2 February 2017

# MEETING MINUTES
# ICH Assembly
# 9 – 10 November 2016, Osaka, Japan

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

ICH Secretariat, Chemin des Mines 9, P.O. Box 195, 1211 Geneva 20, Switzerland

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# List of Assembly Participants

**ICH Assembly Members**

| | |
|---|---|
| Ms. Lenita Lindström-Gommers | Chair |
| Dr. Toshiyoshi Tominaga | Vice-Chair |
| Ms. Ana C. M. Moreira Araujo[1] | ANVISA |
| Ms. Patrícia Pereira[1] | ANVISA |
| Dr. Lila Feisee[1] | BIO |
| Mr. Sébastien Goux | EC |
| Dr. Spiros Vamvakas[2] | EC |
| Mr. Richard Bergström (partly) | EFPIA |
| Mr. Pär Tellner | EFPIA |
| Ms. Joan Wilmarth Blair | FDA |
| Dr. Theresa Mullin | FDA |
| Ms. Catherine Parker | Health Canada |
| Dr. Nicholas Cappuccino | IGBA |
| Ms. Beata Stepniewska | IGBA |
| Dr. Akira Kawahara | JPMA |
| Dr. Hironobu Saito | JPMA |
| Dr. Sun Hee Lee[1] | MFDS |
| Dr. Jeong Yeon Kim[1] | MFDS |
| Mr. Kazuhiko Mori | MHLW |
| Dr. Nobumasa Nakashima | MHLW |
| Mr. Naoyuki Yasuda | MHLW/PMDA |
| Dr. Peter K. Honig | PhRMA |
| Mr. Jerry Stewart | PhRMA |
| Dr. Petra Doerr | Swissmedic |
| Ms. Cordula Landgraf | Swissmedic |
| Mrs. Christelle Anquez-Traxler | WSMI |
| Mr. Motohito Nishizawa | WSMI |

**ICH Assembly Standing Observers:**

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|---|---|
| Dr. David Jefferys | IFPMA |
| Mr. Samvel Azatyan | WHO |
| Mr. Michael Ward | WHO |

**ICH Assembly Observers:**

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|---|---|
| Dr. Hee Sung Kim | APEC |
| Mrs. Marieke van Dalen[3] | APIC |
| Dr. Salmah Bahri | ASEAN |
| Ms. Charunee Krisanaphan | ASEAN |
| Dr. Celeste Sánchez González[4] | CECMED |
| Dr. Lembit Rägo | CIOMS |
| Dr. Mario Alanìs Garza | COFEPRIS |
| Ms. María de la Luz Lara Mendez | COFEPRIS |
| Dr. Susanne Keitel | EDQM |
| Ms. Chua Siew Wei | HSA |
| Prof. Ibrahim A. AlJuffali | GCC |
| Mr. Thamer A. AlSaby | GCC |
| Ms. Janeen Skutnik Wilkinson | IPEC |
| Dr. Alice Tsitsi Sigobodhla[4] | MCC |
| Mrs. Joy E. van Rheede van Oudtshoorn[4] | MCC |
| Dr. Charles Preston | PANDRH |
| Dr. Churn-Shiouh Gau | TFDA |
| Dr. Li-Ling Liu | TFDA |
| Dr John Donohoe | TGA |
| Dr. Katherine Bond | USP |
| Dr. Kevin Moore | USP |

**ICH Assembly *Ad hoc* Observers**

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|---|---|
| Mr. Zhang Hui | CFDA |
| Mr. Wang Xiangyu | CFDA |

**ICH Coordinators:**

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| Mr. Sébastien Goux | EC |
| Mr. Pär Tellner | EFPIA |
| Ms. Amanda Roache | FDA |
| Dr. Celia Lourenco | Health Canada |
| Mr. Nick Orphanos[4] | Health Canada |
| Dr. Norihiro Kawamura | IGBA |
| Mr. Mitsuo Mihara | JPMA |
| Mr. Fumihito Takanashi | MHLW |
| Ms. Camille Jackson | PhRMA |

**ICH Technical Coordinators:**

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|---|---|
| Mr. Milton Bonelli | EC/EMA |
| Dr. Michelle Limoli | FDA |
| Ms. Chieko Hirose | MHLW/PMDA |

[1] At the Assembly meeting in Osaka under agenda 2, ANVISA, BIO and MFDS were welcomed as new ICH Members.

[2] Replacing Dr. Tomas Salmonson

[3] At the Assembly meeting in Osaka under agenda 2, APIC, CECMED and MCC were welcomed as new ICH Observers.

[4] Health Canada was transitioning from Dr. Lourenco, previous ICH Coordinator to Mr. Orphanos, current Coordinator

**Others:**

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| Dr. Kamaruzaman Saleh | ASEAN |
| Mr. Martin Harvey Allchurch | EC/EMA |
| Ms. Agnès Saint-Raymond | EC/EMA |
| Dr. Hironobu Hiyoshi | JPMA |
| Ms. Machiko Sumi | JPMA |
| Ms. Emi Tomotake | JPMA |
| Mr. Toshihiko Tsunenari | JPMA |
| Dr. Masafumi Yokota | JPMA |
| Ms. Enkyoung Lee[1] | MFDS |
| Mr. Yoshihiro Katsura | MHLW/PMDA |
| Ms. Ying-Hsien Fu | TFDA |

**ICH Secretariat:**

Dr. Isabelle Güller
Dr. Dawn Ronan

# Table of Content

**Opening Discussions**

The ICH Assembly meeting in Osaka, Japan held on November 9 – 10, 2016 was chaired by Mrs. Lindström-Gommers (EC, Chair) and Dr. Tominaga (MHLW/PMDA, Vice-Chair).

