ICH
harmonisation for better health

# ICH Association

## Annual Report 2021

# ICH Association

# 2021 Annual Report

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

*Version dated 5 May 2022*

*Approved by the ICH Assembly on 24 May 2022*

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ICH Assembly Chair
EC, Europe

**Dr. Gabriela Zenhäusern**
ICH Assembly Vice Chair
Swissmedic, Switzerland

## Message from Assembly Chair and Vice Chair

Now into ICH's fourth decade of activity, 2021 continued to show the lasting and ever-expanding commitment of ICH Members and Observers to advance global harmonisation for better health. ICH continues to grow, with 19 Members and 35 Observers working together towards developing, implementing and updating high-level guidelines.

Despite challenges presented by the COVID-19 pandemic, harmonisation activities encompassed work on 34 topics on which ICH Working Groups progressed over the year, and an extended strategy to address the training needs of ICH Members and Observers supporting ICH's aim to achieve global harmonised implementation of ICH Guidelines. We would like to extend our gratitude especially to all the ICH Experts for all their efforts in pursuing the important harmonisation work of the ICH Working Groups which is particularly challenging in a virtual setting.

ICH's recent 30-year milestone was marked by the ICH 30$^{th}$ Anniversary Publication and associated Leaflet, two documents intended to disseminate information on ICH's mission, looking back at its history and how its work has contributed to better health, and providing considerations for the next 10 years.

As Chair and Vice-Chair of the Assembly, we are delighted to have the opportunity to see ICH through its continued evolution**. We look forward to stepping into a new year of great achievements where we can hopefully resume in-person ICH meetings.**

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# 1. About ICH

## *1.1. Purpose & Aims*

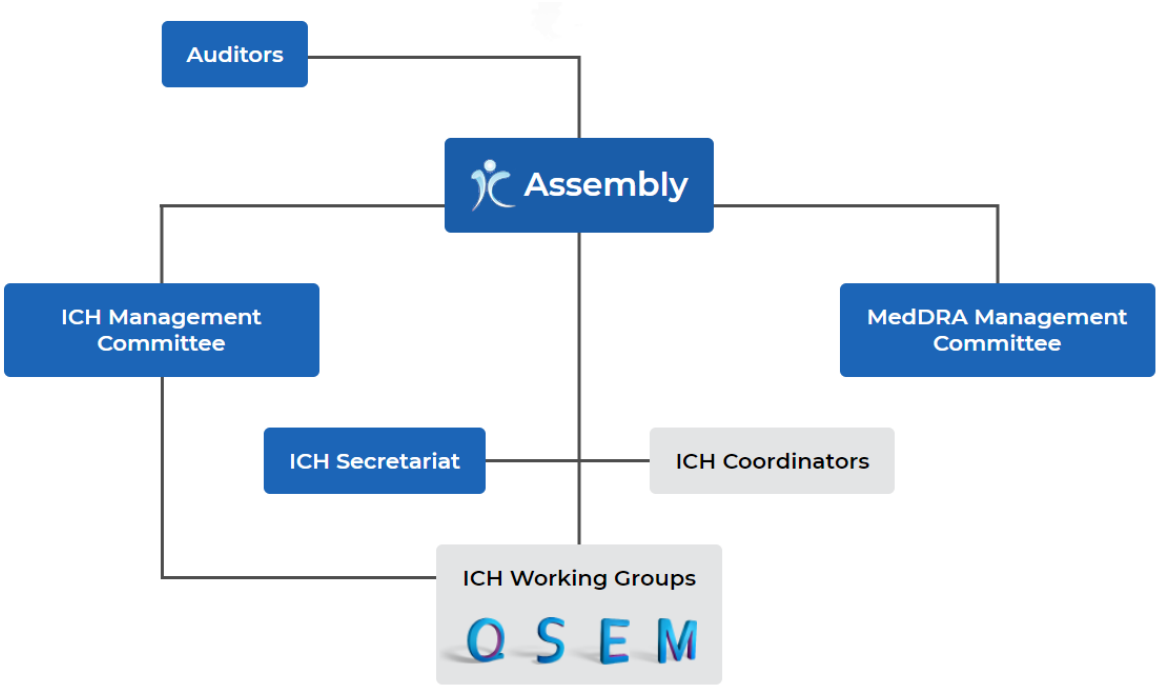
The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (**ICH**) **is an international non-profit organisation** which was established as an association under Swiss law in October 2015. The purpose of ICH is to **promote public health through international 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 adequate **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, 2021 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 2021 the following Subcommittees were supporting the work of Management Committee: Finance, New Topics, Training, and Organising Subcommittee. The 30$^{th}$ Anniversary Organising Subcommittee was disbanded in December 2021 in view of the completion of its work.The full list of the

ICH Management Committee Member Representatives and Observer Delegates as of December 31, 2021 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, 2021 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 2021 are referred to in Section 5.5.
- The full list of ICH Secretariat Staff as of December 31, 2021 is provided in Annex IV.

**Auditors**

- In 2020, 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 2020 and 2021.

**ICH Coordinators**

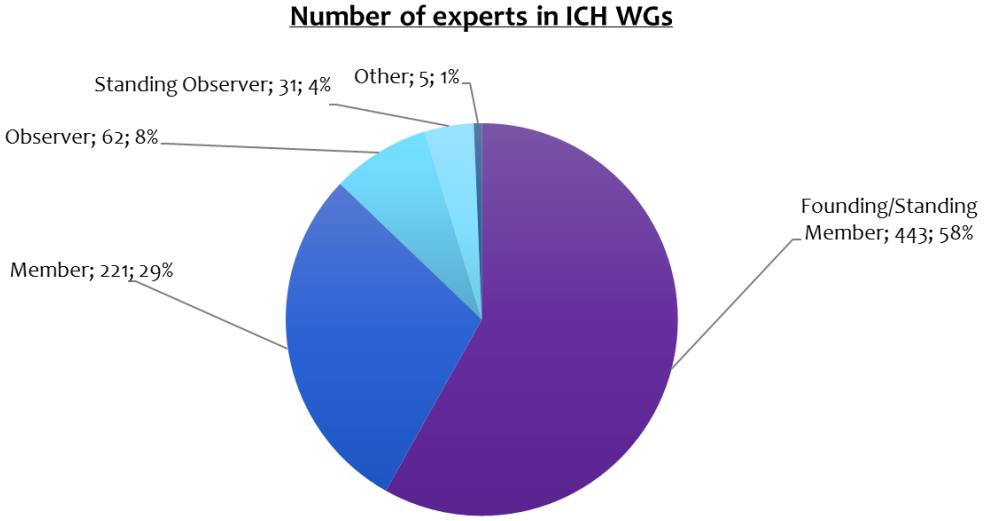
- **Fundamental to the smooth running of ICH** has been the designation of an ICH Coordinator per ICH Member to act as the main contact point with the ICH Secretariat. Coordinators ensure proper distribution of ICH documents to the appropriate persons from their organisation and are responsible for the **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, 2021 is provided in Annex V.

## 2. 2020 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. The year 2021 saw the addition of 2 new Members and 5 new Observers, bringing ICH to a total of **19 Members and 35 Observers**. By the end of 2021 over 1,100 individuals were contributing to the work of ICH, either as Representatives/delegates of ICH bodies, experts on Working Groups (WGs) or in supporting roles.

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 2021 these WGs involved the participation of **over 700 technical experts**.




