ICH ASSOCIATION

2018 ANNUAL REPORT

ICH Association

2018 Annual Report

Prepared by the ICH Secretariat with the ICH Management Committee and MedDRA Management Committee approval of their respective sections.

Version dated 6 May 2019.

Approved by the ICH Assembly on 5 June 2019.

Message from Assembly Chair and Vice Chair

Three years on from the reform of ICH, all organisational changes have been implemented, with 2018 being illustrative of ICH's steady evolution to a more global initiative. ICH is now constituted by 16 Members and 28 Observers, after the ICH Assembly in 2018 approved TFDA, Chinese Taipei as a new Regulatory Member, and MMDA, Moldova, NPRA, Malaysia, NRA, Iran, SCDMTE, Armenia and TİTCK, Turkey as new Observers.

In one of the remaining steps of implementing the 2015 reforms, the Assembly elected additional members to the Management Committee of the ICH Association. The Founding and Standing Members are now joined by five newer ICH Members: NMPA, China, HSA, Singapore and MFDS, South Korea as regulatory members, as well as BIO and IGBA as industry members, all of which have been elected for a three year term.

The increasing number of ICH Members and Observers has further underlined the importance of training in ensuring a globally consistent approach to ICH Guideline implementation. Consideration of training resources is therefore high on ICH's agenda, focusing on the development of training tools for regulators, industry and other stakeholders involved in drug development, manufacturing and post-market safety.

Linked with these efforts, it is important to fully understand how the ICH Guidelines are implemented by ICH Regulatory Members and Observers. As a first step, the terms around implementation have been clearly defined. Currently, a survey is being conducted on the status of implementation of certain guidelines as well as mapping across all guidelines. Once completed, the outcome will be published on the ICH website so that all stakeholders can understand how ICH Guidelines are implemented in their region.

ICH remains dedicated to the mission of achieving greater harmonisation worldwide to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner. We are deeply grateful for the continued commitment of all of the people who are involved in achieving this mission.

Mrs. Lenita Lindström-Gommers
ICH Assembly Chair
EC, Europe

Dr. Petra Doerr
ICH Assembly Vice Chair
Swissmedic, Switzerland

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1. About ICH

1.1. Purpose & Aims

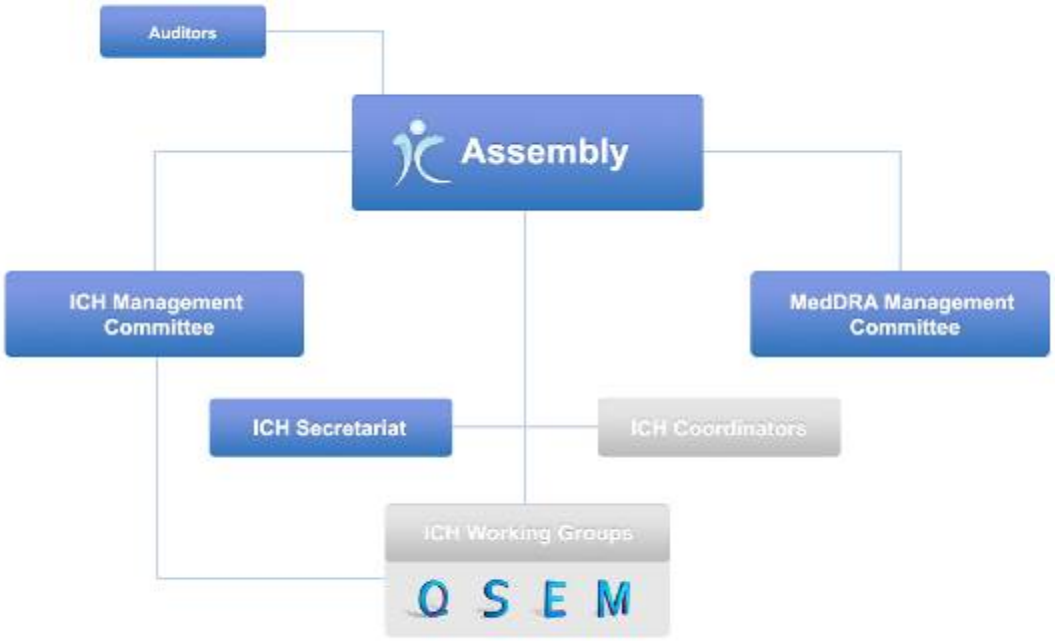
The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (**ICH**) **is an international non-profit organisation** which was established as an association under Swiss law in October 2015. The purpose of ICH is to **promote public health through international harmonisation** of technical requirements that contribute to the timely introduction of new medicines and continued availability of the approved medicines to patients, to the prevention of unnecessary duplication of clinical trials in humans, to the development, registration and manufacturing of safe, effective, and high quality medicines in an efficient and cost-effective manner, and to the minimization of the use of animal testing without compromising safety and effectiveness.

The **ICH's aims** are the following:

- To make recommendations towards achieving **greater harmonisation** in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration and the maintenance of such registrations.
- To maintain a forum for a **constructive dialogue** on scientific issues between regulatory authorities and the pharmaceutical industry on the harmonisation of the technical requirements for pharmaceutical products.
- To contribute to the **protection of public health** in the interest of patients from an international perspective.
- To monitor and update harmonised technical requirements leading to a **greater mutual acceptance** of research and development data.
- To **avoid divergent future requirements** through harmonisation of selected topics needed as a result of therapeutic advances and the development of new technologies for the production of medicinal products.
- To facilitate the adoption of **new or improved technical research and development approaches** which update or replace current practices.
- To encourage the **implementation and integration of common standards** through the dissemination of, the communication of information about and coordination of training of harmonised guidelines and their use.
- And to develop **policy for** the ICH Medical Dictionary for Regulatory Activities Terminology (**MedDRA**) whilst ensuring the scientific and technical maintenance, development and dissemination of MedDRA as a standardised dictionary which facilitates the sharing of regulatory information internationally for medicinal products used by humans.

1.2. Organisational Structure

The bodies of the ICH Association are the: **Assembly**; **ICH Management Committee**; **MedDRA Management Committee**; **ICH Secretariat** and **Auditors**. Although not a body of the Association, ICH Coordinators play an important role in supporting the work of ICH.



Assembly

- The Assembly brings together all Members and Observers of the ICH Association. It is the **overarching governing body** of ICH and adopts decisions in particular on matters such as the ICH Articles of Association, admission of new Members and Observers and adoption of ICH Guidelines.
- The full list of Assembly Member Representatives and Observer Delegates as of December 31, 2018 is provided in Annex I.

ICH Management Committee

- The ICH Management Committee is the body that oversees **operational aspects** of ICH on behalf of all Members, including administrative and financial matters and oversight of the Working Groups (WGs). The ICH Management Committee is responsible for submitting recommendations or proposals to the Assembly in preparation of Assembly discussions.
- The ICH Management Committee may set up Subcommittees for dealing with specific topics to assist the Management Committee. In 2018 the following

Subcommittees were supporting the work of Management Committee: New Topics, Implementation, Training, Communication and Financial.

- The full list of the ICH Management Committee Member Representatives and Observer Delegates as of December 31, 2018 is provided in Annex II.

MedDRA Management Committee

- The MedDRA Management Committee has responsibility for **direction of MedDRA**, the Medical Dictionary for Regulatory Activities, ICH's standardised medical terminology.
- The full list of MedDRA Management Committee Representatives and Observer Delegates as of December 31, 2018 is provided in Annex III.

ICH Secretariat

- The ICH Secretariat is responsible for **day-to-day management** of ICH, coordinating ICH activities as well as providing support to the Assembly, ICH Management Committee and its WGs. The ICH Secretariat also provides support for the MedDRA Management Committee as the "MedDRA Secretariat". The ICH Secretariat is responsible for the implementation of the decisions of ICH's governing bodies. Actions taken by the ICH Secretariat in this regard in 2018 are referred to in Section 5.6.
- The full list of ICH Secretariat Staff as of December 31, 2018 is provided in Annex IV.

Auditors

- In 2018, the Assembly agreed to re-appoint Moore Stephens Refidar SA for a further period of 2 years to audit the **annual financial statements** of the ICH Association.

ICH Coordinators

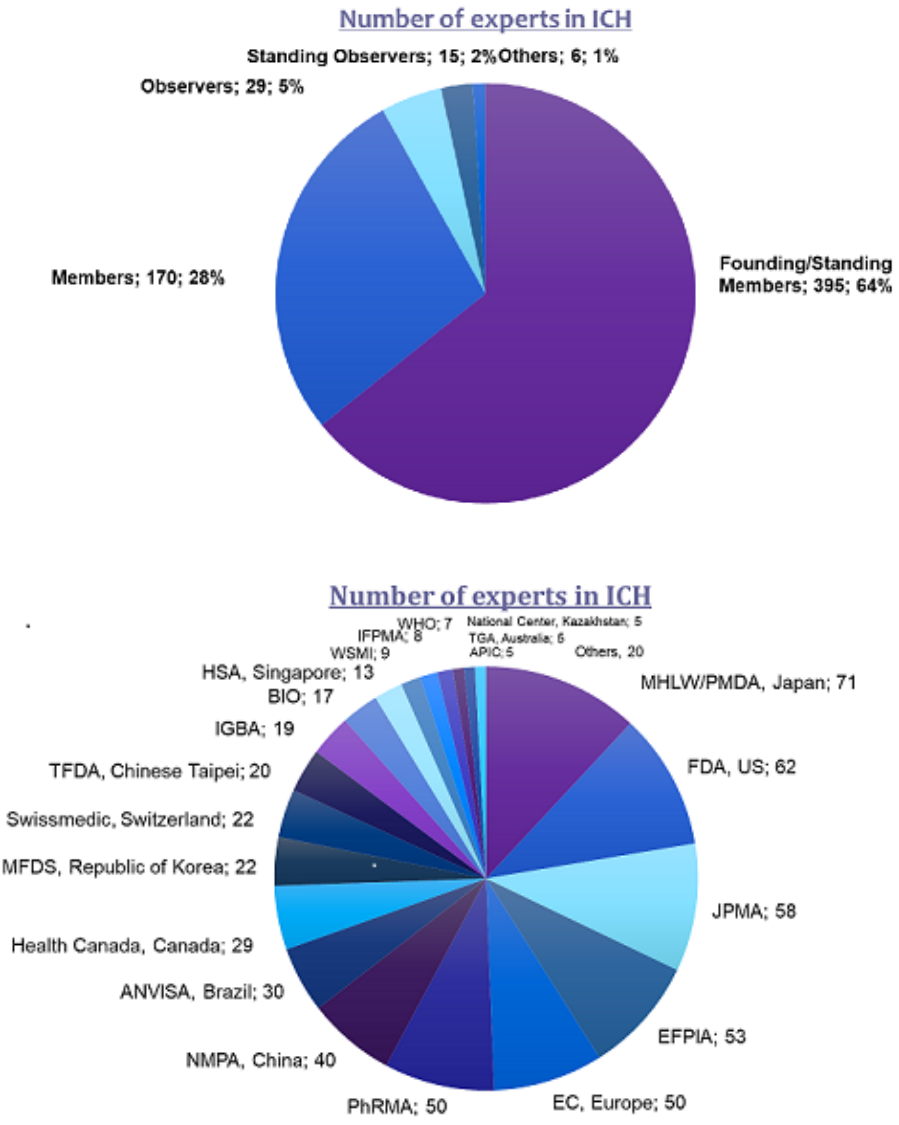
- Fundamental to the smooth running of ICH has been the designation of an ICH Coordinator per ICH Member to act as the main contact point with the ICH Secretariat. Coordinators ensure proper distribution of ICH documents to the appropriate persons from their organisation and are responsible for the **follow-up on actions** within their respective organisation within assigned deadlines. They also assist communication between the ICH Management Committee and/or Assembly and the ICH WGs as needed.
- The full list of ICH Coordinators as of December 31, 2018 is provided in Annex V.