The meeting opened with welcoming remarks offered by Mr. Mori (Councilor for Pharmaceutical Affairs Minister's Secretariat, MHLW).

**Adoption of the Agenda**

The agenda was adopted without modification.

**1. Procedural Matters**

*ICH Articles of Association*

The ICH Secretariat informed the Assembly on several minor amendments proposed to the ICH Articles of Association which were originally approved by the Founding Members at the Inaugural Assembly meeting in October 2015. The changes proposed were aimed at streamlining and smoothening the procedures, in order to maintain the efficiency of ICH's harmonisation activities.

***Decisions/Actions:***

- *The Assembly approved the proposed changes to the ICH Articles of Association;*
- *The revised ICH Articles of Association will be published on the ICH website.*

*Assembly Rules of Procedure*

The ICH Secretariat informed the Assembly on the amendments proposed to the Assembly Rules of Procedure (RoP) which were last updated and approved by the Assembly in June 2016. The Assembly noted that the latest amendments were made to reflect the changes made to the ICH Articles of Association, as well as for clarification and consistency. Included in the amendments was the introduction as an annex of an ICH Donation Policy.

***Decisions/Actions:***

- *The Assembly approved the proposed changes to the Assembly RoP;*
- *The Revised Assembly RoP will be published on the ICH website.*

*Standard Operating Procedures for EWGs/IWGs*

The ICH Secretariat presented to the Assembly the v2.0 of the Standard Operating Procedures for Working Groups (WGs) approved by the ICH Management committee (MC) in Osaka.

***Decisions/Actions:***

- *The Assembly noted the proposed changes to the SOPs v1.0 for WGs and that the ICH MC approved the SOPs v2.0 for WGs at its meeting in Osaka, on November 8, 2016;*
- *The SOPs v2.0 for WGs will be published on the ICH website.*

*MC Rules of Procedure*

The ICH Secretariat presented to the Assembly the amendments proposed to the MC RoP which were last updated and approved by the MC in June 2016. The latest amendments included the addition of new procedures for: the organisation of ICH meetings; selection of new topics; and use of the ICH logo.

***Decisions/Actions:***

- *The Assembly noted the MC RoP that was adopted by the ICH MC at its meeting in Osaka, Japan on November 8, 2016;*
- *The Assembly noted that the MC RoP will be published on the ICH website.*

*MedDRA MC Rules of Procedure*

The Secretariat provided an update on the status of the development of the MedDRA MC's RoP.

***Decisions/Actions:***

- *The Assembly noted the final version of the MedDRA MC RoP that was adopted by the MedDRA MC at its meeting in Osaka, Japan on November 5 – 6, 2016;*
- *The Assembly noted that the MedDRA MC RoP will be published on the ICH website.*

## 2. Membership and Observership

The ICH MC presented to the Assembly an overview of applications for Membership/Observership processed since the Lisbon meeting in June 2016, and its recommendations on these applications. The Chair drew the attention to the high interest in ICH Observership on the part of international organisations referred to in Article 17(1)(d) of the Articles of Association and that while the expression of interest in ICH is positive, it would be important to ensure ICH expands in a manageable way. The Assembly acknowledged a need for reflection on alternative ways of interaction with ICH, as well as on the eligibility criteria for this category of Observer.

***Decisions/Actions:***

- *The Assembly approved in Osaka the following Observership applications on the basis of the recommendation of the MC:*
    - *The Active Pharmaceutical Ingredients Committee (APIC);*
    - *The Centro para el Control Estatal de Medicamentos, Equipos y Dispositivos Médicos (CECMED, Cuba);*
    - *The Medicines Control Council (MCC, South Africa);*
    - *The National Center for the Expertise of Drugs, Medical Devices and Equipment, (National Center, Kazakhstan).*
- *The Assembly approved the following Membership applications on the basis of the recommendation of the MC:*
    - *The Agência Nacional de Vigilância Sanitária (ANVISA, Brazil);*
    - *The Biotechnology Innovation Organisation (BIO);*
    - *The Ministry of Food and Drug Safety (MFDS, Korea).*

## 3. Financial Matters

The ICH MC provided an update on ICH financial matters including: preparation of the 2017 ICH Budget; reflections regarding the level of the annual fee for new Members; development of a Donation Policy and recommendation of an auditing firm for appointment as ICH Auditors.

The ICH Secretariat provided an update on the preparation of the 2017 MedDRA Budget, including the 2017 MSSO MedDRA subscription fees.