***Overview of Expert Participation in ICH, as of October 2021***

Further to the ICH Management Committee's decision taken in 2019 to enable the establishment of a Plenary Working Party (PWP) for each new WG established, at the end of 2021 PWPs had been established for 9 Working Groups (ICH E2D(R1), E6(R3), E20, M4Q(R2), M12, Q3E, Q5A(R2), Q9(R1), S12). This allows interested ICH Members and Observers without an expert in the WG to follow more closely work on ICH Guidelines and to be consulted ahead of *Step 1* and *Step 3* sign-offs. 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 Members and Observers Approved in 2021*

At the virtual meeting in June 2021, the Assembly approved SFDA, Saudi Arabia as a **new ICH Regulatory Member**, in addition to two **new ICH Regulatory Observers**: AEC,

Azerbaijan and MHRA, UK, while at the virtual meeting in November 2021, the Assembly welcomed COFEPRIS, Mexico as a **new ICH Regulatory Member**, in addition to three **new ICH Regulatory Observers**: EDA, Egypt, Indonesian FDA, Indonesia and SECMOH, Ukraine based on the recommendation of the ICH Management Committee.

## 3. 2021 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 2021, these activities were progressed on **34 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, as due to COVID-19 pandemic no face-to-face meetings took place in 2021.

The **key outcomes in 2021** 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 Revised ICH Guidelines**
  - **1 Updated Question & Answer (Q&A) Document and Specification Change Request Document and Implementation Package**

- Reaching of ***Step 2a/b*** of the ICH process and completion of drafts (Please see Section 3.2) of:
  - **2 New ICH Guidelines**
  - **3 Revised** ICH Guidelines

- **3 New** topics were approved in 2021.

An overview of all ICH WG activities and accomplishments in 2021 is presented in Annex VI.

### *3.1. ICH Guidelines & Other WG Work Products Finalised in 2021*

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

**ICH E8(R1) Guideline - General Considerations for Clinical Studies** 

The E8(R1) Guideline reached *Steps 3 and 4* in October 2021.

This revised guideline provides guidance on the clinical development lifecycle, including designing quality into clinical studies, considering the broad range of clinical study designs and data sources used. This modernisation of ICH E8 is the first step towards the Renovation of Good Clinical Practice initiated in 2017. The revision incorporates the most current concepts achieving fit-for-purpose data quality as one of the essential considerations for all clinical trials.

**ICH M8 Electronic Common Technical Document (eCTD) – Revised Q&A, Specification Change Request Document, Specification for Submission Formats, and Implementation Package**

*Step 4* of the eCTD v4.0 Q&As and Specification Change Request Document v1.5, Specification for Submission Formats v1.3, as well as the eCTD v4.0 Implementation Package v.1.4 were reached electronically in June 2021.

*Step 4* of the eCTD v4.0 Q&A Document v1.6 and eCTD v3.2.2 Q&A Document v1.32 were reached in November 2021.

**ICH Q3C(R8) Guideline - Residual Solvents**

*Steps 3 and 4* of the Q3C(R8) Guideline including the Permitted Daily Exposure (PDE) levels for the solvents 2-Methyltetrahydrofuran, Cyclopentyl Methyl Ether and Tertiary-Butyl Alcohol were reached in April 2021.

### *3.2. ICH Guidelines Endorsed at Step 2a/b in 2021*

In 2021 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 M7(R2) Guideline and Addendum - Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk**

*Step 2b* of the M7(R2) draft Guideline and Addendum was reached in October 2021.

The ICH M7(R2) Addendum provides useful information regarding the acceptable limits of known mutagenic impurities/ carcinogenic and supporting monographs. 7 new compounds have been added in this revision: Acetaldehyde, Dibromoethane, Epichlorohydrin, Ethyl Bromide, Formaldehyde, Styrene, and Vinyl Acetate.

**ICH Q9(R1) Guideline - Quality Risk Management**

The Q9(R1) Draft Guideline was endorsed under *Step 2b* in November 2021.

This revised guideline makes limited and specific adjustments to specific chapters and annexes of the ICH Q9 Guideline. This targeted revision, supported by additional training materials (which are expected in 2022), aims to improve understanding in specific areas and consistent application of QRM (Quality Risk Management) by addressing subjectivity in risk assessment/QRM outputs, supply and product availability risks, formality in QRM

and risk-based decision making, as well as the hazard identification and risk review, whilst also recognising the role of other ICH quality guidelines.

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

*Steps 1 and 2a/b* on the Q13 draft Guideline were reached in July 2021.

This new guideline describes scientific and regulatory considerations for the development, implementation, operation, and lifecycle management of continuous manufacturing (CM). Building on existing ICH Quality guidelines, this guideline provides clarification on CM concepts, describes scientific approaches, and presents regulatory considerations specific to CM of drug substances and drug products. This guideline applies to CM of drug substances and drug products for chemical entities and therapeutic proteins. It is applicable to CM for new products (e.g., new drugs, generic drugs, biosimilars) and the conversion of batch manufacturing to CM for existing products. The principles described in this guideline may also apply to other biological/biotechnological entities.

**ICH S1B(R1) Guideline Addendum - Rodent Carcinogenicity Studies for Human Pharmaceuticals** S

*Steps 1 and 2a/b* on the S1B(R1) draft Guideline were reached in May 2021.

This addendum is complementary to the S1 Guidelines (S1A, S1B and S1C(R2)) and, at *Step 4* of the ICH process, will be integrated with the S1B Guideline. This Addendum expands the testing scheme for assessing human carcinogenic risk of small molecule pharmaceuticals by introducing an additional approach that is not described in the original S1B Guideline. Application of this integrative approach would reduce the use of animals in accordance with the 3Rs (reduce/refine/replace) principles, and shift resources to focus onto generating more scientific mechanism-based carcinogenicity assessments, while promoting safe and ethical development of new small molecule pharmaceuticals.

**ICH S12 Guideline - Biodistribution Studies for Gene Therapy Products** S

*Steps 1 and 2a/b* on the S12 draft Guideline were reached in June 2021.

This new guideline aims to provide harmonised recommendations for the conduct of nonclinical biodistribution (BD) studies in the development of gene therapy (GT) products, providing recommendations for the overall design of nonclinical BD assessments, and also providing considerations for interpretation and application of the BD data to support a nonclinical development programme and the design of clinical trials. The recommendations in this guideline endeavour to facilitate the development of GT products while avoiding unnecessary use of animals, in accordance with the 3Rs (reduce/refine/replace) principles.

## *3.3. New Harmonisation Activities*

### 3.3.1. Approval of New Topics

In 2021 the ICH Management Committee and its New Topics Subcommittee assessed **9 New Topic proposals** which had been submitted by ICH Members and Observers by a mid-December 2020 deadline as part of the limited call for New Topics which focused on urgent and high-impact topics, in view of the high number of currently active WGs and the challenges presented by the COVID-19 pandemic, including expert availability, as well as WGs not being able to meet face-to-face. 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 3 new harmonisation activities:

**Revision of ICH Q1 Guidelines on Stability Testing and related ICH Q5C Guideline on Quality of Biotechnological Products: Stability Testing of Biotechnological/Biological Products**

The targeted revisions of the ICH Stability Guideline series aim to include use of science and risk-based approaches in stability, enhanced harmonisation and enabling a holistic view on the stability requirements facilitating early understanding of the current expectations 30 years after the concepts had been developed.

- The Management Committee supported that the informal WG would initiate work in June 2022.

**Revision of ICH Q6A and Q6B on Specifications: Test Procedures and Acceptance Criteria for New Drug Substances and New Drug Products: Chemical Substances and Biotechnological/Biological Products**

This document aims to update and contemporise ICH Q6A/6B Guidelines and clarify expectations for regulatory harmonisation in conjunction with ICH Q3, Q4, Q8-14, M7 and M9 Guidelines, integrating science and risk-based pharmaceutical development concepts that will improve implementation and expedite regulatory review of commercial applications.

