ICH ASSOCIATION

2019 ANNUAL REPORT

ICH Association

2019 Annual Report

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

Version dated 4 May 2020

Approved by the ICH Assembly on 27 May 2020

Message from Assembly Chair and Vice Chair

2019 was a productive year for the ICH Association which has now become well-established in its new format and mode of operation since the implementation of the 2015 reforms. The activities of ICH's 16 Members and 32 Observers in 2019 was focused intently on harmonisation work, including progress of current topics, approval of new topics, implementation and training.

2019 saw harmonisation activities progressed by ICH Working Groups on a record 32 topics, including 7 new topics approved in 2019, with the involvement of over 700 technical experts, more than a third of whom now come from new ICH Members and Observers. And with more than 1,000 individuals now actively contributing to the work of ICH, it has become increasingly important to ensure that the efficiency of the ICH process is maintained. Substantive measures were taken in support of this in 2019, with important changes to ICH procedures related to expert participation in Working Groups.

Advances were also made during the year towards supporting in a strategic manner the training needs of ICH Members and Observers. A call for expressions of interest was conducted successfully to engage accredited non-profit training organisations as Training Associates to deliver training services to ICH. The provision of such services is highly anticipated to get underway in 2020.

A key milestone was also reached this year in understanding how ICH Guidelines are implemented by ICH Regulatory Members with the completion of a survey on the level of implementation and adherence to ICH Guidelines. ICH was pleased by the success of this first survey and is delighted to be able to share its outcome with stakeholders via the ICH website.

As ICH prepares to mark its 30th Anniversary in 2020, ICH's mission and commitment to harmonisation for better health are as strong as ever and we look forward to leading ICH's global membership into a fourth decade of successful activity.

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

Dr. Celia Lourenco
ICH Assembly Vice Chair
Health Canada, Canada

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1. About ICH

1.1. Purpose & Aims

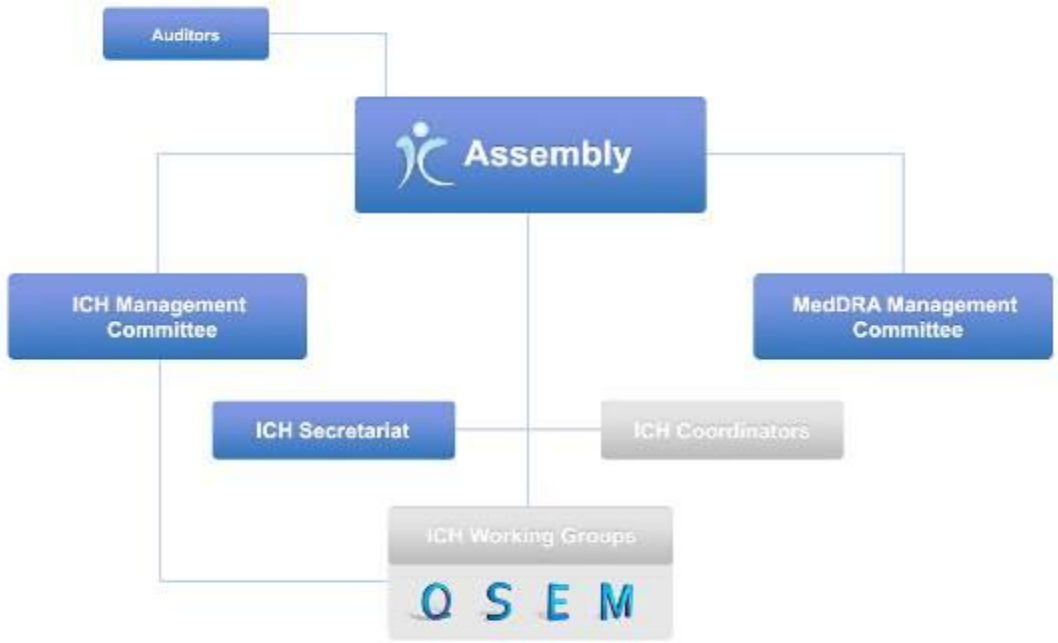
The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (**ICH**) **is an international non-profit organisation** which was established as an association under Swiss law in October 2015. The purpose of ICH is to **promote public health through international 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, 2019 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 2019 the following

Subcommittees were supporting the work of Management Committee: **New Topics, Implementation, Training**, and **30th Anniversary Planning**, although the Implementation Subcommittee was disbanded in June 2019, with leadership of implementation activities transitioned to a Regulatory and Industry Co-Lead. Additionally, a **Planning** Subcommittee was established to work with the E8(R1) EWG on the organisation of an **E8(R1) Stakeholder Meeting** in 2019. A **Financial** Subcommittee was also established at the end of 2019.

- The full list of the ICH Management Committee Member Representatives and Observer Delegates as of December 31, 2019 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.
- A MedDRA Financial Subcommittee was established at the end of 2019.
- The full list of MedDRA Management Committee Representatives and Observer Delegates as of December 31, 2019 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 2019 are referred to in Section 5.5.
- The full list of ICH Secretariat Staff as of December 31, 2019 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 for 2018 and 2019.

ICH Coordinators

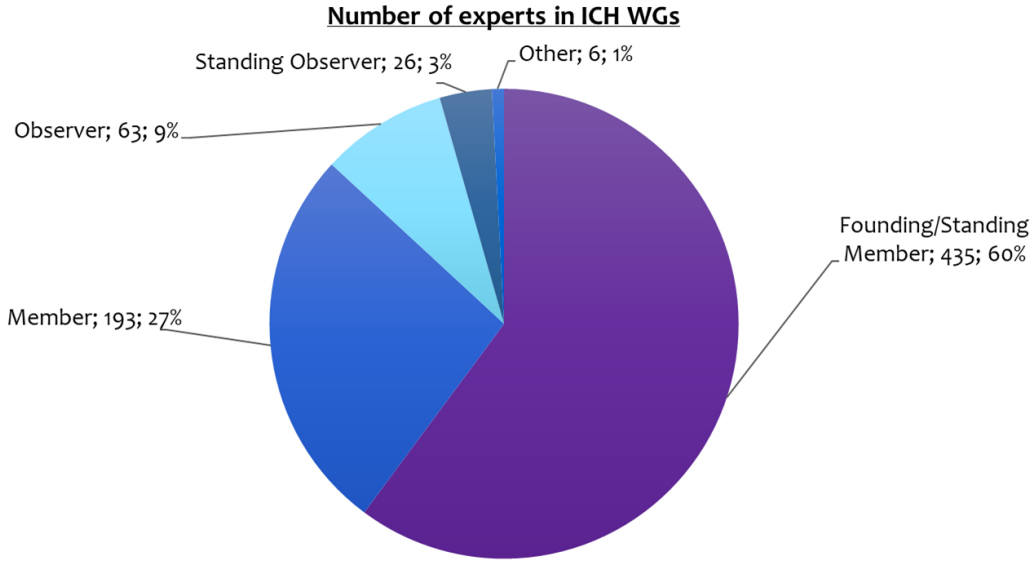
- **Fundamental to the smooth running of ICH** has been the designation of an ICH Coordinator per ICH Member to act as the main contact point with the ICH Secretariat. Coordinators ensure proper distribution of ICH documents to the appropriate persons from their organisation and are responsible for the **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, 2019 is provided in Annex V.

2. 2019 Overview of ICH Membership & Observership

2.1. Continued Expansion of ICH Membership & Observership

A driving factor of ICH's 2015 organisational change was to make ICH a **truly global initiative** and enable an expanded forum for dialogue on scientific issues between regulatory authorities and the pharmaceutical industry on the harmonisation of the technical requirements for pharmaceuticals products. 2019 saw the addition of 4 new Observers, bringing ICH to a total of **16 Members and 32 Observers** and by the end of 2019 over 1,000 individuals were contributing to the work of ICH, either as Representatives/delegates of ICH bodies, experts on Working Groups (WGs) or in supporting roles.

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 2019 these WGs involved the participation of **over 700 technical experts**, with more than a third of these experts coming from new ICH Members and Observers.



Overview of Expert Participation in ICH, as of end of 2019

While the continued growth of ICH is celebrated as advancing global harmonisation efforts, the ICH Management Committee has needed to implement **new rules to manage the size of WGs to ensure the efficiency of activities**. In response to this, and following heavy reflection by the ICH Management Committee, the decision was taken in 2019 to enable the establishment of a **Plenary Working Party (PWP)** for each new WG established. This will allow all ICH Members and Observers without an expert in the WG to follow more closely work on ICH Guidelines by enabling them to appoint an expert to a PWP. Participating in a PWP will provide opportunities to be consulted ahead of the reaching of key milestones in ICH Guideline development, namely prior to *Step 1* and *Step 3* sign-offs. The process, which will also be considered on a case-by-case basis for already

established WGs, furthermore provides the opportunity for the convening of workshops with external industry stakeholders not directly involved in ICH activities. The establishment of PWPs has been welcomed by ICH's Membership and Observership as a way to enable wider involvement, whilst maintaining the efficiency of the process.