***Decisions/Actions:***

- *The Assembly approved the 2017 ICH Budget;*
- *The Assembly approved the annual fee for the ICH Membership Categories: Regulatory Members and Industry Members of CHF 20,000 for publication on the ICH website and confirmed agreement to a 2018 implementation. For administrative reasons the fees were rounded up to CHF 20,000. The Assembly noted that the different amounts of the annual membership fee for the new Members and for the Founding Members do not reflect the differences in their respective rights under the Articles of Association. 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. Any future changes may be made with a view to making fees more proportional for all Members. As per the MC RoP #9.6, the rationale for any changes in the fee level for new members in the future should be communicated and explained at least 6 months before the Assembly decision;*
- *The Assembly approved the publication of the Donation Policy (adopted as part of the Assembly RoP, see Section 1 above) on the ICH website;*
- *The Assembly agreed to appoint the auditing firm Moore Stephens Refidar SA, recommended by the MC, based on an assessment it made, as the ICH Auditors for an initial period of two years to audit the annual financial statements of the Association;*
- *The Assembly approved the 2017 MedDRA Budget, which included the 2017 MSSO MedDRA Subscription fees.*

## 4. Strategic Discussions

The Assembly discussed two topics, proposed by FDA and JPMA respectively, as potential strategic topics: *"GCP Renovation": Modernization of ICH E8 and Subsequent Renovation of ICH E6*; and *Compliance of Reliability for Electronic Records*, and confirmed support for the next steps from this discussion.

***Decisions/Actions:***

- *The Assembly supported that the Reflection Paper on GCP Renovation, once updated based on comments received, will be published on the ICH website in January 2017 as an ICH Reflection Paper for a comment period of 2 months;*
- *The Assembly noted a feasibility group will be set up to further consider the Reflection Paper on Compliance of Reliability for Electronic Records ahead of the June 2017 meeting in Montreal, Canada.*

## 5. New ICH Topics

The MC highlighted the overall status of ICH harmonisation activities on current ICH topics and the process agreed in Lisbon in June 2016 for the selection of new ICH topics.

The MC provided the Assembly with an update on its considerations since the Lisbon meeting in June 2016 of the new proposals on *Safety Data Collection* (proposed by FDA) and *Adaptive Clinical Trials* (proposed by PhRMA). The Assembly noted that for the former, an updated title was proposed in Osaka: *Optimization of Safety Data Collection.*

***Decisions/Actions:***

- *The Assembly adopted the Concept Paper outline on Optimization of Safety Data Collection (code: ICH E19) and agreed on the establishment of an informal WG (with FDA nominated as Lead) to finalise the Concept Paper and develop a Business Plan ahead of the MC Teleconference to be held in spring 2017;*

- *Once the final Concept Paper and the Business Plan will be approved by the MC, the informal WG will be transformed into an EWG, which is expected to meet at the June 2017 meeting in Montreal, Canada;*
- *The Assembly acknowledged that MHLW/PMDA indicated it would only be able to take a position on sign-off at Step 1 of E19 after positive outcome of consultation with its stakeholders;*
- *The ICH Secretariat will launch the nomination process amongst ICH Members and Observers for the establishment of the informal WG;*
- *Further to Article 17(5) of the ICH Articles of Association, any ICH Observer interested to participate in the activities of this new WG would need to inform the ICH Secretariat in writing using the template available in the SOPs for WGs and provide explanations for their interest in the specific WG, information about their available expertise and how they would expect to contribute to the work of the WG;*
- *Any request received by the ICH Secretariat, will be shared with the MC for approval;*
- *The Assembly nominated FDA as the Rapporteur for the ICH E19 EWG;*
- *The Founding Regulatory Members and the Standing Regulatory Members of the MC will confirm the respective Regulatory Chairmanship for the new EWG once established;*
- *The Assembly noted that the new topic proposal on Adaptive Clinical Trials would undergo further revisions with a view to submitting a Concept Paper outline for consideration at the Montreal meeting. The MC at its meeting had supported that PhRMA revises the proposal to encompass a more limited scope, one that is less dependent on statistical considerations given the stated capacity concerns related to some active EWGs (e.g., E9). The revised proposal would be circulated to MC Members for their comments to the revision, with a timeline of submitting the updated proposal ahead of the Montreal meeting.*

## 6. Communication

*Communication Activities*

The MC provided an update on current communication activities including development of: a general slide deck on ICH; a transparency policy; and stakeholder engagement plan.

The Assembly Members and Observers were encouraged to make use of the general slide deck on ICH in their communication about ICH activities, including translating the slide deck into their national language, and noted that the presentation was available on the ICH website. The Assembly also noted other recent updates to the ICH website which included publication of MC meeting minutes/summary reports, and the SOPs for WGs.

***Decision/Action:***

- *The Assembly noted the new ICH Member logo available from the ICH Secretariat for use by ICH Members to denote ICH Membership within their own publications, presentations or on their website, and that a disclaimer would need to be signed beforehand.*

*ICH Regional Public Meetings*

The Assembly was invited to share information on any ICH Regional Public Meetings in their respective regions prior to/following the ICH meeting in Osaka.

The Assembly noted the organisation of a joint FDA/Health Canada public meeting held in Ottawa, Canada on October 24, 2016, to which participants were also able to participate by webcast.

The Assembly was also informed about the organisation of an ICH/DIA Joint Workshop to be held in Tokyo on November 12, 2016 which would present on the recent ICH reform and share the major outcomes of the ICH Osaka meeting.

## 7. Training

*ICH Training Strategy*

The MC presented to the Assembly on the development of an ICH Training Strategy.

