ICH ASSOCIATION

2016 ANNUAL REPORT

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use

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ICH Association
2016 Annual Report

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

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Message from Assembly Chair and Vice Chair

2016 was an exciting year for the ICH Association. It marked the first full year of operation under ICH's new governance structure which saw many new Members and Observers joining ICH. With a key objective of ICH's recent reform aimed at making ICH a more global initiative, the addition of 5 new Members and 16 new Observers marked a major milestone for ICH. Given the expectation for all ICH Regulatory Members to implement ICH Guidelines, the joining of new Regulatory Members from ANVISA - Agência Nacional de Vigilância Sanitária (Brazil) and MFDS - Ministry of Food and Drug Safety (the Republic of Korea) was of significant importance for global harmonisation efforts.

The visible evolution of ICH in 2016 was apparent not only at the level of the Assembly, but also at the heart of ICH's harmonisation activities in ICH's Working Groups. The dedicated scientific experts leading the development of ICH Guidelines included an increasing number of experts from new Members and Observers. It is a true sign of ICH's change that these experts now make-up close to 25% of all experts participating in ICH harmonisation activities. The excellent progress made by ICH in 2016 can be attributed to the successful collaboration of international partners working at various levels of the ICH Association and with a common goal of improving global public health.

Mrs. Lenita Lindström-Gommers
ICH Assembly Chair
EC

Dr. Toshiyoshi Tominaga
ICH Assembly Vice Chair
MHLW/PMDA

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Abbreviation list

ANVISA	*Agência Nacional de Vigilância Sanitária, Brazil*
APEC	*Asia-Pacific Economic Cooperation*
APIC	*Active Pharmaceutical Ingredients Committee*
ASEAN	*Association of Southeast Asian Nations*
BIO	*Biotechnology Innovation Organisation*
CDSCO	*Central Drugs Standard Control Organization, India*
CECMED	*Centro para el Control Estatal de Medicamentos, Equipos y Dispositivos Médicos, Cuba*
CIOMS	*Council for International Organizations of Medical Sciences*
COFEPRIS	*Comisión Federal para la Protección contra Riesgos Sanitarios, Mexico*
CTD	*Common Technical Document*
DIA	*Drug Information Association*
DG	*Discussion Group*
EAC	*East African Community*
EC	*European Commission*
eCTD	*Electronic Common Technical Document*
EDQM	*European Directorate for the Quality of Medicines and HealthCare*
EFPIA	*European Federation of Pharmaceutical Industries and Associations*
EMA	*European Medicines Agency*
EWG	*Expert Working Group*
FDA	*US Food and Drug Administration*
GHC	*Gulf Health Council*
GCP	*Good Clinical Practice*
HSA	*Health Sciences Authority, Singapore*
ICSR	*Individual Case Safety report*
IFPMA	*International Federation of Pharmaceuticals Manufacturers and Associations*
IG	*Implementation Guide*
IGBA	*International Generic and Biosimilar Medicines Association*
IPEC	*International Pharmaceutical Excipient Council*
IPRF	*International Pharmaceutical Regulators Forum*
ISO	*International Organization for Standardization*
IWG	*Implementation Working Group*
JMO	*Japanese Maintenance Organisation*
JPMA	*Japan Pharmaceutical Manufacturers Association*
MCC	*Medicines Control Council, South Africa*
MedDRA	*Medical Dictionary for Regulatory Activities*
MFDS	*Ministry of Food and Drug Safety, Republic of Korea*
MHLW	*Ministry of Health, Labour and Welfare of Japan*
MHRA	*UK Medicines and Healthcare products Regulatory Agency*
MSSO	*MedDRA Maintenance and Support Services Organisation*

PANDRH	*Pan American Network for Drug Regulatory Harmonization*
PDE	*Permitted Daily Exposure*
PhRMA	*Pharmaceutical Research and Manufacturers of America*
PMDA	*Pharmaceuticals and Medical Devices Agency*
PtC	*Points to Consider*
Q&As	*Questions and Answers*
RHIs	*Regional Harmonisation Initiatives*
RoP	*Rules of Procedure*
SADC	*Southern African Development Community*
SMQ	*Standardised MedDRA Queries*
SOC	*System Organ Class*
SOPs	*Standard Operating Procedures*
TFDA	*The Food and Drug Administration, Chinese Taipei*
TGA	*Therapeutic Goods Administration, Australia*
USP	*United States Pharmacopeia*
WHO	*World Health Organization*
WSMI	*World Self-Medication Industry*

1. About ICH

1.1. Purpose & Aims

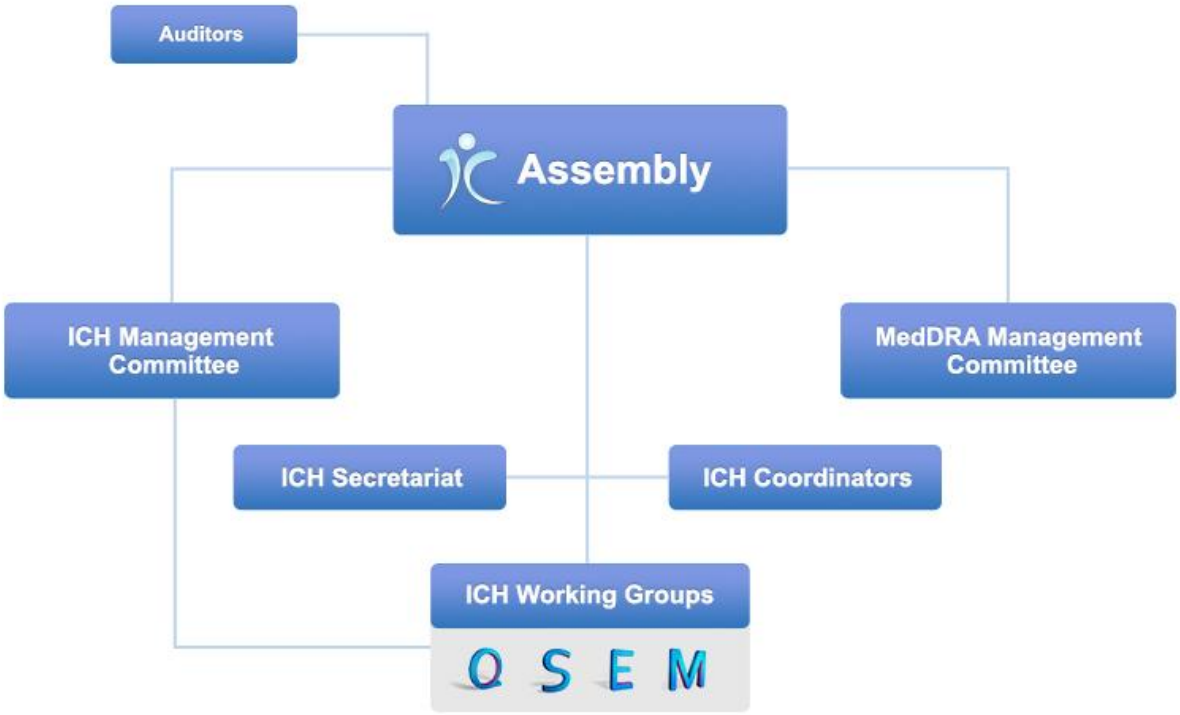
The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) is an international non-profit organisation which was established as an association under Swiss law in October 2015. The purpose of ICH is to promote public health through international harmonisation of technical requirements that contributes 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 provision of training on, 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 on 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, 2016 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. The ICH Management Committee is responsible for submitting recommendations or proposals to the Assembly in preparation of Assembly discussions.
- The full list of the ICH Management Committee Member Representatives and Observer Delegates as of December 31, 2016 is provided in Annex II.

MedDRA Management Committee[1]

- 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, 2016 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 Working Groups. The ICH Secretariat also provides support for the ICH MedDRA Management Board/Committee as the "MedDRA Secretariat".
- The full list of ICH Secretariat Staff as of December 31, 2016 is provided in Annex IV.

Auditors

- In 2016, the Assembly agreed to appoint Moore Stephens Refidar SA for an initial period of 2 years to audit the annual financial statements of the ICH Association.

