September, 20 2016

MEETING MINUTES
ICH Assembly
June 15 – 16, 2016, Lisbon, Portugal

List of Assembly Participants

ICH Assembly Members

Ms. Lenita Lindström-Gommers	EC
Mr. Sébastien Goux	EC
Dr. Tomas Salmonson	EC/EMA
Dr. Sabine Luik	EFPIA
Dr. Theresa Mullin	FDA
Ms. Joan Wilmarth Blair	FDA
Ms. Catherine Parker	Health Canada
Dr. Nicholas Cappuccino[1]	IGBA
Ms. Beata Stepniewska[1]	IGBA
Dr. Hironobu Saito	JPMA
Mr. Takuya Saiki	JPMA
Dr. Toshiyoshi Tominaga	MHLW/PMDA
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-Traxle[1]	WSMI

ICH Assembly Standing Observers:

Mr. Michael Ward	WHO
Mr. Samvel Azatyan	WHO

ICH Assembly Observers:

Ms. Patrícia Pereira	ANVISA
Dr. Hee Sung Kim	APEC
Dr. Dato Eisah Abdul Rahman	ASEAN
Dr. Lila Feisee[2]	BIO
Mr. Wassim Nashabeh[2]	BIO
Dr. Lembit Rägo[2]	CIOMS
Dr. Mario Alanìs Garza[2]	COFEPRIS
Mr. Cuauhtemoc Ruiz[2]	COFEPRIS
Ms. Jane Mashingia	EAC
Mr. Burhani Othman Simai	EAC
Dr. Susanne Keitel[2]	EDQM
Prof. Ibrahim A. Aljuffali	GCC
Prof. Raymond Chua	HSA
Dr. Sun Hee Lee	MFDS
Dr. Jeong Yeon Kim	MFDS
Ms. Fortunate Ntombi Fakudze	SADC
Mt. Joseph Mthetwa	SADC
Dr. Li-Ling Liu	TFDA
Dr. Churn-Shiouh Gau	TFDA
Dr. Robert Femia[2]	USP
Dr. Kevin Moore[2]	USP

ICH Assembly *Ad hoc* Observers

Mr. Qin Xiaoling	CFDA
Ms. Sun Hui	CFDA
Ms. Helena Paula Baião	PIC/S

ICH Coordinators:

Mr. Pär Tellner	EFPIA
Ms. Amanda Roache	FDA
Mr. Nick Orphanos	Health Canada
Mr. Mitsuo Mihara	JPMA
Mr. Fumihito Takanashi	MHLW
Ms. Camille Jackson	PhRMA

Technical Coordinators:

Mr. Milton Bonelli	EC/EMA
Ms. Chieko Hirose	MHLW/PMDA

Others:

Ms. Emer Cooke	EC/EMA
Mr. Martin Harvey	EC/EMA
Dr. Michelle Limoli	FDA
Dr. Juliette Toure	FDA
Mr. Yoshihiro Katsura	MHLW/PMDA
Ms. Enkyoung Lee	MFDS
Ms. Ying-Hsien Fu	TFDA

ICH Secretariat:

Dr. Dawn Ronan
Dr. Sarah Adam
Dr. Isabelle Güller

[1] At the Assembly meeting in Lisbon under agenda 3, IGBA and WSMI were welcomed as the first ICH Industry Members.

[2] At the Assembly meeting in Lisbon under agenda 3
, the Assembly welcomed BIO, COFEPRIS, CIOMS, EDQM and USP as new ICH Observers of the Association.

Table of Content

Adoption of the Agenda

The agenda was adopted without modification.

Opening Discussions

The ICH Assembly meeting in Lisbon Portugal on 15 – 16 June 2016 was chaired by Mrs. Lindström-Gommers (EC, Chair) and Dr. Tominaga (MHLW/PMDA, Vice-Chair).

1. ICH 2015 Annual Report

The ICH Secretariat presented to the Assembly the ICH 2015 Annual Report on the activities of the Association (for the period October 23 – December 31, 2015) which covered the activities undertaken by the Management Committee (MC) and the ICH Secretariat on behalf of the Association.

Decisions/Actions:

- *The Assembly approved the 2015 Annual Report on the activities of the Association for the period October 23 – December 31, 2015;*
- *The Annual Report will be published on the ICH website;*
- *Based on the Annual Report, the Assembly also granted discharge to the MC and the ICH Secretariat for the activities undertaken by these bodies in 2015.*

2. ICH Rules of Procedure and Standard Operating Procedures

The ICH Secretariat presented to the Assembly several minor proposed amendments to the existing version of the Assembly Rules of Procedure (RoP) dated December 10, 2015.