The Assembly noted that work had been undertaken on the following different items:

- Criteria for Topic Selection for Training;
- Coordination with Trusted Providers;
- Training Approaches;
- Resource Implications;

The Assembly noted that in Osaka the MC had endorsed:

- 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 WGs to use when developing presentations;
- A "Best Practices" document that has tips for drafting ICH slide presentations;
- That the Training Strategy Subcommittee becomes a Standing Committee: "Training Subcommittee";
- Partnership with a small group of trusted training providers;
- The Standing Committee to define roles & responsibilities of parties;
- The Standing Committee to define expectations of each party (ex: use of ICH logo; post training avail on ICH Website, etc);
- Draft short agreement/Terms of References (ToR);
- Pilot for 12 months;
- Evaluation and reporting back.

The Assembly also noted the encouragement for the Observers to fill the survey proposed by the Subcommittee and that the results would be updated accordingly.

*APEC Harmonization Center (AHC) Training Programme*

The Assembly congratulated the AHC on: progress made in the development of the pilot programme on the 6 ICH E2 Guidelines in collaboration with ICH; the future Q8, Q9, Q10 training programs planned for 2017 and the translation in English, Spanish and Korean.

The AHC will continue discussing with the MC regarding the development of training materials.

## 8. Update on MedDRA

The Assembly received a report on the ICH MedDRA Management Board/Management Committee (MB/MC) meeting held on 5 – 6 November 2016. The Assembly noted while the MedDRA MC had been established in April 2016, until MedDRA is transferred to the new ICH Association, the MedDRA MB will remain operational and the MedDRA MC will only have responsibilities for MedDRA issues which pertain to the new ICH Association.

The report covered the following matters: 2017 subscription rates; training; tools to facilitate MedDRA's use including the development of an Unqualified Test Name term list; a new

Concept Paper developed by the M1 Point to Consider (PtC) WG; and development of Standardised MedDRA Queries (SMQs) including status of SMQ development and collaboration with the Council for International Organizations of Medical Sciences (CIOMS) and the renewal of the Memorandum of Understanding (MoU) between CIOMS and ICH.

The Assembly was informed of the MedDRA MB/MC's decision to give a reduction in the 2017 Subscription rates, based on the continued growth of MedDRA subscribers throughout the world – currently numbering over 4,500 organisations – and increased efficiencies to contain costs of maintenance and development of MedDRA.

The Assembly also noted the importance of training in helping to facilitate the use of MedDRA and that the MSSO provides free training to Regulators and other MedDRA users as part of their MedDRA subscription package, with training available in several forms: face-to-face training; webinars; and e-learning tools/videocasts. The Assembly heard that by the end of 2016 the MSSO will have had conducted a total of 101 training courses which include 70 face-to-face training classes and 31 webinars. It was noted that a similar scale of training is planned for 2017, with all training offerings advertised on the website www.meddra.org.

The Assembly was also informed of the release of a new Unqualified test name term list approved for development by the MedDRA MB in June 2016 which is intended for use in the E2B test name field and as recommendation only to report adverse events. The list and an explanatory document are available under Related Links on the Support Documentation page on the MedDRA website.

The Assembly also noted the work of the ICH M1 (PtC) WG in facilitating MedDRA's global uptake. The WG has developed condensed versions of the PtC documents for translation into all MedDRA languages (except English and Japanese versions which will remain in full) to support the implementation and use of MedDRA worldwide. These condensed documents will be made available to MedDRA users in 2017. The Assembly was also updated on the WG's new Concept Paper to develop a companion document to the PtC documents, to be available in English and Japanese, which would provide more detailed guidance, examples, and "Questions and Answers" on topics of regulatory importance such as data quality, medication errors, and product quality issues.

The Assembly was also updated on ICH's work with the Council for International Organizations of Medical Sciences **(**CIOMS) to develop Standardised MedDRA Queries (SMQs). In Osaka, the MedDRA MB acknowledged the significant contributions of the CIOMS SMQ WG and the development to-date of 101 SMQs, as well as 1 new SMQ and four new levels 4 SMQs to go into production in v20.0. In addition, the MedDRA MB also congratulated CIOMS for its work on the second edition of the CIOMS SMQ WG's book on *Development and Rational Use of Standardised MedDRA Queries,* which was published on the CIOMS website in August 2016. Furthermore, the MedDRA MB renewed the MoU with CIOMS between ICH and CIOMS for a further year of development of new SMQs.

***Decision/Action:***

- *The Assembly noted the decisions taken by the MedDRA MB/MC.*

## 9. Annual Work Plan and Multi-Annual Strategic Plan of the Association

The ICH Secretariat presented to the Assembly the 2017 ICH Work Plan and Multi-annual Strategic Plan, as well as the MedDRA 2017 Annual Work Plan.

***Decisions/Actions:***

- *The Assembly approved the 2017 Work Plan and Multi-annual Strategic Plan for the Association and agreed to their publication on the ICH website;*

- *The Assembly approved the MedDRA 2017 Annual Work Plan and supported its publication on the ICH website.*

### 10. Implementation of ICH Guidelines

The Assembly noted that as per the Assembly RoP, there should be a process for the Assembly to monitor the progress of international harmonisation and coordinate efforts in this regard. Following the invitation to provide updates, several regulators informed the Assembly on the status of implementation of ICH Guidelines in their respective countries and regions.

