European Federation of Pharmaceutical Industries and Associations

ICH
Overview, training and ICH Q12 Life cycle management

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PharmMedObrashenie-2019

Overview of Presentation

- Overview of ICH
- ICH Training
- ICH Q12 Life cycle management

Overview of ICH

- The full name of the ICH association is the “International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH).”

- Unique harmonisation initiative for regulators and pharmaceutical industry

- Originally founded in 1990

- Reformed as a non-profit legal entity under Swiss Law on October 23, 2015

Overview of ICH

ICH Members 22 May 2019

Members:

- **Founding Regulatory Authorities:** EC/EMA, MHLW/PMDA, FDA
- **Founding Industry Associations:** EFPIA, JPMA, PhRMA
- **Standing Regulatory Authorities:** Swissmedic, Health Canada
- **Industry Associations:** IGBA (Generics), WSMI (OTC) and BIO (Biotech)
- **Regulatory Authorities:** MFDS (South Korea), ANVISA (Brazil), CFDA (China), HSA, (Singapore) and TFDA (Chinese Taipei)

Overview of ICH

ICH Observers 22 May 2019

- **Standing Observers:** WHO, IFPMA

- **Observers:**
  - *Regional harmonisation initiatives (RHIs):* APEC, ASEAN, EAC, GCC, PANDRA and SADC
  - *Regulatory authorities from* Russia, Australia, India, Mexico, Singapore, South Africa, Cuba, Kazakhstan, Columbia, Turkey, Malaysia, Armenia, Moldavia and Iran
  - *International pharmaceutical industry organisations:* APIC
  - *International organisations:* IPEC, CIOMS, EDQM, USP, PIC/S and Bill & Melinda Gates Foundation

- **Ad-hoc observers:** Upon invitation

Overview of ICH

ICH Observers

Regulatory observers (Legislative or administrative authorities)

- Must be authority responsible for regulation of human pharmaceuticals

Regulatory observers (Regional harmonisation initiatives)

- Must represent legislative or administrative authorities with responsibility for the regulation of pharmaceutical products for human use
- For further details on application, please see **https://www.ich.org/about/application-process.html**
- For further details on requirements, please see
  - Article 17.1 (b) of the Articles of Association https://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Articles_Procedures/ArticlesOfAssociation_Approved_2018_0606_v2.pdf

Overview of ICH
ICH Observers

- If Eurasian Economic Commission (EEC) would like to become an observer of ICH, EEC needs to decide if they should apply as a legislative or administrative authority or a regional harmonisation initiative (RHI)
- For the moment my personal assessment is that EEC is a RHI, but in the future it could become a legislative or administrative authority.

Overview of ICH
ICH Observers

- The fact that Rozdravnadzor and National Center, Kazakhstan are ICH observers does does not stop EEC from becoming an observer. Even if Rozdravnadzor and/or the National Center would become member of ICH, EEC could become observer of ICH, provided that not all members of EEC already are members or observers of ICH.
- The reason for these rules, is that ICH would like to avoid double membership via both RHI and its members.
- For further details, please see Assembly Rules of Procedures, section 2.2.1 “Eligibility Criteria for Observers”. **https://www.ich.org/fileadmin/Public_Web_Site/ABOUT_ICH/Articles_Procedures/Assembly_RoPs/AssemblyRoP_Approved_v6-0_2018_1114.pdf**

Overview of ICH
ICH Observers

- Rights of Observers:
  - To attend ICH Assembly meeting, but no right to vote or appoint experts in WGs
  - Standing Observers (WHO and IFPMA) maintain their right to appoint experts in WGs

Overview of ICH

Membership in the Assembly – Eligibility Criteria for Regulators

Engagement in the ICH Process:

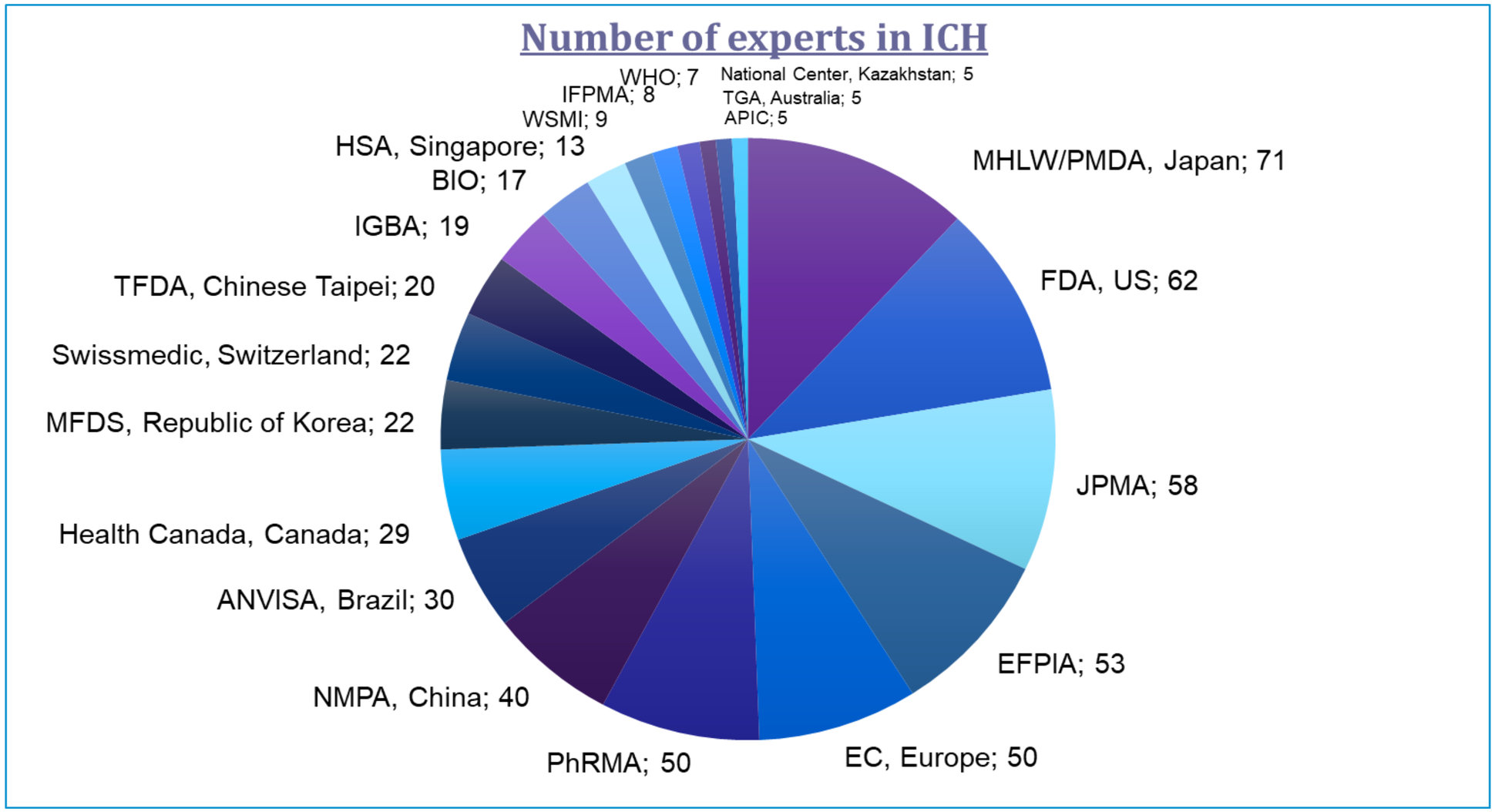
- Past regular attendance in at least 3 ICH meetings during the previous 2 consecutive years
- Past appointment of experts in WGs

Engagement in the ICH Process:

- Having implemented at least the following ICH guidelines
  - Q1: Stability Testing guidelines
  - Q7: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients
  - E6: Good Clinical Practice Guidelines