2. 2018 Overview of ICH Membership & Observership

2.1. Continued Expansion of ICH Membership & Observership

A driving factor of the organisational change celebrated by ICH at the end of 2015 was to make ICH a **truly global initiative**. 2018 built upon 2017's success in expanding ICH's reach, with the addition of more new Members and Observers, bringing ICH to a total of **16 Members and 28 Observers**, thereby further expanding the forum for dialogue on scientific issues between regulatory authorities and the pharmaceutical industry on the harmonisation of the technical requirements for pharmaceuticals products.

These new Members and Observers have demonstrated great interest in participating in the activities of ICH, something which is particularly evident looking at ICH's **WGs**. At the end of 2018 these WGs involved the participation of **over 600 technical experts**, with almost a third of these experts coming from new ICH Members and Observers.



Overview of Expert Participation in ICH, as of end of 2018

While the expansion of ICH is celebrated by all involved, it also brings the challenge of ensuring the continued smooth operation of the Assembly and ICH WGs. In 2018, the ICH Management Committee carefully oversaw the appointment of experts to ICH WGs, weighing decisions on the addition of new experts against the size of WGs and the status of work, which sometimes meant that not all requests to appoint experts could be accommodated. In view of these challenges, the ICH Management Committee initiated reflection on how to manage the size of ICH WGs to maintain efficient and well-managed harmonisation work processes and this is an area that the ICH Management Committee plans to propose changes to in 2019.

In view of this, the MC presented to the Assembly at the June 2018 meeting in Kobe a proposal to enable ICH stakeholders that were not permitted to appoint experts to a WG due to size restrictions, to consult with the WG, and a pilot of the proposed process was launched with the E8(R1) EWG, with a view to further assess the proposal at the end of the pilot for applicability to other ICH WGs.

2.2. New Members & Observers Approved in 2018

The Assembly approved **1 new ICH Regulatory Member** in 2018, based on the recommendation of the ICH Management Committee:

- TFDA, Chinese Taipei

ICH Assembly Kobe, Japan, June meeting

Left to right: Ms. Chao-Yi Wang (TFDA, Chinese Taipei), Ms. Yi-Jing Kuo (TFDA, Chinese Taipei), Ms. Lenita Lindström-Gommers (EC, Europe), Ms. Hsiao-Han Chiang (TFDA, Chinese Taipei), Dr. Toshiyoshi Tominaga (MHLW/PMDA, Japan), Dr.Churn-Shiouh Gau (TFDA, Chinese Taipei).

5 New Observers were also approved by the Assembly in 2018 based on the recommendation of the ICH Management Committee:

- MMDA, Moldova
- NPRA, Malaysia
- NRA, Iran

- SCDMTE, Armenia
- TİTCK, Turkey

In addition to these approved Membership and Observership applications, in 2018 the Assembly also considered one application from an organisation which it considered did not meet the eligibility criteria[1]. The ICH Management Committee also coordinated with the ICH Secretariat in 2018 to respond to further enquiries regarding interest in ICH Membership and Observership from organisations/individuals which in line with the procedures would clearly not be eligible. Furthermore, the revisions to application forms for Regulatory Membership and Observership were approved by the Assembly.

3. 2018 ICH Harmonisation Activities

A major output of ICH's work, in line with the specific aims of the organisation, is the development by Working Groups (WGs) of **harmonised technical guidelines** and other work products to support harmonisation activities on **Q**uality, **S**afety **E**fficacy and **M**ultidisciplinary topics.

In 2018, these activities were progressed on **25 topics** by technical WGs [including Expert Working Groups (EWG), Implementation Working Groups (IWG) and a Discussion Group (DG)], with support from the ICH Secretariat and under the oversight of the ICH Management Committee, with reporting to the Assembly. These activities were undertaken mostly via email and teleconferences, with some of the WGs being approved to meet face-to-face by the ICH Management Committee to progress their activities at the time of ICH's biannual meetings in 2018. The ICH WGs which met in 2018 are presented in Annex VI.

The **key outcomes in 2018** relating to ICH harmonisation efforts include:

- Completion at ***Step* 4** of the ICH process and **finalisation** of work (Please see Section 3.1) on:
  - **1 New** Questions & Answers (Q&A) Document
  - **3 Updated** Q&A Documents
  - **1 Revised** Implementation Package
  - **1 Revised** ICH Guideline (further to a corrigendum)
  - **Updates** of Point to Consider Documents with each MedDRA release
- Reaching of ***Step 2a/b*** of the ICH process and completion of drafts (Please see Section 3.2) of:
  - **2 New** ICH Guidelines
  - **1 Revised** ICH Guideline

[1] In line with the ICH Articles of Association Articles 11, 12 & 17; and Assembly RoP Sections 1 & 2.

- **5 New** topics approved for development.

- **2 Q&As** Documents approved for development.

An overview of all ICH WG activities and accomplishments in 2018 is presented in Annex VII.

3.1. ICH Guidelines & Other WG Work Products Finalised in 2018

3.1.1. ICH Guidelines & Other WG Work Products Adopted at *Step 4*

The following ICH Guidelines and other WG Work Products were adopted by the Regulatory Members of the Assembly at ***Step 4*** of the ICH process in 2018 following the reaching of consensus within the respective ICH WGs and sign-off by the Regulatory Member experts of these WGs under ***Step 3***. Please note that all ICH documents referenced below can be found on the ICH website at www.ich.org.

ICH E2B(R3) Q&A Document – Electronic Transmission of Individual Case Safety Reports (ICSRs)

The **ICH E2B(R3) Q&A Document** provides clarifications for the harmonised interpretation of the E2B(R3) Implementation Guide package and aims to facilitate the implementation of the electronic transmission of Individual Case Safety Reports (ICSRs) in the ICH regions.

In 2018, the following final document was adopted:

- Updated **ICH E2B(R3) Q&As** v2.2 in the ICSR Implementation Guide package.

ICH M8 – Electronic Common Technical Document (eCTD)

ICH M8 is a technical standard and Implementation Guide **to facilitate the exchange of regulatory information prepared in accordance with the requirements of the CTD** in the ICH regions. The M8 EWG/IWG in charge of this standard also assumes the responsibility for the implementation and maintenance of eCTD, as well as development and maintenance of other related documents such as Q&As and Study Tagging File specifications. All electronic standards documents are available on the Electronic Standards for Transfer of Regulatory Information (ESTRI) at http://estri.ich.org.

In 2018, the following documents related to the M8 eCTD were adopted:

- **eCTD v3.2.2 Q&A** and Specification Change Request Document v1.31 (M8);
- **eCTD v4.0** Implementation Package v1.2 (M8);
- **eCTD v4 Q&A** and Specification Change Request Document v1.2 (M8);
- Specification for Submission Formats for **CTD v1.2** (M8).

ICH S9 Q&A Document: Nonclinical Evaluation for Anticancer Pharmaceuticals

The final **ICH S9 Q&A Document** aims to facilitate the implementation of the S9 ICH Guideline and to provide additional clarity around **anticancer pharmaceutical**

development. The Q&A document is also intended to continue progress in the 3Rs of Reduction, Refinement, and Replacement in use of animals.

In 2018, the following final document was adopted:

- **ICH S9 Q&A** on Nonclinical Evaluation for Anticancer Pharmaceuticals.

3.1.2. Other WG Work Products finalised in 2018

The following ICH WG Work Products were finalised in 2018 outside of those items produced as part of the ICH step process.

Q3C(R7) Error Correction for the Permitted Daily Exposure for Ethyleneglycol

The **ICH Q3C(R7) Guideline** is a result of a revision to correct an error in the Permitted Daily Exposure (PDE) for ethyleneglycol in the ICH Q3C(R6) Guideline. Additionally, the **Q3C Support Documents 1, 2 and 3,** which contain the summaries of the toxicity data from which the PDEs were derived for the original ICH Q3C Guideline, were published on the ICH website in October 2018.

In 2018, the following document was finalised:

- The **ICH Q3C(R7) Impurities: Guideline for Residual Solvents.**

MedDRA Points to Consider (PtC) documents on Term Selection and **Data Retrieval and Presentation**

MedDRA is a standardised medical terminology developed by ICH to facilitate sharing of regulatory information internationally for medical products used by humans. Under the governance of the MedDRA Management Committee, MedDRA is continuously enhanced to meet the evolving needs of regulators and industry around the world. The current ICH M1 PtC Working Group develops and maintains two documents on the use of MedDRA for data entry (coding) and data retrieval/analysis. Both documents are updated twice a year, with every MedDRA release.

In 2018, the following documents were finalised:

- The two **MedDRA PtC documents on Term Selection** and **Data Retrieval and Presentation** with MedDRA release versions 21.0 and 21.1;
- The **Companion Document to the PtC Document**, which was endorsed by the MedDRA Management Committee at its meeting in Kobe in June 2018;
- **Translated versions** (in all MedDRA languages) **of the condensed versions of the PtC documents** developed by the ICH M1 PtC WG.

3.2. ICH Guidelines & Other WG Work Products Endorsed at Step 2a/b in 2018

In 2018 the following ICH Guidelines and other WG Work Products were endorsed first at ***Step 2a*** of the ICH process by all Members of the Assembly, followed by endorsement at ***Step 2b*** by the Regulatory Members of the Assembly. This endorsement followed the

reaching of consensus within the respective ICH WGs and sign-off by all Member experts of these WGs, under ***Step 1***.

ICH M9 Guideline - Biopharmaceutics Classification System-based Biowaivers 

The new **draft ICH M9 Guideline** on **Biopharmaceutics Classification System (BCS)-based biowaivers** published for regulatory public consultation in 2018 aims to provide recommendations to support the **biopharmaceutics classification of medicinal products** and recommendations to support the **waiver of bioequivalence studies**. This will result in the harmonisation of current regional guidelines/guidance and support streamlined global drug development.

ICH Q3D(R1) Guideline - Q3D(R1) Revision of Q3D Cadmium Inhalation PDE 

The **draft revised Q3D(R1) Guideline** published for regulatory public consultation in 2018 is a Quality guideline for the control of elemental impurities in drug products (medicinal products), and it establishes Permitted Daily Exposures (PDEs) for 24 Elemental Impurities (EIs) for drug products administered by the oral, parenteral and inhalation routes of administration. The revision aims to **harmonise the calculation method of the PDE level for Cadmium by inhalation**.