The Assembly received presentations on the outcome of the Regional Harmonisation Initiatives (RHIs) and Drug Regulatory Authorities/Department of Health (DRAs/DoH) pre-meetings which were held on June 14, 2016 and where participants (currently Observers) discussed the impact of the ICH Reforms, the Articles of the Association and the Assembly RoP.

The Assembly was also updated on the finalisation of the MC RoP, the development of the RoP for the MedDRA MC as well as the Standard Operating Procedures (SOPs) for Working Groups (WGs).

The Assembly also noted the role of IFPMA (representing the Global Biopharmaceutical Industry) in ICH, and the provision of a platform to national industry organisations that are interested in engaging with ICH as their national authorities become new Regulatory Members.

Decisions/Actions:

- *The Assembly approved the proposed changes to the Assembly RoP;*
- *The Revised Assembly RoP will be published on the ICH website;*
- *The MC RoP, the MedDRA MC RoP as well as the SOPs for WGs once finalised, will be made available on the ICH website.*

3. Membership and Observership Applications

The MC presented to the Assembly its recommendations regarding Membership and Observership applications processed to-date.

Decisions/Actions:

- *The Assembly took note of the following former RHIs and DRAs/DoH who became Observers immediately after the establishment of the Association following submission of a confirmation letter to the ICH Secretariat according to Article 17(3) of the ICH Articles of Association:*
    - *The Brazilian Health Surveillance Agency (ANVISA, Brazil);*
    - *The Asia-Pacific Economic Cooperation (APEC);*
    - *The Association of Southeast Asian Nations (ASEAN);*
    - *The Central Drug Standards Control Organisation (CDSCO, India);*
    - *The East African Community (EAC);*
    - *The Gulf Cooperation Countries (GCC);*
    - *The Pan American Network for Drug Regulatory Harmonisation (PANDRH);*
    - *The Health Sciences Authority (HAS, Singapore);*
    - *The Ministry of Food and Drug Safety (MFDS, Korea);*
    - *The Roszdravnadzor (Russia);*
    - *The Southern African Development Community (SADC);*
    - *The Food and Drug Administration (TFDA, Chinese Taipei);*
    - *The Therapeutic Goods Administration (TGA, Australia);*
- *The Assembly approved in Lisbon the following Observership applications on the basis of the recommendation of the MC:*

  <u>Legislative or Administrative Authority</u>
    - *The Comisión Federal para la Protección contra Riesgos Sanitarios (COFEPRIS, Mexico);*

  <u>International Pharmaceutical Industry Organisation</u>
    - *The Biotechnology Innovation Organisation (BIO);*

  <u>International Organisations with an Interest in Pharmaceuticals</u>
    - *The Council for International Organizations of Medical Sciences (CIOMS);*
    - *The European Directorate for the Quality of Medicines & HealthCare (EDQM);*
    - *The International Pharmaceutical Excipient Council (IPEC);*
    - *The United States Pharmacopeia (USP).*
- *The Assembly approved the following Membership applications on the basis of the recommendation of the MC:*
    - *The International Generics and Biosimilar Medicines Association (IGBA);*
    - *The World Self-Medication Industry (WSMI).*
- *The Assembly did not approve the application for Observership from the Centers for Medicare and Medicaid Services (CMS);*
- *The Assembly supported the request from MFDS to participate in the activities of the Q12 EWG on the basis of the recommendation from the MC.*

4. ICH Communication

Communication Activities

The Assembly noted the ongoing communication activities regarding the newly established ICH Association. It was noted that a Q&A document on Membership had been recently made available on the ICH website. In addition, the Assembly noted the development of a new slide deck on ICH which will also be made available on the ICH website once finalised, the development of a transparency policy and the development of a stakeholder engagement plan to receive feedback from various stakeholders. The Assembly also noted that the ICH website will continue to be improved in advance of the Osaka meeting in November 2016.

ICH Workshops and Regional Public Meetings

The Assembly noted the ICH Information Day organised by the EC/EMA in collaboration with DIA in Hamburg, Germany on April 6, 2016 and, which focused on the recent reform by ICH and its impact on global development of medicines.

The Assembly also noted that JPMA in collaboration with MHLW/PMDA will be organising an ICH regional public meeting in Tokyo, Japan, on July 21, 2016. In addition, JPMA in collaboration with DIA will be also organising in Tokyo, on November 12, 2016 an ICH workshop on ICH E6, E9 and E17 Guidelines.

The Assembly also noted that a U.S. public meeting was held at the FDA's White Oak campus in Silver Spring, MD on May 6, 2016. The meeting was organised by the U.S. FDA and co-hosted with Health Canada (HC), with presenters from FDA, HC, and PhRMA.

In addition, the FDA will also be organising a regional public workshop on August 22-23, 2016 at FDA's White Oak campus in Silver Spring, MD to elaborate key aspects of the ICH Q3D Guideline on *Elemental Impurities*, in order to facilitate a harmonised interpretation and implementation by industry and regulators. The workshop will have presenters from FDA, PhRMA, and USP.