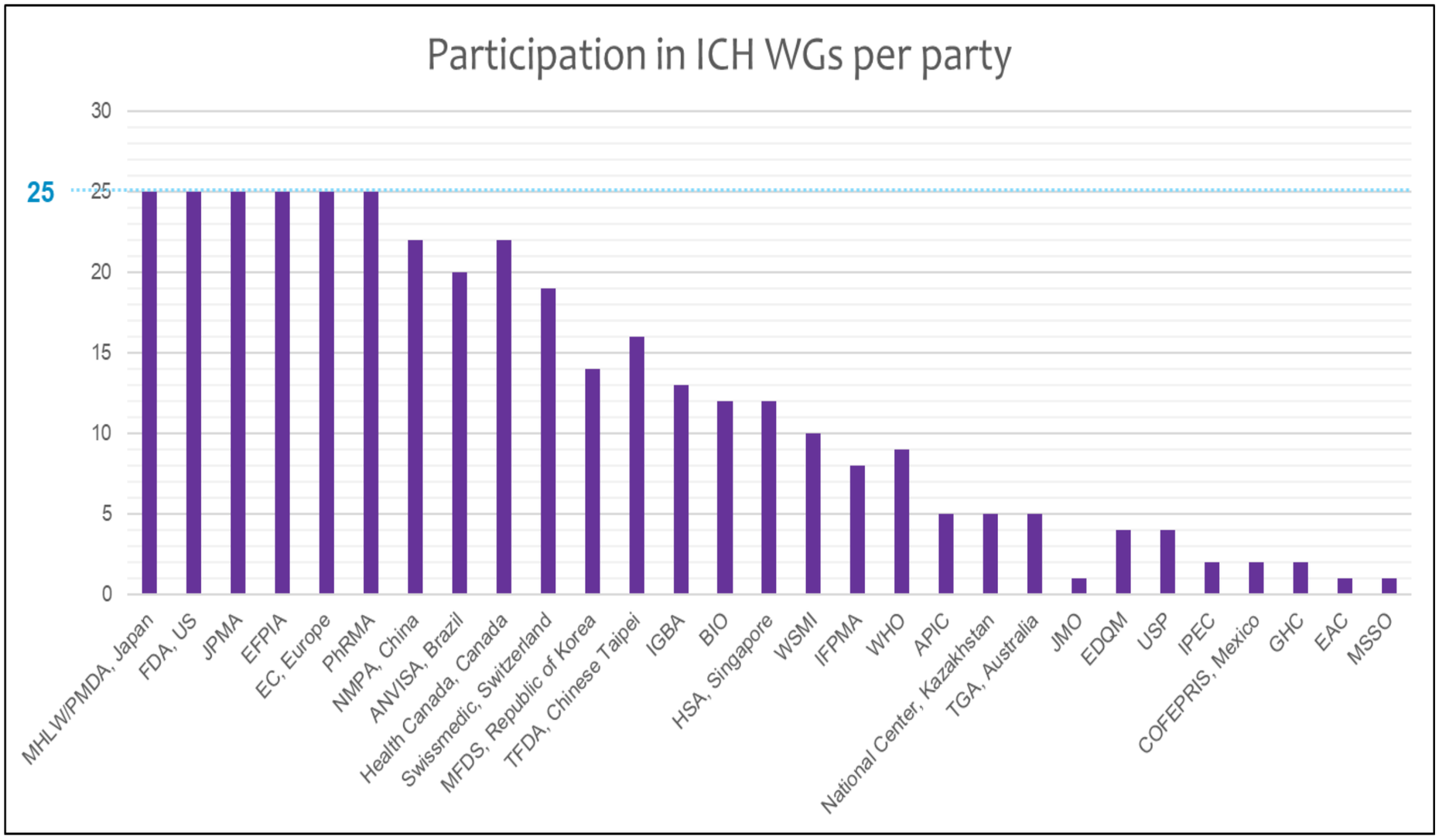
Overview of the participation of current Members and Observers in ICH

5 experts from National Center, Kazakhstan in 25 WGs – as of 15 October 2018



Overview of the participation of current Members and Observers in ICH

615 Experts in 25 WGs– as of 15 October 2018



Overview of ICH

Current focus of ICH MC

The ICH Management Committe is working to:

- **Manage the size of the Expert Working Groups** due to the increasing membership in ICH.

