ICH – Its History, Evolution, Achievements and Challenges

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Focus of Discussion

• Background information
  – History of ICH
  – Process of ICH

• Modification of the ICH process
  – Expansion of participants
  – Outreach to other countries and regions
  – Transparency of process

• Continuum of accomplishments
ICH

INTERNATIONAL CONFERENCE ON HARMONIZATION

of

Technical Requirements for the Registration of Pharmaceuticals for Human Use
A Unique Approach

• ICH was created in 1990
• Agreement between the European Union, Japan and the United States to harmonize technical requirements for registration of pharmaceuticals for human use (EFTA, Canada, WHO)
• Joint effort by regulators and their associated trade associations
  – In May 1996 included generic industry experts in Quality Expert Working Groups (EWG) and OTC industry experts included in Quality and appropriate Efficacy topics
Expert Working Groups

- Safety
- Efficacy
- Quality
- Multidisciplinary

STEERING COMMITTEE
Monitors and Facilitates EWGs
Steps of ICH Harmonization

STEP 1 -- Building Scientific Consensus

STEP 2 -- Agreeing on Draft Text

STEP 3 -- Consulting Regional Regulatory Agencies

STEP 4 -- Adopting Harmonized Guidelines

STEP 5 -- Implementing Guidelines in ICH Regions
Process of Harmonisation

ICH harmonisation activities fall into 4 categories: Formal ICH Procedure, Q&A Procedure, Revision Procedure and Maintenance Procedure, depending on the activity to be undertaken (see below).

- New topic for harmonisation of ICH?
- Clarification needed for an existing ICH Guideline?
- Content of an existing ICH Guideline out of date or no longer valid?
- New information to be added to an existing ICH Guideline?
- Change to be made to either Q2C Guideline or M2 Recommendations?

- Formal ICH Procedure
- Q&A Procedure
- Revision Procedure
- Maintenance Procedure

- Concept Paper & Business Plan required
- Concept Paper required (Business Plan may be required in certain cases)
- Concept Paper required
- Proposal/Concept Paper required for Q3C maintenance. No Concept Paper required for M2 Recommendations maintenance

Each harmonisation activity is initiated by a Concept Paper which is a short summary of the proposal. Depending on the category of harmonisation activity a Business Plan may also be required. The Business Plan outlines the costs and benefits of harmonising the topic proposed by the Concept Paper.

Only when the ICH Steering Committee endorses a Concept Paper, and where appropriate a Business Plan, can the harmonisation activity be initiated.
Examples of ICH Guidelines

ICH: harmonisation for better health

Quality Guidelines

Harmonisation achievements in the Quality area include pivotal milestones such as the conduct of stability studies, defining relevant thresholds for impurities testing and a more flexible approach to pharmaceutical quality based on Good Manufacturing Practice (GMP) risk management.

Zip with all ICH Quality Guidelines in word format.

- Q1A - Q1F Stability
- Q2 Analytical Validation
- Q3A - Q3D Impurities
- Q4 - Q4B Pharmacopoeias
- Q6A - Q6E Quality of Biotechnological Products
- Q6A - Q6B Specifications
- Q7 Good Manufacturing Practice
- Q8 Pharmaceutical Development
US FDA’S Implementation of ICH Guidelines

• Upon completion of the ICH process for a harmonised guideline, the Guideline moves immediately to the final step of the process--regulatory implementation

• This step is carried out according to the same national/regional procedures that apply to other regional regulatory guidelines and requirements, in the European Union, Japan and the United States
US FDA’S Implementation of ICH Guidelines

• In the United States, the finalized ICH Guideline is implemented according to Good Guidance Practices (GGP’s)
• GGP’s are FDA’s polices and procedures for developing, issuing, and using guidance documents.
• Federal Register: September 19, 2000 (Volume 65, Number 182) Page 56468-56480
• This is why the ICH Guidelines posted by FDA are called Guidances and reformatted to comply with GGP’s.
US FDA’S Implementation of ICH Guidelines

• According to GGP’s, FDA Guidances may be categorized as Level 1 or Level 2.