5. ICH Financial Matters

The Assembly was updated on ICH financial matters including the 2016-2018 ICH Secretariat Budget, the proposed fees for new Members and the concept of participation fee for Observers.

Decisions/Actions:

- *The Assembly noted the 2016-2018 ICH Secretariat budget and its publication to the financial section of the ICH website;*
- *The Assembly discussed a proposal for fees for new Members which proposed a range of fees for its consideration: from CHF19,200 to CHF48,000;*
- *The Assembly was invited to provide comments on the proposed fee range for new Members ahead of the Osaka meeting, in November 2016, where a final decision will be made on the level of new members fees;*
- *The Assembly also shared views on the concept of for a participation fee for non-membership fee paying parties (i.e., Observers) to cover costs of meeting participation such as catering. A proposal will be developed including how participation fees will be invoiced, processed and accepted.*

6. Proposal for New ICH Topics

The MC reported on the development of a process for the selection of new ICH technical topics for use in future ICH Meetings.

In addition, the MC presented to the Assembly for its consideration and approval its recommendation to adopt for the following 2 new topics for the development as ICH Guidelines: *Biopharmaceutics Classification System-based Biowaivers* and *Bioanalytical Method Validation.*

The MC also presented a proposal to the Assembly regarding the organisation of strategic topics discussions at the next ICH meeting to be held in Osaka, Japan in November 2016.

Decisions/Actions:

- *The Assembly noted the proposed ICH process for the selection of new ICH topics and supported that the process be run on a yearly basis (6-month process);*
- *The Assembly noted the Concept Paper outlines for the following 2 new ICH topics which were recommended by the MC to the Assembly for its approval:*
  - *Biopharmaceutics Classification System-based Biowaivers (proposed by EC)*
  - *Bioanalytical Method Validation (proposed by MHLW/PMDA)*
- *The Assembly adopted the Concept Paper outline on Biopharmaceutics Classification System-based Biowaivers (code: ICH M9) and agreed on the establishment of an informal Working Group (with EC nominated as Lead) to finalise the Concept Paper and develop a Business Plan ahead of the MC Teleconference to be held in autumn 2016;*
- *The Assembly adopted the Concept Paper outline on Bioanalytical Method Validation (code: ICH M10) and agreed on the establishment of an informal Working Group (with MHLW/PMDA nominated as Lead) to finalise the Concept Paper and develop a Business Plan ahead of the MC Teleconference to be held in autumn 2016;*
- *The ICH Secretariat will launch the nomination process amongst ICH Members for the establishment of the 2 informal Working Groups;*
- *Further to Article 17(5), any ICH Observer interested to participate in the activities of these new Working Groups (WGs) would need to inform the ICH Secretariat in writing and provide explanations for their interest in the specific Working Group, information about their available expertise and how they expect to contribute to the work of the WG;*
- *Any request received by the ICH Secretariat, will be shared with the MC; and the Assembly may, on the basis of the recommendation by the MC, invite Observers to appoint experts in the WGs. The Assembly will be able to take a decision on such invitations at the Osaka meeting in November 2016;*
- *The Assembly nominated EC as the Rapporteur for the ICH M9 EWG and MHLW/PMDA as the Rapporteur for the ICH M10 EWG;*
- *The Founding Regulatory Members and the Standing Regulatory Members will confirm the respective Regulatory Chairmanship for these 2 new EWGs once established;*
- *The Assembly also noted the following 2 additional new topic proposals considered by the MC in Lisbon and recommended that the MC further discussed and provide feedback on these in Osaka:*
  - *Safety Data Collection (proposed by FDA);*
  - *Adaptive Clinical Trials (proposed by PhRMA);*

- *The Assembly also noted the general outline on the organisation of ICH Strategic discussions for which FDA was tasked to develop a proposed approach for the structure and organization of Strategic topics discussions;*
- *The Assembly agreed on a recommendation that proposals are developed for strategic discussions in Osaka on Good Clinical Practices (to be led by FDA) and on Compliance of Reliability for Electronic Data (to be led by JPMA and supported by FDA).*

7. Annual Work Plan and Multi-Annual Strategic Plan of the Association

The ICH Secretariat presented to the Assembly the 2016 Work Plan and Multi-annual Strategic Plan of the Association.

Decision/Action:

- *The Assembly approved the 2016 Work Plan and Multi-annual Strategic Plan for the Association and agreed to their publication on the ICH website.*

8. ICH Training Activities

- ***ICH Cooperation with Other Organisations***

The Assembly received a status report on the AHC e-learning pilot project on the ICH E2 Series of Pharmacovigilance Guidelines. The Assembly noted that the E-Learning Center is expected to launch the pilot programme in Q3 2016 which would be open free of charge for a limited time period (up to 12 months).