2.2. New Observers Approved in 2019

The Assembly approved **4 new ICH Regulatory Observers** in 2019, based on the recommendation of the ICH Management Committee:

- ANMAT, Argentina
- CPED, Israel
- JFDA, Jordan
- SFDA, Saudi Arabia

New ICH Observers in Attendance of Amsterdam, the Netherlands, June meeting

ANMAT, Argentina

Left to right: *Ms. Lenita Lindström-Gommers (EC, Europe), Mr. Sebastian Duarte (ANMAT, Argentina), Dr. Petra Doerr (Swissmedic, Switzerland)*

JFDA, Jordan

Left to right: *Dr. Wesal Haqaish (JFDA, Jordan), Ms. Lenita Lindström-Gommers (EC, Europe), Dr. Petra Doerr (Swissmedic, Switzerland)*

SFDA, Saudi Arabia

Left to right: *Ms. Lenita Lindström-Gommers (EC, Europe), Dr. Mohammed Al Quwaizani (SFDA, Saudi Arabia), Dr. Petra Doerr (Swissmedic, Switzerland)*

3. 2019 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 2019, these activities were progressed on **32 topics** by technical WGs [including Expert Working Groups (EWG), Implementation Working Groups (IWG) and Discussion Groups (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 2019. The ICH WGs which met in 2019 are presented in Annex VI.

The **key outcomes in 2019** relating to ICH harmonisation efforts include:

- Completion at ***Step* 4** of the ICH process and **finalisation** of work (Please see Section 3.1) on:
  - **2 New ICH Guidelines**
  - **1 New Addendum to an ICH Guideline**
  - **1 Updated Question & Answer (Q&A) Document**
  - **1 Revised Permitted Daily Exposure (PDE)**
- **Updates of MedDRA Point to Consider Documents** with each of the two MedDRA releases in March and September 2019

- 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

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

An overview of all ICH WG activities and accomplishments in 2019 is presented in Annex VII.

3.1. ICH Guidelines & Other WG Work Products Finalised in 2019

Please note that all ICH documents referenced below can be found on the ICH website at www.ich.org.

ICH M9 Guideline - Biopharmaceutics Classification System-based Biowaivers

This new ICH M9 Guideline, which reached ICH *Step 4* in November 2019, provides recommendations to support biopharmaceutics classification of medicinal products and waiver of bioequivalence studies and aims to reduce the costs and time of development and prevent unnecessary exposure of mostly healthy volunteers to medicinal products, as in vivo studies to prove the biopharmaceutical quality of the medicinal product would not be needed, and therefore, facilitate the patient's access to medicines or post-approval changes.

ICH Q12 Guideline - Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

This new ICH Q12 Guideline, which reached ICH *Step 4* in November 2019, and is complementary to ICH Quality Guidelines Q8 through Q11, aims to promote innovation and continual improvement in the pharmaceutical sector, and strengthen quality assurance and reliable supply of product, including proactive planning of global supply chain adjustments.

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

An updated version of the ICH E2B(R3) Q&A Document reached ICH *Step 4* in June 2019. The 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.

ICH E9(R1) Guideline - Addendum to Defining the Appropriate Estimand for a Clinical Trial/Sensitivity Analyses

The new Addendum to the ICH E9 Guideline, which reached ICH *Step 4* in November 2019, presents a structured framework to strengthen the dialogue between disciplines involved in the formulation of clinical trial objectives, design, conduct, analysis and

interpretation, as well as between sponsor and regulator regarding the treatment effect(s) of interest that a clinical trial should address.

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

In March 2019, a revision to the Inhalation Permitted Daily Exposure (PDE) for Cadmium reached *Step 4* of the ICH Process. The Q3D(R1) Guideline for the control of elemental impurities in drug products (medicinal products) establishes Permitted Daily Exposures (PDEs) for 24 Elemental Impurities (EIs) for drug products administered by the oral, parenteral and inhalation routes of administration.

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. In 2019, the two MedDRA PtC documents on **Term Selection** and **Data Retrieval and Presentation** were released with **MedDRA versions 22.0 and 22.1**.

While both documents have been updated twice a year, with every MedDRA release, the decision was taken in 2019 to release only one update annually. Related to this decision, is the decision to make the two MedDRA PtC documents available in additional languages. In addition to English and Japanese, the PtC documents will also be made available in Chinese, Korean and Spanish with other translations to be considered based on need and feasibility to develop.

3.2. ICH Guidelines Endorsed at Step 2a/b in 2019

In 2019 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 E8(R1) Revised Draft Guideline - General Considerations for Clinical Studies

The revised draft ICH E8(R1) Guideline, which reached *Step 2b* in May 2019, incorporates the most current concepts achieving fit-for-purpose data quality as one of the essential considerations for all clinical trials, including to: identify a basic set of critical-to-quality factors that can be adapted to different types of trials to support the meaningfulness and reliability of trial results and to protect human subjects; address a broader range of trial designs and data sources; and provide an updated cross-referencing of all other relevant ICH Guidelines that should be referred to when planning clinical

studies. The modernisation of ICH E8 is the first step towards the GCP Renovation initiated in 2017.

ICH E19 Draft Guideline - Optimization of Safety Data Collection E

The new draft ICH E19 Guideline, which reached *Step 2b* in April 2019, provides a harmonised guidance on when it would be appropriate to use a targeted approach to safety data collection in some late-stage pre-marketing or post-marketing studies, and how such an approach would be implemented.

ICH M10 Draft Guideline - Bioanalytical Method Validation M

The new draft ICH M10 Guideline, which reached *Step 2b* in February 2019, provides recommendations on the scientific regulatory requirements for bioanalysis conducted during the development of drugs of both chemical and biological origins.

3.3. New Harmonisation Activities

3.3.1. Approval of New Topics

In 2019 the ICH Management Committee and its New Topics Subcommittee assessed **15 New Topic proposals** which had been submitted by ICH Members and Observers by a mid-December 2018 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 7 new harmonisation activities:

ICH E6(R3) Revision of Guideline - Good Clinical Practice E

The ICH E6(R3) Revision aims to revise the existing ICH E6(R2) Guideline to address the increasing diversity of study types and data sources that are being employed to support regulatory and other health policy decisions in line with the ICH Reflection Paper on GCP Renovation.

- The Assembly adopted the ICH E6(R3) Concept Paper outline at its meeting in June 2019, 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 November 2019.
- The Assembly appointed FDA, United States as Rapporteur.

ICH E2D(R1) Revision of Guideline - Post Approval Safety Data Management: Definition and Standards for Expedited Reporting E

The ICH E2D(R1) Revision of the existing ICH E2D Guideline aims to incorporate pragmatic potentially risk-based approaches of the management of information from existing and any new data sources, to enable a greater focus on the data sources that will optimize signal detection activities and public health.

- The Assembly adopted the ICH E2D(R1) Concept Paper outline at its meeting in June 2019, 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 November 2019.
- The Assembly appointed EFPIA as Rapporteur.

ICH Q5A(R2) Revision of Guideline - Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin

The ICH Q5A(R2) Revision aims to revise the existing ICH Q5A Guideline on technologies for virus detection and quantification, and validation approaches for virus clearance, and expand the scope of the Guideline to include new biotechnology products such as viral-like particles and viral-vectored particles.

- The Assembly adopted the ICH Q5A(R2) Concept Paper outline at its meeting in June 2019, 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 November 2019.
- The Assembly appointed FDA, United States as Rapporteur.

ICH Q3E Guideline - Assessment and Control of Extractables and Leachables (E&L) for Pharmaceuticals and Biologics

The new ICH Q3E Guideline aims to provide harmonised guidance on the assessment and control of extractables and leachables (E&L) in all drug product dosage forms, including clarification of the relationship among existing standards and where possible, harmonise the threshold concepts of reporting, identifying and qualifying impurities.

- The Assembly adopted the ICH Q3E Concept Paper outline at its meeting in November 2019, further to which an informal WG was established to finalise the Concept Paper and Business Plan.
- PhRMA, as the Member who proposed the topic, accepted to lead the informal WG.