ICH Coordinators

- Fundamental to the smooth running of ICH has been the designation of an ICH Coordinator per ICH Member to act as the main contact point with the ICH Secretariat. Coordinators ensure proper distribution of ICH documents to the appropriate persons from their organisation and are responsible for the follow up on actions within their respective organisation within assigned deadlines. They also assist communication between the ICH Management Committee and/or Assembly and the ICH Working Groups as needed.
- The full list of ICH Coordinators as of December 31, 2016 is provided in Annex V.

[1] In 2016, in view of the fact that MedDRA's ownership had not been transferred from trustee IFPMA to the new ICH Association, both the new MedDRA Management Committee and the former MedDRA Management Board operated in parallel, with the MedDRA Management Committee being responsible for MedDRA decision-making pertaining to items relevant for the ICH Association.

2. 2016 Overview of Meetings & Membership

2.1. Meetings

In 2016, ICH activities were progressed via face-to-face meetings and teleconferences, which included the conduct of the biannual ICH week meetings in Lisbon, Portugal on June 11-16 and in Osaka, Japan on November 5-10. 287 participants from ICH Members and Observers attended the Lisbon meeting and 308 the Osaka meeting. ICH's biannual meetings see the meeting of Working Groups for 4-6 days in parallel of Assembly, ICH Management Committee and MedDRA Management Committee meetings, and are important for progressing ICH's work.

The reports of Assembly and ICH Management Committee face-to-face meetings and teleconferences were made available on the ICH website in 2016.

Details on 2016 meetings are provided as follows:

Assembly Meetings

- The Assembly met twice at the time of ICH's biannual meetings: on June 15-16 and on November 9-10.
- Both Assembly meetings were chaired by Mrs. Lindström-Gommers (EC, Chair) and Dr. Tominaga (MHLW/PMDA, Vice-Chair) who were elected in October 2015 for a two-year term.

ICH Assembly, Osaka November 2016

ICH Management Committee Meetings

- The ICH Management Committee met several times: via teleconferences on July 7, September 15, September 30, October 7 and October 25; and face-to-face during ICH's biannual meetings in June and November.

- The chairing of ICH Management Committee meetings in 2016 was as follows: as part of a 6-month rotation, the meetings were initially chaired by Mrs. Lindström-Gommers (EC, Chair) and Dr. Tominaga (MHLW/PMDA, Vice-Chair) up until and including the Lisbon meeting in June; after this by Dr. Tominaga (MHLW/PMDA, Chair) and Ms. Parker (Health Canada, Vice-Chair) up until the Osaka meeting in November; and then with election for a 1-year term of Dr. Mullin (FDA) and Dr. Tominaga (MHLW/PMDA) as Chair and Vice Chair respectively at the end of the Osaka meeting.

MedDRA Management Committee Meetings

- The inaugural MedDRA Management Committee meeting was held virtually on April 19, with Representatives appointed in line with the ICH Articles of Association by the following Founding Regulatory Members: EC, FDA, MHLW/PMDA; and by the following Founding Industry Members: EFPIA, JPMA, PhRMA; and by the following Standing Regulatory Member: the Health Canada; and also by MHRA.
  WHO was named as Observer Delegate in the new MedDRA Management Committee.
- The MedDRA Management Committee met several times: via teleconference on September 13; and face-to-face during ICH's biannual meetings on June 11-12 and November 5-6.
- Following the inaugural meeting chaired by Mr. Goux (EC), an interim rotation system was agreed where the chairmanship would rotate depending on the location of the ICH meeting until such time as the MedDRA Management Committee would become fully operational.
- The chairing of MedDRA Management Committee meetings in 2016 was as follows: by Mr. Goux (EC, Chair) up until and including the Lisbon meeting in June; after this by Dr. Ueno (MHLW/PMDA, Chair) up until the Osaka meeting in November.

ICH Working Group Meetings

A total of 10 Working Groups met at each of the biannual meetings in 2016 and are detailed in Annex VI.

In addition to this, the ICH Management Committee endorsed an interim meeting requested by the ICH Q12 EWG, and that took place in EMA offices in London, United Kingdom on April 6 to 8.

Organisation of Future ICH Meetings

In 2016, the ICH Management Committee took actions regarding the organisation of the 2017 and 2018 biannual ICH meetings. Key decisions are outlined below:

- The ICH Management Committee approved Swissmedic as the host of the autumn 2017 meeting to be held in Switzerland, and MHLW/PMDA and JPMA as the hosts of the spring 2018 meeting to be held in Japan.

- In preparation of the spring 2017 meeting to be held in Montreal, Canada, and hosted by Health Canada, the ICH Management Committee gave its approval for the contract for the meeting venue to be signed-off by ICH (through IFPMA), in line with the approval procedure for contracts of significant monetary value.

2.2. Welcome of New ICH Members & Observers

A driving factor of the organisational change celebrated by ICH at the end of 2015 was to make ICH a truly global initiative. 2016 was an important year for realising this goal, with the welcoming of 5 new Members and 16 new Observers. Indeed with the development of transparent Membership and Observership criteria within the ICH Articles of Association, any party eligible can apply. Approval of applications is a competency of the Assembly, based on a recommendation of the ICH Management Committee.

New Members

The Assembly approved the following 5 new ICH Members, which included 2 Regulatory Members and 3 Industry Members, based on the recommendation of the ICH Management Committee:

New Regulatory Members

- The Agência Nacional de Vigilância Sanitária (ANVISA, Brazil)
- The Ministry of Food and Drug Safety (MFDS, Republic of Korea)

New Industry Members

- The Biotechnology Innovation Organisation (BIO)
- The International Generics and Biosimilar Medicines Association (IGBA)
- The World Self-Medication Industry (WSMI)

Left to right New Members: Ms. Ana C. Moreira M.A.(ANVISA), Ms. Patricia Pereira T.(ANVISA), Ms. Lila Feisee (BIO), Dr. Sun Hee Lee (MFDS)

New Observers

Several new Observers joined in 2016 by availing of the privilege granted to former Global Cooperation Group members under Article 17(3) of the ICH Articles of Association to automatically become ICH Observers by confirming interest within three months of the establishment of the ICH Association. This included the following:

Former Global Cooperation Group New Observers

- The Association of Southeast Asian Nations (ASEAN)
- The Central Drugs Standard Control Organization (CDSCO, India)
- The East African Community (EAC)
- The Health Sciences Authority (HSA, Singapore)
- The Ministry of Food and Drug Safety (MFDS, Republic of Korea)[2]
- The Roszdravnadzor (Russia)
- The Food and Drug Administration (TFDA, Chinese Taipei)
- The Therapeutic Goods Administration (TGA, Australia)

These new Observers joined several other former Global Cooperation Group Members who already joined in 2015. See Annex I for the full list of Observer Delegates at the end of 2016.

The Assembly also approved the following new Regulatory Observer applications based on the recommendation of the ICH Management Committee:

New Regulatory and RHI Observers

- The Centro para el Control Estatal de Medicamentos, Equipos y Dispositivos Médicos (CECMED, Cuba)
- The National Center for the Expertise of Drugs, Medical Devices and Equipment (National Center, Kazakhstan)
- The Comisión Federal para la Protección contra Riesgos Sanitarios (COFEPRIS, Mexico)
- The Medicines Control Council (MCC, South Africa)

Other New Observers

- The Active Pharmaceutical Ingredients Committee (APIC)
- The Biotechnology Innovation Organisation (BIO)[3]
- The Council for International Organizations of Medical Sciences (CIOMS)
- The European Directorate for the Quality of Medicines and HealthCare (EDQM)
- The International Pharmaceutical Excipient Council (IPEC)
- The United States Pharmacopeia (USP)

[2] It should be noted that MFDS initially joined as an Observer before having its Membership Application approved by the Assembly in November 2016.
[3] It should be noted that the Assembly initially approved BIO as an Observer in June 2016, and subsequently approved BIO's Membership in November 2016.

Left to right New Observers: Mrs. Marieke van Dalen (APIC), Dr. Alice Tsitsi Sigobodhla (MCC)

Thanks to these new participants, the Assembly grew in 2016 to a total of 13 Members and 22 Observers, thereby expanding the forum for dialogue on scientific issues between regulatory authorities and the pharmaceutical industry on the harmonisation of the technical requirements for pharmaceuticals products.