Decision/Action:

- *The Assembly congratulated the AHC on progress made in the development of the pilot programme on ICH E2 Guidelines in collaboration with ICH.*

- ***ICH Training Strategy***

The Assembly also received a status report on the MC's development of an ICH Training Strategy.

Decisions/Actions:

- *The Assembly noted that the MC is in the process of developing an ICH Training Strategy;*
- *The AHC will continue discussing with the MC regarding the development of training materials.*

9. Update on MedDRA

The Assembly received a report on the ICH MedDRA Management Board (MB) meeting held on 11 – 12 June 2016.

The report covered the following matters: establishment of the MedDRA Management Committee; completion of the MSSO Call for Tender; 2017 subscription rates; training; development of Standardised MedDRA Queries (SMQs) including status of SMQ development and collaboration with the Council for International Organizations of Medical Sciences (CIOMS); tools to facilitate MedDRA's use; and the MedDRA 2016 Annual Work Plan.

The Assembly was updated on the inaugural MedDRA Management Committee (MC) meeting that was held virtually on April 19, 2016, although several formalities need to be completed before MedDRA can be transferred to the new ICH Association. Once transferred,

the MedDRA MC, which is a body of the ICH Association, will become fully operational. Prior to the transfer, the MedDRA MC will only have responsibilities for MedDRA issues which pertain to the new ICH Association.

The Assembly noted the completion of the Call for Tender for the Maintenance and Support Services Organisation (MSSO) that was launched by ICH in August 2014, with bids invited by October 31, 2014. ICH's Tender Evaluation Panel made its recommendation of the selected bidder to the MedDRA MC and the contract is in the process of being signed off. A specific press release will be published shortly to announce the selected bidder.

The Assembly was informed of the MedDRA MB's consideration 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 MedDRA MB will take a decision on the 2017 rates shortly.

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 in 2016 the MSSO had scheduled a total of 99 training courses which included 68 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 updated on ICH's work with CIOMS to develop Standardised MedDRA Queries (SMQs). In Lisbon, the MedDRA MB acknowledged the significant contributions of the CIOMS SMQ Working Group (WG) and the development to-date of 101 SMQs. 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 is due shortly for publication.

The Assembly was also informed of the release of a new version of the MedDRA Web-Based Browser (WBB) in May 2016 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. Additionally, the Assembly was updated on the coming soon Account Self-Service Application which is a web-based application which allows users to obtain subscription information; add/delete/change point of contact; change of password; download or print Training Certificates.

Decisions/Actions:

- *The Assembly noted the decisions taken by the MedDRA MB;*
- *The Assembly approved MedDRA 2016 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. All ICH Regulators were invited to update the Assembly on the status of implementation of ICH Guidelines in their respective countries and regions.

The Assembly noted that this 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.

Decision/Action:

- *The Assembly Members and Observers shared information on the status of implementation of ICH Guidelines in their respective countries and regions.*

11. Status Report on Topics

At the start of the meeting in Lisbon, 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 Lisbon.

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

The Rapporteur reported to the Assembly on the outcome of the S5(R3) EWG meeting held June 12 – 16, 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 the group's progress related to the completion of the revision of the text for all sections where gaps were identified in the ICH S5(R2) Guideline, the compilation of a draft list of reference compounds, the agreement on: concept of qualification criteria, the exposure multiple for high dose selection, the placental transfer and lactational exposure, and the deferral strategies for Embryo-Foetal Development (EFD) testing. The Assembly also noted some remaining topics to be addressed by the EWG including the design of the reduced EFD study(ies), the foetal morphological variations and the harmonisation of assay qualification for regulatory acceptance.

The Assembly noted that the ICH S5(R3) EWG was expecting to reach *Step 1* and *Step 2a/b* in June 2017.

Action/Decision:

- *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 Paediatric Medicines

The Rapporteur reported to the Assembly on the outcome of the meeting of the S11 EWG held on June 13 – 16, 2016, and progress made towards collecting data on juvenile animal studies and developing the ICH Guideline on *Nonclinical Safety Testing in Support of Development of Paediatric Medicines*.

The Assembly noted the group continued to collect information on juvenile animal studies conducted to support paediatric programs in the last 7 years and reviewed the literature. The Assembly also noted that these data will add to the collective experience in conducting studies and point to areas where specific guidance is needed. Moreover, these data are expected to support the sections of the guideline on how to determine if juvenile animal studies are needed for those studies within scope of S11 and what design elements of juvenile animal studies are most useful.

In addition, the S11 EWG further progressed the development of the sections of the S11 Guideline and agreed with the S9 IWG on the scope regarding oncology products.