The Assembly noted that in addition to providing the updates on the status of implementation of ICH Guidelines, this standing agenda item provides an opportunity for the Regulators to share their experience, explain challenges and how to overcome them; and develop good practice relating to the implementation of ICH Guidelines. The attention was also drawn to the fact that the Rules of Procedures (part 1.1.3) of the Assembly includes some provisions regarding the meaning of implementation.

The Assembly was informed on the development of a table regarding the implementation of ICH Guidelines by all Regulatory Members. This table, which will be maintained by the ICH Secretariat on the basis of input from the Regulatory Members, will be presented at each Assembly meeting as it allows to follow and share the status of ICH Guideline implementation by ICH Regulatory Members.

## REPORTS ON CURRENT TOPICS

### 11. Status Report on Topics

At the start of the meeting in Osaka, the Assembly noted the current status of draft ICH Guidelines and predictions for progress towards *Step 2a/b* and *Step 4*. Updated information was provided during the Assembly meeting by the ICH Rapporteurs of the EWGs/IWGs meeting in Osaka.

Regarding requests from EWGs/IWGs to meet at the next ICH meeting in Montreal on May 27 – June 1, 2017, the Assembly noted that any such requests would be taken under consideration by the MC and that a list of EWG/IWGs agreed by the MC to meet face-to-face in Montreal will be made available to the Assembly, and also on the ICH website, following the MC teleconference to be held in spring 2017.

### 12. S5(R3) EWG: Revision on Detection of Toxicity to Reproduction for Medicinal Products and Toxicity to Male Fertility

The Acting Rapporteur reported on the outcome of the S5(R3) EWG meeting held on November 6-10, 2016 and progress made towards revising the ICH S5(R2) Guideline on *Detection of Toxicity to Reproduction for Medicinal Products and Toxicity to Male Fertility*.

The Assembly noted that the S5(R3) EWG aims to finalise a *Step 1* document in Q2 2017.

***Decisions/Actions:***

- *The Assembly supported that the S5(R3) EWG consult EWG Member constituencies on a preliminary draft in Q1 2017 with feedback received to be considered ahead of the spring ICH meeting, where the group aims to perform line by line revision of the text;*
- *The Assembly endorsed the nomination of the new Rapporteur;*
- *The Assembly endorsed the work plan of the S5(R3) EWG for activities to be undertaken.*

## 13. S11 EWG: ICH Guideline on Nonclinical Safety Testing in Support of Development of Pediatric Medicines

The Rapporteur reported on the outcome of the S11 EWG meeting held on November 6-9, 2016, and progress made towards developing the draft S11 Guideline on *Nonclinical Safety Testing in Support of Pediatric Drug Development*. The Assembly suggested the need for additional detail and specificity in the current draft text. The Assembly recommended the S11 EWG take on a more detailed work plan following the Osaka meeting, including additional teleconferences to develop further specificity. Additionally, the Assembly noted the need to submit a revised work plan and timeline for reaching *Steps 2a/b* and *Step 4* for the MC's consideration.

***Decision/Action:***

- *The S11 EWG will provide a revised work plan to the MC ahead of the MC teleconference to be held in spring 2017 for activities to be undertaken by the EWG.*

## 14. Q12 EWG: ICH Guideline on Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management

The Rapporteur reported on the outcome of the Q12 EWG meeting held on November 5-9, 2016, and progress made towards developing the draft Q12 Technical document on *Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management*. The Assembly noted the EWG's progress made in Osaka in the development of all Q12 chapters including, Established Conditions, Post Approval Change Management Protocols, Product Lifecycle Management Strategy, Effective Pharmaceutical Quality System (Change Management), categorisation of change and data requirements, and the application of Q12 for currently marketed products and lifecycle management plan.

The Assembly noted the Q12 EWG's request for an interim meeting in April 2017 to continue progress on finalising the *Step 1* document in order to reach *Step 1* and *Step 2a/b* in June 2017.

***Decisions/Actions:***

- *The Assembly supported an interim meeting of the Q12 EWG in April 2017 dependent upon subsequent approval by the MC;*
- *The Q12 EWG will provide a revised work plan to the MC ahead of the MC teleconference to be held in spring 2017 for activities to be undertaken by the EWG.*

## 15. E2B(R3) IWG: Revision of the Electronic Submission of Individual Case Safety Reports

The Rapporteur reported on the outcome of the E2B(R3) IWG meeting held on November 7-10, 2016 and progress made towards the completion of a document on how to use the EDQM Routes of Administration; progress towards an editorial update to the Implementation Guide to reflect the Q&A document; and progress towards the determination of any conflicts in ICSR messages based upon review of regional Implementation Guides.