ICH S11 Guideline - Nonclinical Safety Testing in Support of Development of Paediatric Medicines 

The new **draft S11 ICH Guideline** published for regulatory public consultation in 2018 is proposed to provide direction on the **nonclinical safety studies** important to support a **paediatric development programme**. It will recommend standards for the conditions under which nonclinical juvenile animal testing is considered informative and necessary to support paediatric clinical trials, and also provide guidance on the design of the studies. This new ICH Guideline is expected to enable streamlined drug development and higher scientific rigor while minimizing the unnecessary use of animals.

3.3. New Harmonisation Activities

3.3.1. Approval of New Topics

In 2018 the ICH Management Committee and its New Topics Subcommittee assessed **16 New Topic proposals** which had been submitted by ICH Members and Observers by a mid-December 2017 deadline. Further to this, an assessment **of all proposals** was prepared for the Assembly, and a number of **New Topic proposals were recommended** by the ICH Management Committee.

Based on the ICH Management Committee assessment, the Assembly approved the following new harmonisation activities:

ICH M11 Guideline - Clinical electronic Structured Harmonized Protocol (CeSHarP) 

The **M11 new ICH Guideline** aims to provide comprehensive **clinical protocol organisation with standardised content**, with both required and optional components.

The guideline will outline two main sets of harmonised approaches: a template to include identification of headers, common text and a set of data fields and terminologies which will be the basis for efficiencies in data exchange, and a technical specification that uses an open, non-proprietary standard to enable electronic exchange of clinical protocol information.

- The Assembly adopted the M11 Concept Paper outline at its meeting in Kobe in June 2018, further to which an informal WG was established to finalise the Concept Paper and Business Plan which were then endorsed by the ICH Management Committee at its meeting in Charlotte in November 2018.
- The Assembly appointed PhRMA as Rapporteur.

ICH Q2(R2)/Q14 Guideline - Analytical Procedure Development and Revision of Q2 (R1) Analytical Validation

The **Q2(R2)/Q14 EWG** aims to develop a new ICH Quality Guideline, **ICH Q14**, on Analytical Procedure Development, and revise the **ICH Q2(R1) Guideline** on Validation of Analytical Procedures, with a view to potentially combine both documents into one, for simplification and clarity. The scope of the revision of **ICH Q2(R1)** will include **validation principles that cover analytical use of spectroscopic or spectrometry data** some of which often require multivariate statistical analyses. The **Q14 new ICH Guideline** is proposed to harmonise the **scientific approaches of Analytical Procedure Development,** and to provide the principles relating to the description of Analytical Procedure Development process.

- The Assembly adopted the Q2(R2)/Q14 Concept Paper outline at its meeting in Kobe in June 2018, further to which an informal WG was established to finalise the Concept Paper and Business Plan which were endorsed by the ICH Management Committee at its meeting in Charlotte in November 2018.
- The Assembly appointed MHLW/PMDA, Japan as Rapporteur.

ICH Q13 Guideline - Continuous Manufacturing of Drug Substances and Drug Products

The **Q13 new ICH Guideline** aims to capture key technical and regulatory considerations that promote harmonisation, including certain **Current Good Manufacturing Practices (CGMP) elements specific to Continuous Manufacturing (CM).** It will provide guidance to industry and regulatory agencies regarding regulatory expectations on the development, implementation, and assessment of CM technologies used in the manufacture of drug substances and drug products.

- The Assembly adopted the Q13 Concept Paper outline at its meeting in Kobe in June 2018, further to which an informal WG was established to finalise the Concept Paper and Business Plan which were endorsed by the ICH Management Committee at its meeting in Charlotte in November 2018.
- The Assembly appointed FDA, United States as Rapporteur.

ICH E14/S7B Q&As - Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs 

The **E14/S7B Q&As** will provide guidance regarding **best practices for the design, conduct, analysis, interpretation and reporting of in vitro, in silico and in vivo non-clinical assays** in order for these assays to influence non-clinical and clinical evaluations. The Q&As will be developed in two stages to allow for more rapid impact of novel approaches on S7B and subsequently E14 for evolving drug candidates, enabling a more efficient, comprehensive and mechanism-driven process. The objective of the first stage of the proposed harmonisation work is to provide clarity on how to standardise assays such as **multi-ion channel assays, in silico models, in vitro human primary and induced pluripotent cardiomyocyte assays and in vivo evaluation**, and apply these learnings to guide predictions and subsequent clinical assessment. These efforts will provide a customisable **non-clinical strategy that is more informative for clinical development**.

- At its meeting in Charlotte in November 2018, the Assembly endorsed the new area of work for the E14/S7B DG as per the E14/S7B Q&As Concept Paper, further to which the E14/S7B IWG was established.

ICH E20 Guideline - Adaptive Clinical Trials 

The new **E20 new ICH Guideline** aims to define a set of principles for **adaptive trial designs** that guide all aspects of design, conduct, analysis and interpretation that, when followed, are sufficient for regulatory approval. This document aims to **provide a broad overall definition of adaptive trials,** and an overview of types of adaptive trials used in drug development, including regulatory criteria for acceptability of adaptive trials especially for drug approvals. The document will also contain best practices, examples, and case studies to facilitate harmonised implementation.

The Assembly adopted the E20 Concept Paper outline at its meeting in Kobe in June 2018, with the delayed timeframe for establishment of an informal WG by March 2019 confirmed at the Assembly meeting in Charlotte in November 2018.

ICH M12 Guideline - Drug Interaction Studies 

The **M12 new ICH Guideline** aims to provide a consistent approach in **designing, conducting, and interpreting Drug-drug interactions (DDI) studies** that are to evaluate the potential for DDI during the development of a therapeutic product. Harmonising the expectations of the different regulatory agencies on the evaluations of in vitro and in vivo DDI studies can improve the risk-based approaches thereby increasing the safety of drugs and reducing the regulatory burden.

- The Assembly adopted the M12 Concept Paper outline at its meeting in Kobe in June 2018, with the delayed timeframe for establishment of an informal WG by March 2019 confirmed at the Assembly meeting in Charlotte in November 2018.

3.3.2. Other New Harmonisation Activities

In 2018, the following additional new harmonisation activities received the support of the Assembly:

ICH M7(R2) Q&As: Addendum to Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk

The **M7(R2) Q&As** will clarify and address Quality and Safety issues and concerns that have been identified from experience through implementation of M7 since its publication in 2014. This aims to facilitate communication between applicants and assessors. Topics to be discussed are additional clarification on the justification of control strategy for mutagenic impurities in the marketing authorisation dossier, organisation and depth of information reporting of individual mutagenic impurities, (Q)SAR systems, and other safety-related information.

- At its meeting in Charlotte in November 2018, the Assembly endorsed the new area of work of the M7(R2) Maintenance EWG as outlined in the revised Concept Paper which was approved by the ICH Management Committee, further to which the group's code was changed to M7(R2) Maintenance EWG/IWG.

ICH Q4B Maintenance Procedure

The **ICH Q4B Guideline on the Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions**, finalised in November 2007, describes a process for the evaluation and recommendation by the Q4B EWG of selected pharmacopoeial texts to facilitate their recognition by regulatory authorities for use as interchangeable in the Founding ICH regions and Canada. Following favourable evaluations, ICH issued 14 topic-specific annexes, the last of which was published in 2012, which include information about these texts and their implementation intended to avoid redundant testing by industry. The Q4B EWG was disbanded with the conclusion of this work.

- At its meeting in Charlotte in November 2018, the Assembly approved a proposal from the Pharmacopoeial Discussion Group (PDG) for a new Q4B Maintenance Procedure of the ICH Q4B Annexes. The new process will be triggered by PDG's sign-off of a revised text which is the subject of a Q4B Annex. The PDG will then compare the corresponding current ICH Q4B Annex, the PDG sign-off text as well as the corresponding European Pharmacopoeia (Ph. Eur.), Japanese Pharmacopoeia (JP) and United States Pharmacopoeia (USP) chapters as published in the respective Pharmacopoeias. Other pharmacopoeias will be informed of the ongoing review via the contact list of the International Meeting of World Pharmacopoeias (IMWP). Annex 5 of the SOP of the WGs was revised to reflect the new maintenance procedure and describes how this process follows the usual ICH Step process.

3.3.3. Strategic Reflection Papers

In 2018, the ICH Management Committee supported the following activities in relation to the Strategic Reflection Papers aimed at identifying potential areas of work:

- Further to Assembly endorsement in June 2018, the ICH Reflection Paper on **Advancing Biopharmaceutical Quality Standards to Support Continual Improvement and Innovation in Manufacturing Technologies and Approaches** was published on the ICH website in November 2018. In addition, in June 2018 the ICH Management Committee supported the establishment of the Informal Quality Discussion Group (IQDG) with a 2-year mandate during which it would review the need for new ICH Quality-related harmonisation work and review and recommend training needs related to the content and/or implementation of ICH Quality guidelines. The remit document for the IQDG was approved by the ICH Management Committee in Charlotte in November 2018 and published on the ICH website as a part of the Reflection Paper. A call for expression of interest for Members and Observers to nominate experts and to nominate a Rapporteur and a Regulatory Chair of IQDG was subsequently issued by the ICH Secretariat as per the applicable procedures.
- Further to Assembly endorsement of the Reflection Paper on **Further Opportunities for Harmonisation of Standards for Generic Drugs** in Charlotte in November 2018, the ICH Management Committee agreed that it would be published on the ICH website along with the remit of the Informal Generic drug Discussion Group (IGDG), once approved.

In 2018, the ICH MC also provided input into several other Reflection Papers being developed by Members which may potentially be submitted to the Assembly for consideration in 2019

3.4. Implementation of ICH Guidelines

At *Step 5* of the ICH process, harmonised ICH Guidelines are implemented by ICH Regulatory Members and Observers within their respective country/region. This is in line with the ICH Articles of Association and the aim and intention that **all ICH Regulatory Members should implement all ICH Guidelines**. At the time of Membership application to ICH, each Regulator is expected to have implemented the **"Tier 1" ICH Guidelines**: **Q1, Q7 and E6,** and have specific plans with identified milestones and timeframes for implementation of the following **"Tier 2" ICH Guidelines** within the next five years: **E2A, E2B, E2D, M4 (CTD) and M1 (MedDRA)**. The other, remaining ICH Guidelines should be implemented in the near term and as soon as possible.

According to ICH Regulatory Member reporting, implementation activity by ICH Regulatory Members was high during 2018, with ***Step 5* (implementation)** of the ICH process being **reached 56 times** for new and existing ICH Guidelines by both new and old ICH Members.

ICH Guideline implementation information is published on the ICH website www.ich.org under each ICH Guideline section for Founding and Standing Regulatory Members. Information from new Regulatory Members will be added in 2019 as part of a website update which will enable optimal presentation of this information.