The Assembly noted that the ICH S11 EWG was expecting to reach *Step 1* and *Step 2a/b* in June 2017.

Action/Decision:

- *The Assembly endorsed the work plan of the S11 EWG for activities to be undertaken.*

14. Q11 IWG: Q&As on API Starting Materials

The Rapporteur reported to the Assembly on the outcome of the Q11 IWG meeting held on June 13 – 16, 2016 and progress made towards developing the draft Q11 Q&A document on *API Starting Materials*.

The Assembly noted the IWG progress made in Lisbon regarding assessing and editing the 16 Q&As based on constituent feedback received, including clarifying and proposing revised text for the Question 6.

The Assembly also noted that the ICH Q11 IWG was expecting to reach *Step 1* and *Step 2a*/b by November 2016.

Action/Decision:

- *The Assembly endorsed the work plan of the Q11 IWG for activities to be undertaken.*

15. 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 June 12 – 16, 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 Lisbon 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 lifecyle management plan.

The Assembly noted that the ICH Q12 EWG was expecting to reach *Step 1* and *Step 2a/b* in June 2017.

Decision/Action:

- *The Q12 EWG will provide a revised work plan for activities to be undertaken to the MC ahead of its teleconference to be held in autumn 2016.*

16. E6(R2) EWG: Integrated Addendum to Good Clinical Practice (GCP)

The Rapporteur reported on the outcome of the E6(R2) EWG meeting held on June 13 – 16, 2016 and progress made towards finalising the draft E6 Integrated Addendum on *Good Clinical Practice*.

The Assembly noted that in Lisbon the EWG went through all comments received during the public consultation and finalised the draft Integrated Addendum under *Step 3* of the ICH process. The content of the Integrated Addendum was presented to the Assembly.

Decisions/Actions:

- *The E6(R2) Regulatory Experts signed-off Step 3 of the E6 Integrated Addendum;*
- *Step 4 of the E6 Integrated Addendum will be for adoption at the next Assembly meeting in Osaka in November 2016 following the completion of MHLW/PMDA internal consultation.*

17. 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 June 13 – 16, 2016 and progress made towards developing the draft E9 Addendum on *Defining the Appropriate Estimand for a Clinical Trial/Sensitivity Analyses*.

The Assembly noted the EWG progress made in Lisbon in the development of the Technical document for the Addendum to the E9 Guideline including the EWG agreement on content for the scope, the framework for positioning an estimands, the definition of estimands, and the classification for different choices of estimands. It was noted that the EWG proposes to promote specification and possibly discussion of the estimand choice in the trial protocol.

The Assembly noted the group's proposal to insert footnotes in the Guideline where the existing guidance is superseded by E9 Addendum (e.g., on analysis sets, missing data and sensitivity analysis).

The Assembly also noted the impact of the Addendum on other ICH Guidelines: E3, E6(R2), and E8.

The Assembly also noted that the Addendum to ICH E9 was expected to reach *Step 1* and *Step 2a/b* in November 2016; and that the EWG was reflecting on the organisation of the consultation process (*Step 3*) amongst stakeholders.

Decisions/Actions:

- *The Assembly agreed that the E9(R1) EWG should further consider how the changes could be made in a clear manner and requested that the MC also consider how best to do this procedurally;*
- *The Assembly noted the impact of the work of the EWG on the E6(R2) Guideline and recommended that the comments received from the E9(R1) EWG be considered in Osaka when a strategic discussion will be organised at the Assembly level;*
- *The Assembly also noted the impact of the work of the EWG on the E8 Guideline and recommended that E9(R1) EWG develops a proposal for MC consideration;*
- *The Assembly agreed that the MC should discuss further the development of an engagement plan including the need of a broader consultation amongst stakeholders to facilitate understanding of the impact of the E9 Addendum on the E9(R1) Guideline;*
- *The Assembly endorsed the work plan of the E9(R1) EWG for activities to be undertaken.*

18. E11(R1) EWG: Addendum to Paediatric Drug Development

The Rapporteur reported on the outcome of the E11(R1) EWG meeting held on June 13 – 16, 2016 and progress made towards developing the draft E11 Addendum on *Paediatric Drug Development.*

The Assembly noted that some additional work would be needed to ensure clarity/accuracy of new sections, especially Extrapolation and Modelling & Simulation, based on comments received after an internal review amongst Members and the output of 3 Extrapolation workshops held in 2015 and 2016.

The Assembly noted that *Step 1* and *Step 2a/b* for the Addendum to ICH E11(R1) were expected by August 2016.

The Assembly also noted the EWG proposal to update the Concept Paper template with some text to ensure early consideration of paediatric populations in the development of any future new ICH Guidelines.