- **Ensure adequate implementation of ICH guidelines** in a harmonized manner by all Regulatory Members. A survey on the implementation of guidelines by regulatory members has therefore been sent out to companies and regulatory members to get data on implementation in practice.

- **Facilitate the provision of training on ICH guidelines** to ensure that members fully understand the guidelines. This is specially important for the implementation of guidelines by regulatory members.

ICH Training
Remit / Deliverable ICH Training subcommittee

Objectives

- Facilitate harmonized implementation of ICH guidelines through training to strengthen the regulatory framework and improve regulatory efficiencies to promote innovation and protect patients

Desired future

- Provide effective training tools to enable regulators, industry and those involved in drug development to successfully and consistently implement approaches described in ICH guidelines

Deliverables	Stakeholder	Milestone	Status
List of upcoming training events. Please see https://www.ich.org/trainings/training.html	Public	Keep current	Implemented
Collaboration with training providers: • Training Programme Provider Eligibility Criteria • Terms of Reference for Training Providers • Procedure for Organisations Interested in Developing an ICH Recognised Training Programme • ICH Training Programme Provider Application Form	Potential training providers	Goal for 2018	Endorsed
ICH Training Subcommittee to assess training providers and training associates	Candidates for collaboration	ICH approval for collaboration	Ongoing
Collaboration with training associates • Call for expression of interest published on ICH Training site	Potential training providers	Goal for 2019	Under review

ICH Training
Developing ICH Training Material

- **Current and future ICH working groups should develop training material**
  - Step 2 guideline – for information
  - Step 4 guideline – at least the introductory format
- **Priority list of existing guidelines**
  - **Tier 1 Guidelines**
    - Stability Q1 (NEU)
    - GMP for APIs Q7 (PDA)
    - GCP E6 (Harvard MRCT)
  - **Tier 2 Guidelines**
    - Safety Data E2A,B,D (incl. C,E; AHC)
    - CTD M4 (RAPS)
    - MeDRA M1 (established via ICH)
- **Major Tier 3 guidelines priorities for training**
  - Impurities Q3 (priority Q3C), M7
  - Biotech Q5 (priority Q5E), S6 (R1)
  - Specification Q6A&B
  - QbD Q8-11
  - Non-clinical toxicology E5
  - Trial design & data analysis E17
  - Timing of safety studies M3 (R2)
  - E-CTD M8

ICH Training
Relationships to Organizations

ICH Training Provider

- A non-for profit organization/institution which ICH Training Subcommittee approved to provide an individual training program. “ICH Training Provider” is only allowed to use the "ICH Recognised Training Programme" logo for the approved individual program

ICH Training Associates

- An accredited non-profit training organization/institution which will be recognized by ICH, and its’ scope is to act as ‘ICH training provider’ and in addition provide consultancy services about a conceptional group of ICH guidelines (e.g. Q1, Q8-12, Pharmacovigilance) for a comprehensive training approach among different regions

ICH Training
ICH Online Training Providers

Developing introductory online programs in 2019

Q1 , Stability	Northeastern University (NEU)
Q7, GMP for API	Parenteral Drug Association (PDA)/Pharmaceutical Inspection Co-operation Scheme (PICs)
E6 GCP	Harvard MRCT (Multiregional Clinical Trials)
E2 Pharmacovig.	The APEC Harmonisation Center (AHC)
M4 CTD	Regulatory Affairs Professional Society (RAPS)