Value of ICH Membership

Recognising the growing interest in ICH Membership, 2016 also saw ICH Management Committee development of a document on the Value of ICH Membership for the information of Assembly Members and Observers. It was agreed that on the basis of this document, the ICH Secretariat publish a page on the ICH website to communicate more widely on the value of ICH Membership.

ICH Member Logo

The ICH Management Committee also approved a new ICH Member Logo developed by the ICH Secretariat to enable ICH Members to communicate their Membership in ICH within their own publications, presentations or on their website after the signing of a disclaimer.

3. 2016 ICH Harmonisation Activities

A major output of ICH's work, in line with the specific aims of the organisation is the development of harmonised technical guidelines on Quality, Safety Efficacy and Multidisciplinary topics. In 2016, these activities were progressed on 23 topics by technical Working Groups [including Expert Working Groups (EWG), Implementation Working Groups (IWG) and Discussion Group (DG)], with support from the ICH Secretariat and under the oversight of the ICH Management Committee, with reporting to the Assembly. These activities were progressed via email and teleconferences, with some of the Working Groups being approved by the ICH Management Committee to meet face-to-face to progress their activities at the time of ICH's biannual meetings in 2016. The ICH Working Groups which met in 2016 are presented in Annex VI.

The key outcomes in 2016 relating to ICH harmonisation efforts include delivery of finalised *Step 4* documents, draft *Step 2a/b* documents, and other documents as mentioned below, in addition to the approval of New Topics for harmonisation. An overview of all ICH Working Groups activities and accomplishments in 2016 is presented in Annex VII.

3.1. ICH Guidelines & Other Documents Adopted at Step 4 in 2016

The following ICH Guidelines and other documents were adopted by the Regulatory Members of the Assembly at *Step 4* of the ICH process in 2016 following the reaching of consensus within the respective ICH Working Groups tasked with their development and sign-off by the Regulatory Member experts of these Working Groups under *Step 3*.

ICH E6 Guideline – Good Clinical Practice (GCP)

The ICH E6(R1) Guideline on Clinical Good Practice was revised with an integrated Addendum and then was renamed as E6(R2). The integrated Addendum aims to encourage sponsors to implement improved oversight and management of clinical trials, while continuing to ensure protection of human subjects participating in trials and clinical trial data integrity. Further to this revision on the GCP Guideline, ICH has discussed further work to modernise the ICH E8 Guideline on General Considerations for Clinical Trials and subsequently renovate the ICH E6 Guideline.

ICH M4 Guideline – Common Technical Document (CTD)

The agreement to assemble all the Quality, Safety and Efficacy information in a common format called CTD has revolutionised regulatory review processes, led to harmonised electronic submission that, in turn, enabled implementation of good review practices.

The CTD is organised into five modules, and some modules are further described in three other guidelines specific to the Quality (M4Q), Safety (M4S) and Efficacy (M4E) sections of the CTD.

In 2016, two of these guidelines were revised:

- The Granularity document included in the ICH M4(R3) Guideline as an Annex was revised to add Module 2 and 3 tables and Appendices for eCTD v4, as well as corrections to Module 2 and 3 tables for eCTD v3.2.2 and then was renamed as ICH M4(R4);
- The ICH M4E(R1) was revised to include greater specificity on the format and structure of benefit-risk information, harmonising the presentation of this information in regulatory submissions, and then was renamed as ICH M4E(R2).

ICH M8 – Electronic Common Technical Document (eCTD)

ICH M8 is a technical standard and Implementation Guide to facilitate the exchange of regulatory information prepared in accordance with the requirements of the CTD in the ICH regions. The M8 EWG/IWG in charge of this standard also assumes the responsibility for the implementation and maintenance of eCTD, as well as development and maintenance of other related documents such as Q&As and Study Tagging File specifications.

In 2016, several documents related to the M8 eCTD were adopted:

- The eCTD v4.0 Implementation Package v1.2;
- The eCTD v4.0 Q&A and Change Request Document v1.00;
- The eCTD v3.2.2 Q&A and Specification Change Request Documents v1.28 and v1.29;
- The Specification for Submission Formats for eCTD v1.1;
- The Valid Values File v5.

ICH E2B Guideline – Clinical Safety Data Management: Data Elements for Transmission of Individual Case Safety Reports (ICSR)

The ICH E2B Guideline aims to standardise the essential clinical safety data with recommendation on their specifications for electronic transmission.

In 2016, the following documents were adopted:

- The ICSR Implementation Guide v5.02;
- The ICSR Q&A Documents v1.0 and v2.0 in the Implementation Guide package v5.02;
- The Backwards and Forwards Compatibility (BFC) Specification v2.02.

ICH Q3C Guideline – Impurities: Guideline for Residual Solvents

The ICH Q3C Guideline recommends the use of less toxic solvents in the manufacture of drug substances and dosage forms, and sets pharmaceutical limits for residual solvents

(organic volatile impurities) qualitatively and quantitatively in drug products and excipients. A Maintenance process has been established to revise Permitted Daily Exposure (PDE), as new toxicological data for solvents become available.

In 2016, the PDE for Triethylamine was added as a new solvent and the PDE for Methylisobutylketone was revised in the ICH Q3C(R5) Guideline which was then renamed ICH Q3C(R6).

3.2. ICH Guidelines & Other Documents Endorsed at Step 2a/b in 2016

In 2016 the following ICH Guidelines and other documents 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 Working Groups tasked with their development and sign-off by all Member experts of these Working Groups, under *Step 1*.

ICH E17 Guideline – General Principles for Planning and Designing of Multi-Regional Clinical Trials

A new draft ICH E17 Guideline was developed on Multi-Regional Clinical Trials which is intended, in view of the move to global development of medicines, to support the planning and design of multi-regional clinical trials, a reduction in unnecessary duplication of studies and the subsequent acceptability to regulators of data from those trials.

ICH E11 Guideline – Clinical Trials in Pediatric Population

A revision to the existing ICH E11 Guideline on Clinical Investigation of Medicinal Products in the Pediatric Population reached *Step 2 a/b* of the ICH process in 2016. This draft Addendum proposed to address new scientific and technical knowledge advances in paediatric drug development.

ICH S3A Guideline – Note for Guidance on Toxicokinetics: The Assessment of Systemic Exposure in Toxicity Studies

A Q&A document was developed in support of the ICH S3A Guideline. The draft ICH S3A Q&A document has been developed to provide additional guidance and facilitate the interpretation of the S3A Guideline; and especially to address the benefit and use of microsampling techniques in main study animals.

ICH S9 Guideline – Nonclinical Evaluation for Anticancer Pharmaceuticals

A Q&A document was developed in support of the ICH S9 Guideline. The draft ICH S9 Q&A document aims to clarify the scope and implementation of the ICH S9 Guideline on non-clinical evaluation of anticancer products, and support the development and evaluation of medicines for faster access for patients with serious and life-threatening cancers.

ICH Q11 Guideline – Development and Manufacture of Drug Substances

A Q&A document was developed in support of the ICH Q11 Guideline. The draft ICH Q11 Q&A document focuses on selection and justification of starting materials (chemical entities and biotechnological/biological entities) for the manufacture of drug substances.

3.3. Other Working Groups Outputs

The following highlights other noteworthy outputs of ICH Working Groups in 2016 outside of those items produced as part of the ICH step process. (See Section 3.6 for Working Group outputs related to training).

- In March and September, the ICH M1 Point to Consider (PtC) WG updated the two PtC documents on Term Selection and Data Retrieval and Presentation with MedDRA release versions 19.0 and 19.1;
- In April, further to the update of the Regulatory Notice Document (RND) published in January 2016 (endorsed by the Assembly in December 2015), the S1 Expert Working Group completed a Prospective Evaluation Period Status Report. This Status Report which provided a brief overview of the study's progress and actions taken by the Working Group to ensure successful completion of the study was made available on the ICH website.
- In June and November, the Assembly endorsed the eCTD v4.0 Support Documentation v1.1 and v1.2, as well as the Orientation Materials v1.1 and v1.2, developed and updated by the M8 EWG/IWG to support the eCTD v4.0 Implementation Guide;
- In November, the MedDRA Management Board approved a new ICH M1 PtC Concept Paper to extend the remit of the M1 PtC WG to include development of a companion document to the PtC documents, to be available in English and Japanese, which would provide more detailed guidance, examples, and "Q&A" on topics of regulatory importance such as data quality, medication errors and product quality issues.