ICH Q9(R1) Revision – Quality Risk Management

The ICH Q9(R1) Revision aims to further accelerate and enable the practical realisation of ICH Q9 by providing useful guidance for industry and regulators alike on addressing the issues of subjectivity in risk assessment and Quality Risk Management (QRM) work. It will also help the implementation of ICH Q8, Q10 and Q12 Guidelines.

- The Assembly adopted the ICH Q9(R1) Concept Paper outline at its meeting in November 2019, and agreed that an informal WG would be established at a later stage to be determined by the ICH Management Committee to finalise the Concept Paper and Business Plan.
- EC, Europe, as the Member who proposed the topic, accepted to lead the informal WG.

ICH S12 Guideline - Nonclinical Biodistribution Studies for Gene Therapy Products

The new ICH S12 Guideline aims to recommend types of non-clinical studies with which collection of biodistribution data is considered informative and/or necessary to support dosing in early clinical trials, and which will provide guidance on the design of the studies. This will result in streamlined development of gene therapy products with higher scientific rigor while minimising the unnecessary use of animals.

- The Assembly adopted the ICH S12 Concept Paper outline at its meeting in June 2019, 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 November 2019.
- The Assembly appointed MHLW/PMDA, Japan as Rapporteur.

ICH M13 Guideline - Bioequivalence for Immediate-Release Solid Oral Dosage Forms

The new ICH M13 Guideline aims to harmonise bioequivalence (BE) assessments for immediate-release solid oral dosage forms by creating common study design and assessment methodologies for BE determination in order to streamline generic drug development and make it more cost effective.

- The Assembly adopted the ICH M13 Concept Paper outline at its meeting in November 2019, further to which an informal WG was established to finalise the Concept Paper and Business Plan.
- FDA, United States, as the Member who proposed the topic, accepted to lead the informal WG.

Furthermore, in 2019, the ICH Management Committee approved the following Concept Papers for the following 2 new topics which had been adopted by the ICH Assembly in June 2018, but with a delayed timeframe for the establishment of the informal WGs which were eventually established in mid-2019:

ICH E20 Guideline - Adaptive Clinical Trials

The new ICH E20 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 appointed PhRMA as Rapporteur.

ICH M12 Drug Interaction Studies

The new ICH M12 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 appointed FDA, United States as Rapporteur.

3.3.2. Other New Harmonisation Activities

In 2019, the following activity received the support of the Assembly:

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.

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 Standard Operating Procedures (SOP) of the WGs had been revised in November 2018 to reflect the new maintenance procedure and describes how this process follows the usual ICH Step process.

In November 2019, the ICH Assembly noted PDG plans to revise 14 Q4B Annexes by mid-2020 to align the annexes with the current editions of the three pharmacopoeias, and by end of 2020, to revise the Q4B Guideline to align it with the Q4B Maintenance Procedure described in Annex 5 of the SOP of the WGs.

3.3.3. Strategic Reflection Papers

In 2019, the Assembly endorsed a Reflection Paper on **Strategic Approach to International Harmonization of Technical Scientific Requirements for Pharmacoepidemiological Studies Submitted to Regulatory Agencies to Advance More Effective Utilization of Real-World Data** and supported the establishment of a Pharmacoepidemiology DG (**PEpiDG**) with a 2-year remit, with MHLW/PMDA, Japan appointed as Rapporteur.

Additionally, following on from ICH Assembly approval of two other Reflection Papers in 2018 (**Advancing Biopharmaceutical Quality Standards to Support Continual**

Improvement and Innovation in Manufacturing Technologies and Approaches, and **Further Opportunities for Harmonisation of Standards for Generic Drugs**), two further DG were established in 2019, the Quality DG (**QDG**) and Generic drug DG (**GDG**), with PhRMA and FDA, United States appointed as the respective Rapporteurs.

In 2019, the ICH Management Committee also provided input into other Reflection Papers being developed by Members which may potentially be submitted to the Assembly for consideration in 2020. Furthermore, procedures were developed related to Reflection Paper development and review. These procedures layout a number of considerations regarding the need and value of a Reflection Paper which the ICH Management Committee should reflect upon before a Member or Observer proceeds to undertake work to develop one. These new procedures were further complemented by additional new procedures regarding general principles for DGs, as well as work on a strategic framework to help ICH identify near and long-term priorities.

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 2019, with ***Step 5*** **(implementation)** of the ICH process being **reached 41 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, with a new searchable database tool rolled-out in 2019 which allows information on the status of implementation of any ICH Guideline by any ICH Regulatory Member to be readily retrieved by all stakeholders.

Monitoring the progress of international harmonisation and coordinating efforts in this regard is an important ICH focus. ICH is working to understand the level of implementation and adherence to ICH Guidelines within Regulatory Member and Observer countries/regions. In support of this effort, an **ICH-driven survey** was completed in 2019 in coordination with the Centre for Innovation in Regulatory Science (CIRS), an independent third party contracted by ICH to conduct the survey. The scope of the survey included 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). A **publication communicating the outcome of the survey** was published on the ICH website in November 2019.

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. In 2019, ICH additionally lauched a YouTube Channel to share high resolution ICH Training videos and furthermore initiated planning for the development of a training library for the ICH website which would make it easier to consult ICH's growing catalogue of training materials.

3.5.1. ICH Training Strategy

Work was progressed on several fronts in 2019 in furtherance of efforts to ensure the availability of high quality training on ICH Guidelines. This included: continued delivery of **ICH Recognised Training Programmes** organised by Training Providers; the initiation of efforts to contract accredited non-profit training organisations/institutions as **ICH Training Associates** to deliver online training materials and other support according to ICH needs; and the financial support of training on ICH Guidelines organised by ICH Regulatory Members.

ICH Recognised Training Programmes:

In 2019 the following **training programmes** from Training Providers, supported as **ICH Recognised Training Programmes** by the ICH Management Committee's Training Subcommittee, were delivered:

- APEC PKU Regulatory Sciences CoE: MRCT & GCP-Related Considerations, Beijing, China, November 2019;
- NEU: ICH-Q1: Drug Stability Training, Burlington, MA, USA, October 2019;
- DIA-NIFDS: Workshop on Pharmacovigilance, Seoul, Korea, September 2019;
- DIA India: ICH Day, Mumbai, India, August 2019;
- NEU: Training Seminar on ICH Stability Guidelines (ICH-Q1), Kuala Lumpur, Malaysia, August 2019;
- MHLW/PMDA, Japan: Symposium for the draft revision on the ICH E8(R1), Tokyo, Japan, July 2019;

- DIA China: ICH Day, Beijing, China, May 2019;
- CPA: Training Workshop on ICH M4Q and Regional Administrative Information, Beijing, China, May 2019.
- APEC PKU Regulatory Sciences CoE: Pharmacovigilance Seminar, Beijing, China, April 2019;
- DIA Japan: ICH Day, Tokyo, Japan, April 2019;
- CoRE Duke NUS Medical School: Chemistry, Manufacturing and Controls (CMC) Workshop, Singapore, March 2019;
- MRCT Center and Health Canada, Canada: ICH GCP and MRCT Training: ICH E6(R2) and ICH E17, Ottawa, Ontario, Canada, February 2019.

In coordination with the Training Subcommittee, work was also progressed in 2019 by Training Providers to develop **introductory online training courses** for Tier 1 and 2 Guidelines. This included:

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

The first of these **online training courses on the Q7 ICH Guideline was published by PDA in November 2019**, with a link to the material posted on the ICH website. Links to the other training materials will also be posted on the ICH website once they become available.

Additionally, in relation to this activity the ICH Management Committee provided its approval in 2019 to: an ICH Recognised Training Programme Online Presentation Template; revised Terms of Reference for Training Providers; a revised ICH Recognised Training Programme Logo Disclaimer Template; and revised General Guidance for ICH Training Providers.

ICH Training Associates:

The ICH Management Committee was also pleased to announce a new ICH training initiative in 2019, providing its support for the launch of a Call for Expression of Interest in April 2019 for ICH Training Associates. This initiative aims to contract appropriate accredited non-profit training organisations/institutions as **Training Associates to assist ICH in its efforts to address in a strategic manner the training needs of its Regulatory and Industry Members and Observers**. The Call received a good level of interest, with the ICH Management Committee establishing a Review Committee to conduct, with the support of the ICH Secretariat, an anonymised assessment of applications, based on the eligibility criteria and ability to meet the statement of work. Further to this, two organisations were short-listed and work commenced to develop contracts with detailed specifications on the first work items to be delivered by these

organisations. It is expected that work will get underway in the first half of 2020 following successful conclusion of contracts with these organisations.

