information (ESTRI)
- CTD/eCTD
- MedDRA (standardised medical terminology)

https://www.ich.org/page/ich-guidelines

The ICH Guideline Work Process Involves 5 Steps

ICH Guideline is published -& Regulators seek public comment in every region

TRAINING on the new ICH Guideline for both Regulators and Industry

https://www.ich.org/page/formal-ich-procedure

ICH Quality Guidelines

ICH Quality Guidelines -- include focus on pivotal milestones such as the conduct of stability studies, defining relevant thresholds for impurities testing and a more flexible approach to management of pharmaceutical quality, product life cycle, continuous manufacturing and other topics.

- Stability (Q1)
- Analytical Validation (Q2)
- Impurities (Q3)
- Specifications (Q6)
- Good Manufacturing Practice for APIs (Q7)
- Pharmaceutical Development (Q8)
- Quality Risk Management (Q9)
- Pharmaceutical Quality System (Q10)
- Lifecycle Management (Q12)
- Continuous Manufacturing of Drug Substances and Drug Products (Q13)

ICH Q10 Annex 1:
Opportunities to Enhance Science & Risk-Based Approaches

Scenario	Potential Opportunity
1. Comply with GMPs	Compliance – status quo
2. **Demonstrate effective pharmaceutical quality system,** including effective use of quality risk management principles (e.g., ICH Q9 and ICH Q10).	Opportunity to: • **increase use of risk based approaches for regulatory inspections.**
3. **Demonstrate product and process understanding**, including effective use of quality risk management principles (e.g., ICH Q8 and ICH Q9).	Opportunity to: • facilitate science based pharmaceutical quality assessment; • enable innovative approaches to process validation; • establish real-time release mechanisms.
4. **Demonstrate effective pharmaceutical quality system and product and process understanding,** including the use of quality risk management principles (e.g., ICH Q8, ICH Q9 and ICH Q10).	Opportunity to: • increase use of risk based approaches for regulatory inspections; • facilitate science based pharmaceutical quality assessment; • optimise science and risk based post-approval change processes to maximise benefits from innovation and continual improvement; • enable innovative approaches to process validation; • establish real-time release mechanisms.

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

- Provides framework to facilitate the management of post-approval changes in a more predictable, efficient manner.
- How increased product and process knowledge can help reduce the number of regulatory submissions, using these tools and enablers:

1. Categorization of Post-Approval CMC Changes
2. **Established Conditions (ECs)**
3. **Post-Approval Change Management Protocol (PACMP)**
4. **Product Lifecycle Management (PLCM)**
5. Pharmaceutical Quality System (PQS) and Change Management
6. Relationship Between Regulatory Assessment and Inspection
7. Post-Approval Changes for Marketed Products

Summary

- Effective pharmaceutical quality management requires a life-cycle approach that includes Post Approval Changes (PACs) to regulatory filings
- Many PACs require separate prior approval by each regulatory authority where the product is marketed => regulatory complexity and operational challenges
- ICH works to harmonize technical requirements for quality management and regulatory submission formats – produces ICH Q and M Guidelines
  - ICH harmonization work is undertaken by regulatory and industry experts can take several years of intensive work to produce a consensus guideline.
  - Resulting guidelines enable regulatory consistency and efficiency and reduce the regulatory uncertainty and risk for manufacturers in managing quality.
- Effective management of quality helps ensure the availability of critical medicines for the patients who need them--globally

Thank you!