Decisions/Actions:

- *The Assembly requested that once Step 1 is reached, the Secretariat organises a written postal sign-off (under Step 1) at the expert level which will be followed by Step 2a electronic endorsement by the Assembly and Step 2b electronic endorsement by the Regulatory Members of the Assembly;*
- *The Assembly supported the proposed update of the Template Concept Paper to include considerations of paediatric populations in ICH Guidelines;*
- *The Assembly endorsed the work plan of the E11(R1) EWG for activities to be undertaken.*

19. 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 June 12 – 16, 2016 and progress made towards the finalisation of additional Q&As and the revision of documents in the Implementation Guide Package.

The Assembly noted the completion of the additional Q&As. *Step 3* was signed-off by the IWG in Lisbon and the Regulatory Members of the Assembly were invited to adopt as final under *Step 4* the additional Q&As in Lisbon, in June 2016.

The Assembly was updated on the current status of E2B(R3) implementation in the different regions with FDA and MHLW/PMDA having started the implementation, and EC and Health Canada to transition to E2B(R3) within the next years.

The Assembly also noted the need of the E2B(R3) IWG to have M2 EWG's support regarding SDO monitoring and ISO standards.

The Assembly was also updated on E2B discussion with EDQM on Dose Forms (DF) and Routes of Administration (RoA) and was invited to endorse the designation of EDQM as the maintenance organization for DF and RoA TermIDs for E2B(R3), pending the approval of the EDQM governance board.

Decisions/Actions:

- *The E2B(R3) Regulatory Experts signed-off Step 3 of the additional Q&As in the Implementation Guide Package;*
- *The Regulatory Members of the Assembly adopted Step 4 of the additional Q&As in the Implementation Guide Package;*
- *The EDQM will be designated as the maintenance organisation for DF and RoA TermIDs for E2B(R3) (pending the approval of the EDQM governance board);*
- *The E2B(R3) IWG will provide an updated work plan for activities to be undertaken to the MC ahead of its teleconference to be held in autumn 2016.*

20. M1 PtC WG: MedDRA Points to Consider (PtC)

The Rapporteur reported on the outcome of the M1 PtC WG meeting held on June 13 – 16, 2016 and the group's current activities with respect to the updating with each MedDRA release of the two PtC documents on *Term Selection* and *Data Retrieval and Presentation*.

The Assembly noted the current activities of the M1 PtC WG including the review and update of PtC documents for MedDRA version 19.1 to be released on September 1, 2016, the review of proposed revisions to the Medication error and Product use issue hierarchy and the development of condensed versions of both PtC documents in order to translate them in the 9 other MedDRA languages (to be released in 2017). The Assembly noted that the full

documents will remain in English and Japanese and will continue to be maintained with each MedDRA version.

Decision/Action:

- *The Assembly endorsed the work plan of the M1 PtC WG for activities to be undertaken.*

21. M4E(R2) EWG: Revision of CTD-Efficacy Guideline

The Rapporteur reported on the outcome of the M4E(R2) EWG meeting held on June 12 – 16, 2016 and progress made towards updating the draft M4E(R2) Guideline on *CTD-Efficacy* with comments received from the public consultation in the ICH regions.

The Assembly noted the completion of the revised Section 2.5.6. of the *CTD-Efficacy* Guideline. The Rapporteur presented the revised structure of Section 2.5.6 and its general principles for a submitted guideline which should represent the thought process behind the applicant's weighing of benefits and risks; be a critical and succinct presentation by the applicant; and it should not present new efficacy or safety data. The revised section captures pan-regional thinking on content, format, and the flexibility to apply different approaches to Benefits and Risks.

The Assembly noted that *Step 3* was signed-off by the Regulatory Experts of the EWG in Lisbon and the Regulatory Members of the Assembly were invited to adopt as final under *Step 4* the M4E(R2) Guideline on *CTD-Efficacy* in Lisbon, in June 2016.

Decisions/Actions:

- *The M4E(R2) Regulatory Experts signed-off Step 3 of the M4E(R2) Guideline on CTD-Efficacy;*
- *The Regulatory Members of the Assembly adopted Step 4 of the M4E(R2) Guideline on CTD-Efficacy;*
- *The Assembly noted that the M4E(R2) EWG completed its work.*

22. EWGs/IWGs/Discussion Groups not Meeting in Lisbon, Portugal

- ***S1 EWG: Revision of the Rodent Carcinogenicity Studies for Human Pharmaceuticals Guideline***

  The S1 EWG did not meet in Lisbon.

  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 was 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 autumn 2016 for activities to be undertaken.*

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

The S3A IWG did not meet in Lisbon.

The Assembly noted the current activities of the S3A IWG which reached *Step 2b* upon electronic endorsement by the Regulatory Members of the Assembly in May 2016. The Assembly also noted that the public consultation (under *Step 3)* had been launched by ICH Regulatory Members.