ICH Regulatory Training

2019 also saw the ICH Management Committee approve the **provision of ICH funding support to training programmes on ICH Guidelines organised by 4 ICH Regulatory Members**. This came further to a Call for Expression of Interest launched by the ICH Management Committee at the end of 2018 and saw support provided for training organised by:

- Health Canada, Canada on ICH E6(R2) and ICH E17 Guidelines;
- MHLW/PMDA, Japan on the ICH E8(R1) Draft Guideline;
- MFDS, Republic of Korea on a number of ICH Q, S, E and M Guidelines;
- NMPA, China on ICH E8(R1), E9(R1); E17; M3(R2); and Q8-11 Guidelines

Each of the Regulatory Members submitted written reports to the ICH Management Committee on the successful outcomes of their respective programmes.

In view of the success of this initiative, the ICH Management Committee sought the support of the ICH Assembly to allocate budget towards a repeat of the process in 2020, this time extending it to ICH Regulatory Observers.

3.5.2. Training Materials Developed by ICH Working Groups

Further to support provided by the Assembly and ICH Management Committee for WGs to pursue training material development to help **assist understanding of new concepts** and implementation of their respective ICH Guidelines, training materials were finalised in 2019 on the following topics:

- ICH E17 Guideline on Multi-Regional Clinical Trials (MRCT)
- ICH Q11 Questions and Answers (Q&As) on the Development and Manufacture of Drug Substances (Chemical Entities and Biotechnological/Biological Entities)

The materials include **informative slide decks**, as well as training videos which were developed with the assistance of Founding Regulatory Member FDA, United States which provided the support of its studios for the production of the videos. The materials are made available on the ICH website, with higher resolution versions of the videos published on ICH's YouTube Channel.

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 2019, the following presentations were made available:

- ICH E8(R1) *Step 2* Informational Presentation
- ICH M10 *Step 2* Informational Presentation

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.

2019 was a significant year for MedDRA, marking 20 years since its first release on 1 March 1999. The moment was marked by presentations at MedDRA User Group meetings in China, Europe, India, Japan and the USA, as well as special edition of MedDRA Messenger featuring perspectives from several MedDRA Management Committee Members.

One of the indicators of the successful adoption of MedDRA over the past 20 years as a worldwide standard in the protection of public health, has been the continued growth in the number of users. At the end of 2019, this included **over 6,000 subscribing organisations from 125 countries**. In view of this continued user growth, 2019 saw continued expansion in the support provided to facilitate the use of MedDRA in a broader set of countries/regions. This included release to users of **Korean and Russian MedDRA translations**, initiation of work to develop a **Brazilian Portuguese MedDRA translation** and specific translations of MedDRA Points to Consider documents, as well as expanded training and helpdesk support with the assistance of **local support staff in Europe, India, China, Republic of Korea, Latin America, the USA and other regions**.

3.6.1. Overview of 2019 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" which is provided by the ICH Secretariat. (MedDRA Secretariat implementation of key MedDRA Management Committee decisions are referred to in Section 5.5 below)

The following key decisions were taken in 2019 related to MedDRA's management:

Financial:

- The MedDRA Management Committee supported the **2020 Budget** including the **2020 MSSO Subscription Fees** for presentation to the Assembly. The 2020 Budget and Subscription Fees were subsequently approved by the Assembly.
- The MedDRA Management Committee approved the **2020 MSSO Business Plan**.

- The MedDRA Management Committee agreed to plan a **market analysis** for 2020 with the support of an external consultant to inform the determination of Subscription Fees moving forward.

Operational:

- The MedDRA Management Committee supported the **2020 Annual MedDRA Work Plan** for submission to the Assembly, which was subsequently approved by the Assembly.
- The MedDRA Management Committee supported the continued 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 with support provided for the filing of ICH opposition against 2 applications for the registration of trademarks similar to MedDRA trademarks.
- The MedDRA Management Committee tasked the MSSO to initiate efforts towards engaging an IT Consultant, whose appointment and work would be under the governance of the MedDRA Management Committee, to provide advice towards a **digital transformation of operations**, leveraging technological advances.
- The MedDRA Management Committee supported that the MedDRA Secretariat hire an additional new staff to be better able to support additional MedDRA activities.
- The MedDRA Management Committee established a Financial Subcommittee to coordinate with the ICH Management Committee's Financial Subcommittee to review overall ICH and MedDRA multi-year budget planning in view of overall ICH Association activities.

Facilitating Global Use of MedDRA:

- The MedDRA Management Committee agreed for MSSO to hire an additional two local support in China to support high training needs until 2022.
- The MedDRA Management Committee supported **translation into Chinese, Korean, and Spanish of the two MedDRA PtC documents**: MedDRA Term Selection: Points to Consider and MedDRA Data Retrieval and Presentation: Points to Consider. The ICH Assembly furthermore supported this change in policy from making these documents available only in English and Japanese, to the MedDRA Management Committee determining on a case-by-case the development of additional translations, based on need expressed and feasibility.
- The MedDRA Management Committee agreed to provide MHRA, UK 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: (1) supported establishment of a Memorandum of Understanding with the International Medical

Device Regulators Forum (**IMDRF**) concerning cooperation on the maintenance of a mapping between MedDRA and IMDRF's terminology: terminology: Annex E: Health Effects – Clinical Signs, Symptoms and Conditions Terms and Codes, which was furthermore supported by the ICH Assembly; and (2) investigated development of a bi-directional mapping between MedDRA and **ICD** 11 and/or 10;

Development of SMQs:

- The MedDRA Management Committee approved 1 new Standardised MedDRA Query (SMQ) – the SMQ Opportunistic Infections, for release to MedDRA users. The addition of this new SMQs will result in a total of **106 SMQs developed to-date** by the CIOMS WG on SMQs.
- With the development of the last two SMQs by the CIOMS WG coming to conclusion – SMQ Progressive multifocal leukoencephalopathy and SMQ Immune-mediated/autoimmune disorders – the MedDRA Management Committee acknowledged the completion of a very successful current phase of SMQ development between ICH and CIOMS, which was furthermore supported by the Assembly.
- The MedDRA Management Committee supported that MSSO continue consulting the PtC WG on any new *ad hoc* SMQ requests received, with any considered candidate SMQs for development to utilize volunteers from Regulatory Authorities and Industry to support testing.

3.6.2. Oversight of 2019 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 2019, which were overseen by the MedDRA Management Committee:

- Conduct of **157 training courses** for MSSO MedDRA users, including **31 webinars** and **126 face-to-face training courses** with **3,664 persons trained** at face-to-face training courses and 3,221 webinar connections. Trainees came from over 73 countries.
- Release to users of MedDRA versions 22.0 and 22.1.
- Release to MedDRA users of a **Korean MedDRA translation**, the draft of which was developed by ICH Regulatory Member MFDS, Republic of Korea.
- Release to MedDRA users of a **Russian MedDRA translation** developed in close coordination with ICH Regulatory Observer Roszdravnadzor, Russia.
- Initiation of work on a **Brazilian Portuguese MedDRA translation** to be developed in close coordination with ICH Regulatory Member ANVISA, Brazil.
- **Cooperation with the WHO and its Collaborating Centre, the Uppsala Monitoring Centre (UMC)** which resulted in further joint MSSO MedDRA and UMC WHO-Drug user group meetings in India (March 2019) and in the USA (October 2019), as well as MSSO participation to provide MedDRA training at the Annual Meeting of Representatives of National Pharmacovigilance Centres

participating in the WHO Programme for International Drug Monitoring held in Colombia (November 2019).

- Liaison with the **IMDRF** Adverse Event Terminology and Coding Working Group regarding maintenance of its mapping of its Annex E (Health Effects – Clinical Signs, Symptoms and Conditions Terms and Codes) terminology to MedDRA LLTs.
- Support of the work of the **ICH M1 PtC WG** to update with each MedDRA release the PtC documents on Term Selection and Data Retrieval and Presentation.
- 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 **Innovative Medicines Initiative (IMI) WEB-RADR 2 Project** in Work Package 4, focusing on a **bi-directional mapping between MedDRA and SNOMED** terminologies, including developing a model for the ownership, maintenance and distribution of a mapping.

4. 2019 Overview of Meetings & Planning

4.1. 2019 Meetings

In 2019, ICH activities were progressed via face-to-face meetings and teleconferences. ICH's biannual meetings see the meeting of WGs usually for 4-5 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 **Amsterdam, the Netherlands on** 1 to 6 June, and the second meeting in **Singapore** on 16 to 20 November. Both meetings were well attended by ICH's growing numbers of Members and Observers, with the Amsterdam meeting being the largest biannual meeting in ICH history with close to 500 participants.

The new schedule for the ICH biannual meeting week came into effect with the Singapore meeting with the week now starting on Sunday, and the Assembly meeting taking place on Tuesday and Wednesday.