***Decisions/Actions:***

- *The E2B(R3) IWG Regulatory Experts signed-off Step 3 of the new format of the additional Q&As in the Implementation Guide Package, the Implementation Guide v5.02 and the BFC Specification v2.02;*

- *The Regulatory Members of the Assembly adopted Step 4 of the new format of the additional Q&As in the Implementation Guide Package, the Implementation Guide v5.02 and the BFC Specification v2.02;*
- *The E2B(R3) Experts signed-off the Technical Information document and E2B Code List #25;*
- *The Assembly endorsed the Technical Information document and E2B Code List #25;*
- *The Assembly noted that these documents will be published on the ESTRI website;*
- *The Assembly supported the temporary change in the Rapporteurship of the E2B(R3) IWG;*
- *The Assembly endorsed the work plan of the E2B(R3) IWG for activities to be undertaken by the IWG.*

## 16. E9(R1) EWG: Addendum to Defining the Appropriate Estimand for a Clinical Trial/Sensitivity Analyses

The Rapporteur reported on the outcome of the E9(R1) EWG meeting held on November 4-8, 2016 and progress made towards developing the draft E9 Addendum on *Defining the Appropriate Estimand for a Clinical Trial/Sensitivity Analyses*.

***Decisions/Actions:***

- *The Assembly supported that the E9(R1) EWG performs internal EWG Member consultation on the draft currently being developed ahead of the spring ICH meeting based upon which the E9(R1) EWG will make a proposal on whether non-statisticians will need to support the group in reviewing the draft technical document ahead of the spring ICH meeting;*
- *The Assembly endorsed the work plan of the E9(R1) EWG for activities to be undertaken by the EWG.*

## 17. E17 EWG: ICH Guideline on Multi-Regional Clinical Trials

The Rapporteur reported on the outcome of the E17 EWG meeting held on November 7-10, 2016 and progress made towards updating the draft E17 Guideline on *Multi-Regional Clinical Trials* with comments received during the consultation period in the ICH regions.

The Assembly noted that the E17 EWG expects to reach *Step 3* sign off and *Step 4* adoption in Q4 2017.

***Decision/Action:***

- *The Assembly endorsed the work plan of the E17 EWG for activities to be undertaken by the EWG.*

## 18. E18 EWG: ICH Guideline on Genomic Sampling and Management of Genomic Data

The Rapporteur reported on the outcome of the E18 EWG meeting held on November 7-10, 2016 and progress made towards updating the draft E18 Guideline on *Genomic Sampling and Management of Genomic Data* with comments received during the consultation period in the ICH regions.

The Assembly noted that the E18 EWG expects to reach *Step 3* sign off and *Step 4* adoption in Q2 2017.

***Decision/Action:***

- *The Assembly endorsed the work plan of the E18 EWG for activities to be undertaken by the EWG.*

## 19. M8 EWG/IWG: The Electronic Common Technical Document: eCTD

The Rapporteur reported on the outcome of the M8 EWG/IWG meeting held on November 7-10, 2016 and progress made on the current activities of the M8 EWG/IWG including: updating the Implementation Package and Specification Change Request document; developing the v4.0 Q&A v1.0; and communication with vendors.

***Decisions/Actions:***

- *The M8 Regulatory Experts signed-off Step 3 of the eCTD v3.2.2 Q&A and Change Request Document v1.29, the eCTD v4.0 Q&A and Change Request Document v1.00, eCTD v4.0 Implementation Package v1.2, Specification for Submission Formats for eCTD v1.1 and the Valid Values File v5;*
- *The Regulatory Members of the Assembly adopted under Step 4 of the eCTD v3.2.2 Q&A and Change Request Document v1.29, the eCTD v4.0 Q&A and Change Request Document v1.00, eCTD v4.0 Implementation Package v1.2, Specification for Submission Formats for eCTD v1.1 and the Valid Values File v5;*
- *The M8 Experts signed-off the eCTD v4.0 Support Documentation v1.2 and the eCTD v.4 Orientation Material v1.2;*
- *The Assembly endorsed the eCTD v4.0 Support Documentation v1.2 and the eCTD v.4 Orientation Material v1.2;*
- *The Assembly noted that these documents will be published on the ICH and ESTRI websites;*
- *The Assembly endorsed the M8 proposal for interaction with vendors;*
- *The Assembly noted the pending nomination of the new Regulatory Chair by the Founding Regulatory and Standing Regulatory Members of the MC;*
- *The Assembly endorsed the work plan of the M8 EWG/IWG for activities to be undertaken by the EWG/IWG.*

## 20. M9 EWG: Biopharmaceutics Classification System-based Biowaivers

The Rapporteur reported on the outcome of the first meeting of the M9 EWG held on November 7-10, 2016 and progress made towards developing the draft guideline on *Biopharmaceutics Classification System-based Biowaivers*. The M9 EWG started its work by performing a mapping of the relevant regional perspectives and guidelines, and will further exchange documents and supportive data on the issues under discussion, with the plan of discussing these by teleconference in early 2017.

The Assembly noted that the M9 EWG expects to reach *Step 1* by the spring 2018 meeting.

***Decisions/Actions:***

- *The Assembly noted the nomination of the new Regulatory Chair by the Founding Regulatory and Standing Regulatory Members of the MC;*
- *The Assembly endorsed the work plan of the M9 EWG for activities to be undertaken by the EWG.*

## 21. M10 EWG: Bioanalytical Method Validation

The Rapporteur reported on the outcome of the first meeting of the M10 EWG held on November 7-10, 2016 and progress made towards developing the draft guideline on *Bioanalytical Method Validation*.

The Assembly noted that the M10 EWG will prepare the first draft technical document after the Osaka meeting in November 2016.