- The informal WG will be established with a delayed start following the initiation of the revision of ICH Q1 topic.

**General Principles on Planning and Designing Pharmacoepidemiological Studies that Utilize Real-World Data (RWD) for Safety Assessment of a Medicine**

This document aims to provide recommendations on general considerations when utilising RWD for drug safety assessments, including data source selection, study design, definitions of target populations, exposure and outcome(s), and analytic approaches.

- The M14 informal Working Group has been established in the second half of 2021 to develop a Concept Paper and Business Plan.

### 3.3.2. Other New Harmonisation Activities

In 2021, the Assembly approved the final Concept Paper and Business Plan concerning a revision procedure: M4Q(R2) Common Technical Document (CTD) on Quality Guidance, focusing on revision of CTD Quality sections in Modules 2 and 3 to capture quality information for the registration and lifecycle management of pharmaceuticals for human use.

### 3.3.3. Strategic Reflection Papers

The ICH Assembly supported an updated version of the ICH Reflection Paper on Patient-Focused Drug Development (PFDD) endorsed in November 2020. The paper presents opportunities for development of new ICH Guidelines to provide a globally harmonised approach to the inclusion of the patient's perspective in a way that is methodologically sound and fit-for-purpose for both regulated industry and regulatory authorities.

The updated version reflects modifications based on public stakeholder comments received during the public consultation until March 2021 and which are summarized in an Outcome of Public Consultation Document, published on the ICH website.

## *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.

ICH Guideline implementation information is published on the ICH website www.ich.org, with a searchable database tool rolled-out in 2019 and periodically updated by the ICH Secretariat 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 launched for the second time in December 2020 in coordination with the Centre for Innovation in Regulatory Science (CIRS), an independent third party contracted by ICH to conduct the survey. The objective of the study was principally to assist in determining whether Regulatory Members would meet the eligibility criteria for the Management Committee elections in 2021 and to also allow participating Observers interested in future ICH Membership to reference survey findings. The scope of the survey included Tier 1 ICH Guidelines for Regulatory Observers, and Tier 2 and Tier 3 ICH Guidelines for ICH non-Founding and non-Standing Regulatory

Members, based on the criteria of ICH Membership and Management Committee Elections. The results of the study were presented at the ICH virtual meeting in June 2021, and subsequently a report was developed by CIRS and published on the ICH website in September 2021.

The results show evidence of a strong level of implementation and adherence to the ICH Guidelines by the participating 6 ICH non-Founding and non-Standing Regulatory Members and the 4 ICH Regulatory Observers, with a good alignment between the perception of the participating 30 pharmaceutical companies and the self-declaration from the assessed authorities.

Furthermore, following the same approach as for the Phase 2a survey, in 2021 the Management Committee supported the conduct of an analysis of the free-text entries from the 2021 Phase 2b Implementation Survey, including development by CIRS of two types of report: a main report, with overall trends across all guidelines and specific reports for each participating regulatory authority. Both types of reports were delivered by CIRS in Q4 2021, with a main report to be finalised in early 2022.

With the Public Report and the Free Text Analysis being the last deliverables of the Phase 2b Implementation Survey, the Management Committee decided that support of future survey work will be provided by the ICH Secretariat.

### *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 an effort to ensure the availability of high-quality training on ICH Guidelines, despite continuing challenges faced in view of the global pandemic situation, work included continued delivery of **ICH Recognised Training Programmes** organised by Training Providers and the **financial support of training on ICH Guidelines** organised by ICH Regulatory Members and Observers.

Additionally, the Assembly supported an expedited approach to address the training needs of ICH Members and Observers as part of a 5-year strategic plan focused on expanding work with **ICH Training Associates** to develop online training materials for all ICH Guidelines, in addition to offering tailored training.

ICH Recognised Training Programmes:

In 2021 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 HeSAY Regulatory Science CoE: Pharmacovigilance Seminar, Beijing, China, 31 October - 4 November 2021 (in person and online);
- King's College London: ICH Q8 Pharmaceutical Development Guidelines, 8 November 2021 (online).

ICH Training Associates:

Further expansion of the ICH Training Associates programme was seen in 2021, with progress of work on the ICH Q1 in-depth training modules by the first ICH Training Associate contracted in 2020, as well as contracting a second Training Associate in May 2021 for the development of training materials on ICH M4 and ICH E2.

Moreover, in 2021 the Assembly endorsed a **multi-year training approach and supported** a general concept of ICH training on specific Guidelines and crosscutting training approach including entering into cooperation with three proposed future Training Associates on developing online training materials, as well as offering of tailored training for regulatory authorities. This concept also included a 5-year budget plan supported by the Assembly as a part of the new multi-year approach. The continued aim of the ICH Training Associates programme is **to assist ICH in its efforts to address in a strategic manner the training needs of its Regulatory and Industry Members and Observers**. The work of new potential Training Associates is to be initiated in early 2022.

ICH Regulatory Training

2021 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 and 1 ICH Regulatory Observer**. This came further to a Call for Expression of Interest launched by the ICH Management Committee in January 2021 and saw support provided for training planned by:

- ANVISA, Brazil on ICH Efficacy Guidelines;
- Health Canada, Canada on the ICH Q12 Guideline;
- JFDA, Jordan on ICH Q1, Q3, Q5-7 Guidelines;
- MHLW/PMDA, Japan on ICH Quality Guidelines;
- NMPA, China on ICH Q8-Q12 Guidelines.

In view of the COVID-19 pandemic, only one training event approved in 2021 and organised by MHLW/PMDA, Japan took place in 2021, with others being postponed to 2022.

In addition, out of the trainings approved in 2020, only that applied for by FDA, United States for Inspectorate training on ICH Q12 developed by PIC/S, took place in 2021, with other trainings, which were initially postponed to 2021, also delayed to 2022. The ICH Assembly approved carry over in the 2022 ICH budget to support these postponed training events in 2022.

Furthermore, the ICH Assembly supported budget towards a new Call for Expression of Interest process in 2022 for ICH Regulatory Members and Observers and also supported funding of regulatory training as a standing yearly process, subject to confirmation of the yearly budget.

### 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, in 2021 work was initiated and/or progressed on developing training materials on the following ICH topics, with the assistance of Founding Regulatory Member FDA, United States which made available the support of its studios for the production of videos:

- E9(R1);
- E2B(R3);
- Q12.

In June 2022 the ICH Q12 Training Materials Modules 0-7 were finalised by ICH Q12 IWG, with continued work on the development of Training Material Module 8 (case studies) as well as on a broad-audience video with the support of the FDA, United States studios to be finalised in 2022.

### 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 2021, the following presentations were made available:

- ICH Q9(R1) *Step 2* Informational Presentation;
- ICH Q13 *Step 2* Informational Presentation;
- ICH S12 *Step 2* Informational Presentation;
- ICH S1B(R1) *Step 2* Informational Presentation;
- ICH M7(R2) *Step 2* Informational Presentation;
- ICH Q3C(R8) *Step 4* Introductory Training 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.


Despite the global COVID-19 pandemic, MedDRA's number of users continued to grow globally in 2021, reaching close to 7500 subscribers (of which over 700 new subscribers) in almost 130 countries.