To further facilitate the goal of enabling the **Assembly to monitor ICH Guideline implementation and the progress of international harmonisation**, and to achieve a common understanding on the meaning of implementation, the following activities received the support of the Assembly in 2018:

- The Assembly approved new definitions to be used with respect to the degrees of implementation of and adherence to ICH Guidelines, developed by an ICH Management Committee Implementation Subcommittee which recognised the need to have a common view on different degrees of implementation.
- The Assembly supported the scope and design of the Phase 2a Study for an ICH-driven survey on monitoring the Implementation of and Adherence to ICH Guidelines within Regulatory Member and Observer countries/regions, led by an independent third party with the aim of launching the survey early 2019 and providing the results to the Assembly at the June 2019 ICH meeting. The agreed scope of the survey includes Tier 1 and Tier 2 ICH Guidelines, as well as Tier 3 ICH Guidelines identified as a priority in terms of the Implementation survey (M3, M8 and E17).

3.5. Training on ICH Guidelines

As part of its effort to achieve **global harmonised implementation of ICH Guidelines,** ICH is working on ensuring that high quality training is available based upon scientific and regulatory principles outlined in the ICH Guidelines. Training materials developed by/with ICH can be accessed with the respective ICH Guideline as they become available.

3.5.1. ICH Training Strategy

In 2018, work was further progressed by an ICH Management Committee Training Subcommittee on an ICH training strategy, by further developing the work with selected Training Providers to promote their delivery of in-person training programmes on ICH Guidelines for regulators, industry and other stakeholders involved in drug development. In 2018 the following **6 training programmes** submitted by Training Providers were supported as ICH Recognised Training Programmes:

- CNDA/DIA Joint ICH Day, Beijing, China, 22 May 2018;
- Northeastern University, ICH Q1 Stability Training, Brasilia, Brazil, 7-8 August 2018;

- Northeastern University, ICH Q1 Stability Training, Boston, MA, USA, 10-12 October, 2018;
- MRCT Center and Health Canada, Canada, ICH GCP and MRCT Training: ICH E6(R2) and ICH E17, Ottawa, Ontario, Canada, 26-28 February 2019;
- CoRE - Duke NUS, ICH Workshop Chemistry, Manufacturing and Controls (CMC), Singapore, 21-22 March 2019;
- Chinese Pharmaceutical Association (CPA), ICH M4 Training Workshop, Beijing, China, first half of 2019.

Another focus of the Training Subcommittee in 2018 was to seek development by Training Providers of at least **one introductory** and **one in-depth** online training for **Tier 1 & 2 Guidelines** (except MedDRA) in English by 2021. In order to reach this objective, the Training Subcommittee selected the following Training Providers[2] in 2018:

- NEU for the Q1 ICH Guideline;
- PDA/PICs for the Q7 ICH Guideline;
- Harvard MRCT for E6 ICH Guideline;
- AHC for E2 series of ICH Guidelines;
- RAPS for M4 ICH Guideline.

The training materials will be made available on the website of the respective ICH Training Provider once they are finalised. A link to each training material will be posted on the ICH website.

The following additional decisions were taken by the Assembly and/or ICH Management Committee in 2018 in relation to training activities:

- The ICH Management Committee supported the following documents in regards to the Training Providers' process: ICH Training Provider application form, Procedures for Organisations Interested in Developing an ICH Recognised Training Programme and revised ICH Training Programme Providers' Eligibility Criteria;
- The ICH Management Committee endorsed the list of **Tier 3 ICH Guidelines prioritised for training purposes**[3], noting that the list should be revised by the Training Subcommittee and submitted for ICH Management Committee approval on a yearly basis;
- The ICH Management Committee supported the revisions to the ICH Training Subcommittee mission statement and its subsequent publication on the ICH website.

The ICH Management Committee furthermore discussed exploring the use of ICH funds to support various additional training activities. At the end of 2018 a Call for Expression

[2] ICH Training Programme Providers Eligibility Criteria: https://www.ich.org/fileadmin/Public_Web_Site/Training/ICH_TrainingProviderEligibilityCriteria_2018_1026.pdf

[3] Prioritised Tier 3 ICH Guidelines for Training Purposes: ICH E2 (E2C(R2), E2E, E2F), ICH E5, ICH E17, ICH Q3 (Priority Q3C), ICH Q5 (priority Q5E), ICH Q6 (A & B), ICH Q8-11 as a package, ICH M3(R2), ICH M7(R1), ICH M8, ICH S6(R1).

of Interest from ICH Regulatory Members interested to receive support for the organisation of training on ICH Guidelines in 2019 was launched. And consideration was also given by the ICH Management Committee to the development of a new training process in 2019 in which ICH might potentially engage non-profit training organisations/institutions to: develop training materials for ICH ownership; deliver training; and provide consultancy services to ICH.

3.5.2. Training Materials Developed by ICH Working Groups

Support was also provided by the Assembly and ICH Management Committee in 2018 for several WGs to develop training materials to help **assist understanding of new concepts** and implementation of their respective ICH Guidelines. Please note that finalised materials are /will be made available on the ICH website.

In 2018, the following received the support of the Assembly and/or ICH Management Committee:

- **ICH E9(R1) Draft Guideline – Addendum: Statistical Principles for Clinical Trials:** Following the Assembly's approval, the **ICH E9(R1) *Step 2* Training Material** produced by the ICH E9(R1) Expert Working Group was published on the ICH website in August 2018. It was intended to accompany the Draft ICH E9(R1) Addendum and to support the scientific community in the comprehension of a new framework to define estimands based on the trial objective and considering intercurrent events. The training material is accompanied by examples and case studies.
- **ICH Q11 Questions and Answers (Q&As) on the Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities):** A first supportive slide deck training presentation developed by the Implementation Working Group was agreed by the ICH Management Committee at its meeting in Kobe in June 2018 and published on the ICH website after expert sign-off in July 2018. A training material based upon the slide deck, will be developed as a video in early 2019.
- **E17 ICH Guideline on Multi-Regional Clinical Trials (MRCT):** Following the adoption of the **E17 Guideline,** an Implementation Working Group (IWG) was established to promote the efficient and consistent implementation of the guideline in the context of an evolving drug development environment, in order to facilitate more appropriate MRCT execution and greater overall efficiency in drug development, resulting in fewer redundancies in drug development programmes and facilitating better regulatory decision-making. The E17 IWG is developing **innovative training materials on the E17 Guideline,** by making effective use of multimedia materials and content delivery methods as appropriate.

In addition, Founding Regulatory Member FDA, United States has been able to provide the support of its studios for the production of ICH E9(R1), ICH Q11 and ICH E17 training videos.

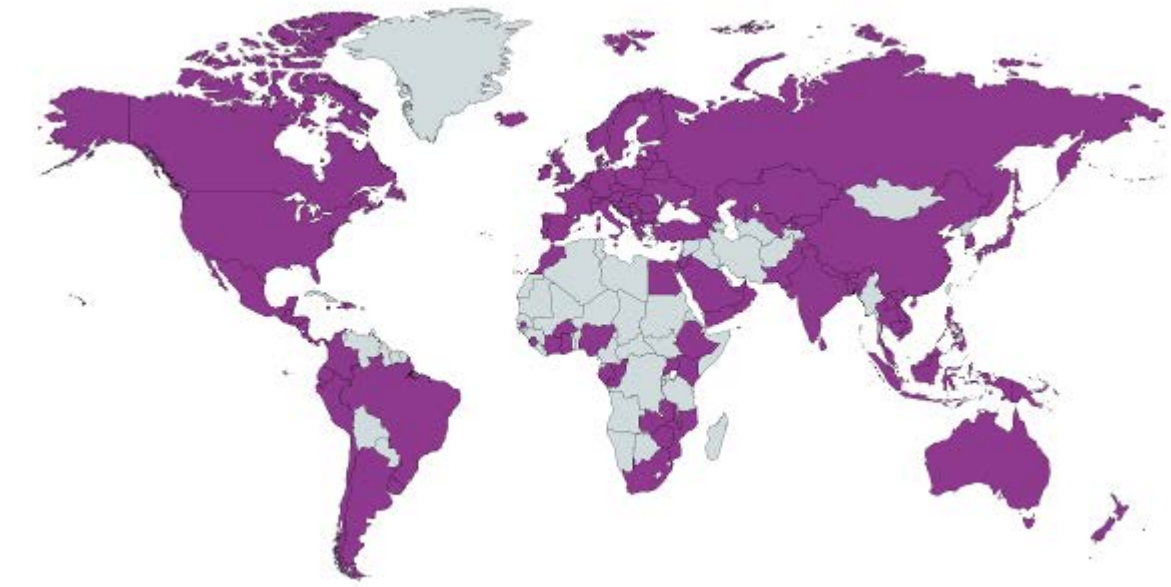
3.5.3. Working Group *Step 2/Step 4* Presentations

In line with ICH procedures, when an ICH Guideline reaches *Step 2b* or *Step 4* of the ICH process, each ICH WG develops a presentation to be included by the ICH Secretariat on the ICH website. In 2018, the Assembly supported the revised templates for ICH WG *Step 2* Informational Presentation and *Step 4* Introductory Training Presentation, which were made available to ICH WGs.

3.6. MedDRA Activities

MedDRA, the **Medical Dictionary for Regulatory Activities**, is a rich and highly specific standardised medical terminology developed by ICH to facilitate sharing of regulatory information internationally for medical products used by humans. It is used for **registration, documentation and safety monitoring of medical products** both before and after a product has been authorised for use.

2018 was a successful year of continued growth and development of MedDRA which now has **over 5,500 subscribing organisations in 120 countries worldwide**, which represents an approximate 10% growth compared to the previous year. The table below shows the countries with MedDRA Subscribing Organisations.



Countries with MedDRA Subscribing Organisations, as of 2018

3.6.1. Overview of 2018 MedDRA Management & Key Decisions

The MedDRA Management Committee is responsible for overseeing the main activities of the MSSO (Maintenance and Support Services Organisation), as well as providing oversight and direction to the MedDRA Secretariat. (MedDRA Secretariat implementation of key MedDRA Management Committee decisions are referred to in Section 5.6 below)

The following key decisions were taken in 2018 related to MedDRA's management:

Financial:

- The MedDRA Management Committee supported the **2019 Budget** including the **2019 MSSO Subscription Fees** for presentation to the Assembly, with the granting of a **5% reduction for the 2019 subscription rates for all users**. The 2019 Budget and Subscription Fees were subsequently approved by the Assembly.
- The MedDRA Management Committee approved the **2019 MSSO Business Plan**.
- The MedDRA Management Committee supported that the MSSO proceed in 2018 with the recruitment of 7 new MSSO staff to provide local support in various countries and to provide additional IT support related to Mapping and to Terminology Maintenance. This proposal was subsequently approved by the Assembly.

Operational:

- The MedDRA Management Committee supported the 2019 Annual MedDRA Work Plan for submission to the Assembly, which was subsequently approved by the Assembly.
- The MedDRA Management Committee supported the implementation of a **MedDRA trademark strategy** by the MedDRA Secretariat for the registration of the MedDRA name mark and the MedDRA logo (device) mark in a broad set of countries.
- Noting that the ICH Management Committee had approved a change in the ICH Employee Handbook to allow for 3 signatories from the ICH Secretariat, the MedDRA Management Committee agreed to name Dr. Anne Latrive as an additional ICH MedDRA signatory (with joint by two signatory rights), alongside existing ICH Secretariat signatories.