***Decisions/Actions:***

- *The Assembly noted the nomination of the new Regulatory Chair by the Founding Regulatory and Standing Regulatory Members of the MC;*
- *The Assembly endorsed the work plan of the M10 EWG for activities to be undertaken by the EWG.*

## 22. EWGs/IWGs/Discussion Groups Not Meeting in Osaka

### ❖ *S1 EWG: Revision of the Rodent Carcinogenicity Studies for Human Pharmaceuticals*

The S1 EWG did not meet in Osaka.

The Assembly noted the current activities of the S1 EWG including the progress made towards the collection and review of confidential submissions of Carcinogenicity Assessment Documents (CADs) and summary report submissions by sponsors to Drug Regulatory Authorities (DRAs) within each region and considerations regarding the timeframe for drafting the S1 Technical document. A CAD addresses the carcinogenic potential of an investigational pharmaceutical and predicts the outcome and value of the planned 2 year rat carcinogenicity study, and based on the level of certainty a company is expected to indicate the need for such a study or to claim a (virtual) waiver. The predicted value and outcome of the 2 year rat study in the CADs will be then checked against the actual value and outcome of the 2 year rat studies as they are completed and reported to the DRAs.

The Assembly noted that the ICH S1 document is expected to reach *Step 1* and *Step 2a/b* in June or November 2019.

***Decision/Action:***

- *The S1 EWG will provide a work plan to the MC ahead of its teleconference to be held in spring 2017 for activities to be undertaken by the EWG.*

### ❖ *S3A IWG: Q&As on Note for Guidance on Toxicokinetics*

The S3A IWG did not meet in Osaka.

The Assembly was updated on the current activities of the S3A IWG and the progress made by the group to collect comments on the draft S3A Q&As in the respective ICH regions.

***Decisions/Actions:***

- *The S3A IWG will work by email and teleconference on the finalisation of the Q&As, with Step 3 sign off and Step 4 adoption expected by June 2017;*
- *The S3A IWG will provide a work plan to the MC ahead of the teleconference to be held in spring 2017 for activities to be undertaken by the IWG.*

❖ ***S9 IWG: Q&As on Nonclinical Evaluation for Anticancer Pharmaceuticals***

The S9 IWG did not meet in Osaka.

The Assembly noted the current activities of the S9 IWG and that the draft guideline had been issued for regional regulatory consultation. The Assembly was informed that following completion of the regional regulatory consultation, the IWG will resume its activities to develop a revised guideline. The Assembly noted that the ICH S9 IWG is expected to reach *Step 3* and *Step 4* by June 2017.

***Decision/Action:***

➢ *The S9 IWG will provide a work plan to the MC ahead of the teleconference to be held in spring 2017 for activities to be undertaken by the IWG.*

❖ ***Q3C(R6) Maintenance EWG: Maintenance of the Guideline for Residual Solvents***

The Q3C(R6) Maintenance EWG did not meet in Osaka.
The Assembly was updated on the current activities of the Q3C(R6) EWG including: the progress made towards reaching *Step 3* and *Step 4*. The Assembly noted that a new Q3C Rapporteur will be appointed for the period 2017-2018 in line with the Q3C maintenance procedure.

***Decisions/Actions:***

➢ *The Q3C(R6) Regulatory Experts signed-off Step 3 of the Q3C(R6) Guideline (via written postal procedure) in advance of the Assembly meeting;*
➢ *The Regulatory Members of the Assembly adopted Step 4 of the Q3C(R6) Guideline as final;*
➢ *The Assembly noted that per the maintenance procedure, the role of Rapporteur will rotate to FDA at the beginning of 2017;*
➢ *The Q3C(R6) Maintenance EWG will provide a work plan to the MC ahead of the teleconference to be held in spring 2017 for activities to be undertaken.*

❖ ***Q3D(R1) Maintenance EWG: Guideline for Elemental Impurities***

The Q3D(R1) EWG did not meet in Osaka.
The Assembly was informed that the Q3D training package was finalised and had been published on the ICH website. Additionally, it was noted that the regional training workshops held in the founding ICH regions in 2016 had been completed.
The Assembly was informed that the Q3D(R1) EWG had updated its Concept Paper and will begin work to develop Permitted Daily Exposure levels and permitted concentrations of elemental impurities for products administered by the cutaneous and transdermal route of administration following confirmation of the experts who will participate in the EWG.

***Decision/Action:***

➢ *The Q3D(R1) EWG will provide a work plan to the MC ahead of the teleconference to be held in spring 2017 for activities to be undertaken by the EWG.*

❖ ***Q11 IWG: Q&As on API Starting Materials***

The Q11 IWG did not meet in Osaka.

The Assembly was given an update on the status of the Q11 IWG activities, including the completion of the *Step 1* expert sign-off of the Q&A document on Selection and Justification of API Starting Materials.

The Assembly noted the recommendation from the Q11 IWG on a timeframe of approximately 1-3 months for public consultation in each region.

***Decisions/Actions:***

- *The Q11 Experts signed-off Step 1 of the Q11 Q&As (via written postal procedure) in advance of the Assembly meeting;*
- *The Assembly Members endorsed Step 2a of the Q11 Q&As;*
- *The Regulatory Members of the Assembly endorsed Step 2b of the Q11 Q&As;*
- *The Assembly endorsed the nomination of the new Rapporteur;*
- *The Q11 IWG will provide a work plan to the MC ahead of its teleconference to be held in spring 2017 for activities to be undertaken.*

❖ ***E6(R2) EWG: Integrated Addendum to Good Clinical Practice (GCP)***

The E6(R2) EWG did not meet in Osaka.