The Assembly noted that the ICH S3A Q&As document was expected to reach *Step 3* and *Step 4* by June 2017.

Decision/Action:

- *The S3A IWG will provide a work plan to the MC ahead of its teleconference to be held in autumn 2016 for activities to be undertaken.*

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

The S9 IWG did not meet in Lisbon.

The Assembly noted the current activities of the S9 IWG including the finalisation of the Technical Document for the S9 Q&As.

The Assembly noted that the S9 IWG experts signed-off electronically *Step 1* in early June.

The Assembly noted that the ICH S9 Q&As document was expected to reach *Step 3* and *Step 4* by June 2017.

Decisions/Actions:

- *The S9 Experts signed-off Step 1 of the S9 Q&As (via written postal procedure) in advance of the Assembly meeting;*
- *The Assembly Members endorsed Step 2a of the S9 Q&As;*
- *The Regulatory Members of the Assembly endorsed Step 2b of the S9 Q&As;*
- *The S9 IWG will provide a work plan to the MC (including the length of time for the public consultation period in each region) ahead of its teleconference to be held in autumn 2016 for activities to be undertaken.*

❖ ***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 Lisbon.

The Assembly noted the current activities of the M7(R1) EWG including the progress made towards addressing comments received on the M7(R1) Addendum on *Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk*. The Assembly noted that the draft Addendum presents calculated Acceptable Intake (AI) or Permissible Daily Exposure (PDE) values derived for 15 chemicals that are mutagens and carcinogens and are selected because they are commonly used in pharmaceutical manufacturing, or are useful to illustrate the principles for deriving compound-specific intakes described in ICH M7.

The Assembly noted that the ICH M7(R1) work plan indicated that the Addendum was expected to reach *Step 3* and *Step 4* by December 2016, however, the EWG will try to complete its work ahead of the next Assembly meeting in November so that the Addendum could be presented to the Assembly for adoption in November.

It was also noted that following the finalisation of the Addendum, the EWG would propose to the Assembly to assess 10 remaining compounds and determine whether PDEs or AI's should be developed for these remaining compounds.

Decisions/Actions:

- *Once Step 3 is reached, the Secretariat will organise a written postal sign-off (under Step 3) at the Regulatory expert level;*
- *The Assembly noted that the Regulatory Members of the Assembly would be invited to adopt as final under Step 4 the M7(R1) Addendum at the next Assembly meeting in Osaka in November 2016;*
- *The M7(R1) EWG will provide a work plan to the MC ahead of its teleconference to be held in autumn 2016 for activities to be undertaken.*

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

The Q3C(R6) Maintenance EWG did not meet in Lisbon.

The Assembly noted the current activities of the Q3C(R6) EWG, including the progress made towards finalising the maintenance of the Q3C(R5) Guideline to revise PDE for methylisobutylketone and include PDE for triethylamine and maintenance procedure for collecting new Q3C/Q3D proposals.

The Assembly noted that the ICH Q3C(R6) Guideline was expected to reach *Step 3* and *Step 4* after June 2016.

It was noted that the leadership of the Maintenance EWG is changing every 2 years and that it will rotate to FDA in 2017-2018.

Decisions/Actions:

- *Once Step 3 is reached, the Secretariat will organise a postal sign-off (under Step 3) at the Regulatory expert level;*
- *The Assembly noted that the Regulatory Members of the Assembly would be invited to adopt as final under Step 4, the ICH Q3C(R6) Guideline at the next Assembly meeting in Osaka in November 2016;*
- *The Q3C(R6) Maintenance EWG will provide a work plan to the MC ahead of its teleconference to be held in autumn 2016 for activities to be undertaken.*

❖ ***Q3D IWG: Guideline for Metal Impurities***

The Q3D EWG/IWG did not meet in Lisbon.

The Assembly noted the current activities of the Q3D IWG, and the finalisation of Modules 8-9 of the Q3D training package.

It was noted that a regional Q3D workshop will be organised on August 22-23, 2016 at FDA's White Oak campus in Silver Spring, MD, USA (see also Section 4 of this report).

Decisions/Actions:

- *The Q3D Experts signed-off the final training modules 8 and 9;*
- *The Assembly endorsed the final training modules 8 and 9;*
- *The Assembly noted that these training modules would be made available on the ICH public website;*
- *The Q3D IWG will provide a work plan to the MC ahead of its teleconference to be held in autumn 2016.*

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

The M4Q(R1) IWG did not meet in Lisbon.

The Assembly noted that the M4Q(R1) (CTD-Quality) IWG completed its work regarding the revision of the Granularity Document with the M8 EWG, and the development of a process to address future CTD-Q related questions.