The reports of Assembly and ICH Management Committee face-to-face meetings and teleconferences from 2019 are made available on the **ICH website**.

Both 2019 meetings were supported by a Professional Conference Organiser (PCO) contracted to work closely with ICH in support of its meetings. With the agreement of the ICH Management Committee, ICH applied for a grant in support of the Singapore meeting.

Details on 2019 meetings are provided as follows:

Assembly Meetings

- The **Assembly met twice during 2019**, at the time of ICH's biannual meetings: on 5 to 6 June and on 19 to 20 November.

- In June 2019 the Assembly was chaired by **Mrs. Lenita Lindström-Gommers (EC, Europe Chair) and Dr. Petra Doerr (Swissmedic, Switzerland, Vice-Chair)**. With Dr. Doerr needing to step down from the position at the end of the June 2019 meeting, **Dr. Celia Lourenco (Health Canada, Canada)** was appointed for a 6-month term until the Singapore meeting in November 2019, where both she and Mrs. Lindström-Gommers were re-elected to the respective positions of Assembly Vice-Chair and Chair to serve a 2-year term.
- The ICH Management Committee supported the participation of Ad-Hoc Observer Delegates to ICH Assembly meetings in June 2019 from: ANMAT, Argentina; JFDA, Jordan and SFDA, Saudi Arabia. These Ad-Hoc Observers were subsequently approved as ICH Observers.

ICH Assembly, Singapore, November 2019

ICH Management Committee Meetings

- The ICH Management Committee met several times throughout the year:
  - **9 times via teleconference** on the following dates: 30 January, 12 March, 25 March, 12 April, 8 May, 10 September, 13 September, 7 October and 23 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 Brussels, Belgium.
- Additionally, **close** to **20 ICH Management Committee Subcommittee teleconferences** were held (on New Topics, Implementation, Training, E8(R1) Stakeholder Meeting Planning, and Organisation of 30th Anniversary Event).
- All meetings in 2019 were chaired by **Dr. Theresa Mullin (FDA, United States, Chair)** and **Dr. Nobumasa Nakashima (MHLW/PMDA, Japan, Vice Chair)**. In November 2019 the ICH Management Committee re-elected Dr. Mullin as Chair and Dr. Nakashima as Vice-Chair to serve a further 1-year term.
- In Singapore, in November 2019, the Assembly elected **Mr. Diogo Penha Soares and Mr. Gustavo Lima Mendes Santos from ANVISA, Brazil, as ICH Management Committee Elected Representatives**, to serve until the next ICH Management Committee elections in June 2021, thereby filling the one vacant seat on the ICH Management Committee.

New ICH Management Committee Member Singapore, November meeting

ANVISA, Brazil

Left to right: *Mr. Diogo Penha Soares (ANVISA, Brazil), Dr. Nobumasa Nakashima (MHLW/PMDA, Japan), Dr. Celia Lourenco (Health Canada, Canada), Ms. Ana Carolina Moreira Marino Araujo (ANVISA, Brazil), Dr. Theresa Mullin (FDA, United States), Ms. Lenita Lindström-Gommers (EC, Europe), Mr. Gustavo Lima Mendes Santos (ANVISA, Brazil)*

MedDRA Management Committee Meetings

- The MedDRA Management Committee met several times:
  - **6 times via teleconference** on 25 April, 21 June, 31 June, 4 September, 19 September and 8 October.
  - **2 times face-to-face** during ICH's biannual meetings on 1 to 2 June and 17 to 18 November.
- All meetings in 2019 were chaired by **Mr. Mick Foy (MHRA, UK)**, who the MedDRA Management Committee re-elected as Chair in June 2019 for a further 1-year term.

ICH Working Group Meetings

A total of **16** and **14 WGs met face-to-face** respectively at the May/June and November 2019 biannual meetings, and are detailed in Annex VI.

4.2. Planning of Future ICH Meetings

In 2019, the ICH Management Committee took decisions regarding the organisation of future ICH meetings. **Key decisions** are outlined below:

- The ICH Management Committee supported **Vancouver, Canada** and **Athens, Greece** as the respective locations for the **May and November 2020** meetings, as well as **Incheon, Republic of Korea** as the location of the **May/June 2021 meeting**.
- The ICH Management Committee agreed on the following dates for the 2021 and 2022 meetings:
    - From 13 to 17 November 2021;
    - From 21 to 25 May 2022 or 11-15 June 2022.
- The ICH Management Committee agreed to an interim meeting to take place on 19 to 20 March 2020 in **Brussels, Belgium** organised by the PCO.
- The ICH Management Committee agreed to renew the contract with the current PCO for an additional year to cover the 2022 ICH biannual meetings for organisation.
- The ICH Management Committee supported that a **call for tenders** would be conducted by the ICH Secretariat in 2020 to receive offers for the organisation of ICH meetings from 2023 and beyond, which may also include an offer from the current PCO.

5. 2019 ICH Operational Matters

5.1. ICH Articles & Procedures

5 Documents support the governance of the ICH Association and were each updated in 2019 in view of 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.

Significant changes were made in 2019 related to procedures on participation in WGs. These changes came further to careful reflections by the ICH Management Committee on how to manage the size of WGs in view of the growing number of ICH Members and Observers and maintain efficient and well-managed harmonisation work processes.

Starting first with a successfully conducted pilot with the E8(R1) EWG which enabled ICH stakeholders not participating in the WG to consult on the draft revised Technical Document prior to *Step 1*, the ICH Management Committee extended this mechanism for consultation by providing for the establishment of **Plenary Working Parties (PWPs)**. PWPs may be established for all new WGs with participation from Members/Observers who are either unable to participate in those WGs due to size limitations, or who are unable to devote the necessary level of effort to participate actively in those WGs' activities, but who wish to nonetheless follow the progress of the WG. PWPs will be consulted on draft documents prior to the reaching of *Step 1* and *Step 3*, with the possibility for the organisation of workshops with external industry stakeholders during

the public regulatory consultation phase for the draft ICH Guideline, as well as after the ICH Guideline is finalised.

Additionally, the Membership of each new WG was limited to a maximum 2 representatives per ICH Founding Regulatory Member, and 1 representative per Standing Regulatory Member, Regulatory Member, Founding Industry Member, Industry Member, and ICH Observer, with a special mechanism implemented to enable industry as a group to nominate up to 3 additional experts which could be used to enable experts from regions outside of the 3 Founding Members to participate so as to achieve appropriate diversity in representation of industry perspectives.

The following highlights the key decisions taken in 2019 regarding these documents:

ICH Articles of Association

- The Assembly approved several amendments to the ICH Articles of Association in 2019, with approval of version 3.0 in June and version 4.0 in November. Amendments related to: management of the size of ICH WGs in view of ICH's growing number of Members and Observers; definitions of the degrees of implementation of ICH Guidelines approved by the Assembly in Charlotte, NC, USA in November 2018; ICH cooperation with other organisations; reflection of the ICH Training mission statement supported in Charlotte, NC, USA in November 2018; replacement of ICH Management Committee Elected Representatives; and clarification on the synchronization of the terms of office of the Assembly Chair and Vice-Chair.

Assembly RoP

- The Assembly approved several amendments to the Assembly RoP in 2019, with approval of version 7.0 in June and version 8.0 in November. Amendments related to: management of the size of ICH WGs in view of ICH's growing number of Members and Observers; definitions of the degrees of implementation of ICH Guidelines approved by the Assembly in Charlotte, NC, USA in November 2018; ICH cooperation with other organisations; replacement of ICH Management Committee Elected Representatives; clarification on the synchronization of the terms of office of the Assembly Chair and Vice-Chair; process for nominating experts to the 3 additional industry seats; process for development of Reflection Papers; general principles for Discussion Groups; attendance of experts to WG meetings; and synchronization of the terms of office of ICH Management Committee Elected Representatives.

ICH Management Committee RoP

- The ICH Management Committee approved several amendments to its RoP in 2019, with approval of version 7.0 in June and version 8.0 in November. Amendments related to: management of the size of ICH WGs in view of ICH's growing number of Members and Observers; definitions of the degrees of implementation of ICH Guidelines approved by the Assembly in Charlotte, NC, USA in November 2018;

ICH cooperation with other organisations; ICH Management Committee and Subcommittee interim meetings; process for development of Reflection Papers; general principles for Discussion Groups; replacement of ICH Management Committee Elected Representatives; and synchronisation of the terms of office of the ICH Management Committee Chair and Vice-Chair.

MedDRA Management Committee RoP

- The MedDRA Management Committee approved amendments to its RoP in 2019 with approval of version 5.0 in June. Amendments included changes related to efficiency in the approval of reports, as well as for alignment with the ICH Articles of Association on the concept of cooperation with other organisations.