The Assembly was updated on the status of the finalisation of the draft E6 Integrated Addendum on Good Clinical Practice. The Assembly noted that the Regulatory Experts signed-off at *Step 3* of the Integrated Addendum and that the internal consultation of MHLW/PMDA was complete.

***Decisions/Actions:***

- *The E6(R2) Regulatory Experts signed-off Step 3 of the E6(R2) Integrated Addendum (via written postal procedure) in advance of the Assembly meeting;*
- *The Regulatory Members of the Assembly adopted Step 4 of the E6(R2) Integrated Addendum as final;*
- *The Assembly noted that the E6(R2) EWG completed its work and supported the disbandment of the EWG.*

❖ ***E11(R1) EWG: Addendum to Pediatric Drug Development***

The E11(R1) EWG did not meet in Osaka.

The Assembly was updated on the current activities of the E11(R1) EWG including progress made towards collecting comments on the draft E11 Addendum on Paediatric Drug Development which was endorsed by the Regulatory Members of the Assembly under *Step 2b* of the ICH process in September 2016.

***Decisions/Actions:***

- *The Assembly endorsed the nomination of the new Rapporteur;*
- *The E11(R1) EWG will provide a work plan to the MC ahead of the teleconference to be held in spring 2017 for activities to be undertaken.*

❖ ***E14/S7B Discussion Group (DG): The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs***

The E14/S7B DG did not meet in Osaka.

The Assembly noted the current activities of the E14/S7B DG including its proposal to review advances in science and methods related to the clinical assessment of QT prolongation and to monitor the progress of the discussion of the Comprehensive In vitro Proarrythmia Assessment Initiative. The Assembly noted that the E14/S7B DG recommendation on whether to reopen the E14 Guideline for a complete revision was expected by December 2017.

***Decision/Action:***

➢ *The E14/S7B DG will provide a work plan to the MC ahead of its teleconference to be held in spring 2017 for activities to be undertaken.*

❖ ***M1 PtC WG: MedDRA Points to Consider***

The M1 PtC WG did not meet in Osaka.

The Assembly was updated on the current activities of the M1 PtC WG with respect to the updating with each MedDRA release of the two PtC documents on Term Selection and Data Retrieval and Presentation; and the development of a proposal for a new area of work.

***Decisions/Actions:***

➢ *The Assembly also noted the endorsement of the MedDRA MB on the Concept Paper for the Extension of the Remit for the Points to Consider WG (M1 PtC) to Develop and Maintain a Companion Document to the PtC Documents;*
➢ *The M1 PtC WG will provide a work plan to the MC and MedDRA MB ahead of the teleconference to be held in spring 2017 for activities to be undertaken by the WG.*

❖ ***M2 EWG: Electronic Standards for the Transfer of Regulatory Information***

The M2 EWG did not meet in Osaka.

The Assembly was updated on the outcome of MC discussions in Osaka regarding M2 activities.

***Decisions/Actions:***

➢ *The Assembly noted that the MC had supported that the M2 EWG be supplemented by a small Steering Group in place of a single Rapporteur and that the M2 EWG will establish the steering group's working practice;*
➢ *The Assembly noted the nomination of the new Regulatory Chair by the MC;*
➢ *The M2 EWG will provide a work plan to the MC ahead of the teleconference to be held in spring 2017 for activities to be undertaken by the EWG.*

❖ ***M4Q(R1) (CTD-Quality) IWG: Addressing CTD-Q-Related Questions***

The M4Q(R1) EWG did not meet in Osaka.

The Assembly noted that the M4Q(R1) (CTD-Quality) IWG had completed its work regarding the revision of the Granularity Document with the M8 EWG. The Assembly was provided a recommendation on the decision to disband the M4Q(R1) IWG. The Assembly acknowledged the potential for questions to be received following the implementation of the M4 Granularity document.

***Decisions/Actions:***

- *The M4Q(R1) IWG will become dormant and will not be requested to update their work plan;*
- *A decision on the disbandment of the M4Q(R1) (CTD-Quality) IWG will be deferred to the next ICH meeting in spring 2017.*

❖ ***M7(R1) EWG: Addendum to Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk***

The M7(R1) EWG did not meet in Osaka.

The Assembly was updated on the current activities of the M7(R1) EWG including the progress made towards finalising the M7(R1) Addendum to Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk. The Assembly was informed that *Step 3* sign-off is expected by December 2016 and *Step 4* is expected by June 2017 for the 14 compounds Acceptable Intake and Permitted Daily Exposure levels have been developed for. Additionally, it was noted that the remaining 10 compounds will be reassessed following completion of this work.

***Decision/Action:***

- *The M7(R1) EWG will provide a work plan to the MC ahead of the teleconference to be held in spring 2017 for activities to be undertaken by the EWG.*

**DATES/LOCATION OF NEXT MEETINGS FOR 2017/2018**

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|---|---|
| May 27 – June 1, 2017 | Montreal, Canada |
| November 11– 16, 2017 | Geneva, Switzerland |
| June 2 – 7, 2018 | Japan (location to be confirmed) |