3.4. New Harmonisation Topics

During 2016, a process was established for the selection of new topics proposed for harmonisation by ICH Members and Observers. The process was documented in the ICH Management Committee and Assembly Rules of Procedure, as well as in the Standard Operating Procedures for Working Groups. The process was piloted in 2016 on the basis of several new topic proposals submitted by Members ahead of the Lisbon meeting in June. Topics were ranked according to priority by the ICH Management Committee, who then recommended those with the highest priority rankings to the Assembly for approval on the basis of Concept Paper outlines.

In 2016, 3 new topics for harmonisation were recommended by the ICH Management Committee and approved by the Assembly:

ICH M9 Guideline – Biopharmaceutics Classification System-based Biowaivers

The ICH M9 Guideline aims to achieve worldwide harmonisation of the applicability of biowaivers and the data needed to support such applications. The public health benefits include reducing unnecessary clinical trials, and facilitating the production and availability of good quality medicines especially in low and middle-income countries.

- The Assembly approved the M9 Concept Paper outline at its meeting in Lisbon in June and agreed to the establishment of an informal Working Group to finalise the Concept Paper and Business Plan.
- The ICH Management Committee approved the Concept Paper and Business Plan at its teleconference on October 7 and agreed to the establishment of an Expert Working Group.
- The Assembly appointed EC as Rapporteur and the ICH Management Committee appointed FDA as Regulatory Chair.

ICH M10 Guideline – Bioanalytical Method Validation

The ICH M10 Guideline related to bioanalytical method validation, for which recent regulatory requirements have been introduced in EU, Japan and USA, is aimed at addressing the discrepancies between these provisions and those from other ICH Regulatory Members. A harmonisation approach will promote rational and effective studies and facilitate global drug development, thereby advancing the mission of ICH.

- The Assembly approved the M10 Concept Paper outline at its meeting in Lisbon in June and agreed to the establishment of an informal Working Group to finalise the Concept Paper and Business Plan.
- The ICH Management Committee approved the Concept Paper and Business Plan at its teleconference on October 7 and agreed to the establishment of an Expert Working Group.
- The Assembly appointed MHLW/PMDA as Rapporteur and the ICH Management Committee appointed MHLW/PMDA as Regulatory Chair.

ICH E19 Guideline – Optimization of Safety Data Collection

The ICH E19 Guideline is expected to harmonise requirements on the optimal collection of safety data during late stage pre-market and post-approval clinical investigations of new drugs and new indications for approved drugs. This aims to improve global health by encouraging study on long-term effects, rare events and new indications of drugs through reducing resources required for these studies.

- The Assembly approved the E19 Concept Paper outline at its meeting in Osaka in November and agreed to the establishment of an informal Working Group to finalise the Concept Paper and Business Plan.
- The Assembly appointed FDA as Rapporteur.

Strategic Approach to New Topic Selection

In 2016, the ICH Management Committee also discussed a strategic approach to the selection of future ICH topics for harmonisation aimed at identifying potential areas of work. Discussion was initiated by the ICH Management Committee on two potential strategic topics for ICH:

GCP Renovation: Modernisation of ICH E8 and Subsequent Renovation of ICH E6

- The ICH Management Committee provided input on a Reflection Paper on GCP Renovation, the development of which was led by FDA.
- In Osaka in November, the Assembly supported the publication on the ICH website of the Reflection Paper for a comment period of 2 months.

Compliance of Reliability for Electronic Records

- The ICH Management Committee agreed in Osaka in November to establish a feasibility group to further consider the development of a Reflection Paper on Compliance of Reliability for Electronic Records, which was led by JPMA.

3.5. Implementation of ICH Guidelines

The aim and intention is that all ICH Regulators should implement all ICH Guidelines. At the time of Membership application to ICH each Regulator is expected to have implemented the ICH Q1, ICH Q7 and ICH E6 Guidelines ("Tier 1 guidelines"), 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.

During 2016, a total of 20 ICH Guidelines were implemented by ICH Regulatory Members EC, Health Canada, FDA, MHLW/PMDA and Swissmedic.

The implementation dates for each guideline by each Regulatory Member are indicated on the ICH website www.ich.org.

The following decisions were also taken in relation to ICH Guideline implementation:

- With the joining of new ICH Regulatory Members in 2016, the ICH Management Committee directed the ICH Secretariat to update the ICH website with implementation information relating to the new Members.
- At the Osaka meeting in November, the Assembly discussed the establishment of a process, in line with the Assembly Rules of Procedure, to enable it to monitor ICH Guideline implementation, the progress of international harmonisation, and coordinate efforts in this regard.
- The ICH Management Committee tasked the ICH Secretariat to develop and maintain a table regarding the implementation of ICH Guidelines by all Regulatory Members to provide an overview on the status of implementation for discussion at the Assembly.

3.6. Training on ICH Guidelines

ICH recognises that training is important to the successful implementation of ICH Guidelines globally.

ICH Training Strategy

In 2016, work was progressed by an ICH Management Committee Subcommittee on an ICH training strategy. The following decisions were taken by the ICH Management Committee in November in relation to this work:

- The ICH Management Committee agreed that the Training Strategy Subcommittee becomes a Standing Committee: "Training Subcommittee".
- The ICH Management Committee endorsed the Training Subcommittee's partnership with a small group of trusted training providers as part of a 12 month pilot, during which the Subcommittee would work on Terms of Reference and defining the roles and responsibilities of the parties. The pilot work will be evaluated and a report made back to the ICH Management Committee and the Assembly.
- The ICH Management Committee supported the following items developed by the Subcommittee: a list of training modalities and which methods might work best for certain topics, criteria for training approaches, and various techniques and tools; a slide template for ICH Working Groups to use when developing presentations; and a "Best Practices" document that has tips for drafting ICH slide presentations.

Training Materials Developed by ICH Working Groups

In line with ICH procedures, when an ICH Guideline reaches *Step 2b* or *Step 4*, each ICH Working Group develops a presentation to be included by the ICH Secretariat in a library of presentations and implementation materials made available on the ICH public website.

- In 2016, the ICH Secretariat updated the ICH website with the following presentations developed by the respective Working Groups:

  ***Step 2* presentations:**

  - Q&As on ICH S3A Guideline
  - Q&As on ICH S9 Guideline
  - Q&As on ICH Q11 Guideline

- Addendum to the ICH E11 Guideline
- New ICH E17 Guideline

Step 4 **presentations:**

- Integrated Addendum to the ICH E6(R2) Guideline
- Revision of the ICH M4E(R1) Guideline
- Revision of the ICH Q3C(R5) Guideline

Some ICH Working Groups are tasked with the development of detailed training materials to support the implementation of an ICH Guideline.

- In 2016, the Expert Working Group which had developed the ICH Q3D Guideline on Elemental Impurities (*Step 4* reached in December 2014) completed work on a package of ICH Q3D Training Modules 0-9 (Module 0: Overview; Modules 1-7: Key Safety and Quality Topics; Module 8: Case Studies; and Modules 9: FAQ Document). The ICH Q3D Guideline aims to provide a global policy for limiting elemental impurities in drug products. The development of a comprehensive training programme and supporting documentation was considered necessary by ICH, to ensure the proper interpretation and effective utilisation of the ICH Q3D Guideline by industry and regulators alike, to enable a harmonised and smooth implementation of ICH Q3D on a global basis.
- With the support of the Assembly, the ICH Q3D training modules were published on the ICH website.
- Training Workshops supported by the ICH Q3D Working Group were held as follows in 2016: in Tokyo, Japan on March 11; in London, UK on April 5-6 and in Silver Spring, US on August 22-23.