ICH Training
Some Training Events in 2019

- **Some training events by ICH Training Providers in 2019 (taken from ICH Training site)**
  - ICH GCP and MRCT Training: ICH E6(R2) and ICH E17, Ottawa, Ontario, Canada, 26-28 February 2019
  - ICH Workshop Chemistry, Manufacturing and Controls (CMC), Singapore, 21-22 March 2019
  - ICH Day, Tokyo, Japan, 18 April 2019
  - Pharmacovigilance Seminar, Beijing, China, 23-25 April 2019

ICH Training
by regulators partly funded by ICH (Jan 2019)

Training organiser (ICH Regulatory Member)	Training provider/co-organizer	Title	Guideline(s)	Date	Place
Health Canada, Canada	Harvard MRCT	ICH GCP and MRCT Training: ICH E6(R2) and ICH E17	E6(R2) and E17	26-28 February 2019	Ottawa, Canada
MHLW/PMDA, Japan	Co-organized with JPMA and supported by non-profit Japanese academia organization (under confirmation).	Seminar for ICH E8 (R1) draft guideline	E8 (R1) draft Guideline	July 2019 (one day)	Tokyo, Japan
MFDS, Republic of Korea	NA	ICH Guideline Training	Quality (3), Safety (3), Efficacy (3) and Multidisciplinary (3): 12 in total	September 2019 (4 days)	Seoul, Korea
NMPA, China	APEC PKU Regulatory Science CoE	General Principles for planning and Design of MRCT (E17)	E17 (and E5, E6, E8, E9, E10, and E18)	September 2019 (4 days)	Beijing, China
NMPA, China	Pending	ICH M3(R2) Nonclinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals	M3(R2)	June/July/September or October 2019 (2 days)	Beijing, China
NMPA, China	Regulatory Affairs Professionals Society (RAPS)	ICH M8 Electronic Common Technical Document (eCTD)	M8 (and M4)	June/July/September or October 2019 (2 days)	Beijing, China
NMPA, China	Northeastern University America (NEU)	ICH Q8-Q11 Guidelines package	Q8-11	June/July/September or October 2019 (3 days)	Beijing, China

Q12 Objectives and Potential Benefits

✱ Objectives

- …Harmonize change management…in a more transparent and efficient manner…across ICH regions
- …Facilitate risk-based regulatory oversight…
- Emphasize…control strategy as a key component of the…dossier
- Enhance use of regulatory tools for prospective change management…enabling strategic management of post-approval changes…

✱ Potential Benefits

- Reduce unnecessary cost and time burdens on industry and regulators, while assuring that patients reliably have access to high quality therapies
- Support continual improvement…which can result in decreased product variability and increased manufacturing efficiency
- Help to mitigate drug shortages related to manufacturing and quality issues
- Facilitate the introduction of innovations in manufacturing…

Q12 Scope

A framework to facilitate the management of post-approval CMC changes in a more predictable and efficient manner

Scope

- Pharmaceutical drug substances (i.e., active pharmaceutical ingredients) and pharmaceutical drug products
    - Includes marketed chemical and biotechnological/biological products
- Drug-device combination products that meet the definition of a pharmaceutical or biotechnological/biological product
- Does not include changes needed to comply with Pharmacopeial monographs

Q12 (Step 2b Draft) Table of Contents

Core Guideline:

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

* Appendix 1: CTD Sections That Contain ECs
* Appendix 2: Principles of Change Management

Annex:

Annex I: ECs – Illustrative Examples

Annex I A: Chemical Product

Annex I B: Biological Product

Annex II: PACMP – Illustrative Examples

Annex II A: PACMP Example 1

Annex II B: PACMP Example 2

Annex III: Product Lifecycle Management Document

Illustrative Example

Q12 Product Lifecycle Management Update

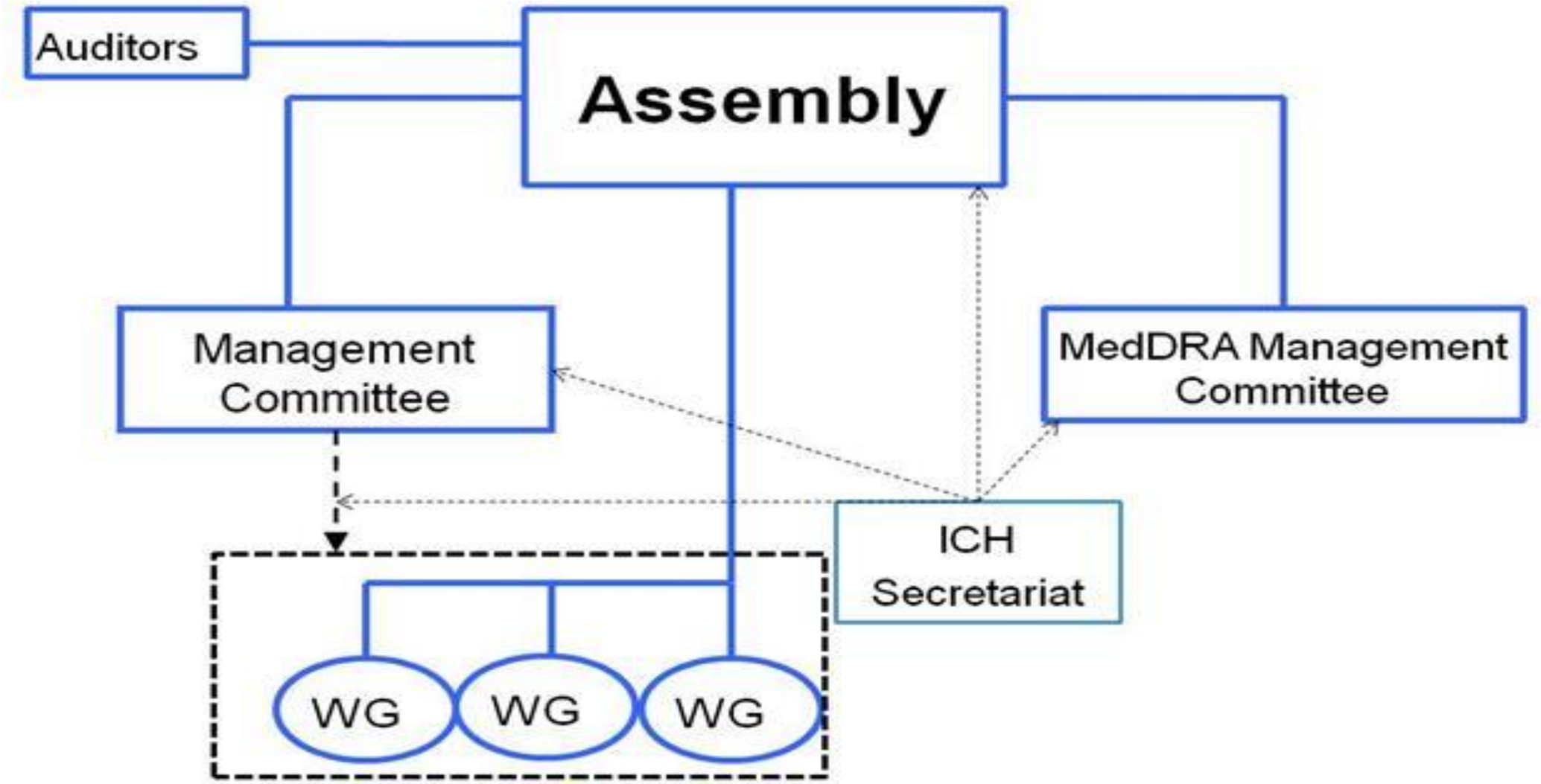
- Q12 EWG Interim meeting (11-15 Feb. 2019; Tokyo, Japan)
  - Preparation for Step 4 (approx. 900 consolidated comments received)
  - Good progress made addressing key issues
  - ‘EWG Meeting Report and updated Workplan prepared for ICH Management Committee
  - EWG formed 11 subteams to continue working on priority issues
- Step 4 Guideline
  - Target for ICH 1-6 June 2019; Amsterdam
- EWG to meet in Singapore?
  - From updated Workplan:

    ‘Note that given the large number of comments received, it may not be possible to complete training materials during the June meeting. In such case, the EWG may request approval to meet in Singapore (November 2019) to complete the training materials.’