• Level 1 guidance documents include guidance documents that:
  – (i) Set forth initial interpretations of statutory or regulatory requirements;
  – (ii) Set forth changes in interpretation or policy that are of more than a minor nature;
  – (iii) Include complex scientific issues; or
  – (iv) Cover highly controversial issues.
US FDA’S Implementation of ICH Guidelines

• Level 2 guidance documents" are guidance documents that set forth existing practices or minor changes in interpretation or policy

• In the context of ICH, Level 1 Guidances are generally ICH Guidelines that go through the 4 Step ICH Process and Level 2 Guidances are generally Q and A’s or addendums to established ICH Guidelines
ICH Public Conferences

1st Conference: Brussels 1991
2nd Conference: Orlando 1993
3rd Conference: Yokohama 1995
4th Conference: Brussels 1997
5th Conference: San Diego 2000
   Focused on the CTD
6th Conference: Osaka 2003
Applications composed of ICH Guidelines
In 1996 ICH industry representatives proposed assembling the information generated by these harmonized guidances in the same order
Goal was to decrease the amount of time and staff needed to assemble and disassemble documents for submission to ICH regions
CTD Finalized in 2000 at ICH 5

SC and CTD EWG: Q, E, & S Members
ICH CTD

1.0 Regional Administrative Information
1.1 ToC of Module 1 or overall ToC, including Module 1

2.1 ToC of the CTD (Mod 2,3,4,5)
2.2 Introduction
2.3 Quality Overall Summary
2.4 Nonclinical Overview
2.5 Clinical Overview
2.6 Nonclinical Summary
2.7 Clinical Summary

Source: ICH Implementation Coordination Group
Shift in Information Flow

ICH Guidelines

CTD

Initial

Current

REVIEW
ICH Anniversary Publications

10th - 2000

20th - 2010
The CTD Changed ICH

Catalyst for modification of the ICH process to be more inclusive

– Expanded participation
– Outreach to other countries
– Increased transparency
Expanded Participation

- **November 2003** — Regional Harmonization Initiatives (RHI) invited to ICH-6 in Osaka to discuss their participation in the Global Cooperation Group
  - APEC, ASEAN, GCC, PANDRH, SADC
- **November 2005** — RHIs invited to observe ICH Experts Working Group meetings
ASEAN

Association of Southeast Asian Nations

Brunei Darussalam
Cambodia
Indonesia
Laos
Malaysia
Myanmar
The Philippines
Singapore
Thailand
Viet Nam
21 Member Economies

Russia
China
Hong Kong
Chinese Taipei
Japan
Korea
Brunei Darussalam
Indonesia
Malaysia
The Philippines
Singapore
Thailand
Viet Nam

Canada
Chile
Mexico
Peru
United States

Australia
New Zealand
Papua New Guinea
The Cooperation Council for the Arab States of the Gulf

Bahrain
Kuwait
Oman
Qatar
Saudi Arabia
United Arab Emirates
PANDRH

Pan American Network for Drug Regulatory Harmonization

- NAFTA
  USA, Canada, Mexico
- MERCOSUR
  Argentina, Brazil, Paraguay, Uruguay
- Andean Group
  Bolivia, Columbia, Ecuador, Peru, Venezuela
- CARICOM
  Caribbean Community
- SICA
  Central America Integration System
SADC

Angola
Botswana
Dem Rep Congo
Lesotho
Malawi
Mauritius
Mozambique
Namibia
Seychelles
South Africa
Swaziland
Tanzania
Zambia
Zimbabwe
East African Community

Member GCG
June 2011

Burundi
Kenya
Rwanda
Tanzania
Uganda
Expanded Participation

- **June 2008** — Regulators Forum, separate and distinct from ICH, was created to include India, China and Brazil and other countries interested in implementation of ICH Guidelines

- **June 2008** — ICH Global Cooperation Group (GCG) expanded to include individual countries
  
  – Australia, Brazil, China, Chinese Taipei, India, Korea, Russia, Singapore
# ICH Week

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**ICH Working Groups**

**Complementary**
Expanded Participation

• April 2011 — ICH SC opens Expert Working Groups to RHIs, DRAs, DoH as expert members (not only as observers), with following criteria:
  – Demonstrated support for the use of ICH guidelines
  – Experts possess appropriate knowledge
  – Commitment to participate in all discussions over life of topic development
  – Self-financed travel
  – Timely registration
Increased Transparency