The continued growth in the number of users of MedDRA is a clear indicator of the successful adoption of MedDRA over the past 22 years as a worldwide standard in the protection of public health. In view of this continued user growth, 2021 saw further expansion in the support provided to facilitate the use of MedDRA in a broader set of countries/regions. This included initiation of a multi-year project in 2021 which will see the translation of MedDRA into the remaining 16 languages of the European Economic Area in collaboration with individual European National Competent Authorities, and release of Russian translations of MedDRA Points to Consider documents adding to other translations of the PtC documents (Chinese, English, Japanese, Korean, and Spanish. Work on developing translations initiated in 2021 include, Swedish, Latvian, Maltese, Greek, and Polish. Additionally, preparation towards initiating an Arabic MedDRA translation in 2022 has been made.

Expanding training and helpdesk support came with addition in 2021 of local support in Russia further to local support staff already in place **in Europe, India, China, Republic of Korea, Latin America, the USA and other regions**.

#### 3.6.1. Overview of 2021 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 2021 related to MedDRA's management:

***Financial:***

- The MedDRA Management Committee supported the **2022 Budget** including the **2022 MSSO Subscription Fees,** subsequently approved by the Assembly.

- The MedDRA Management Committee approved the **2022 MSSO Business Plan**.

***Operational:***

- The MedDRA Management Committee supported the **2022 Annual MedDRA Management Committee Work Plan** for submission to the Assembly, which was subsequently approved by the Assembly.
- The MedDRA Management Committee, with the support of the ICH Assembly, supported a transfer of the MSSO agreement from the Contractor Northrop Grumman to Peraton, effective end of August 2021 This transfer was necessitated by Peraton's acquisition of the Northrop Grumman business entity which had been providing the MSSO.
- The MedDRA Management Committee supported work to identify auditors in support of a multi-year MSSO audit plan covering Clinical-Quality-Procedural, IT and Financial aspects.
- 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 new ICH Member/Observer countries/regions as ICH grows, and in 2021 this included Azerbaijan.
- The MedDRA Management Committee supported the continued implementation of several recommendations informed by an assessment performed by an external IT consultant in 2020 for a digital transformation of MedDRA operations, leveraging technological advances.
- The MedDRA Management Committee, with the support of the ICH Assembly, initiated work towards the conduct of a study to support ICH considerations on long-term MedDRA operations.

***Interoperability with other terminologies:***

- As part of the efforts to facilitate the use of MedDRA through **mapping with other terminologies**, the MedDRA Management Committee: (1) cooperated with the International Medical Device Regulators Forum (**IMDRF**) in 2021 on the maintenance of the mapping between MedDRA and IMDRF's terminology: terminology: Annex E: Health Effects – Clinical Signs, Symptoms and Conditions Terms and Codes; (2) entered into cooperation with **SNOMED International, with ICH Assembly's approval**, for the maintenance and distribution of a bi-directional MedDRA/SNOMED mapping **released to MedDRA and SNOMED users on 30 April 2021**; and (3) continued to investigate a mapping between MedDRA and **WHO's ICD-10/11**.

***Development of SMQs:***

- The MedDRA Management Committee approved 1 new Standardised MedDRA Queries (SMQ) – Sexual dysfunction – included in MedDRA version 24.1. The addition of this new SMQ resulted in a total of **109 SMQs developed to-date**.

3.6.2. Oversight of 2021 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 2021, which were overseen by the MedDRA Management Committee:

- The MSSO conducted 9 face-to-face trainings in China and 177 webinars worldwide, and trained over 15,000 participants in 2021. MSSO has also added new topics, including but not limited to: MSSO Tool Demonstration; Introduction to MedDRA APIs for non-IT Personnel; and MedDRA – SNOMED CT mapping.
- Release to users of MedDRA versions 24.0 and 24.1.
- Continued work towards the **translation of MedDRA into the remaining 16 languages of the European Economic Area** in collaboration with individual European National Competent Authorities, and initiated preparations for work on an **Arabic translation in 2022 in coordination with ICH Member, SFDA, Saudi Arabia**.
- **Cooperation with the WHO and its Collaborating Centre, the Uppsala Monitoring Centre (UMC)** for organising a MedDRA and WHO Drug User Group virtual event, and in organising in-person and virtual User Group meetings.
- 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 the March release of MedDRA the PtC documents on Term Selection and Data Retrieval and Presentation, and to develop Russian translations of these PtC documents.
- Further to participating in the **Innovative Medicines Initiative (IMI) WEB-RADR 2 Project**, liaison with SNOMED International on the **bi-directional mapping between MedDRA and SNOMED** terminologies, released to MedDRA and SNOMED users on 30 April 2021.

# 4. 2021 Overview of Meetings & Planning

## *4.1. 2021 Meetings*

In 2021, due to the ongoing exceptional circumstances of the COVID-19 pandemic, all ICH meetings and activities were held as virtual biannual meetings and teleconferences of the WGs, the Assembly, ICH Management Committee, and MedDRA Management Committee.

The first of the biannual virtual meetings of the year for the Assembly, ICH Management Committee, and MedDRA Management Committee was held over several days between 18 May and 3 June, and the second between 25 October and 18 November. Both virtual meetings were well attended by ICH's growing numbers of Members and Observers with over 80 participants to the Assembly meetings.

The reports of Assembly and ICH Management Committee face-to-face meetings and teleconferences from 2021 are made available on the **ICH website**.

Details on 2021 meetings are provided as follows:

**Assembly Meetings**

- The **Assembly met twice during 2021**, at the time of ICH's biannual virtual meetings: on 2-3 June and 17-18 November.
- Both meetings were chaired by **Mrs. Lenita Lindström-Gommers (EC, Europe Chair) and Dr. Celia Lourenco (Health Canada, Canada, Vice-Chair)**. At the November meetings, Mrs. Lindström-Gommers was re-elected as Assembly Chair and **Dr. Gabriela Zenhaeusern (Swissmedic, Switzerland)** was elected as Assembly Vice-Chair to serve a two-year term.
- The ICH Management Committee supported the participation of Ad-Hoc Observer Delegates to the ICH Assembly meeting in November 2021 from EDA, Egypt, Indonesian FDA, Indonesia and SECMOH, Ukraine, which were subsequently approved as ICH Observers.

**ICH Management Committee Meetings**

- The ICH Management Committee met several times virtually throughout the year:
  - **9 times via teleconference** on the following dates: 2 February, 29 March, 30 March, 11 May, 26 April, 8 September, 17 September, 30 September, 18 October.
  - **3 virtual meetings:** during ICH's biannual meetings on 25 May and 1 June, and on 9, 15 and 16 November, and during its interim meeting on 15 and 16 March.
- Additionally, **more than 15 ICH Management Committee Subcommittee teleconferences** were held (on New Topics, Training, Finance, and Organisation of 30th Anniversary Event).
- All meetings in 2021 were chaired by **Dr. Theresa Mullin (FDA, United States, Chair)** and **Dr. Nobumasa Nakashima (MHLW/PMDA, Japan, Vice Chair)**. In November 2021 the ICH Management Committee re-elected Dr. Mullin as Chair and Dr. Nakashima as Vice-Chair to serve a further 2-year term.
- In line with ICH procedures, in June 2021 new elections were held for ICH Management Committee Elected Representatives, and the Assembly elected the following Representatives from Regulatory and Industry Members, for a 3-year term:
  - Regulatory Member Representatives: **Mr. Diogo Penha Soares and Mr. Gustavo Mendes Lima Santos from ANVISA, Brazil; Dr. Seogyoun Kang and Dr. Youngjoo Park from MFDS, Republic of Korea; Dr. Sheng Yang and Dr. Siyuan Zhou from NMPA, China;**
  - Industry Member Representatives: **Dr. Joseph Damond and Dr. Wassim Nashabeh from BIO; Dr. Nicholas Cappuccino and Ms. Beata Stepniewska from IGBA.**

**MedDRA Management Committee Meetings**

- The MedDRA Management Committee met several times:

- **8 times via teleconference** on 18 February, 22 March, 12 April, 28 June, 23 August, 28 September, 13 October, and 2 December.
- **2 virtual meetings (composed of 3 teleconferences each):** at the time of ICH's biannual meetings on 18, 20 and 27 May and on 25, 28 October and 4 November.