Back-up slides

Overview of ICH

Structure of the ICH Association



Overview of ICH

ICH Observers

Industry observers

- The organisation and/or its members must be regulated or affected by ICH guidelines
- International organisations whose members are already represented by other members or observers are not eligible to become observers for regulation of human pharmaceutical products

Overview of ICH

Membership in the Assembly – Eligibility Criteria for Industry

Engagement in the ICH Process:

- Past regular attendance in at least 3 ICH meetings during the previous 2 consecutive years
- Past appointment of experts in WGs

Type of Organisation:

- Be an international pharmaceutical industry organisation representing a global constituency

Impact of ICH Guidelines:

- The organisation and/or its members must be regulated or affected by ICH guidelines

Process for selection of new topics

1. ICH members submit proposals for new/revised topics using template by **15 December.** At EFPIA, relevant expert working groups e g Technical Development expert groupup for quality topics endorse new topic proposals before submission.
2. Topic proposals are presented by experts to ICH New topics subcommittee in January/February.
3. A shortlist of topics and an assessment summary report are selected by the new topics subcommittee at the ICH interim meeting, which takes place in the period 15 March – 15 April
4. The ICH Management Committee (MC) approves the assessment summary report from the new topics subcommittee 15 April – 1 May.
5. Assessment summary report and proposals for topics are submitted to ICH Assembly one month before Assembly meeting
6. Final decision at ICH Assembly on new topics at the ICH June meeting

New topics for ICH

At the June 2018 meeting in Kobe, Japan, ICH decided to initiate three new topics for harmonisation:

- Q13: Continuous manufacturing
- Q14/Q2(R2): Analytical Procedure Development and Revision of Q2(R1) Analytical Validation
- M11: Clinical electronic Structured Harmonised Protocol (CeSHarP)

New topics for ICH

Strategic discussion on harmonisation needs

At the June 2018 meeting in Kobe, we endorsed a quality reflection paper and agreed to develop a generic reflection paper further. In addition agreement was made to develop proposals for strategic discussions on:

- Model Informed Drug Development (Modelling & Simulation)

At the ICH meeting in Kobe a draft reflection paper on vaccines were discussed. However the ICH Assembly decided not to continue the development of the vaccines reflection paper.

A reflection paper on Good Clinical Practice has also been developed. Please see link below.
http://www.ich.org/products/gcp-renovation.html

Steps in the ICH Process for Guideline Development

Step 5	Implementation
Step 4	Adoption of an ICH Harmonised Guideline
Step 3	Regulatory consultation and Discussion
Step 2	a. ICH Parties consensus on Technical Document / b. Draft Guideline adoption by Regulators
Step 1	Consensus building - Technical Document

The ICH Step Process (1)

- *Step 1:*
  - *<u>WG</u> works to prepare a consensus draft of the technical document.*
- *Step2:*
  - ✓ *Step 2a:*
    - *<u>The Assembly</u> is invited to endorse the technical document.*
  - ✓ *Step 2b*:
    - *<u>The ICH Regulatory Members</u> of the Assembly are invited to endorse the draft Guideline.*

Cont.

The ICH Step Process (2)

- *Step 3:*
  - *Public consultation by the ICH Regulatory Members and ICH Secretariat. All comments are considered by the WG.*
  - *Step 3 is finalised once concensus is reached in the WG.*
- *Step 4:*
  - *The Regulatory Members of the Assembly adopt the final document.*
- *Step 5:*
  - *Implementation by the ICH Regulatory Members.*

European Federation of Pharmaceutical Industries and Associations

Thank you!

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