ICH Support of Other Training Initiatives

In 2016, with the support of the ICH Management Committee, and in continuation of an activity initiated prior to the establishment of the new ICH Association, an ICH Committee of experts reviewed ICH's package of training materials on the ICH E2 series of pharmacovigilance Guidelines for use by the APEC Harmonisation Center (AHC) as part of an AHC ICH e-learning pilot programme on these ICH Guidelines. This course on the E2A-E2F ICH Guidelines is open for a pilot period from August 29, 2016 to August 31, 2017 and is available to anyone without charge by signing-up to the course with the AHC e-Learning Center. Further information is provided on the ICH website www.ich.org.

3.7. 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 sale.

2016 was a successful year of continued growth and development of MedDRA. Important steps were taken such as the conduct of the inaugural MedDRA Management Committee meeting, the approval of the ICH Association's award of a new 7-year contract for the MedDRA Maintenance and Support Services Organisation (MSSO), and the approval of a significant reduction of the 2017 Subscription fees based on the continued growth of worldwide MedDRA users.

3.7.1. Overview of 2016 MedDRA Management & Key Decisions

In 2016, considering that MedDRA's ownership had not been transferred yet from IFPMA, as trustee of the former International Conference on Harmonisation, to the new ICH Association, the MedDRA Management Board, which was established under the former ICH, ran in parallel with the new MedDRA Management Committee.

In 2016, the MedDRA Management Board remained responsible for overseeing the main activities of the MSSO, as well as providing oversight and direction to the MedDRA Secretariat. The MedDRA Management Board addressed also the necessary legal and fiscal matters along with the ICH Management Committee and Secretariat, to enable the transfer of MedDRA, as part of the overall transfer of ICH assets, from IFPMA (as trustee of the International Conference on Harmonisation Steering Committee) to the new ICH Association. The MedDRA Management Committee was in turn responsible for the MedDRA matters related to the new ICH Association.

The following key decisions were taken in 2016 related to MedDRA's management:

- Approval by the MedDRA Management Committee of the ICH Association's award of the new 7-year contract for the MedDRA MSSO to Northrop Grumman's Health Solutions Business Unit on the basis of a recommendation from the ICH Tender Evaluation Panel, and provision of direction to the persons entitled to represent the ICH Association on MedDRA matters to sign-off the new contract.

- Approval by the MedDRA Management Board of the amendment of the current MSSO/ICH (IFPMA) contract to enable the contract to be extended beyond December 31, 2016 until MedDRA's ownership is transferred to the new ICH Association.
- Approval by the MedDRA Management Board of the amendment of the current Sub-licensing agreement between MSSO/JMO (Japanese Maintenance Organisation) to enable the contract to be extended beyond December 31, 2016 until MedDRA's ownership is transferred to the new ICH Association.
- Approval by the MedDRA Management Committee/MedDRA Management Board of the 2017 MSSO Business Plan and Budget.
- Approval by the MedDRA Management Committee/MedDRA Management Board of the 2017 MSSO Subscription fees, including a significant reduction based on the continued growth of MedDRA users throughout the world and increased efficiencies to contain costs of maintenance and development of MedDRA.
- Approval by the MedDRA Management Board of the renewal for another year of the Memorandum of Understanding ICH has (through trustee IFPMA) with the Council for the International Organizations of Medical Sciences (CIOMS) to develop Standardised MedDRA Queries (SMQs).
- Approval by the MedDRA Management Board for the ICH Secretariat to organise an audit of MSSO IT tools and systems.

3.7.2. Oversight of 2016 MedDRA MSSO Activities

Although not entirely under the purview of the ICH Association in 2016, for completeness, a summary is provided as follows of the main activities of the MSSO in 2016 which the MedDRA Management Board oversaw and provided the necessary approvals for, including MedDRA development activities and support of MedDRA users:

- Release of a new 27th SOC (System Organ Class) with MedDRA v19.0 in March named Product issues.
- Development of an updated version of the MedDRA Web-Based Browser in May, which updates the user interface in all MedDRA languages, includes hierarchy information when exporting MedDRA terms, as well as search results displayed in more than one language.
- Release of a new Unqualified test name term list intended for use in the E2B test name field and not used to code adverse events. The list is intended as recommendation only to improve data quality.
- Development of a "patient friendly" list of MedDRA terms that would be pilot tested in 2017.
- Development of an Account Self-Service Application to allow MSSO Subscribers to obtain subscription information; add/delete/change point of contact; change of password; download or print Training Certificates without needing to contact the MSSO Helpdesk.

- Maintenance of ISO 9001:2008 certification and preparation for transitioning to the new ISO standard 9001:2015 in 2017.
- Support of the work of the ICH MedDRA Points to Consider Working Group to (i) update with each MedDRA release the PtC documents on Term Selection and Data Retrieval and Presentation, and (ii) develop a condensed version of the PtC documents which could be easily translated in languages where a MedDRA translation exists.
- Conduct of training for MSSO MedDRA users, including Regulators in Canada, Czech Republic, France, Germany, Mexico, Republic of Serbia, the Netherlands, the United Kingdom, and the United States (101 training courses including 70 face-to-face training classes and 31 webinars to approximately 4,400 people).
- Provision of assistance to Regulators expressing interested in MedDRA or working towards a MedDRA translation in their national language.

4. 2016 ICH Operational Matters

4.1. ICH Articles & Procedures

As 2016 represented the first complete year of activity of the newly created ICH Association, efforts were made to develop and clarify procedures to support ICH activities. Five documents currently 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) for the ICH Working Groups. Each of these documents is available on the ICH website.

The following highlights the key decisions taken in 2016 regarding these documents:

ICH Articles of Association

- The Assembly approved several minor amendments to the ICH Articles of Association in November. The Articles had originally been approved by the Founding Members at the Inaugural Assembly meeting in October 2015. The changes approved were based on experience with a year of operation and aimed at streamlining the procedures, in order to maintain the efficiency of ICH's harmonisation activities.

Assembly RoP

- The Assembly approved two sets of amendments to the Assembly RoP, in June and November respectively. The changes approved included those consistent with the amendments to the ICH Articles of Association, in addition to the introduction of an ICH Donation Policy and a number of clarifications aimed at maintaining the efficiency of ICH's harmonisation activities.

ICH Management Committee RoP

- The ICH Management Committee approved the first version of its RoPs in June, with several amendments subsequently approved in November. The changes made in November included addition of new procedures related to: the organisation of ICH meetings; selection of new topics for harmonisation; and use of the ICH logo.

MedDRA Management Committee RoP

- The MedDRA Management Committee approved the first version of its RoPs in November during the Osaka meeting.

SOPs for the ICH Working Groups

- The ICH Management Committee approved Version 1.0 of the SOPs for Working Groups in June, followed by Version 2.0 in November.

4.2. ICH Funding

ICH Funding

In line with the ICH Articles of Association, 2016 was a transitional period for the ICH Association, whereby, as per Article 59, until the Assembly approves membership fees and other financial means to be raised and which are payable by all Members, the ICH Management Committee ensured the funding of the ICH Association.

In 2016, the following decisions were taken related to the funding of ICH:

- The Assembly approved the 2017 ICH Budget on the basis of a recommendation from the ICH Management Committee.
- The Assembly approved a recommendation from the ICH Management Committee to implement from the start of 2018 a Membership Fee of CHF 20,000 for Regulatory and Industry Members. The Assembly acknowledged that the need to revise the annual membership fee for Regulatory and Industry Members will be assessed periodically depending on the budget situation and the number of members. No decision to modify the Membership Fees for Founding Regulatory, Founding Industry and Standing Regulatory Members was taken. The Assembly supported publication on the ICH website of the 2018 Membership Fees. The 2018 Membership Fees are provided in Table 1 below:

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

Table 1: 2018 Membership Fees

MedDRA Funding

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

- In 2016, the Assembly approved the 2017 MedDRA Budget, which included the 2017 MSSO MedDRA Subscription fees, on the basis of a recommendation from the MedDRA Management Committee.

Financial Audit

In line with Articles 55 and 56 of the ICH Articles of Association, Auditors should be appointed by the Assembly to audit the financial statements of the ICH Association upon conclusion of each Fiscal Year. They should ensure that the accounting of the ICH Association complies with Swiss law and generally accepted Swiss accounting principles.