- **November 2005** — Decision to publish summary of SC actions and decisions (summarized report) on ICH website
- **June 2006** (SC Decision) — Posting of concept papers and business plans for new topics. This provided for earlier notice of topics under discussion instead of at Step 2 when documents were posted for comment
Increased Transparency

• Anyone can comment on ICH Guidelines
• Standing section on the ICH Web
• Help to Shape the ICH Guidelines:

  *By responding to one of our consultations, your contribution will then be considered by the relevant ICH Working Group with links to Draft Guidelines and Q&A Documents*
Recent Changes

• The ICH Global Cooperation Group was integrated into sessions of the ICH Steering Committee in order to promote greater involvement of global regulators

• International Pharmaceutical Regulators Forum (IPRF) established
  • Issue specific discussion and information sharing related to ICH and other topics
International Pharmaceutical Regulators Forum

- Regulators have a distinct role and greater responsibility in ICH
- Desire to maximize the value of Regulator’s discussions
  - Public health issues
  - Technical issues
  - Development/implementation of ICH Guidelines
Formally established in June 2013

- Evolved from the Regulators Forum held on the margins of ICH meetings since 2008
  - IPRF benefits from good relationships built in ICH GCG and the Regulators Forum
- Participants include DRA/RHI/DOH and meetings are adjacent to ICH meeting to provide for expanded time for discussion of issues and information sharing
- IPRF Chair: Swissmedic & Co-Chair: MHLW
International Pharmaceutical Regulators Forum (IPRF)

Purpose
The purpose of the International Pharmaceutical Regulators Forum (IPRF) is to create an environment for pharmaceutical regulators to exchange information on issues of mutual concern and regulatory cooperation. This dedicated venue for global regulators will maximize potential efficiencies in addressing the increasingly complex global context of medicines regulation, will facilitate the implementation of ICH and other internationally harmonized technical guidelines for pharmaceuticals for human use and will contribute to the coordination of a range of international efforts related to regulation of medicines.

Goals
The International Pharmaceutical Regulators Forum provides members a unique opportunity to leverage the expert scientific knowledge, regulatory and operational experience, on-going technical harmonization work and information access of other participating regulators.

The first goal is to enable all parties to identify new approaches and specific best practices, and develop smart strategies for dealing with the challenges of a rapidly evolving globalized pharmaceutical industry.

The second goal is to provide a global overview of the different regulatory developments at national and international level and enable open sharing of information and ideas among regulatory leaders with hands-on operational responsibilities. This information sharing will allow the forum participants to discuss issues at an actionable level of detail.

The third goal is to support international regulatory cooperation in areas which are not covered by existing initiatives.
### New ICH Week

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<td>Regulators Meetings</td>
<td>IPRF International Pharmaceutical Regulators Forum</td>
<td>IPRF Industry Caucus</td>
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**GCG now incorporated into ½ day of Steering Committee**

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**ICH Working Groups**
Continuing Evolution

• Given the global environment in which we now operate, the continued success and relevance of ICH will depend upon broader use of ICH guidelines and standards

• ICH must evolve to meet the changing global paradigm
Dissemination and Uptake of ICH Guidelines

- FDA
- EMEA
- MHLW
- Swiss
- HC

GMP, GCP
PCV
GRP, CTD

APEC
RED PARE
PANDRH
The ICH Study Group in China was founded in July 2009, led by the Drug Registration Department of the State Food and Drug Administration (SFDA), involving regulators and representatives from industry and academia. The objectives of the group are to study and disseminate ICH Guidelines, strengthen cooperation and exchange with ICH, and promote harmonisation of China drug registration standard with global standard. Translating and publishing ICH Guidelines and related documents are part of the important tasks. Adaptation, dissemination and utilisation of ICH Guidelines are part of a long-term and dynamic program of the group.
UPDATE-ICH Steering Committee Meetings—Lisbon, Portugal, November 2014

- A broader range of membership and governance reforms continue to be considered
- Includes greater clarity regarding the distinct and separate roles of the ICH regulatory and industry parties in ICH.
- ICH reform discussions have also been addressing parameters for creating a new legal entity for ICH and the future approach to funding
Continuing Evolution

• Expansion of ICH represents a natural evolution and a changing world reality
• Expanded participation in ICH is expected to benefit, industry, regulators and patients
• Will promote faster access to innovative medicines
Many Thanks for Your Attention