SOPs of the ICH Working Groups

- The ICH Management Committee several amendments to the SOPs of the WGs in 2019, with approval of version 8.0 in June and version 9.0 in November. Amendments related to: management of the size of ICH WGs in view of ICH's growing number of Members and Observers; definitions of the degrees of implementation of ICH Guidelines approved by the Assembly in Charlotte, NC, USA in November 2018; ICH Management Committee and Subcommittee interim meetings; replacement of a WG's Regulatory Chair in the event of resignation; appointment of a Rapporteur; development of Work Plans by WGs; clarification on WG quorum; alignment of sign-off templates for *Steps 1* and *3* with procedures; update of forms for Industry and Observer requests to nominate experts to WGs; process for nominating experts to the 3 additional industry seats; process for development of Reflection Papers; general principles for Discussion Groups; S5 Annexes maintenance procedure; and attendance of experts to their WG meetings.

5.2. ICH Funding

ICH Financial Audit

In June 2019 **the Assembly approved the 2018 Audited Accounts and Financial Statements of the ICH Association**, supporting their submission along with ICH's 2018 tax return in July 2019.

ICH Funding

2019 Membership Fees were paid as follows by all ICH Members in line with the decision taken by the Assembly in 2018:

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

2019 Membership Fees

Further to decisions taken in 2018 and 2019, the Assembly furthermore approved the same level of fees for 2020 and 2021.

In February 2019, the Assembly approved a revision to the 2019 ICH Budget to include additional funds for 2019 ICH training related activities. Later in the year, the Assembly approved the updated 2020 ICH Budget and provisional 2021 ICH budget.

Information can be found on the ICH website regarding yearly ICH Budgets 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 November 2019, the **Assembly approved the 2020 MedDRA Budget, including 2020 MSSO MedDRA Subscription Fee levels,** which were kept stable from 2019. It was furthermore noted that in 2020 the MedDRA Management Committee planned to undertake a market analysis with the support of an external consultant which would potentially be informative for the setting of future Subscription Fee levels.

Information can be found on the ICH website regarding the 2020 MedDRA Budget.

Financial Management

In 2019, the ICH Management Committee continued work to develop a **plan regarding use of surplus funds to further strategic activities** such as training, outreach and stakeholder engagement. In parallel of this exercise, the ICH Management Committee also progressed efforts towards the **establishment of a sustainable ICH funding model**, which is not reliant to the use of surplus funds to cover core operational activities. In support of this effort, an ICH Management Committee Financial Subcommittee was established and consideration given to future Membership Fee increases, particularly at the ICH Member level, as well as a possible introduction of a meeting fee for participants from Observers that do not pay Membership Fees. It was furthermore agreed for the ICH Management Committee Financial Subcommittee to hold joint sessions with a newly established MedDRA Management Committee Financial Subcommittee. The aim of which being to enable more active coordination between the two Committees, and facilitate a joint review of overall ICH and MedDRA multi-year budget planning, surplus needs and the appropriate level of reserve to maintain in view of overall ICH Association activities. This effort will continue into 2020.

With the support of the ICH and MedDRA Management Committees, 2019 also saw efforts to offset currency depreciation, with placement of an amount of US Dollar ICH surplus funds in a fixed-term interest earning account.

5.3. ICH Communication

The following should be noted in relation to communication activities in 2019:

- On 31 October 2019, as part of the GCP renovation plan, ICH held a public meeting entitled **"ICH Global Meeting on E8(R1) Guideline on General Considerations for Clinical Trials"** hosted by FDA, United States at its headquarters in Silver Spring, MD, USA. The purpose of the public meeting was to provide information and solicit input from a broad range of non-ICH Member/Observer stakeholders on the draft revised E8(R1) Guideline on General Considerations for Clinical Trials. Additionally, a public symposium was also organised on this topic by MHLW, PMDA, Japan and JPMA in Tokyo, Japan on 25 July 2019.
- Acknowledging a benefit for more routine engagement with the **Pharmaceutical Inspection Co-operation Scheme (PIC/S)** on ICH Guideline work with relevance to both Regulatory Assessor and Inspector disciplines, the ICH Management Committee took steps in 2019 towards a pilot process to facilitate further communication with PIC/S with respect to relevant ICH Guideline. The implementation of this pilot will be further explored with PIC/S in 2020.
- Work was also initiated by the ICH Management Committee in 2019 towards the commemoration in 2020 of **ICH's 30th Anniversary**. An Organising Subcommittee was established, with plans initiated to hold a one-day conference on Saturday, 14 November 2020 in Athens, Greece, ahead of the start of the ICH meeting. Additionally a short ICH film will be released to mark the occasion on ICH's 30th Anniversary and special sessions focusing on ICH's milestone will be held in conjunction with regional DIA meetings in Europe, Japan and USA in 2020.

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. In 2019 the following ICH Members held regional public meetings: ANVISA, Brazil; FDA, United States together with Health Canada, Canada; and MHLW/PMDA, Japan together with JPMA.

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 presenting on ICH and its Guidelines in other fora in 2019. One such presentation was delivered by Mrs. Lenita Lindström-Gommers (ICH Assembly Chair, EC, Europe) at the 13th Middle East Regulatory Conference (MERC) held in October 2019 in Cairo, Egypt.

5.4. Cooperation with the IPRP

Further to the renewal of the Memorandum of Understanding (MoU) between ICH and the IPRP (International Pharmaceutical Regulators Programme) in June 2018, the ICH Secretariat continued in 2019 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 2019, 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 2020.

5.5. ICH Secretariat

Staffing

The following highlights key points and decisions related to ICH Secretariat staffing in 2019:

- ICH Secretariat staffing was planned at **7 FTEs (Full Time Equivalents) for 2019**, allocated between ICH (~4.6 FTEs) and MedDRA (~1.9 FTEs) activities, as well as IPRP support (~0.5 FTEs). The ICH Secretariat operated at just less than full capacity in 2019, with approximately 6.3 FTEs, due to staff leave.
- The year saw the hiring in March 2019 of **Ms. Léa Bolle Buenano Mora** in the position of temporary Administrative Assistant to allow a reorganisation of ICH Secretariat activities during other staff leave.

- In view of the growing number of administrative tasks associated with independent ICH Secretariat operations, as well as MedDRA Management Committee interest to further increase the activities supported by the ICH Secretariat, the MedDRA Management Committee gave its approval for the ICH Secretariat to hire an additional new staff from 2020 to support MedDRA Secretariat activities.

2019 ICH Secretariat Key Activities

The following outlines key activities undertaken by the ICH Secretariat in 2019 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.

2019 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 Amsterdam in May/June 2019 and in Singapore in November 2019, and in March 2019 for the interim ICH Management Committee meeting in Brussels, Belgium; as well as for the following **teleconferences** which were organised by the ICH Secretariat in 2019: **9** ICH Management Committee teleconferences, in addition to support of close to **20** ICH Management Committee Subcommittee teleconferences; **2** ICH Coordinator teleconferences; and **6** MedDRA Management Committee teleconferences.
- **Supporting ICH harmonisation activities** and the work of **32 ICH WGs** in 2019, including keeping up-to-date membership lists and establishing 9 new WGs in 2019.
- **Providing support and input for the work of the ICH Management Committee Subcommittees** on: Financials; Training; New Topics; E8(R1) Stakeholder Meeting Planning and Organisation of 30th ICH Anniversary.
- **Drafting ICH Association Reports and Work Plans** in support of ICH Management Committee and MedDRA Management Committee reporting to the Assembly, including: 2018 Annual Report; 2020 ICH Work Plan and ICH Multi-Annual Strategic Plan; and 2020 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, final ICH Guidelines, *Step 2* and *Step 4* presentations, regional public consultation dates, guideline implementation status and dates, ICH Management Committee and Assembly Meeting Reports, ICH WG Training Materials, Press Releases, and information on ICH Recognised Training Programmes.
  - Maintaining up-to-date the publication on the ICH website, as part of **ICH's communication strategy and transparency policy,** the photographs and short biographies of all ICH Assembly, ICH Management Committee and MedDRA

Management Committee Representatives, Member Coordinators and ICH Secretariat, as well as the list of experts' names for all active WGs.

- Overseeing, inputting into and reviewing the work of the website developer contracted to: perform **upgrades to the ICH, Private Platform, and MedDRA websites**, work which was ongoing at the end of 2019; change the Content Management System for the **ICH Public website** and develop **new tools** to allow straightforward search of ICH Guidelines and easy retrieval of information on the status of implementation of ICH Guidelines, work which was completed in October 2019; and **develop an internal database interfaced with the websites** which was completed in March 2019 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.
- Managing the hosting of ICH websites, which in 2019 saw the migration of the ICH Public Website to a new hosting provider on a server located in Switzerland.