- In 2016, the Assembly agreed to appoint the auditing firm Moore Stephens Refidar SA for an initial period of two years based on a recommendation from the ICH Management Committee following its assessment of proposals solicited by the ICH Secretariat.

Donation Policy

Article 57.3 of the ICH Articles of Association identifies financial contributions as a mean by which the costs of the ICH Association may be covered. Since this may include donations from Members, Observers or external parties, an ICH Donation Policy was developed.

- In 2016, the Assembly approved an ICH Donation Policy as part of the revisions made to the Assembly Rules of Procedure document.

4.3. ICH Communication

One of the key areas of work foreseen for the ICH Association is to ensure appropriate communication and transparency with stakeholders on ICH activities. The ICH Management Committee has established a Communications Subcommittee to support ICH Communication Activities.

In 2016, the Communication Subcommittee progressed development of an ICH communication and stakeholder engagement plan, as well as a transparency policy. The Subcommittee also identified enhancements to be made to the ICH website, and supported the development of some documents to enhance communication.

ICH Website

The ICH public website www.ich.org represents the main line of communication and is updated in real-time by the ICH Secretariat.

2016 saw publication by the ICH Secretariat on the ICH website of a number of new documents supported by the Assembly and the ICH Management Committee aimed at providing stakeholders with information on ICH and its processes. This included:

- Procedural Documents – In addition to the ICH Articles of Association and Assembly Rules of Procedure already published in 2015, 2016 saw publication of: ICH Management Committee Rules of Procedure; MedDRA Management Committee Rules of Procedure; and Standard Operating Procedures for ICH Working Groups.
- Work Plans and Reports – this included: the 2016 ICH Work Plan; ICH Multi-annual Strategic Plan; 2016 MedDRA Work Plan; 2015 Annual Report.

- Meeting Documents – In addition to the Assembly agendas and reports already published, 2016 saw publication of minutes of ICH Management Committee face-to-face meetings, as well as summary reports of the teleconference held between meetings.
- Information on ICH Membership and Observership – this included publication of application forms, as well as a Questions and Answers document.
- The 2016-2018 ICH Provisional Multi-Year Budget.
- A general slide deck on ICH.

ICH Regional Public Meetings

While ICH no longer organises the large international ICH Conferences that it did between 1991 and 2003, public meetings are still considered important for disseminating information of ICH activities. ICH Members periodically hold dedicated ICH regional public meetings, either independently or in collaboration with other non-profit organisations. Information on these meetings is made available by the ICH Secretariat on the ICH website.

In 2016, Members held the following ICH regional public meetings:

Europe

On April 6, the Drug Information Association (DIA) in collaboration with EC and the European Medicines Agency (EMA) organised an "Information Day on ICH" in conjunction with the DIA Euro meeting in Hamburg, Germany. The Information Day focused on the recent reforms by ICH and what this means for global development of medicines.

Japan

JPMA in collaboration with MHLW/PMDA organised an ICH regional public meeting in Tokyo, Japan, on July 21 and again on November 12 in collaboration with DIA.

United States & Canada

Health Canada and the FDA held a joint public consultation meeting on ICH Guidelines currently under development prior to each of the 2016 biannual ICH face-to-face meeting. A meeting was held at the FDA's White Oak campus in Silver Spring, MD on May 6 and then on October 24 at the Tunney's Pasture campus of Health Canada in Ottawa, Ontario.

4.4. ICH Secretariat

ICH Secretariat Operations

The ICH Secretariat is responsible for the day-to-day management of ICH, coordinating ICH activities as well as providing support to the Assembly, the ICH Management Committee, its Working Groups and the MedDRA Management Board/Committee.

The following highlights key points and decisions related to Secretariat staffing in 2016:

- Secretariat staffing was planned at 4.8 FTEs (Full Time Equivalents) for 2016, allocated between support for ICH activities (3.0 FTEs) and MedDRA activities (1.8 FTEs). Due to staffing changes, the ICH Secretariat operated at less than full capacity with 4.2 FTEs over the full year.
- The year saw the hiring of Dr. Isabelle Güller in January, who filled a vacant Manager position, and the hiring of Ms. Emilie Macara in October, who filled a vacant Administrative Assistant position. And the departure of Dr. Sarah Adam in October, followed by launching of the recruitment of a replacement Manager.
- Acknowledging an increase in the activities needing ICH Secretariat support since the establishment of the new ICH Association in October 2015, the ICH Management Committee approved the following:
  - An increase of 0.4 FTE for ICH Manager support, adding to 0.3 FTE previously approved in Lisbon in June 2016, allowing capacity to be increased by 0.7 FTE in support of ICH activities;
  - In view of the future provision of services to the International Pharmaceutical Regulators Forum (IPRF), hiring of a new full-time Manager to help the ICH Secretariat through the transition period after which point the allocation to ICH would be reduced to 0.5FTE.

The following highlights key activities of the Secretariat in 2016:

- Preparation of agenda papers and reports for the biannual face-to-face meetings of the Assembly, the ICH Management Committee and the MedDRA Management Board/Committee, as well as for the following teleconferences: 11 ICH Management Committee teleconferences; 2 ICH Coordinator teleconferences; and 3 ICH MedDRA Management Board/Committee teleconferences.
- Supporting ICH harmonisation activities and the work of 23 ICH Working Groups in 2016, including the establishment of 2 new Expert Working Groups in 2016.
- Administration of the ICH website including:
  - Keeping the ICH website up-to-date with publication of draft documents for public consultation, *Step 2* and *Step 4* presentations, Press Releases, regional public consultation dates and guideline implementation dates;
  - Managing the working areas for the ICH Management Committee, MedDRA Management Committee/MedDRA Management Board and ICH Working Groups, with the provision of assistance to an additional 5 Working Groups in 2016 to make use of the working area, bringing the total number of Working Groups using the working area to 15 by the end of 2016.
- Responding to stakeholder enquiries received via the ICH mailbox with input solicited as necessary from ICH experts and ICH Coordinators, and which in 2016 represented close to 200 enquiries.
- Drafting documents in support of ICH Management Committee and MedDRA Management Board/Committee reporting to the Assembly, including: 2015 Annual Report (for the period October 23 – December 31, 2015); 2016 and 2017 ICH Work Plans and ICH Multi-annual Strategic Plan; and 2016 and 2017 MedDRA Work Plans.

- Provision of support and input for the work of the ICH Management Committee Subcommittees on; Financials; Training; Communication; Standard Operating Procedures for Working Groups; Membership; and New Topics.
- Financial administration, including: drafting of 2017 ICH and MedDRA budgets; preparation of closing reports; soliciting proposals from potential auditors for consideration by the ICH Management Committee; and submitting items required for the FDA Grant (in 2016 this was the quarterly Federal Financial Report and the requesting of a delay in the drawing of funds pending the transfer of assets from IFPMA to the ICH Association).
- Contract management, including those related to day-to-day operations (e.g., website hosting and maintenance), as well as support of the MedDRA Management Board/Committee's oversight of the MSSO Contractor, which in 2016 included the completion of the MedDRA MSSO Call for Tender process and the award of a 7-year contract for the MedDRA MSSO.

Operationalising the New ICH Association

In 2016, work was progressed by the ICH Secretariat under the direction of the ICH Management Committee towards making fully operational the ICH Association established in October 2015 under Swiss law. This included work to address the necessary legal and fiscal matters to enable the transfer of all ICH assets from IFPMA (as trustee of the International Conference on Harmonisation Steering Committee) to the new ICH Association. The ICH Secretariat was supported in this work by external legal and fiscal advisors:

- Submission to the Geneva Fiscal Administration a request for a tax exemption for the ICH Association.
- Seeking clarification from the Swiss Federal Tax Administration on VAT aspects related to ICH activities.
- Preparation for the transfer of assets from IFPMA to ICH including: work on the asset transfer agreement and accompanying documents; and identifying contractors necessary to support the independent operation of the ICH Secretariat (e.g., external fiduciary services firm; IT support etc…).
- Consideration of the insurances which will need to be taken upon the ICH Association becoming fully operational – the taking of legal insurance for the ICH Association (complimentary to the Directors and Officers insurance acquired in 2015) was postponed until this time.