- All meetings in 2021 were chaired by **Mr. Mick Foy (MHRA, UK)**, who the MedDRA Management Committee re-elected as Chair in May 2021 for a further 1-year term.

**ICH Working Group Meetings**

In the absence of face-to-face meetings, WGs were encouraged to continue their activities remotely, replacing as far as possible any planned face-to-face meetings with virtual meetings in the form of series of teleconferences over several days.

At the end of 2021, and to assist considerations on meetings in 2022, the ICH Management Committee agreed to the conduct of a study of the impact and lessons learned by a selection of actively operating WGs from ICH's recent shift from face-to-face to virtual meetings necessitated by the pandemic.

### *4.2. Planning of Future ICH Meetings*

In 2021, the ICH Management Committee took decisions regarding the organisation of future ICH meetings. **Key decisions** are outlined below:

- The ICH Management Committee agreed to maintain planning for its next biannual meeting in Athens, Greece in May 2022 in a face-to-face setting, with planning to be made for hybrid in-person/virtual formats as needed.
- The Management Committee agreed to re-schedule the 2021 meetings due to have been held in **Incheon, Republic of Korea** and **Vancouver, Canada** to **November 2022 and June 2023** respectively.
- The ICH Management Committee agreed on the following dates for the 2023 and 2024 meetings:
  - From 28 October to 1 November or 11 to 15 November 2023;
  - From 18 to 22 May or 1 to 5 June 2024.
- Work continued in 2021 further to a **call for tenders** conducted in 2020 for the Professional Conference Organiser (PCO) to support the organisation of ICH meetings from 2023.

## 5. 2021 ICH Operational Matters

### *5.1. ICH Articles & Procedures*

**5 Documents support the governance 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 2021 regarding these documents:

**Assembly RoP**

- The Assembly approved several amendments to the Assembly RoP with approval of version 10.0 in June. Amendments related to: clarifying the rules on confidentiality and on additional participants at meetings.

**ICH Management Committee RoP**

- The ICH Management Committee approved several amendments to its RoP in 2021, with approval of version 11.0 in May. Amendments related to: clarifying the rules on confidentiality and on additional participants at meetings; addition of a rule on the illustrative use of the ICH logo by third parties; and adjustment to the ICH budget approval cycle and periodic adjustment of ICH Membership Fees further to the recommendations of the ICH Finance Committee.

**MedDRA Management Committee RoP**

- The MedDRA Management Committee approved v6.0 at its virtual meeting in May 2021, including amendments related to: virtual meetings in extraordinary circumstances; removing outdated text; clarifying the process for press releases; and addition of principles for 5-year budget planning and for periodic adjustment of the MedDRA subscription fees further to the recommendations of the ICH Finance Committee.

**SOPs of the ICH Working Groups**

- The ICH Management Committee has approved v11.0 in October 2021. Amendments related to: publishing the names of Rapporteur Supporters on the ICH website in recognition of their work; clarifying the M2 recommendations approval process via a sign-off by M2 Topic Leaders followed by an approval by the Assembly Members; and ensuring more clarity on the matter for public comment on draft Guidelines undergoing a maintenance procedure by publishing under *Step 3* consultation a document listing only the changes to the core Guideline or Addendum.

## *5.2. ICH Funding*

**ICH Financial Audit**

In May 2021 **the Assembly approved the 2020 Audited Accounts and Financial Statements of the ICH Association**, supporting their submission along with ICH's 2020 tax return in July 2021.

**ICH Funding[1]**

[1] ICH notes that in lieu of the membership fee payment required of ICH Founding Members, for the period 2016 to-date, FDA, United States has supported ICH through an equivalent level of funding via a grant mechanism. ICH (2016 to-date) is supported by the Food and Drug Administration (FDA) of the U.S. Department of Health and Human Services (HHS) as part of a financial assistance award [FAIN] totaling $1,928,598 with 16% funded by FDA/HHS, and $11,804,605 and 84% funded by non-U.S. government sources. The contents are those of the authors and do not necessarily represent the official views of, nor an endorsement, by FDA/HHS, or the U.S. Government.

2021 Membership Fees were paid as follows by all ICH Members in line with the decision taken by the Assembly in November 2020:

| 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 |

***2021 Membership Fees***

The Assembly furthermore approved the same level of fees for 2022.

In November 2021, the Assembly approved the 2022 ICH and MedDRA budgets and supported the 5-Year ICH and MedDRA budget projection for 2022-2026. Information can be found on the ICH website regarding the combined provisional ICH and MedDRA 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 November 2021, the **Assembly approved the 2022 MedDRA Budget, including 2022 MSSO MedDRA Subscription Fee levels,** which were kept stable from 2021.

Information can be found on the ICH website regarding the 2021 MedDRA Budget.

**Financial Management**

In 2021, the ICH Finance Committee, which includes representation from both the ICH and MedDRA Management Committees, provided support for ICH financial management. In addition to support provided in 2021 for 2022 ICH and MedDRA budget preparation and 5-Year ICH and MedDRA budget planning for 2022-2026, the Finance Committee also worked on items including: alignment of the ICH and MedDRA budget cycles; an approach for a periodic 5-year cycle of adjustment of ICH Membership Fees and MedDRA Subscription Fees; and the development of an asset preservation policy.

## *5.3. ICH Communication*

The following should be noted in relation to communication activities in 2021:

- As a part of the **Good Clinical Practice (GCP) renovation plan,** the ICH E6 EWG held a public web conference on 18 and 19 May 2021, to provide an update on the progress on the draft principles of GCP, published on the ICH website in April 2021, and to facilitate broad dissemination of and public engagement on the principles of

GCP. The Web Conference Report was made available for download on the ICH website and a recorded presentation from the web conference has been made available on the ICH YouTube channel.

- In October 2021, the ICH 30th Anniversary Publication was published on the ICH website. It provides an overview of ICH's history and current work, as well as views of different stakeholders on how ICH has contributed to better health and ICH's future directions in the next 10 years. In addition to the electronic format, a printed format will be available in early 2022, and is intended to serve as an ICH communication document beyond the anniversary celebration to allow sharing of information on ICH in various forums, as well as by ICH Members and Observers. A leaflet on ICH has also been developed based on the ICH 30th Anniversary Publication and finalised in December 2021. It provides a brief overview of ICH's mission, structure and current work, and would be available on the ICH website in January 2022.
- In view of the COVID-19 pandemic preventing face-to-face meetings in 2021 and in view of the lower added value of an online event, the plans to organise a postponed 30th Anniversary commemorative event in 2021 were cancelled. It was discussed that other options to commemorate ICH's anniversary on a smaller scale may be considered in 2022.
- Acknowledging the importance of relevant patient stakeholder engagement in ICH and input from the patient community on ICH Guidelines, especially those referring to pre-market or post-market activities that would directly involve or affect patients, the ICH Management Committee agreed that ICH Members should be encouraged to do appropriate outreach to patient communities to ensure awareness of existing opportunities for input at the ICH Regional meetings organised by ICH Members. The Management Committee furthermore agreed to continue discussion in 2022 on patient stakeholder engagement.
- At the November 2021 virtual meeting, the Assembly supported a proposal for an ICH Award for Outstanding Leadership and Contributions, intended to show recognition to those ICH WG experts meeting the criteria of a sustained participation in ICH over multiple years, having served in leadership role(s) and made outstanding contributions to ICH work, with a process to be launched in early 2022.