MSSO/JMO Sub-Licensing Agreement:

- The MedDRA Management Committee in coordination with the Japanese Management Board (JMB) supported the removal of the fee for MSSO Subscribers to access the Japanese translation of MedDRA maintained by the Japanese Maintenance Organisation (JMO), in line with the MedDRA Management Committee's policy that all translations should be accessible as part of a standard MedDRA subscription.

Facilitating Global Use of MedDRA:

- In addition to MedDRA translations already newly under development, namely Russian and Korean, the MedDRA Management Committee also approved the development of a Brazilian Portuguese MedDRA translation in coordination with ANVISA, Brazil, with development of the translation by a translation firm under the MSSO, with review and input into the translation by ANVISA, Brazil.
- The MedDRA Management Committee agreed on the provision in 2018 of MSSO local support in additional countries and regions which have an increasing number of subscribers, namely China and India in addition to the Republic of Korea and Latin America which had been approved in 2017, which will see MSSO providing in-country/region MedDRA experts who speak the local language.
- The MedDRA Management Committee agreed to provide MFDS, Republic of Korea a MedDRA Special License to be used by companies having a turnover under the threshold limit of the MSSO Commercial Level 1 company. Special Licenses allow MedDRA's use without charge in a non-downloadable format within a Regulatory Agency's electronic tools designed to allow companies to meet their regulatory reporting.
- As part of the efforts to facilitate the use of MedDRA through mapping with other terminologies, the MedDRA Management Committee supported the necessary formalities be undertaken for ICH become a partner in the Innovative Medicines Initiative (IMI) WEB-RADR 2 Project, which is a project composed of several Work Packages (WP). ICH will participate specifically in WP4, which focuses on a bi-directional mapping between MedDRA and SNOMED terminologies. A revision to the MSSO Contractor Service Agreement was also approved by the MedDRA Management Committee in support of this activity. Furthermore, the MedDRA Management Committee also supported that a discussion be initiated with WHO for the development of a mapping between MedDRA and ICD 10/11.

Development of SMQs:

- The MedDRA Management Committee approved **1 new Standardised MedDRA Query (SMQ)** – the SMQ Hypokalaemia, for release to MedDRA users. The addition of this new SMQs resulted in a **total of 103 SMQs** developed to-date by a CIOMS WG on SMQs.
- The MedDRA Management Committee supported the renewal for another year of the Memorandum of Understanding ICH has with the CIOMS to develop SMQs.
- The MedDRA Management Committee supported that MSSO continue consulting the PtC WG on new SMQ requests and coordinating with the CIOMS WG on SMQs (if available) for development of any approved requests, in consideration that the majority of common medical concepts have already been developed as SMQs.

3.6.2. Oversight of 2018 MedDRA MSSO Activities

A summary is provided as follows on the main activities of the MSSO related to MedDRA development and support of MedDRA users in 2018, which were overseen by the MedDRA Management Committee:

- Conduct of **98 training courses** for MSSO MedDRA users, including regulators, including **27 webinars** and **71 face-to-face training courses** provided in multiple locations worldwide, including Canada, Central America, China, Colombia, Europe, Japan (via the JMO), Mexico, Republic of Korea and the United States.
- **Cooperation with the WHO and its Collaborating Centre, the Uppsala Monitoring Centre (UMC)** which resulted in a further joint MSSO MedDRA and UMC WHO-Drug user group meeting in Bengaluru, India (February 2018), and a MedDRA presentation at the 2018 WHO Annual Meeting of National Pharmacovigilance Centres (NPCs) in Geneva, Switzerland (November 2018).
- Liaison with the **International Medical Device Regulatory Forum (IMDRF)** regarding considerations for addressing the differences between MedDRA and a draft IMDRF term list on Patient Problems as well as considerations for the maintenance of the list.
- Support of the work of the **ICH M1 PtC WG** to (i) update with each MedDRA release the PtC documents on Term Selection and Data Retrieval and Presentation, (ii) develop a **condensed version of the PtC documents,** which is intended to support the global implementation and use of MedDRA and published on the MedDRA website in November 2018 in all languages except English and Japanese (as these versions will continue to be maintained as the full reference documents), and (iii) develop a **companion document to the PtC documents,** which was endorsed by the MedDRA Management Committee and published on the MedDRA website in June 2018.
- Consolidation of all four **MedDRA Best Practice documents** into a single document available in all 11 MedDRA translation languages, which was published on the MedDRA website.
- Provision of assistance to Regulators expressing interest in MedDRA or working towards a MedDRA translation in their national language.
- Participation as ICH's contractor in the IMI WEB-RADR 2 Project in WP4, which focusing on a bi-directional mapping between MedDRA and SNOMED terminologies.
- Initiation of work on the development of additional IT support tools for MedDRA users including a Mobile Web-Based Browser and an online chat function as part of the help-desk service.

4. 2018 Overview of Meetings & Planning

4.1. 2018 Meetings

In 2018, ICH activities were progressed via face-to-face meetings and teleconferences. ICH's biannual meetings see the meeting of WGs for 3.5-5 days in parallel of Assembly, ICH Management Committee, and MedDRA Management Committee meetings, and are important for progressing ICH's work.

The first of the biannual meetings of the year took place in **Kobe, Japan** on 2 to 7 June, and the second meeting in **Charlotte, North Carolina, United States** on 10 to 15

November, with ICH Founding Industry Members JPMA and PhRMA playing an important role in ensuring the smooth running of meetings in their respective regions. With ICH's growing Membership and Observership, between **350 - 400 experts** attended each of the meetings.

The reports of Assembly and ICH Management Committee face-to-face meetings and teleconferences from 2018 are made available on the **ICH website**.

Details on 2018 meetings are provided as follows:

Assembly Meetings

- The **Assembly met twice during 2018**, at the time of ICH's biannual meetings: on 6 to 7 June and on 14 to 15 November.
- In June 2018 the Assembly was chaired by Mrs. Lenita Lindström-Gommers (EC, Europe Chair) and Dr. Toshiyoshi Tominaga (MHLW/PMDA, Japan, Vice-Chair) who were elected in November 2017 for a second 2-year term. Following Dr. Tominaga's resignation from the position in mid-2018, Dr. Nobumasa Nakashima from MHLW/PMDA, Japan was appointed interim Assembly Vice-Chair to serve until the November 2018 meeting in Charlotte, which he chaired along with Mrs. Lindström-Gommers. In November 2018 the Assembly elected Dr. Petra Doerr (Swissmedic, Switzerland) as Assembly Vice-Chair and supported that she would serve for a one-year term.
- The ICH Management Committee supported the participation of Ad-Hoc Observer Delegates to ICH Assembly meetings in 2018, one from NPRA, Malaysia and the other from TITCK, Turkey, in the ICH Assembly meeting in Kobe, and one Ad-Hoc Observer Delegate from NorthEastern University in the ICH Assembly meeting in Charlotte.

ICH Assembly, Kobe
June 2018

ICH Assembly, Charlotte, NC, USA
November 2018

ICH Management Committee Meetings

- The ICH Management Committee met several times throughout the year:
  - **10 times via teleconference** on the following dates: 24 January, 20 March, 22 March, 10 April, 25 April, 15 May, 19 September, 20 September, 10 October, 22 October.
  - **3 face-to-face meetings:** twice during ICH's biannual meetings in June and November, and once during the interim meeting in March in London, United Kingdom.
- Additionally, approximately 20 ICH Management Committee Subcommittee teleconferences were held (on New Topics, Implementation, Training, Communication and Financials), and a face-to-face meeting of 4 Subcommittees organised during the interim meeting in March in London, United Kingdom.
- In June 2018 the ICH Management Committee was chaired by Dr. Theresa Mullin (FDA, United States, Chair) and Dr. Toshiyoshi Tominaga (MHLW/PMDA, Japan, Vice Chair) who were elected in November 2017 for a second 1-year term. Following Dr. Tominaga's resignation from the position in mid-2018, Dr. Nobumasa Nakashima from MHLW/PMDA, Japan was appointed interim Assembly Vice-Chair to serve until the November 2018 meeting in Charlotte, which he chaired along with Dr. Mullin. In November 2018 the ICH Management Committee re-elected Dr. Mullin as Chair and elected Dr. Nakashima as Vice-Chair to serve a 1-year term.

MedDRA Management Committee Meetings

- The MedDRA Management Committee met several times:
  - **4 times via teleconference** on 19 April, 23 August, 14 September, and 3 October.
  - **2 times face-to-face** during ICH's biannual meetings on 2 to 3 June and 10 to 11 November.
- With the stepping down of MedDRA Management Committee Chair Ms. Sommerer (Health Canada, Canada) in early 2018, Ms. Heather Morrison (Health Canada, Canada) assumed the role of Interim Chair until elections were held at the meeting in Kobe, Japan in June 2018 where Mr. Mick Foy (MHRA, UK) was **elected** by the MedDRA Management Committee as Chair for a 1-year term.

ICH Working Group Meetings

A total of **11** and **13 WGs met face-to-face** respectively at the June and November 2018 biannual meetings, and are detailed in Annex VI.

4.2. Planning of Future ICH Meetings

In 2018, the ICH Management Committee took decisions regarding the organisation of future ICH meetings. **Key decisions** are outlined below:

- The ICH Management Committee supported the selection of a Professional Conference Organiser (PCO) for organisation of ICH meetings from 2019 onwards.

- The ICH Management Committee supported **Amsterdam, the Netherlands** as the location for the June 2019 meeting, as the first meeting to be organised by the ICH in collaboration with the PCO, and **Singapore** as the location for the November 2019 meeting.
- The ICH Management Committee supported a new schedule for the ICH biannual meeting week with the week to start on Sunday, and the Assembly meeting taking place on Tuesday and Wednesday. The new schedule will be implemented for meetings starting from November 2019.
- The ICH Management Committee agreed on the following dates for the 2020 and 2021 meetings:
  - From Sunday, 24 May to Thursday, 28 May 2020;
  - From Sunday, 15 November to Thursday, 19 November 2020;
  - From Sunday 30 May to Thursday 3 June, 2021.
- The ICH Management Committee agreed that as part of the selection process, ICH meetings will be held with a three-region rotation (North America/South America, Europe/Africa, Asia) and that within a region with more than one ICH Member, the PCO is to identify the three best options (based on the agreed selection criteria) looking across ICH Member countries/regions, with one of the options to come from the country/region of a Founding or Standing ICH Member, with the ICH Management Committee to take a final decision.
- The ICH Management Committee agreed to an interim meeting to take place on 1-2 April 2019 in Brussels, Belgium, hosted by EC, Europe.

5. 2018 ICH Operational Matters

5.1. ICH Articles & Procedures

5 Documents support the governance of the ICH Association and were each updated in 2018 in view of experience gained with the evolution of the operations of the ICH Association: the ICH Articles of Association, the Assembly Rules of Procedures (RoP), the ICH Management Committee RoP, the MedDRA Management Committee RoP and the Standard Operating Procedures (SOPs) of the ICH WGs. Each of these documents is available on the ICH website.