Annex I

Assembly Member Representatives & Observer Delegates

December 31, 2016

Founding Regulatory Members

The European Commission (EC)
Mrs. Lenita Lindström-Gommers *(Chair)*
Dr. Tomas Salmonson
Dr. Aurélien Perez

The Ministry of Health, Labour and Welfare of Japan (MHLW), also represented by the Pharmaceuticals and Medical Devices Agency (PMDA)
Dr. Toshiyoshi Tominaga *(Vice Chair)*
Dr. Nobumasa Nakashima
Mr. Naoyuki Yasuda

The US Food and Drug Administration (FDA)
Dr. Theresa Mullin
Ms. Joan Wilmarth Blair

Founding Industry Members

The European Federation of Pharmaceutical Industries and Associations (EFPIA)
Dr. Sabine Luik
Mr. Pär Tellner

The Japan Pharmaceutical Manufacturers Association (JPMA)
Dr. Hironobu Hiyoshi
Dr. Masafumi Yokota

The Pharmaceutical Research and Manufacturers of America (PhRMA)
Mr. Jerry Stewart
Dr. Peter Honig

Standing Regulatory Members

Swissmedic
Dr. Petra Doerr
Ms. Cordula Landgraf

Health Canada
Ms. Catherine Parker
Dr. Celia Lourenco

Regulatory Members

The Agência Nacional de Vigilância Sanitária (ANVISA, Brazil)
Ms. Patrícia Pereira Tagliari
Mr. Renato Alencar Porto

The Ministry of Food and Drug Safety (MFDS, Korea)
Dr. Sun Hee Lee
Dr. Won Sik Lee

Industry Members

The Biotechnology Innovation Organisation (BIO)
Ms. Lila Feisee
Ms. Kay Holcomb

The International Generic and Biosimilar Medicines Association (IGBA)
Dr. Nick Cappuccino
Ms. Beata Stepniewska

The World Self-Medication Industry (WSMI)
Mrs. Christelle Anquez-Traxler
Dr. Gerald Dziekan

Standing Observers

WHO
Mr. Mike Ward
Dr. Samvel Azatyan

IFPMA
Mr. Eduardo Pisani
Dr. David Jefferys

Observers

The Central Drugs Standard Control Organization (CDSCO, India)
Dr. S. Eswara Reddy
Dr. Gyanendra Nath Singh

The Centro para el Control Estatal de Medicamentos, Equipos y Dispositivos Médicos (CECMED, Cuba)
Dr. Celeste Sánchez González
Ms. Lisette Pérez Ojeda

The Comisión Federal para la Protección contra Riesgos Sanitarios (COFEPRIS, Mexico)
Dr. Mario Alanis Garza
Mr. Cuauhtémoc Ruiz

The Health Sciences Authority (HSA, Singapore)
Dr. Dorothy Toh
Ms. Chua Siew Wei

The Medicines Control Council (MCC, South Africa)
Dr. Jeanette Lotter
Mr. Tohlang Sehloho

The National Center for the Expertise of Drugs, Medical Devices and Equipment (National Center, Kazakhstan)
Ms. Moldasheva Aiman Borashevna
Pr. Kulzhanov Maksut Karimovich

The Roszdravnadzor (Russia)
Dr. Mikhail A. Murashko
Dr. Sergey Glagolev

The Food and Drug Administration (TFDA, Chinese Taipei)
Ms. Li-Ling Liu
Dr. Churn-Shiouh Gau

The Therapeutic Goods Administration (TGA, Australia)

The Asia-Pacific Economic Cooperation (APEC)
Dr. Young Ju Choi
Dr. Churn-Shiouh Gau

The Association of Southeast Asian Nations (ASEAN)
Ms. Charunee Krisanaphan
Dr. Salmah Bahri

The East African Community (EAC)
Ms. Jane H. Mashingia
Dr. Stanley Sonoiya

The Gulf Health Council (GHC)
Dr. Ibrahim A. Aljuffali

The Pan American Network for Drug Regulatory Harmonization (PANDRH)
Ms. Analía Porrás
Ms. Ana Paula Jucá Silva

The Southern African Development Community (SADC)
Mrs. Fortunate Ntombi Fakudze
Mr. Joseph Mthetwa

The Active Pharmaceutical Ingredients Committee (APIC)
Mr. Tony Storey
Mrs. Marieke van Dalen

The Council for International Organizations of Medical Sciences (CIOMS)
Dr. Lembit Rägo
Ms. Sue le Roux

The European Directorate for the Quality of Medicines and HealthCare (EDQM)
Dr. Susanne Keitel

The International Pharmaceutical Excipient Council (IPEC)
Ms. Janeen SkutnikWilkinson

The United States Pharmacopeia (USP)
Dr. Katherine Bond
Dr. Kevin Moore

Annex II

ICH Management Committee Representatives

December 31, 2016

Founding Regulatory Members

The European Commission (EC)
Ms. Lenita Lindström-Gommers
Dr. Spiros Vamvakas

The Ministry of Health, Labour and Welfare of Japan (MHLW), also represented by the Pharmaceuticals and Medical Devices Agency (PMDA)
Dr. Toshiyoshi Tominaga *(Vice Chair)*
Dr. Nobumasa Nakashima
Mr. Naoyuki Yasuda

The US Food and Drug Administration (FDA)
Dr. Theresa Mullin *(Chair)*
Ms. Joan Wilmarth Blair

Founding Industry Members

The European Federation of Pharmaceutical Industries and Associations (EFPIA)
Dr. Sabine Luik
Mr. Pär Tellner

The Japan Pharmaceutical Manufacturers Association (JPMA)
Dr. Hironobu Hiyoshi
Dr. Masafumi Yokota

The Pharmaceutical Research and Manufacturers of America (PhRMA)
Mr. Jerry Stewart
Dr. Peter Honig

Standing Regulatory Members

Swissmedic
Dr. Petra Doerr
Ms. Cordula Landgraf

Health Canada
Ms. Catherine Parker
Dr. Celia Lourenco

Standing Observers

WHO
Mr. Mike Ward
Dr. Samvel Azatyan

IFPMA
Mr. Eduardo Pisani
Dr. David Jefferys

Annex III

MedDRA Management Committee Representatives

December 31, 2016[4]

Founding Regulatory Members

The European Commission (EC)
Mr. Sébastien Goux
Dr. Sabine Brosch

The Ministry of Health, Labour and Welfare of Japan (MHLW), also represented by the Pharmaceuticals and Medical Devices Agency (PMDA)
Dr. Kiyomi Ueno
Mr. Takayuki Okubo

The US Food and Drug Administration (FDA)
Ms. Mary Ann Slack
Dr. Christopher Jankosky

Founding Industry Members

The European Federation of Pharmaceutical Industries and Associations (EFPIA)
Ms. Hilary Vass
Dr. Christina Winter

The Japan Pharmaceutical Manufacturers Association (JPMA)
Mr. Yo Tanaka
Mr. Hisaya Motojima

The Pharmaceutical Research and Manufacturers of America (PhRMA)
Dr. Peter Honig
Ms. Camille Jackson

Standing Regulatory Member

Health Canada
Ms. Heather Morrison
Ms. Sophie Sommerer

The UK Medicines and Healthcare products Regulatory Agency (MHRA)

Mr. Mick Foy

WHO Observer Delegate

WHO
Dr. Daisuke Tanaka
Mr. Mike Ward

[4] The representation on the MedDRA Management Committee and MedDRA Management Board was equivalent in 2016.