**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 2021 the ICH Members holding regional public meetings were Health Canada, Canada together with FDA, United States; and 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 2021. Such presentations were delivered at the regional DIA China ICH Day in May 2021.

## *5.4. Cooperation with the IPRP*

Under a Memorandum of Understanding (MoU) between ICH and the IPRP (International Pharmaceutical Regulators Programme), the ICH Secretariat continued in 2021 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 July 2021, the ICH Assembly further approved the renewal of the MoU for another year so that the ICH Secretariat would continue the provision of support services to the IPRP for the year 2022.

## *5.5. ICH Secretariat*

### *2021 Staffing*

The following highlights key points and decisions related to ICH Secretariat staffing in 2021:

- ICH Secretariat staffing was initially planned at **8.8 FTEs (Full Time Equivalents) for 2021**, allocated between ICH (~ 5 FTEs) and MedDRA (~ 3.3 FTEs) activities, as well as IPRP support (~ 0.5 FTEs). However, the ICH Secretariat operated at less than full capacity in 2021, with closer to 7.5 FTEs active during the year due to staff leave, as well as delays in hiring support to cover leaves.
- The year saw **Ms. Amina Mir**, **Dr. Marine Lacroix**, and **Ms. Anca-Elena Matei** join the team in August, October and November respectively in the positions of **Administrative Assistant**, **Manager** and **Project Coordinator**, with **Managers Dr. Anne Latrive** and **Ms. Nadia Myers Biggs** leaving the ICH Secretariat at the end of 2021.
- At its virtual meeting in November 2021, the Assembly approved 1 additional Secretariat staff from 2022 in view of increased training projects, along with continued expansion of ICH.
- Staff continued working principally from home in view of the COVID-19 pandemic and consideration of the recommendations of the Swiss Federal Office of Public Health.

### *2021 ICH Secretariat Key Activities*

The following outlines key activities undertaken by the ICH Secretariat in 2021 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.

**2021 Day-to-Day Management Key Activities:**

- **Preparing agenda papers and reports** for meetings of the Assembly, the ICH Management Committee and the MedDRA Management Committee, all of which had to be organised virtually by the ICH Secretariat in 2021 due to the COVID-19 pandemic. This included the biannual meetings of these governing bodies in May/June 2021 and in October/November 2021, and in March 2021 for the interim ICH Management Committee meeting.
- **Supporting ICH harmonisation activities** and the work of **34 ICH WGs** in 2021, including keeping up-to-date membership lists, establishing 3 new WGs and providing support for the use of MS SharePoint tool by all WGs.
- **Providing support and input for the work of the following ICH Management Committee Subcommittees**: Finance; Training; New Topics; and Organising Subcommittee.
- **Drafting ICH Association Reports and Work Plans** in support of ICH Management Committee and MedDRA Management Committee reporting to the Assembly, including: 2020 Annual Report; 2022 ICH Work Plan and ICH Multi-Annual Strategic Plan; and 2022 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: (i) develop **the ICH, Private Platform, and MedDRA websites**, and (ii) maintain these websites, along with the **internal database interfaced with the websites**.
  - **Managing the hosting of ICH websites**.
- **Responding to stakeholder enquiries** received via the ICH mailbox with input solicited as necessary from ICH experts and ICH Coordinators in accordance with the 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 Swiss tax authorities for items including

submission of 2020 tax return, quarterly VAT declarations, and recovery of withholding tax deducted from interest earned in 2020 from fixed-term deposit bank account; managing ICH's grant agreement with FDA, United States, which in 2020 included submitting quarterly and annual Federal Financial Reports.

- **Entering into and managing contracts**, including those related to day-to-day operations (e.g., office support, website hosting/maintenance, MS SharePoint, web conferencing tools etc.), specific projects (e.g., Training Associate), 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 ICH biannual meetings and ICH Management Committee interim meeting** including: regular coordination with and oversight of the PCO. In 2021, work was undertaken in coordination with the PCO in view of the COVID-19 pandemic to cancel/re-schedule meetings originally planned for 2021.

**2021 New/One-Time/Key Activities:**

- **Supporting the ICH Management Committee in commissioning a third-party to conduct a study** of the impact and lessons learned by a selection of actively operating WGs from ICH's recent shift from face-to-face to virtual meetings necessitated by the pandemic.
- **Supporting ICH WG collaboration** by facilitating the use of MS Teams as a web conferencing tool in April 2021 to all WGs interested in using it, further to conducing a successful pilot with 4 WGs in 2020.
- **Supporting the ICH Management Committee in efforts to engage new Training Associates**, with work to put in place an agreement with a second Training Associate in 2021 for the delivery of training materials on ICH E2 and ICH M4, and initiation of contract negotiations with three additional potential Training Associates.
- **Supporting development and publication on the ICH website of the ICH 30th Anniversary Publication and development of an associated ICH Leaflet.**
- **Supporting ICH Guideline implementation activities**: further to the Phase 2b ICH Survey on Guideline Implementation, the results of which were presented to the ICH Assembly at the June 2021 Virtual meeting, the public report was developed by CIRS and published on the ICH website.
- **Supporting the selection of a new PCO** further to a call for tenders for the organisation of ICH meetings from 2023 and beyond.
- **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. This effort included provision of input to the trademark lawyers for: class descriptions; responding to trademark authority questions and refusals; supporting an opposition filed by ICH in 2019 against an application for the registration of a trademark similar to the MedDRA trademark; and considering other new applications for trademarks similar to ICH and MedDRA trademarks, as well as sign-off of Powers of Attorney (with arrangement of

notarisation as required) to facilitate the follow-ups by lawyers in each jurisdiction, and follow-up with ICH and MedDRA Management Committee Chairs on key decision items.

- **Supporting the MedDRA Management Committee** with activities including:
    - Follow-up on **contract related matters**, including seeking the necessary legal input and seeking the appropriate support of ICH Management Committee / Assembly, and concluding agreements which in 2021 included: a transfer agreement to facilitate the transition of the MSSO from Northrop Grumman to Peraton; an agreement between ICH and SNOMED International regarding the maintenance and distribution of a bidirectional mapping between MedDRA and SNOMED mapping; and an amendment to the MSSO agreement;
    - Support for a multi-year MSSO audit plan covering Clinical-Quality-Procedural, IT and Financial aspects;
    - Support related to the conduct of a study to support ICH considerations on long-term MedDRA operations.
- **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.

### *5.6. ICH Management Appointed Signatories*

At the end of 2021, with the stepping down as ICH Assembly Chair of Dr. Celia Lourenco and departure of Dr. Anne Latrive from the ICH Secretariat, ICH signatories in line with Article 36 2(e) and 47 2(e) of the ICH Articles of Association, to represent the ICH Association vis-à-vis third parties are: ICH Assembly Chair Ms. Lenita Lindström-Gommers, and ICH Secretariat staff Ms. Emilie Macara and Dr. Dawn Ronan. All signatories have joint (by two) signatory rights.