The following highlights the key decisions taken in 2018 regarding these documents:

ICH Articles of Association

- The Assembly approved several refinements to the ICH Articles of Association in June 2018, which included: revisions to the ICH Membership/Observership criteria for Regional Harmonisation Initiatives and their respective individual members with a view to avoiding double representation in ICH; and changes to management of the size of WGs by revising the process for appointing experts.

Assembly RoP

- The Assembly approved several amendments to the Assembly RoP in 2018, including several in June 2018 aligned with the changes made to the ICH Articles of Association (see above for details).The Assembly RoP was further revised in November 2018 to clarify the process for the replacement of Assembly Chair and Vice-Chair in the event of his/her resignation, and to maintain the synchronisation of the terms of the Assembly Chair and Vice-Chair; to provide clarifications regarding confidentiality; the timing of the press release; and clarification of the process for appointment of Rapporteurs and Regulatory Chairs.

ICH Management Committee RoP

- The ICH Management Committee approved several updates to their RoP in 2018, including: clarifications regarding the participation of Assembly Members/Observers to DGs; the process for the replacement of the Chair and Vice-Chair in the event of his/her resignation; clarification of the process for appointment of Rapporteurs and Regulatory Chairs; and the recording and communication of decisions of the ICH Management Committee. Moreover, minor revisions were made to provide consistency with the current approved process for the selection of New Topic proposals and with the current decision-making process.

MedDRA Management Committee RoP

- The MedDRA Management Committee approved changes to its RoP in 2018 to clarify procedures related to the respective roles of the ICH Management Committee, MedDRA Management Committee and ICH Assembly with respect to MedDRA financial matters; and the procedure regarding use of the MedDRA logo.

SOPs of the ICH Working Groups

- The ICH Management Committee approved 4 versions of the SOPs for WGs in 2018. Version 4.1 in March, Version 5.0 in June, Version 6.0 in October and Version 7.0 in November 2018. Version 4.1 included a minor edit to the Business Plan template in Annex 10. Version 5.0 included changes proposed for consistency with revisions to the Articles of Association and the Assembly RoP, as well as minor edits proposed by the ICH Secretariat. Version 6.0 included further changes based on the need for clarity and consistency between the ICH procedure documents such as: clarifications regarding the participation of Assembly Members to DGs; the management of the size of Working Groups; the process for endorsement of new activities; and clarification of the process for appointment of Rapporteurs and Regulatory Chairs. Version 7.0 included further clarifications of the process for appointment of Rapporteurs and Regulatory Chairs.

5.2. ICH Funding

ICH Financial Audit

In June 2018 **the Assembly approved the 2017 Audited Accounts and Financial Statements of the ICH Association**, supporting their submission along with ICH's 2017 tax return in July 2018. Furthermore, the Assembly took the decision to re-appoint Moore Stephens Refidar SA for a further two years to perform the audit of the 2018 and 2019 financial statements of the ICH Association.

ICH Funding

2018 saw the implementation of Membership Fees for all ICH Members in line with the decision taken by the Assembly in 2016 and payable as follow:

Membership Category	Membership Fee (CHF / Swiss Franc)
Founding Regulatory Member	CHF 233,000
Founding Industry Member	CHF 233,000
Standing Regulatory Member	CHF 96,000
Regulatory Member	CHF 20,000
Industry Member	CHF 20,000
Standing Observer	N/A
Observer	N/A

2018 Membership Fees

In November 2018, the **Assembly approved the updated 2019 ICH Budget** and confirmed that the amount of the 2019 Membership Fees would remain unchanged compared to 2018. As part of the 2019 ICH Budget, the Assembly supported increasing the funding available to support the organisation of the biannual ICH meetings, which will now also include a buffer to accommodate currency fluctuations. This decision was linked with the fact that Kobe and Charlotte meetings came in over budget. The ICH Management Committee was supportive that the ICH Secretariat reimburse the respective meeting hosts the additional costs and supported requesting the Assembly to increase the budget in future years. Furthermore, the Assembly supported the provisional 2020 ICH Budget and 2020 Membership Fees, with no change in the fees compared to 2019.

Information can be found on the ICH website regarding the 2019 ICH Budget and Membership Fees.

MedDRA Funding

MedDRA activities are self-financed through the collection of annual subscription fees from organisations which are subscribers to MedDRA.

In February 2018, the **Assembly approved a revision to the 2018 MedDRA Budget** in view of a need identified by the MedDRA Management Committee to support expanded

2018 activities related to the increasing global uptake of MedDRA, including costs related to local support and trademark registrations. In November 2018, the **Assembly approved the updated 2019 MedDRA Budget**, which included a **5% reduction across all MSSO MedDRA Subscription Fee levels**.

Information can be found on the ICH website regarding the 2019 MedDRA Budget.

Surplus Funds

The ICH Assembly noted the status of surplus ICH funds in 2018, including planned usage for contingencies, and considerations related to multi-year ICH Association budget needs. In November 2018, the Assembly approved the use of surplus funds in 2019 in line with the 2019 MedDRA Budget.

The Assembly furthermore noted the ICH Management Committee's intent to develop a plan regarding use of surplus funds to further strategic activities such as training, outreach and stakeholder engagement.

5.3. ICH Communication

In 2018, work was progressed in view of further **enhancing communication and transparency with stakeholders** on ICH activities.

The following should be noted in relation to communication activities in 2018:

- The ICH Management Committee supported the further implementation of the **ICH Transparency Policy**, which included publication on the ICH website of **photographs and biographies** of the Member Representatives and Observer Delegates of the ICH Management Committee, MedDRA Management Committee and Assembly, as well as those of ICH Coordinators and the ICH Secretariat; publication of WG Expert Lists and Work Plans, and ICH documents: Agendas and Reports, Budgets etc.
- The ICH Management Committee supported the development of the GCP Renovation Stakeholder Engagement Plan for 2018-2019 led by the E8(R1) EWG.
- The Assembly supported the following future activities of ICH Secretariat: improvements to the ICH website to be implemented in early 2019, maintenance of the ICH transparency policy for publication of agendas, reports and other WG documents on the ICH website, ICH presence on online platforms such as Wikipedia, as well as plans to update the ICH history webpage and develop a flyer about ICH for dissemination purposes.
- The ICH Management Committee reviewed a draft article in 2018 which was developed by Mrs. Lenita Lindström-Gommers (ICH Assembly Chair) and Dr. Theresa Mullin (ICH Management Committee Chair) entitled "ICH: Recent Reforms as a Driver of Global Regulatory Harmonization and Innovation in Medical Products" and planned for submission to the journal Clinical Pharmacology & Therapeutics.
- The ICH Management Committee noted the publication of a book in Japanese developed by MHLW/PMDA, Japan and JPMA, which summaries ICH activities and ICH Guidelines.

ICH Regional Public Meetings

While ICH no longer organises the large international ICH Conferences that it did between 1991 and 2003, public meetings are still considered important for disseminating information of ICH activities. ICH Members periodically hold **dedicated ICH regional public meetings**, either independently or in collaboration with other non-profit organisations. Information on these meetings is made available by the ICH Secretariat on the ICH website. It should be noted, that in addition to these regional public meetings, ICH Members were also active in finding opportunities to present on ICH and its Guidelines in other fora in 2018.

In 2018, Members held the following ICH regional public meetings:

ANVISA, Brazil

In 2018 ANVISA, Brazil organised a meeting to raise awareness of ICH Guidelines: in May on the Q12 draft ICH Guideline, and in November on the M9 draft ICH Guideline and its public consultation in Brazil. Moreover, in October ANVISA, Brazil hosted an ICH Public Meeting to raise awareness and share information on the advances achieved by the Working Groups of the ICH and on the process of implementation of ICH Guidelines by ANVISA, Brazil.

MHLW/PMDA, Japan and JPMA

JPMA in collaboration with MHLW/PMDA, Japan and PMRJ organised 38th and 39th ICH Public Meetings in Japan respectively on 18 July and 14 December to report on the preceding ICH meetings.

MFDS, Republic of Korea

MFDS, Republic of Korea held two ICH Public Meetings with stakeholders: the first in May 2018, and the second in October 2018 to share with Regulators and Industry the main results of the ICH Assembly meeting in June and the major agenda items of the upcoming ICH Assembly meeting in November.

FDA, United States & Health Canada, Canada

Health Canada, Canada and the FDA, United States held joint public meetings ahead of each of the 2018 ICH meetings. The first was held in Silver Spring, MD, USA on 6 April, and the second was held in Ottawa, Canada on 17 October.

5.4. Elected ICH Management Committee Representatives

In accordance with the ICH Articles of Association, in one of the remaining steps of implementing the 2015 reforms of ICH, the Assembly elected additional members to the ICH Management Committee in June 2018.

The following Regulatory Member Applicants were elected as ICH Management Committee Elected Representatives:

- Mr. Xiaoling Qin and Mr. Siyuan Zhou from NMPA, China;

- Dr. Nakyung Kim and Dr. Won Sik Lee from MFDS, Republic of Korea;
- Ms. Siew Wei Chua and Dr. Dorothy Toh from HSA, Singapore.

The following Industry Member Applicants were elected as ICH Management Committee Elected Representatives:

- Ms. Lila Feisee and Dr. Wassim Nashabeh from BIO;
- Dr. Nick Cappuccino and Ms. Beata Stepniewska from IGBA.

The new Elected Representatives will also have the opportunity to participate in any Subcommittees and DGs set-up under the ICH Management Committee.

5.5. Cooperation with the IPRP

Further to the signing of a Memorandum of Understanding (MoU) between ICH and the IPRP (International Pharmaceutical Regulators Programme) in January 2018, the ICH Secretariat initiated the provision of support services to the IPRP, which are funded by IPRP Members and conducted separately from the support of ICH activities. IPRP is a venue which addresses the increasingly complex global regulatory environment, facilitates the implementation of ICH and other internationally harmonised technical guidelines for pharmaceuticals for human use, promotes collaboration and regulatory convergence, and contributes to the coordination of a range of international efforts related to regulation of medicinal products for human use.

In June 2018, the ICH Assembly further approved the renewal of the MoU for one year so that the ICH Secretariat would continue the provision of support services to the IPRP for the year 2019.

5.6. ICH Secretariat

Staffing

The following highlights key points and decisions related to ICH/MedDRA Secretariat staffing in 2018:

- Secretariat staffing was planned at **7 FTEs (Full Time Equivalents) for 2018** (compared with 6 FTE in 2017), allocated between ICH (~4.6 FTEs) and MedDRA (~1.9 FTEs) activities, as well as IPRP support (~0.5 FTEs). The Secretariat however operated at less than full capacity in 2018, with approximately 4 FTEs in the first half of the year and 6 FTEs in the second, due to delays in the hiring of new staff as well as staff leave.
- The year saw the hiring in May 2018 of Ms. Nadia Myers Biggs, who filled a vacant Manager position, and Ms. Nikoleta Luludi who filled a newly created Project Coordinator position.