Annex IV

ICH Secretariat Staff

December 31, 2016

Director
Dr. Dawn Ronan

Manager
Dr. Isabelle Güller

Administrative Assistant
Ms. Coralie Angulo
Ms. Emilie Macara

Left to right ICH Secretariat: Ms. Coralie Angulo, Ms. Emilie Macara, Dr. Isabelle Güller, Dr. Dawn Ronan

Annex V

Assembly Member Representatives & Observer Delegates

December 31, 2016

Founding Regulatory Members

The European Commission (EC)
Mr. Sébastien Goux
Dr. Spiros Vamvakas (Technical Coordinator)
Dr. Milton Bonelli

The Ministry of Health, Labour and Welfare of Japan (MHLW), also represented by the Pharmaceuticals and Medical Devices Agency (PMDA)
Mr. Fumihito Takanashi
Ms. Chieko Hirose

The US Food and Drug Administration (FDA)
Ms. Amanda Roache
Dr. Michelle Limoli

Founding Industry Members

The European Federation of Pharmaceutical Industries and Associations (EFPIA)
Mr. Pär Tellner

The Japan Pharmaceutical Manufacturers Association (JPMA)
Mr. Mitsuo Mihara

The Pharmaceutical Research and Manufacturers of America (PhRMA)
Ms. Camille Jackson

Standing Regulatory Members

Swissmedic
Ms. Tsvetina Vasileva

Health Canada
Mr. Nick Orphanos

Regulatory Member

The Agência Nacional de Vigilância Sanitária (ANVISA, Brazil)
Ms. Ana Carolina Moreira Marino Araujo

The Ministry of Food and Drug Safety (MFDS, Korea)
Ms. Pan Soon Kim

Industry Members

The Biotechnology Innovation Organisation (BIO)
Ms. Lila Feisee

The International Generic and Biosimilar Medicines Association (IGBA)
Dr. Norihiro Kawamura

The World Self-Medication Industry (WSMI)
Mrs. Christelle Anquez-Traxler

Annex VI

ICH Working Groups which met face-to-face at ICH's biannual meetings in 2016

Lisbon, Portugal in June 11 – 16

Group Code	Topic	Meeting Days
S5(R3) EWG	Revision on Detection of Toxicity to Reproduction for Medicinal Products and Toxicity to Male Fertility	5 days
S11 EWG	Nonclinical Safety Testing in Support of Development of Paediatric Medicines	4 days
Q11 IWG	Q&As on API Starting Materials	4 days
Q12 EWG	Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management	5 days
E6(R2) EWG	Addendum to Good Clinical Practice	4 days
E9(R1) EWG	Addendum To Defining The Appropriate Estimand For A Clinical Trial/Sensitivity Analyses	4 days
E11(R1) EWG	Addendum to Paediatric Drug Development	4 days
E2B(R3) IWG	Revision of the Electronic Submission of Individual Case Safety Reports	5 days
M1 PTC WG	MedDRA Points to Consider Working Group	4 days
M4E(R2) EWG	Revision of CTD-Efficacy	5 days

Osaka, Japan in November 6 – 10

Group Code	Topic	Meeting Days
S5(R3) EWG	Revision on Detection of Toxicity to Reproduction for Medicinal Products and Toxicity to Male Fertility	5 days
S11 EWG	Nonclinical Safety Testing in Support of Development of Paediatric Medicines	4 days
Q12 EWG	Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management	5 days
E9(R1) EWG	Addendum to Defining the Appropriate Estimand for a Clinical Trial/Sensitivity Analyses	5 days
E17 EWG	Multi-Regional Clinical Trials	4 days
E18 EWG	Genomic Sampling and Management of Genomic Data	4 days
M8 EWG/IWG	The Electronic Common Technical Document: eCTD	4 days
E2B(R3) IWG	Revision of the Electronic Submission of Individual Case Safety Reports	4 days
M9 EWG	Biopharmaceutics Classification System-based Biowaivers	4 days
M10 EWG	Bioanalytical Method Validation	4 days

Annex VII

Overview of harmonisation activities and accomplishments in 2016

Topic Code	Type of Working Group	Topic Name	Accomplishments	Anticipated Milestones (at the end of 2016)
S1	EWG	Revision of Rodent Carcinogenicity Studies for Human Pharmaceuticals	Prospective Evaluation Period Status Report published on the S1 EWG's Regulatory Testing Paradigm of Carcinogenicity in rats	*Steps 1* and *2a/b* are expected by June or November 2019
S3A	IWG	Q&As on Note for Guidance on Toxicokinetics	Reached *Steps 1* and *2a/b* in June 2016	*Steps 3* and *4* are expected by June 2017
S5(R3)	EWG	Revision on Detection of Toxicity to Reproduction for Medicinal Products and Toxicity to Male Fertility	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2a/b* are expected by Q2 2017
S9	IWG	Q&As on Nonclinical Evaluation for Anticancer Pharmaceuticals	Reached *Steps 1* and *2a/b* in June 2016	*Steps 3* and *4* are expected by June 2017
S11	EWG	ICH Guideline on Nonclinical Safety Testing - Paediatric Medicines	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2a/b* are expected by Q2 2017

Topic Code	Type of Working Group	Topic Name	Accomplishments	Anticipated Milestones (at the end of 2016)
M7(R1)	EWG	Addendum to Assessment and Control of DNA Reactive Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 3* and *4* are expected by Q1/Q2 2017
Q3C(R6)	Maintenance EWG	Maintenance of the Guideline for Residual Solvents	Reached *Steps 3* and *4* to revise the Permitted Daily Exposure for Methyl isobutyl ketone (MIBK), and to add Triethylamine (TEA) as a new solvent	N/A (Ongoing Activity)
Q3D(R1)	Maintenance EWG	Maintenance of the Guideline for Elemental Impurities	Package of Training Modules published on the Q3D Guideline for Elemental Impurities New activity approved to update Q3D Guideline to develop Permitted Daily Exposure levels and permitted concentrations of elemental impurities for products administered by the cutaneous and transdermal route of administration	N/A (Ongoing Activity)
Q11	IWG	Q&As on API Starting Materials	Reached *Steps 1* and *2a/b* in November 2016	*Steps 3* and *4* are expected in November 2017

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Q12	EWG	ICH Guideline on Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2a/b* are expected by June 2017
M4Q(R1)	IWG	Addressing CTD-Q-Related Questions	Reached *Steps 3* and *4* in June 2016 of Revised Granularity Document	Activity Completed
E6(R2)	EWG	Integrated Addendum to Good Clinical Practice	Reached *Steps 3* and *4* in November 2016	Activity Completed
E9(R1)	EWG	Addendum to Defining Appropriate Estimand for a Clinical Trial/Sensitivity Analyses	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 1* and *2a/b* are expected by June 2017
E11(R1)	EWG	Addendum to Pediatric Drug Development	Reached *Steps 1* and *2a/b* in September 2016	*Steps 3* and *4* are expected by May 2017
E14/S7B	Discussion Group	Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs	Activities progressed in line with Concept Paper/Business Plan/Work Plan	N/A (Ongoing Activity)

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E17	EWG	ICH Guideline on Multi-Regional Clinical Trials	Reached *Steps 1* and *2a/b* in June 2016	*Steps 3* and *4* are expected by early Q4 2017
E18	EWG	ICH Guideline on Genomic Sampling and Management of Genomic Data	Activities progressed in line with Concept Paper/Business Plan/Work Plan	*Steps 3* and *4* are expected by Q2 2017
E19	EWG	Optimization of Safety Data Collection	New topic approved for harmonisation in November 2016	To be confirmed
M4E(R2)	EWG	Revision of CTD-Efficacy Guideline	Reached *Steps 3* and *4* in June 2016	Activity Completed
E2B(R3)	EWG/IWG	Revision of Electronic Submission of ICSRs	Reached *Steps 3* and *4* in June 2016 for: additional Q&As; and update to Implementation Guide and related document	N/A (Ongoing Activity)
M2	EWG	Electronic Standards for the Transfer of Regulatory Information	New operating model developed	N/A (Ongoing Activity)
M8	EWG/IWG	Electronic Common Technical Document: eCTD	Reached *Steps 3* and *4* for: updated eCTD version 4.0 Implementation Guide and related documents; and Q&As and Change Request documents for eCTD versions 3.2.2 and 4.0;	N/A (Ongoing Activity)

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M1	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 19.0 and 19.1; and new area of work approved	N/A (Ongoing Activity)
M9	EWG	Biopharmaceutics Classification System-based Biowaivers	New topic approved for harmonisation in June 2016	*Steps 1* and *2a/b* are expected by June 2018
M10	EWG	Bioanalytical Method Validation	New topic approved for harmonisation in June 2016	*Steps 1* and *2a/b* are expected by June 2018