# Annex I

## Assembly Member Representatives & Observer Delegates

December 31, 2021

### Founding Regulatory Members

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

***FDA, United States***
Dr. Theresa Mullin
Dr. Michelle Limoli

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

### Founding Industry Members

***EFPIA***
Dr. Sue Forda
Mr. Pär Tellner

***JPMA***
Dr. Manabu Yanagisawa
Dr. Masafumi Yokota

***PhRMA***
Dr. Michelle Rohrer
Ms. Janet Vessotskie

### Standing Regulatory Members

***Health Canada, Canada***
Dr. Léo Bouthillier
Mr. Bruce Randall

***Swissmedic, Switzerland***
Dr. Andreas Pfenninger
Dr. Jörg Schläpfer

### Regulatory Members

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

***COFEPRIS, Mexico***
Ms. Miriam Jackeline Loera Rosales
Dr. Alejandro Ernesto Svarch Pérez

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

***MFDS, Republic of Korea***
Dr. Seogyoun Kang
Dr. Younjoo Park

***NMPA, China***
Dr. Sheng Yang
Mr. Siyuan Zhou

***SFDA, Saudi Arabia***
Dr. Abdullah Hamad Al Hatareshah
Dr. Adel Alharf

***TFDA, Chinese Taipei***
Dr. Jo-Feng Chi
Mr. Kevin Ming-Hsun Liu

***TITCK, Turkey***
Dr. Elif İnci Ergönül
Ms. Handan Öztunca

### Industry Members

***BIO***
Mr. Joseph Damond
Dr. Wassim Nashabeh

***Global Self-Care Federation***
Dr. Padmaja Kamath
Ms. Judy Stenmark

***IGBA***
Dr. Nick Cappuccino
Ms. Beata Stepniewska

## Standing Observers

***WHO***
Dr. Samvel Azatyan

***IFPMA***
Ms. Angelika Joos
Dr. Sharon Olmstead

## Observers

***AEC, Azerbaijan***
Mr. Farid Hasanov

***ANMAT, Argentina***
Dr. Manuel Limeres

***APEC***
Dr. Youngju Choi

***APIC***
Dr. Rainer Fendt

***ASEAN***
Ms. Charunee Krisanaphan

***Bill and Melinda Gates Foundation***
Dr. Murray Lumpkin

***CDSCO, India***
Dr. Venugopal Girdharilal Somani

***CECMED, Cuba***
Dr. Celeste Sánchez González

***CIOMS***
Dr. Lembit Rägo

***CPED, Israel***
Dr. Ofra Axelrod

***EAC***
Ms. Jane Mashingia

***EDA, Egypt***
Ms. Asmaa Fouad

***EDQM***
Dr. Petra Doerr

***GHC***
Dr. Hajed M. Hashan

***IFPMA***
Ms. Angelika Joos
Ms. Judith MacDonald

***INVIMA, Colombia***
Ms. Yenny Marcela Suárez González

***IPEC***
Ms. Janeen Skutnik-Wilkinson

***JFDA, Jordan***
Dr. Wesal Haqaish

***MHRA, UK***
Mr. Jamie Convisser

***MMDA, Moldova***
Mr. Dumitru Saghin

***MOPH, Lebanon***
Dr. Colette Raidy

***NPRA, Malaysia***
Dr. Roshayati Mohamad Sani

***NRA, Iran***
Dr. Mahmoud Alebouyeh

***National Center, Kazakhstan***
Dr. Sabina Chukumova

***PANDRH***
Dr. Analía Porrás

***Roszdravnadzor, Russia***
Ms. Anastasia Nikitina

***SADC***
Ms. Fortunate Ntombi Bhembe

***SAHPRA, South Africa***
Ms. Portia Nkambule

***SCDMTE, Armenia***
Ms. Aida Malkhasyan

***SECMOH, Ukraine***
Dr. Mykhailo Babenko

***TGA, Australia***
Mr. Benjamin Noyen

***USP***
Dr. Kevin Moore

***WHO***
Dr. Samvel Azatyan

# Annex II

## ICH Management Committee Representatives

December 31, 2021

### Founding Regulatory Members

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

***FDA, United States***
Dr. Theresa Mullin *(Chair)*
Dr. Michelle Limoli

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

### Founding Industry Members

***EFPIA***
Dr. Sue Forda
Mr. Pär Tellner

***JPMA***
Dr. Manabu Yanagisawa
Dr. Masafumi Yokota

***PhRMA***
Dr. Michelle Rohrer
Ms. Janet Vessotskie

### Standing Regulatory Members

***Swissmedic, Switzerland***
Dr. Andreas Pfenninger
Dr. Jörg Schläpfer

***Health Canada, Canada***
Dr. Léo Bouthillier
Mr. Bruce Randall

### Standing Observers

***WHO***
Dr. Samvel Azatyan

***IFPMA***
Ms. Angelika Joos
Dr. Sharon Olmstead

### Regulatory Members

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

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

***MFDS, Republic of Korea***
Dr. Seogyoun Kang
Dr. Younjoo Park

***NMPA, China***
Dr. Sheng Yang
Mr. Siyuan Zhou

### Industry Members

***BIO***
Mr. Joseph Damond
Dr. Wassim Nashabeh

***IGBA***
Dr. Nick Cappuccino
Ms. Beata Stepniewska

# Annex III

## MedDRA Management Committee Representatives

31 December, 2021

### Founding Regulatory Members

***EC, Europe***
Dr. Georgios Balkamos
Dr. Sabine Brosch

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

***MHLW/PMDA, Japan***
Mr. Masahiro Inada
Ms. Akiko Takahashi

### Founding Industry Members

***EFPIA***
Ms. Claudia Lehmann
Dr. Christina Winter

***JPMA***
Ms. Mamiko Kasho (Konishi)
Ms. Yasuyo Suzuki

***PhRMA***
Ms. Amanda Roache

### Standing Regulatory Member

***Health Canada, Canada***
Ms. Heather Morrison

### MHRA, UK

Mr. Mick Foy
Mr. Philip Tregunno

### WHO Observer

***WHO***
Mr. Fumihito Takanashi

# Annex IV

## ICH Secretariat Staff

31 December, 2021

### Director
Dr. Dawn Ronan

### Managers
Mr. Masaki Fujita
Dr. Marine Lacroix
Dr. Anne Latrive

### Coordinators
Ms. Clarisse Bertherat
Ms. Nikoleta Luludi
Ms. Emilie Macara
Ms. Anca-Elena Matei

### Administrative Assistant
Ms. Nadja Leuba
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# Annex V

## Assembly Member ICH Coordinators

31 December, 2021

### Founding Regulatory Members

***EC, Europe***
Dr. Georgios Balkamos
Dr. Zahra Hanaizi (Technical Coordinator)

***MHLW/PMDA, Japan***
Mr. Hirooki Tanabe
Ms. Mami Ueda (Technical Coordinator)

***FDA, United States***
Ms. Jill Adleberg
Dr. Michelle Limoli (Technical Coordinator)

### Founding Industry Members

***EFPIA***
Ms. Andreea Iordache

***JPMA***
Mr. Hiroaki Hagiwara

***PhRMA***
Ms. Amanda Roache

### Standing Regulatory Members

***Swissmedic, Switzerland***
Dr. Gabriela Zenhaeusern

***Health Canada, Canada***
Mr. Nick Orphanos

### Regulatory Members

***ANVISA, Brazil***
Ms. Ana Carolina Moreira Marino Araujo

***COFEPRIS, Mexico***
Ms. Margarita Contreras Olvera

***NMPA, China***
Mr. Baoshu Wen

***HSA, Singapore***
Ms. Junhan Shang

***MFDS, Republic of Korea***
Ms. Miyoung Hyun

***SFDA, Saudi Arabia***
Mr. Yahya Al-Nujaym

***TFDA, Chinese Taipei***
Ms. Pao-Hsuan Huang

***TITCK, Turkey***
Dr. Elif İnci Ergönül

### Industry Members

***BIO***
Mr. David Dee

***IGBA***
Dr. Shinichiro Hirose

***Global Self-Care Federation***
Dr. Padmaja Kamath

# Annex VI

## Overview of harmonisation activities and accomplishments in 2021

| Topic Code | Type of Working Group | Topic Name | Accomplishments | Anticipated Milestones |
|---|---|---|---|---|
| Standing Paediatric | Standing EWG | Expert consultation and guidance to ICH WGs on paediatric considerations | | N/A<br><br>Dormant state pending requests for paediatric advice. |
| E2B(R3) | EWG/IWG | Revision of Electronic Submission of ICSRs | Information Paper regarding the Use of ISO IDMP Standards in ICH E2B(R3) Messages finalised in June 2021. | *Step 3 sign-off* of the ICSR BFC (Backwards and Forwards Compatibility) Recommendation document expected in early 2022. |