Final Step in the Set-up of Fully Operational Independent ICH Secretariat

The completion of the transfer of assets in November 2017 to the ICH Association from IFPMA, as trustee of the former ICH (International Conference on Harmonisation)

Steering Committee, paved the way for the ICH Secretariat to relocate offices in April 2018 from its co-location with IFPMA, and enabled the completion of some final administrative steps. Key activities undertaken by the ICH Secretariat in this regard included:

- Entering into a multi-year rental agreement for an office located in Geneva, Switzerland, with arrangement of the required bank guarantee, as well the monthly rental of staff parking spaces.
- Organising office relocation in April 2018 with set-up of new office infrastructure, including: installation of internet and phone lines; acquiring phones and phone numbers; photocopier rental; purchasing of furniture, office equipment and supplies; opening of a post office box; and adjustment of office and content related insurances.
- Organising data migration from old to new server, with implementation of back-up system, contracting of IT support, and acquiring the necessary IT licences, certificates etc.
- Putting in place various service provider contracts for items including: phone, internet, webconferencing, cleaning service, travel support etc.
- Setting-up of accounting system with contracted fiduciary firm.
- Seeking assignment of trademarks with the competent trademark authorities in each of the jurisdictions where a MedDRA trademark was registered by IFPMA in its capacity as trustee with a view to having all trademarks assigned to ICH ownership in 2019.

2018 ICH Secretariat Key Activities

The following outlines key activities undertaken by the ICH Secretariat in 2018 in accordance with its responsibilities for day-to-day ICH management, WG support, and the support of the Assembly, the ICH Management Committee and the MedDRA Management Committee and the implementation of their respective decisions and directives.

2018 Day-to-Day Management Key Activities:

- **Preparing agenda papers and reports** for the biannual face-to-face meetings of the Assembly, the ICH Management Committee and the MedDRA Management Committee in Kobe, Japan in June 2018 and in Charlotte, North Carolina, United States in November 2018, and in March 2018 for an interim ICH Management Committee/New Topics, Implementation, Training and Communication Subcommittee meeting in London, United Kingdom; as well as for the following **teleconferences** which were organised by the Secretariat in 2018: **10** ICH Management Committee teleconferences, in addition to support of approximately **20** ICH Management Committee Subcommittee teleconferences; **2** ICH Coordinator teleconferences; and **4** ICH MedDRA Management Committee teleconferences.
- **Supporting ICH harmonisation activities** and the work of **25 ICH WGs** in 2018, including keeping up-to-date membership lists and establishing 3 new WGs in 2018.
- **Providing support and input for the work of the ICH Management Committee Subcommittees** on: Financials; Training; Communication; Membership; and New

Topics, and assuming the lead for related activities following the ICH Management Committee's decision to disband the Financial, Communication and Membership Subcommittees in June 2018.

- **Drafting ICH Association Reports and Work Plans** in support of ICH Management Committee and MedDRA Management Committee reporting to the Assembly, including: 2017 Annual Report; 2019 ICH Work Plan and ICH Multi-Annual Strategic Plan; and 2019 MedDRA Work Plan. All documents were approved by the ICH Assembly.
- **Maintaining the ICH website** including:
  - **Keeping the ICH website up-to-date** with publication of draft documents for public consultation, *Step 2* and *Step 4* presentations, Press Releases, regional public consultation dates and guideline implementation dates.
  - **Implementing ICH's communication strategy and transparency policy**, including completion of the publication on the ICH website of the photographs and short biographies of all ICH and MedDRA Management Committee Representatives, Member Coordinators and ICH Secretariat, as well as the list of experts' names for all active WGs.
  - Including a new ICH Privacy Statement on the ICH Public website to provide clarity regarding treatment of the personal data of website visitors.
  - Contracting a developer and preparing ICH requirements to support: **upgrades to the ICH Members Only, ICH WGs and MedDRA.org websites**; the change of the Content Management System for the ICH Public website; and the **development of an internal database interfaced with the websites** to enable the efficient update of multiple data points on the websites through a single database entry and efficient management of data on ICH Guidelines and Experts/Representatives.
- **Responding to stakeholder enquiries** received via the ICH mailbox with input solicited as necessary from ICH experts and ICH Coordinators, and which in 2018 represented close to **200 enquiries**.
- **Managing ICH's financial administration**, including: regular coordination with fiduciary firm providing accountancy services to ICH; authorisation of payments; drafting of ICH and MedDRA budgets and multi-year budget plans; preparation of closing reports; organising the financial audit; liaising with the relevant tax authorities for items including submission of 2017 tax return to Swiss authorities, quarterly VAT declarations to Swiss authorities, and other administrative aspects; managing ICH's grant agreement with FDA, United States (in 2018 this included submissions of: quarterly Federal Financial Report, the annual Research Performance Progress Report, and a request for additional funding based on ICH Management Committee approval).
- **Entering into and managing contracts**, including those related to day-to-day operations (e.g., office support, website hosting/maintenance etc.), as well as support of the MedDRA Management Committee's oversight of the MSSO Contractor.
- **Controlling use of the ICH logo** (including ICH Member logo and ICH Recognised Training Programme logo) in line with the agreed procedures governing its use and

seeking ICH Management Committee approval as necessary, for example to confirm support for ICH logo use to illustrate ICH participation in the IMI WEB-RADR 2 project.

- **General operational administration**, including revision (with the approval of the ICH Management Committee) of the **ICH Employee Handbook** to update ICH signatory and budget administration rules, to include additional data privacy considerations and to support implementation of flexi-time system for ICH Secretariat staff; as well as taking the necessary steps to add Assembly Vice-Chair Dr. Petra Doerr (Swissmedic, Switzerland) and Dr. Anne Latrive from ICH Secretariat as **new ICH signatories** with joint (by two) signatory powers, further to ICH Management Committee approval.

2018 Other Key Activities:

- Supporting the ICH Management Committee with the **selection and contracting of a Professional Conference Organiser (PCO)** tasked with organising ICH's biannual meetings starting in 2019, with the provision thereafter of oversight and input to ensure alignment with contract and the meeting of ICH requirements.
- Supporting the ICH Management Committee's Implementation Subcommittee with the contracting of an independent third party to conduct an **ICH-driven survey on ICH Guideline Implementation** in new ICH Regulatory Member countries/regions and ICH Guideline Adherence in ICH Founding/Standing Regulatory Member countries/regions.
- **Implementing ICH's trademark registration strategy** for the ICH logo (device) which was approved by the ICH Management Committee, and for the MedDRA logo (device) and name, which was approved by the MedDRA Management Committee, including provision of input to the trademark lawyers (for class descriptions and to respond to trademark authority questions), as well as sign-off of Powers of Attorney (with arrangement of notarisation as required) to facilitate the filing of registrations by lawyers in each jurisdiction, and the necessary legal follow-ups.
- Supporting the MedDRA Management Committee facilitate **ICH participation in the IMI WEB-RADR 2 project** regarding the development a proof-of-concept bidirectional **mapping between MedDRA and SNOMED**, with coordination of legal input, registration of ICH in the online European Participant Portal, and sign-off of Declaration of Honour, Consortium Agreement, Grant Agreement, and an amendment to the MSSO Contractor Service Agreement.

2018 Other Activities in support of the IPRP:

- As part of support provided to the IPRP in 2018, the ICH Secretariat supported the launching of the IPRP public website including the contracting of the necessary providers for website development, hosting and maintenance.

Annex I

Assembly Member Representatives & Observer Delegates

December 31, 2018

Founding Regulatory Members

EC, Europe
Dr. Georgios Balkamos
Mrs. Lenita Lindström-Gommers *(Chair)*
Dr. Harald Enzmann

MHLW/PMDA, Japan
Dr. Nobumasa Nakashima
Dr. Junko Sato
Mr. Naoyuki Yasuda

FDA, United States
Dr. Theresa Mullin
Ms. Joan Wilmarth Blair

Founding Industry Members

EFPIA
Dr. Sabine Luik
Mr. Pär Tellner

JPMA
Dr. Hironobu Hiyoshi
Dr. Masafumi Yokota

PhRMA
Mr. Jerry Stewart
Dr. Peter Honig

Standing Regulatory Members

Swissmedic, Switzerland
Dr. Petra Doerr *(Vice Chair)*
Ms. Cordula Landgraf

Health Canada, Canada
Dr. Celia Lourenco
Ms. Catherine Parker

Regulatory Members

ANVISA, Brazil
Ms. Patrícia Pereira Tagliari
Dr. Raphael Sanches Pereira

HSA, Singapore
Dr. Dorothy Toh
Ms. Chua Siew Wei

MFDS, Republic of Korea
Dr. Nakyung Kim

NMPA, China
Mr. Xiaoling Qin
Mr. Siyuan Zhou

TFDA, Chinese Taipei
Dr. Jo-Feng Chi
Ms. Shiang-Ing (Shirley) Pan

Industry Members

BIO
Ms. Lila Feisee
Dr. Wassim Nashabeh

IGBA
Dr. Nick Cappuccino
Ms. Beata Stepniewska

WSMI
Ms. Caroline Mendy
Ms. Judy Stenmark

Standing Observers

WHO
Mr. Mike Ward
Dr. Samvel Azatyan

IFPMA
Dr. David Jefferys
Mr. Thomas B. Cueni

Observers

Bill and Melinda Gates Foundation
Dr. Murray Lumpkin

CDSCO, India
Dr. S. Eswara Reddy
Dr. Gyanendra Nath Singh

CECMED, Cuba
Dr. Celeste Sánchez González

COFEPRIS, Mexico
Dr. Mario Alanis Garza

INVIMA, Colombia
Mr. Javier Humberto Guzmán Cruz

MMDA, Moldova
Ms. Corina Iacob

National Center, Kazakhstan
Mrs. Aliya Kessikova

NPRA, Malaysia
Dr. Kamaruzaman Saleh

NRA, Iran
Mr. Mahmoud Alebouyeh

Roszdravnadzor, Russia
Dr. Sergey Glagolev
Dr. Mikhail A. Murashko

SAHPRA, South Africa
Ms. Portia Nkambule

SCDMTE, Armenia
Ms. Aida Malkhasyan

TGA, Australia
Dr. Kaylene Raynes

TITCK, Turkey
Ms. Hacer Coşkun Çetintaş

APEC
Dr. Young Ju Choi

ASEAN
Ms. Charunee Krisanaphan

EAC
Ms. Jane Mashingia
Mr. John Patrick Mwesigye

GHC
Dr. Hajed M. Hashan

PANDRH
Ms. Analía Porrás

SADC
Mrs. Fortunate Ntombi Fakudze

APIC
Mrs. Marieke van Dalen

CIOMS
Dr. Lembit Rägo

EDQM
Dr. Susanne Keitel

IPEC
Ms. Janeen Skutnik-Wilkinson

PIC/S
Mr. David Churchward

USP
Dr. Kevin Moore

Annex II

ICH Management Committee Representatives

December 31, 2018

Founding Regulatory Members

EC, Europe
Dr. Milton Bonelli
Ms. Lenita Lindström-Gommers

MHLW/PMDA, Japan
Dr. Nobumasa Nakashima *(Vice Chair)*
Dr. Junko Sato
Mr. Naoyuki Yasuda

FDA, United States
Dr. Theresa Mullin *(Chair)*
Ms. Joan Wilmarth Blair
Ms. Pujita Vaidya