- **Responding to stakeholder enquiries** received via the ICH mailbox with input solicited as necessary from ICH experts and ICH Coordinators, and implementing with the support of the ICH Management Committee a new process for managing technical questions received.
- **Managing ICH's financial administration**, including: regular coordination with the fiduciary firm providing accountancy services to ICH; authorisation of payments; drafting of ICH and MedDRA budgets and multi-year budget plans; preparation of separate year-end closing expense reports for ICH and MedDRA; organising the financial audit; liaising with the relevant tax authorities for items including submission of 2018 tax return to Swiss authorities, quarterly VAT declarations to Swiss authorities, and other administrative aspects; setting-up and managing renewal of a fixed-term deposit bank account; managing ICH's grant agreement with FDA, United States, which in 2019 included: submissions of quarterly and annual Federal Financial Reports and the annual Research Performance Progress Report, in addition to submission of a request for additional funding based on ICH Management Committee approval to support the continued Rapporteurship through the grant of a former FDA, United States expert with the establishment of an agreement to facilitate their provision of consultancy services to ICH.
- **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.
- **Supporting the logistical organisation of current and future year ICH biannual meetings and ICH Management Committee interim meeting** including: regular coordination with and oversight of the PCO in their (1) selection of potential meeting venues for presentation to the ICH Management Committee, (2) contracting of meeting venues and support services, such as translators and audio-visual equipment, and (3) organisation of meetings with registration and meeting information provided to participants followed by logistical set-up of meeting venues to ensure ICH meeting

requirements are met appropriately to support the successful meetings of ICH governing bodies and WGs.

2019 Other Key Activities:

- **Supporting ICH WG interest for a more advanced collaborative platform** than the ICH Groups platform used to-date, with conduct of a pilot of SharePoint for a number of WGs, and following the successful outcome of the pilot, and with the support of the ICH Management Committee, initiating a plan to **transition all WGs from the ICH Groups platform to SharePoint** by end of 2020 with a view to retiring the ICH Groups platform.
- **Supporting the ICH Management Committee in efforts towards the selection and contracting of Training Associates**, with development of materials for a Call for Expression of Interest launched in April 2019, triaging questions received during the Call, assisting ICH Management Committee anonymised assessment of the responses received, and coordinating the development and negotiation of agreements with solicitation of the appropriate legal input.
- **Supporting ICH Guideline implementation activities**, including: supporting the ICH Management Committee's Implementation Subcommittee until its disbandment in June 2019; supporting the ICH Management Committee Co-Leads assigned to this activity thereafter; coordination with CIRS, the independent third party contracted to conduct the survey and develop a publication on its outcome, with publication of this report on the ICH website in November 2019; making current up-to-date information on ICH Guideline implementation available on the ICH website, which in 2019 included liaison with ICH Members on the status of implementation and publication of this information in a new searchable tool on the ICH website.
- **Managing 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; coordination with trademark lawyers and ICH and MedDRA Management Committee Chairs regarding issues, which in 2019 resulted in ICH Secretariat support of filing of ICH opposition against 2 applications for the registration of trademarks similar to MedDRA trademarks.
- **Supporting the MedDRA Management Committee** oversight of the MSSO Contractor's participation in the **IMI WEB-RADR 2 project** which ICH joined in 2018 in support the development a proof-of-concept bidirectional **mapping between MedDRA and SNOMED**, and support of efforts towards establishing an agreement between ICH and SNOMED Internationals regarding the maintenance and distribution of the mapping.

- **Identifying opportunities for enhanced efficiencies** in the ICH Secretariat's management of the day-to-day operations of the ICH Association to ensure a mindful and well-appropriated use of ICH Secretariat resources.

Annex I

Assembly Member Representatives & Observer Delegates

December 31, 2019

Founding Regulatory Members

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

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

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

Founding Industry Members

EFPIA
Dr. Sue Forda
Mr. Pär Tellner

JPMA
Dr. Hironobu Hiyoshi
Dr. Masafumi Yokota

PhRMA
Dr. Peter Honig

Standing Regulatory Members

Swissmedic, Switzerland
Dr. Jörg Schläpfer

Health Canada, Canada
Dr. Celia Lourenco *(Vice Chair)*
Dr. Léo Bouthillier

Regulatory Members

ANVISA, Brazil
Mr. Diogo Penha Soares
Mr. Gustavo Mendes Lima Santos

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

MFDS, Republic of Korea
Dr. Young-Ok Kim
Dr. Kyung Won Seo

NMPA, China
Dr. Sheng Yang
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

Global Self-Care Federation
Ms. Caroline Mendy
Ms. Judy Stenmark

Standing Observers

WHO
Dr. Samvel Azatyan

IFPMA
Dr. Sharon Olmstead

Observers

Bill and Melinda Gates Foundation
Dr. Murray Lumpkin

CDSCO, India
Dr. S. Eswara Reddy

CECMED, Cuba
Dr. Celeste Sánchez González

COFEPRIS, Mexico
Dr. Ofra Axelrod

CPED, Israel
COFEPRIS Secretariat

INVIMA, Colombia
Dr. Judith del Carmen Mestre Arellano

JFDA, Jordan
Dr. Wesal Haqaish

MMDA, Moldova
Mr. Dumitru Saghin

National Center, Kazakhstan
Ms. Sabina Chukumova

NPRA, Malaysia
NPRA Secretariat

NRA, Iran
Mr. Mahmoud Alebouyeh

Roszdravnadzor, Russia
Dr. Sergey Glagolev

SAHPRA, South Africa
Ms. Portia Nkambule

SCDMTE, Armenia
Ms. Aida Malkhasyan

SFDA, Saudi Arabia
Dr. Adel Alharf

TGA, Australia
TGA Secretariat

TITCK, Turkey
Ms. Hacer Coşkun Çetintaş

APEC
Dr. Joung-weon Oh

ASEAN
Ms. Charunee Krisanaphan

EAC
Ms. Jane Mashingia

GHC
Dr. Hajed M. Hashan

PANDRH
Ms. Analía Porrás

SADC
Ms. Fortunate Ntombi Bhembe

APIC
Dr. Rainer Fendt

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, 2019

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

Founding Industry Members

EFPIA
Dr. Sue Forda
Mr. Pär Tellner

JPMA
Dr. Hironobu Hiyoshi
Dr. Masafumi Yokota

PhRMA
Dr. Peter K. Honig

Standing Regulatory Members

Swissmedic, Switzerland
Dr. Jörg Schläpfer

Health Canada, Canada
Dr. Celia Lourenco
Dr. Léo Bouthillier

Standing Observers

WHO
Dr. Samvel Azatyan

IFPMA
Dr. Sharon Olmstead

Regulatory Members

ANVISA, Brazil
Mr. Diogo Penha Soares
Mr. Gustavo Mendes Lima Santos

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

MFDS, Republic of Korea
Dr. Young-Ok Kim
Dr. Kyung Won Seo

NMPA, China
Dr. Sheng Yang
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, 2019

Founding Regulatory Members

EC, Europe
Dr. Georgios Balkamos
Dr. Sabine Brosch

MHLW/PMDA, Japan
Dr. Daisuke Tanaka
Mr. Masahiro Inada

FDA, United States
Ms. MaryAnn 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