The Assembly noted that in Osaka, the MC will provide its recommendation to the Assembly on whether the group should be dissolved or continue its work depending on whether questions would have been received following the implementation of the M4 Granularity Document.

Decision/Action:

- *If needed, the M4Q(R1) IWG will provide a work plan to the MC ahead of its teleconference to be held in autumn 2016.*

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

The E14/S7B DG did not meet in Lisbon.

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 Proarythmia 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 autumn 2016 for activities to be undertaken.*

❖ ***E17 EWG: ICH Guideline on Multi-Regional Clinical Trials***

The E17 EWG did not meet in Lisbon.

The Assembly noted the current activities of the E17 EWG including the finalisation of the draft E17 Technical document on *Multi-Regional Clinical Trials* (MRCTs) and initiation of the consultation process. The Assembly noted that the primary focus of this guideline is on MRCTs designed to provide data that will be submitted to multiple regulatory authorities for drug approval (including approval of additional indications, new formulations and new dosing regimens) and for studies conducted to satisfy post-marketing requirements.

The Assembly noted that the E17 EWG experts signed-off electronically *Step 1* in early June.

The Assembly also noted that the ICH E17 was expected to reach *Step 3* and *Step 4* in June 2017.

Decisions/Actions:

- *The E17 Experts signed-off Step 1 of the E17 Technical Document (via written postal procedure) in advance of the Assembly meeting;*
- *The Assembly Members endorsed Step 2a of the E17 Technical Document;*
- *The Regulatory Members of the Assembly endorsed Step 2b of the E17 Technical Document;*

- *The E17 EWG will provide a work plan to the MC (including the length of time for the public consultation period in each region) ahead of its teleconference to be held in autumn 2016 for activities to be undertaken.*

❖ ***E18 EWG: ICH Guideline on Genomic Sampling and Management of Genomic Data***

The E18 EWG did not meet in Lisbon.

The Assembly noted the current activities of the E18 EWG including 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 also noted that the ICH E18 was expected to reach *Step 3* and *Step 4* in June 2017.

Decision/Action:

- *The E18 EWG will provide a work plan to the MC ahead of its teleconference to be held in autumn 2016 for activities to be undertaken.*

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

The M2 EWG did not meet in Lisbon.

The Assembly noted the current activities of the M2 EWG and the progress made towards development of a new M2 Operating Model; finalisation of the Information Paper on Redaction by June 2016; harmonisation of the PDF Specification; finalisation of the Technology Watch Report by June 2016; finalisation of report of M8 SDO Project survey results by M8 EWG/IWG for its review and comments.

Decision/Action:

- *The M2 EWG will provide a work plan to the MC ahead of its teleconference to be held in autumn 2016 for activities to be undertaken.*

❖ ***M8 EWG/IWG: The Electronic Common Technical Document: eCTD***

The M8 EWG/IWG did not meet in Lisbon.

The Assembly noted the current activities of the M8 EWG/IWG, including Q&As session with eCTD Tool Vendors; finalisation of the eCTD v4.0 Orientation Materials; finalisation of the revised Granularity Document included in the M4(R3) Guideline on Organisation with M4Q(R1) IWG agreement; and work on an updated version of the eCTD v3.2.2 Q&As/Change Request document.

The Assembly also noted the eCTD v4.0 Q&As and Change Request Document is expected to reach *Step 3* and *Step 4* at the next meeting in Osaka in November 2016.

Decisions/Actions:

- *The M8 Regulatory Experts signed-off Step 3 of the revised Granularity Document included in the M4(R3) Guideline on Organisation and the eCTD v3.2.2 Q&As and Specification Change Request v1.28 Document;*
- *The Regulatory Members of the Assembly adopted under Step 4 the revised Granularity Document included in the M4(R3) Guideline on Organisation and the eCTD v3.2.2 Q&As and Specification Change Request v1.28 Document;*
- *The M4(R4) Guideline on Organisation will be published on the ICH website;*
- *The eCTD v3.2.2 Q&As and Specification Change Request v1.28 Document will be published on the ICH website;*
- *The M8 Experts signed-off the Support Document and Orientation Materials;*

- *The Assembly endorsed the Support Document and Orientation Materials;*
- *The Assembly noted that these documents will be published on the ESTRI website;*
- *The M8 EWG/IWG will provide a work plan to the MC ahead of its teleconference to be held in autumn 2016 for activities to be undertaken.*

Dates of Next Meetings for 2016/2017

November 5 – 10, 2016	Osaka, Japan
Spring 2017	Montreal, Canada (dates to be confirmed)

EWG/IWGs Meeting in Osaka, Japan

A list of EWG/IWGs which will meet face-to-face at the next ICH meeting in Osaka on November 5 – 10, 2016 will be made available on the ICH public website following the Management Committee teleconference to be held in autumn 2016.