Founding Industry Members

EFPIA
Dr. Sabine Luik
Mr. Pär Tellner

JPMA
Dr. Hironobu Hiyoshi
Dr. Masafumi Yokota

PhRMA
Mr. Jerry Stewart
Dr. Peter K. Honig

Standing Regulatory Members

Swissmedic, Switzerland
Dr. Petra Doerr
Ms. Cordula Landgraf

Health Canada, Canada
Ms. Catherine Parker
Dr. Celia Lourenco

Standing Observers

WHO
Mr. Mike Ward
Dr. Samvel Azatyan

IFPMA
Mr. Thomas B. Cueni
Dr. David Jefferys

Regulatory Members

HSA, Singapore
Ms. Siew Wei Chua
Dr. Dorothy Toh

MFDS, Republic of Korea
Dr. Nakyung Kim

NMPA, China
Mr. Xiaoling Qin
Mr. Siyuan Zhou

Industry Members

BIO
Ms. Lila Feisee
Dr. Wassim Nashabeh

IGBA
Dr. Nick Cappuccino
Ms. Beata Stepniewska

Annex III

MedDRA Management Committee Representatives

31 December, 2018

Founding Regulatory Members

EC, Europe
Dr. Georgios Balkamos
Dr. Sabine Brosch

MHLW/PMDA, Japan
Mr. Hideo Eno
Mr. Masahiro Inada

FDA, United States
Ms. Mary Ann Slack
Dr. Barbee I. Whitaker

Founding Industry Members

EFPIA
Mrs. Claudia Lehmann
Dr. Christina Winter

JPMA
Mr. Yo Tanaka
Ms. Yoko Hattori

PhRMA
Dr. Maria Apostolaros
Dr. Peter K. Honig

Standing Regulatory Member

Health Canada, Canada
Dr. Gayatri Jayaraman
Ms. Heather Morrison

MHRA UK

Mr. Mick Foy
Mr. Philip Tregunno

WHO Observer Delegate

WHO
Mr.Takahiro Goto
Mr. Mike Ward

Annex IV

ICH Secretariat Staff

31 December, 2018

Director
Dr. Dawn Ronan

Managers
Dr. Isabelle Güller
Dr. Anne Latrive
Ms. Nadia Myers Biggs

Coordinators
Ms. Coralie Angulo
Ms. Nikoleta Luludi
Ms. Emilie Macara

Annex V

Assembly Member ICH Coordinators

31 December, 2018

Founding Regulatory Members

EC, Europe
Dr. Georgios Balkamos
Dr. Milton Bonelli (Technical Coordinator)

MHLW/PMDA, Japan
Mr. Fumihito Takanashi
Dr. Yasuhiro Kishioka (Technical Coordinator)

FDA, United States
Ms. Amanda Roache
Dr. Michelle Limoli (Technical Coordinator)

Founding Industry Members

EFPIA
Ms. Giovanna Rizzetto

JPMA
Mr. Mitsuo Mihara

PhRMA
Ms. Camille Jackson

Standing Regulatory Members

Swissmedic, Switzerland
Ms. Anna Sieg

Health Canada, Canada
Mr. Nick Orphanos

Regulatory Member

ANVISA, Brazil
Ms. Ana Carolina Moreira Marino Araujo

NMPA, China
Dr. Wei Zhou

HSA, Singapore
Ms. Chua Siew Wei

MFDS, Republic of Korea
Ms. Pan Soon Kim

TFDA, Chinese Taipei
Ms. Yi-Jing Kuo

Industry Members

BIO
Ms. Lila Feisee
Dr. Ingrid Markovic

IGBA
Dr. Shinichiro Hirose

WSMI
Ms. Caroline Mendy

Annex VI

ICH Working Groups which met face-to-face at ICH's biannual meetings in 2018

Kobe, Japan on 1 – 7 June

Group Code	Topic	Meeting Days
E2B(R3) EWG/IWG	Revision of the Electronic Submission of Individual Case Safety Reports	5 days
E8(R1) EWG	Revision on General Considerations for Clinical Trials	5 days
E9(R1) EWG	Addendum to Defining the Appropriate Estimand for a Clinical Trial/Sensitivity Analyses	4 days
E11A EWG	Paediatric Extrapolation	5 days
E19 EWG	Optimization of Safety Data Collection	4 days
M2 EWG	Electronic Standards for the Transfer of Regulatory Information (ESTRI)	4 days
M8 EWG/IWG	The Electronic Common Technical Document (eCTD)	4 days
M9 EWG	Biopharmaceutics Classification System-based Biowaivers	4 days
M10 EWG	Bioanalytical Method Validation	5 days
S5(R3) EWG	Revision on Detection of Toxicity to Reproduction for Human Pharmaceuticals	4 days
S11 EWG	Nonclinical Safety Testing in Support of Development of Paediatric Medicines	4 days

Charlotte, NC, USA on 10 – 15 November

Group Code	Topic	Meeting Days
E8(R1) EWG	Revision on General Considerations for Clinical Trials	5 days
E9(R1) EWG	Addendum to Defining the Appropriate Estimand for a Clinical Trial/Sensitivity Analyses	4 days
E11A EWG	Paediatric Extrapolation	4 days
E14/S7B DG	The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs	4 days
E17 IWG	Multi-Regional Clinical Trials	3.5 days
E19 EWG	Optimization of Safety Data Collection	4 days
M7(R2) Maintenance EWG	Addendum to Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk	4 days
M10 EWG	Bioanalytical Method Validation	5 days
M11 informal WG	Clinical electronic Structured Harmonized Protocol (CeSHarP)	4 days
Q2(R2)/Q14 informal WG	Analytical Procedure Development and Revision of Q2(R1) Validation of Analytical Procedures	4 days
Q13 informal WG	Continuous Manufacturing	4 days
S1(R1) EWG	Revision of the Rodent Carcinogenicity Studies for Human Pharmaceuticals Guideline	4 days
S5(R3) EWG	Revision on Detection of Toxicity to Reproduction for Human Pharmaceuticals	5 days

Annex VII

Overview of harmonisation activities and accomplishments in 2018

Topic Code	Type of Working Group	Topic Name	Accomplishments	Anticipated Milestones
Standing Paediatric	Standing EWG	Addendum to Pediatric Drug Development	The Standing EWG stay available for requests for pediatric expertise from other ICH WGs	N/A (Ongoing Activity)
E11A	EWG	Paediatric Extrapolation	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2a/b* are expected in November 2020
E14/S7B	IWG	Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs	Establishment of the IWG in November 2018	*Steps 1* and *2a/b* are expected in June 2020
E17	IWG	ICH Guideline on Multi-Regional Clinical Trials	Activities progressed in line with Concept Paper/Business Plan/Work Plan	Finalisation of Training Materials is expected by June 2019
E19	EWG	ICH Guideline on Optimization of Safety Data Collection	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2a/b* are expected in early 2019
E2B(R3)	EWG/IWG	Revision of Electronic Submission of ICSRs	Reached *Steps 3* and *4* in June 2018 of the Revision of Q&As for the Electronic Submission of	N/A (Ongoing Activity)

			Individual Case Study Reports	
E8(R1)	EWG	Revision of ICH Guideline on General Considerations for Clinical Trials	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2 a/b* are expected in early 2019
E9(R1)	EWG	Addendum to Defining Appropriate Estimand for a Clinical Trial/Sensitivity Analyses	Activities progressed in line with Concept Paper/Business Plan/Work Plan. Publication of training materials on the ICH website in July 2018	*Steps 3* and *4* are expected in June 2019
M1	PtC WG	MedDRA Points to Consider	Updated the two Points to Consider (PtC) documents on Term Selection and Data Retrieval and Presentation with MedDRA release versions 21.0 & 21.1. Published the Companion Document in November 2018.	N/A (Ongoing Activity)
M10	EWG	Bioanalytical Method Validation	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2 a/b* are expected by early 2019
M11	EWG	Clinical electronic Structured Harmonised Protocol (CeSHarP)	EWG established in November 2018	*Step 1* and *2 a/b* are expected in June 2020
M2	EWG	Electronic Standards for the Transfer of Regulatory	Progressed development of project opportunities	N/A (Ongoing Activity)

		Information	proposals. Finalised the revisions of recommendations on Electronic Transfer of Regulatory Information (ESTRI)	
M7(R2)	Maintenance EWG	Addendum to Assessment and Control of DNA Reactive Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2 a/b* are expected in November 2019
M8	EWG/IWG	Electronic Common Technical Document: eCTD	Reached *Step 3* and *4* in June 2018 of: - eCTD v3.2.2 Q&A and Specification Change Request Document v1.31; - eCTD v4.0 Implementation Package v1.2; - eCTD v4 Q&A and Specification Change Request Document v1.2; - Specification for Submission Formats for CTD v1.2.	N/A (Ongoing Activity)
M9	EWG	Biopharmaceutics Classification System-based Biowaivers	Reached *Steps 1* in June and *2a/b* in June 2018.	*Steps 3* and *4* are expected by November 2019
Q11	IWG	Q&As on API Starting Materials	Activities progressed in line with Work Plan	Finalisation of training materials is expected in

				early 2019
Q12	EWG	ICH Guideline on Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 3* and *4* are expected by November 2019
Q13	EWG	Continuous Manufacturing of Drug Substances and Drug Products	EWG established in November 2018	*Step 1* and *2 a/b* are expected in June 2020
Q2(R2)/Q14	EWG	Analytical Procedure Development and Revision of Q2 (R1) Analytical Validation	EWG established in November 2018	*Step 1* and *2 a/b* are expected in June 2020
Q3C(R8)	Maintenance EWG	Maintenance of the Guideline for Residual Solvents	- ICH Management Committee approval of the revised Q3C(R7) Guideline further to the error correction in the Permitted Daily Exposure (PDE) for ethyleneglycol - Progressed work to develop Permitted Daily Exposure (PDE) levels for 3 new solvents adopted in June 2017: 2-methyltetrahydrofuran, cyclopentylmethyleher and tert-butanol.	(Ongoing Activity) *Step 1* and *2 a/b* are expected in early 2019
Q3D(R1)/(R2)	Maintenance EWG	Maintenance of the Guideline for Elemental Impurities	Progressed work on Addendum to Q3D Guideline to include PDEs for cutaneous	(Ongoing Activity) *Step 1* and *2 a/b* are

			and transdermal products. Reached *Steps 1* and *2 a/b* on the revision Q3D(R1) for the Cadmium inhalation PDE in May 2018.	expected by November 2019 for Q3D(R2) Addendum *Steps 3* and *4* are expected in early 2019 for the Q3D(R1) Cadmium inhalation PDE
S1(R1)	EWG	Revision of Rodent Carcinogenicity Studies for Human Pharmaceuticals	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2a/b* are expected in early 2020
S11	EWG	ICH Guideline on Nonclinical Safety Testing - Paediatric Medicines	Reached *Step 1* in June and *Step 2a*/b in September 2018	*Steps 3* and *4* are expected in November 2019
S5(R3)	EWG	Revision on Detection of Toxicity to Reproduction for Medicinal Products and Toxicity to Male Fertility	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 3* and *4* are expected in November 2019
S9	IWG	Q&As on Nonclinical Evaluation for Anticancer Pharmaceuticals	Reached *Step 3* and *4* in April 2018	The IWG has been disbanded following *Step 4*