Standing Regulatory Member

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

MHRA, UK

Mr. Mick Foy
Mr. Philip Tregunno

WHO Observer

WHO
Mr.Takahiro Goto

Annex IV

ICH Secretariat Staff

31 December, 2019

Director
Dr. Dawn Ronan

Managers
Dr. Anne Latrive
Ms. Nadia Myers Biggs

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

Administrative Assistant
Ms. Léa Bolle Buenano Mora

Annex V

Assembly Member ICH Coordinators

31 December, 2019

Founding Regulatory Members

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

MHLW/PMDA, Japan
Mr. Ryo Iwase

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

Founding Industry Members

EFPIA
Ms. Giovanna Rizzetto

JPMA
Dr. Manabu Yanagisawa

PhRMA
Ms. Camille Jackson

Standing Regulatory Members

Swissmedic, Switzerland
Dr. Gabriela Zenhaeusern

Health Canada, Canada
Mr. Nick Orphanos

Regulatory Members

ANVISA, Brazil
Ms. Ana Carolina Moreira Marino Araujo

NMPA, China
Dr. Yang Wang

HSA, Singapore
Ms. Chua Siew Wei

MFDS, Republic of Korea
Ms. Pan Soon Kim

TFDA, Chinese Taipei
Ms. Yi-Jing Kuo

Industry Members

BIO
Dr. Ingrid Markovic

IGBA
Dr. Shinichiro Hirose

Global Self-Care Federation
Ms. Caroline Mendy

Annex VI

ICH Working Groups which met face-to-face at ICH's biannual meetings in 2019

Amsterdam, the Netherlands on 1 – 7 June 2019

Group Code	Group Name	Meeting Days
E2B(R3) EWG/IWG	Revision of the Electronic Submission of Individual Case Safety Reports	4 days
E8(R1) EWG	Revision on General Considerations for Clinical Trials	4 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 IWG	The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs	4 days
E17 IWG	Multi-Regional Clinical Trials	3 days
M2 EWG	Electronic Standards for the Transfer of Regulatory Information (ESTRI)	4 days
M7(R2) Maintenance EWG/IWG	Addendum to Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk	4 days
M9 EWG	Biopharmaceutics Classification System-based Biowaivers	4 days
M11 EWG	Clinical electronic Structured Harmonized Protocol (CeSHarP)	4 days
Q2(R2)/Q14 EWG	Analytical Procedure Development and Revision of Q2(R1) Validation of Analytical Procedures	4 days
Q3D(R2) Maintenance EWG	Maintenance of the Guideline for Elemental Impurities	2 days
Q12 EWG	Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management	6 days
Q13 EWG	Continuous Manufacturing	4 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

Singapore on 16 – 20 November 2019

Group Code	Group Name	Meeting Days
E2D(R1) informal WG	Revision of ICH E2D Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting	4 days
E6(R3) informal WG	Revision of ICH E6 Good Clinical Practice	4 days
E11A EWG	Paediatric Extrapolation	5 days
E14/S7B IWG	The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs	4 days
E19 EWG	Optimization of Safety Data Collection	4 days
E20 informal WG	Adaptive Clinical Trials	4 days
M10 EWG	Bioanalytical Method Validation	4 days
M11 EWG	Clinical electronic Structured Harmonized Protocol (CeSHarP)	4 days
M12 informal WG	Drug Interaction Studies	4 days
Q2(R2)/Q14 EWG	Analytical Procedure Development and Revision of Q2(R1) Validation of Analytical Procedures	4 days
Q5A(R2) informal WG	Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin	4 days
Q12 EWG	Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management	5 days
Q13 EWG	Continuous Manufacturing of Drug Substances and Drug Products	4 days
S12 informal WG	Non-clinical Biodistribution Studies for Gene Therapy Products	4 days

Annex VII

Overview of harmonisation activities and accomplishments in 2019

Topic Code	Type of Working Group	Topic Name	Accomplishments	Anticipated Milestones
Standing Pediatric	Standing EWG		The Standing EWG stays available for requests for pediatric expertise from other ICH WGs	N/A (Ongoing Activity)
E2B(R3)	EWG/IWG	Revision of Electronic Submission of ICSRs	Reached *Steps 3* and *4* in June 2019 of the Revision of Q&As for the Electronic Submission of Individual Case Study Reports	N/A (Ongoing Activity)
E2D(R1)	EWG	Revision of Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting	EWG established in November 2019	*Steps 1* and *2 a/b* are expected by November 2021
E6(R3)	EWG	Revision of Good Clinical Practice	EWG established in November 2019	*Steps 1* and *2 a/b* are expected for Annex 1 by November 2021 *Steps 1* and *2 a/b* for Annex 2 to be determined (work to be undertaken following reaching of *Steps 1* and *2 a/b* for Annex 1)
E8(R1)	EWG	Revision of General Considerations for Clinical Studies	Reached *Steps 1/2* in April/May 2019	*Steps 3* and *4* are expected by June 2020
E9(R1)	EWG	Addendum to Defining Appropriate Estimand for a Clinical Trial/Sensitivity	Reached *Steps 3* and *4* in November 2019	Training materials are expected to be finalised by early 2020

		Analyses		
E11A	EWG	Paediatric Extrapolation	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2a/b* are expected by November 2020
E14/S7B	IWG	Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs	Activities progressed in line with Concept Paper/Work Plan	Finalisation of the first stage of Q&As is expected by June 2020
E17	IWG	ICH Guideline on Multi-Regional Clinical Trials	Final Training Materials published in September 2019	The work of this IWG is now complete
E19	EWG	ICH Guideline on Optimization of Safety Data Collection	Reached *Steps 1/2* in March/April 2019	*Steps 3* and *4* are expected by June 2021
E20	EWG	Adaptive Clinical Trials	EWG established in November 2019	*Steps 1* and *2 a/b* are expected by November 2021
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 22.0 & 22.1.	N/A (Ongoing Activity)
M2	EWG	Electronic Standards for the Transfer of Regulatory Information	Developed White Paper on HL7 Fast Healthcare Interoperability Resources (FHIR) Considerations for ICH Progressed development of project opportunities proposal.	N/A (Ongoing Activity)
M7(R2)	Maintenance EWG	Addendum to Assessment and Control of DNA	Activities progressed in line with Concept Paper /Work Plan	*Steps 1* and *2 a/b* for the revised M7(R2) Draft Guideline

		Reactive Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk Development of Q&As		(including the revised second Addendum) and Q&As are expected by first half of 2020
M8	EWG/IWG	Electronic Common Technical Document: eCTD	Progressed work on eCTD v4.0 Change Requests	N/A (Ongoing Activity)
M9	EWG	Biopharmaceutics Classification System-based Biowaivers	Reached *Steps 3* and *4* in November 2019	The work of this EWG is now complete
M10	EWG	Bioanalytical Method Validation	Reached *Steps 1/2* in January/February 2019	*Steps 3* and *4* are expected by November 2020
M11	EWG	Clinical electronic Structured Harmonised Protocol (CeSHarP)	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2 a/b* are expected by November 2020
M12	EWG	Drug Interaction Studies	EWG established in November 2019	*Steps 1* and *2 a/b* are expected by November 2021
Q2(R2)/Q 14	EWG	Analytical Procedure Development and Revision of Q2 (R1) Analytical Validation	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2 a/b* are expected by May 2020
Q3C(R6)	Maintenance EWG	Maintenance of the Guideline for Residual Solvents	Following a correction with release of Q3C(R7) in 2018, for what had been considered an error regarding the PDE for ethyleneglycol, the change was in 2019 reversed and the former PDE and Q3C(R6) reinstated, based on archival documents and literature review which confirmed the PDE for ethyleneglycol as 6.2	N/A

			mg/day (620 ppm). A cover statement was publish on the ICH website to explain the reason for the reversion.	
Q3C(R8)	Maintenance EWG	Maintenance of the Guideline for Residual Solvents	Progressed work to develop PDE levels for 3 new solvents adopted in June 2017: 2-methyltetrahydrofuran, cyclopentylmethyleher and tert-butanol.	(Ongoing Activity) *Steps 1* and *2 a/b* are expected by early 2020
Q3D(R1)/(R2)	Maintenance EWG	Maintenance of the Guideline for Elemental Impurities	Progressed work on Addendum to Q3D Guideline to include PDEs for cutaneous and transdermal products. Reached *Steps 3* and *4* on the revision Q3D(R1) for the Cadmium inhalation PDE in March 2019.	(Ongoing Activity) *Steps 1* and *2 a/b* are expected by early 2020 for Q3D(R2) Addendum
Q5A(R2)	EWG	Revision of Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin	EWG established in November 2019	*Steps 1* and *2 a/b* are expected by June 2021
Q11	IWG	Q&As on API Starting Materials	Training Materials finalised and published on ICH website in 2019	The work of this IWG is now complete
Q12	EWG	ICH Guideline on Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management	Reached *Steps 3* and *4* for new Q12 Guideline in November 2019	Concept Paper to be approved regarding establishment of a IWG for the development of training materials
Q13	EWG	Continuous Manufacturing of Drug Substances and	Activities progressed in line with Concept Paper/Business	*Steps 1* and *2 a/b* are expected by May 2020

		Drug Products	Plan/Work Plan	
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 by May 2020
S5(R3)	EWG	Revision on Detection of Toxicity to Reproduction for Human Pharmaceuticals	Activities progressed in line with Concept Paper/ Work Plan	*Steps 3* and *4* are expected by early 2020
S11	EWG	Nonclinical Safety Testing in Support of Development of Paediatric Medicines	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 3* and *4* are expected by early 2020 Training materials expected to be finalised by June 2020
S12	EWG	Nonclinical Biodistribution Considerations for Gene Therapy Products	EWG established in November 2019	*Steps 1* and *2 a/b* are expected by June 2021