| E2D(R1) | EWG | Revision of Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting | | *Steps 1* and *2a/b* expected by November 2022. |
| E6(R3) | EWG | Revision of Good Clinical Practice | Global web conference held on 18-19 May 2021 to facilitate broad dissemination of and public engagement on the principles of Good Clinical Practice.<br><br>Draft principles of Good Clinical Practice published on the ICH website May 2021. | *Steps 1* and *2 a/b* for Principles and Annex 1 expected by October 2022.<br><br>Revised E6(R3) Concept Paper updated in regards to Annex 2 expected by September 2022. |

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| E8(R1) | EWG | Revision on General Considerations for Clinical Studies | *Steps 3 and 4* reached in October 2021. | Training materials expected by early 2022. |
| E9(R1) | EWG | Addendum to Defining Appropriate Estimand for a Clinical Trial/Sensitivity Analyses | | Training materials expected early 2022. |
| E11A | EWG | Paediatric Extrapolation | | *Steps 1* and *2a/b* expected by January 2022. |
| E14/S7B | IWG | Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs | | *Steps 3* and *4* of the first stage of Q&As expected early 2022. |
| E19 | EWG | Optimization of Safety Data Collection | | *Steps 3* and *4* expected by April 2022. |
| E20 | EWG | Adaptive Clinical Trials | | *Steps 1* and *2a/b* expected by June 2023. |
| M1 | PtC WG | MedDRA Points to Consider (PtC) | Updated "MedDRA Term Selection: Points to Consider" and "MedDRA Data Retrieval and Presentation: Points to Consider" documents (based on MedDRA Version 24.0) in English, Japanese, Chinese, Korean, and Spanish translations released in March 2021. | Updated "MedDRA Term Selection: Points to Consider" and "MedDRA Data Retrieval and Presentation: Points to Consider" documents in English, Japanese, Chinese, Korean, Spanish, and Russian expected in March 2022 (based on MedDRA Version 25.0).<br>Release of v3.0 of the Companion document expected in Q2 2022. |
| M2 | EWG | Electronic Standards for the Transfer of | Revised M2 Recommendation | N/A (Ongoing activity) |

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| | | Regulatory Information (ESTRI) | documents in October 2021. | |
| M4Q(R2) | EWG | Revision of M4Q(R1) CTD on Quality guidance | Concept Paper and Business Plan endorsed November 2021.<br><br>M4Q(R2) informal WG established in November 2021. | |
| M7(R2) | Maintenance EWG/IWG | Addendum to Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk | *Steps 1 and 2a/b* of the M7(R2) draft Guideline reached in October 2021. | *Steps 3* and *4* of the M7(R2) Q&As expected by June 2022. |
| M8 | EWG/IWG | Electronic Common Technical Document: eCTD | *Step 4* of the eCTD v4.0 Q&A Document v.1.5, Specification for Submission Format v1.3, as well as the eCTD v4.0 Implementation Package v.1.4 reached in June 2021.<br><br>*Step 4* the eCTD v4.0 Q&A Document v1.6 and eCTD v3.2.2 Q&A Document v1.32 reached in November 2021. | N/A (Ongoing Activity) |
| M10 | EWG | Bioanalytical Method Validation | | *Steps 3* and *4* expected by May 2022. |

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| | | | | Training materials expected after completion of the M10 Guideline. |
| M11 | EWG | Clinical electronic Structured Harmonised Protocol (CeSHarP) | | *Steps 1* and *2 a/b* for the Guideline, Template, and Technical Implementation Guide expected by May 2022. |
| M12 | EWG | Drug Interaction Studies | | *Steps 1* and *2a/b* expected by May 2022. |
| M13 | EWG | Bioequivalence for Immediate-Release Solid Oral Dosage Forms | | *Steps 1* and *2 a/b* are expected by June 2022. |
| M14 | Informal WG | General principles on planning and designing pharmacoepidemiologic al studies that utilize real-world data for safety assessment of a medicine | M14 informal WG established in December 2021. | |
| Q2(R2)/Q14 | EWG | Analytical Procedure Development and Revision of Q2(R1) Validation of Analytical Procedures | | *Steps 1* and *2 a/b* expected by early 2022. |
| Q3C(R9) | Maintenance EWG | Maintenance of the Guideline for Residual Solvents | *Steps 3* and *4* of the Q3C(R8) Guideline reached in April 2021. | N/A<br>Dormant state until proposals for revisions are received. |
| Q3D(R2) | Maintenance EWG | Maintenance of the Guideline for Elemental Impurities | | *Steps 3* and *4* expected by January 2022. |
| Q3E | EWG | Impurity: Assessment and Control of Extractables and Leachables for | | *Steps 1* and *2a/b* expected by November 2022. |

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| | | Pharmaceuticals and Biologics | | |
| Q5A(R2) | EWG | Revision of Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin | | *Steps 1* and *2 a/b* expected by May 2022. |
| Q9(R1) | EWG | Quality Risk Management | *Steps 1* and *Step 2a/b* reached in November 2021. | Training materials expected by August 2022. |
| Q12 | IWG | Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management | Training Materials Modules 0-7 finalised in June 2021. | Work ongoing on Module 8 and case studies. |
| Q13 | EWG | Continuous Manufacturing of Drug Substances and Drug Products | *Steps 1* and *2a/b* on reached in July 2021. | *Steps 3* and *4* expected by November 2022. |
| S1B(R1) | EWG | Revision of the Rodent Carcinogenicity Studies for Human Pharmaceuticals | *Steps 1* and *2a/b* reached in May 2021.<br>4th Status Report from Regulatory Authorities published in August 2021. | *Steps 3* and *4* expected by May 2022. |
| S5(R4) | Maintenance EWG | Maintenance of Annexes 1 and 2 of the S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals | | N/A<br>Dormant state until proposals for revisions are received. |

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| S12 | EWG | Biodistribution Studies for Gene Therapy Products | *Steps 1* and *2 a/b* reached in June 2021. | *Steps 3* and *4* expected by May 2023. |
| GDG | DG | Generic drug Discussion Group | Report on finalisation of GDG activities. | N/A<br>Dormant state. |
| QDG | DG | Quality Discussion Group | QDG Recommendation Report published in December 2021. | N/A |
| PEpiDG | DG | Pharmacoepidemiology Discussion Group | New Topic proposal and Concept Paper outline, supported by the Assembly in June 2021. | N/A<br>Activity completed. |
| MIDD DG | DG | Model-Informed Drug Development Discussion Group | Concept Paper outline on General Considerations for Model-Informed Drug Development endorsed in November 2021, with new M15 informal WG to be established in June 2022. | N/A<br>Activity completed. |