05 July 2023

FINAL MINUTES

ICH ASSEMBLY VANCOUVER MEETING

12 – 13 JUNE 2023

Please find hereafter the final minutes of the Assembly Meeting held in Vancouver, Canada on 12 and 13 June 2023.

List of Assembly Participants

Chair: Ms. Lenita Lindström
Vice-Chair: Dr. Gabriela Zenhaeusern

ICH Assembly Member Representatives:

Mr. Nélio Cezar De Aquino	ANVISA, Brazil
Ms. Bianca Zimon Giacomini Ribeiro	ANVISA, Brazil
Dr. Wassim Nashabeh	BIO
Ms. Nancy Schwalje Travis	BIO
Ms. Miriam Jackeline Loera Rosales	COFEPRIS, Mexico
Ms. Margarita Contreras Olvera**	COFEPRIS, Mexico
Dr. Georgios Balkamos	EC, Europe
Dr. Bruno Sepodes	EC, Europe
Ms. Asmaa Fouad	EDA, Egypt[1]
Mr. Raun Kupiec	EFPIA
Mr. Pär Tellner	EFPIA
Dr. Michelle Limoli	FDA, United States
Dr. Theresa Mullin	FDA, United States
Mr. Douglas MacKay**	Global Self-Care Federation
Dr. Leo Bouthillier	Health Canada, Canada
Mr. Bruce Randall	Health Canada, Canada
Ms. Siew Wei Chua*	HSA, Singapore
Dr. Dorothy Toh	HSA, Singapore
Dr. Nicholas Cappuccino	IGBA
Ms. Beata Stepniewska	IGBA
Dr. Manabu Yanagisawa	JPMA
Dr. Masafumi Yokota	JPMA
Ms. Minyoung Lim	MFDS, Republic of Korea
Dr. Younjoo Park	MFDS, Republic of Korea
Mr. Naoyuki Yasuda	MHLW/PMDA, Japan
Ms. Catherine Lenihan**	MHRA, UK
Mr. Julian Beach**	MHRA, UK
Mr. Siyuan Zhou	NMPA, China
Ms. Michelle Rohrer	PhRMA
Ms. Janet Vessotskie	PhRMA
Dr. Adel Al Harf	SFDA, Saudi Arabia
Dr. Abdullah AL-Hatareshah	SFDA, Saudi Arabia
Dr. Andreas Pfenninger	Swissmedic, Switzerland
Dr. Yi Chu Lin	TFDA, Chinese Taipei
Ms. Elif Inci Ergonul	TITCK, Turkey
Ms. Handan Oztunca	TITCK, Turkey

[1] At the Assembly meeting under Agenda item 2, EDA, Egypt was welcomed as a new ICH Member
* Virtual attendance
** Replacement for Vancouver meeting only

ICH Management Committee Member Representatives:

Dr. Milton Bonelli	EC, Europe
Dr. Shinichi Okudaira	MHLW/PMDA, Japan

ICH Assembly Coordinators:

Ms. Ana Carolina Moreira Marino Araujo	ANVISA, Brazil
Ms. Casey Rosner	BIO
Dr. Georgios Balkamos	EC, Europe
Dr. Jyothsna Krishnan	EFPIA
Ms. Jill Adleberg	FDA, United States
Dr. Padmaja Kamath	Global Self-Care Federation
Mr. Nick Orphanos	Health Canada, Canada
Ms. Shu Yi Ong*	HSA, Singapore
Dr. Shinichiro Hirose	IGBA
Ms. Mariko Kato	JPMA
Dr. Hyun Song	MFDS, Republic of Korea
Ms. Mao Yanagisawa	MHLW/PMDA, Japan
Ms. Nannan Li**	NMPA, China
Ms. Amanda Roache	PhRMA
Mr. Yahya Al-Nujaym	SFDA, Saudi Arabia
Ms. Sarah Koechlin	Swissmedic, Switzerland
Ms. Yi Ju (May) Lin	TFDA, Chinese Taipei
Ms. Elif Inci Ergönül	TITCK, Turkey

ICH Assembly Technical Coordinators:

Dr. Kevin Cunningham	EC, Europe
Dr. Takashi Misu	MHLW/PMDA, Japan

ICH Assembly Standing Observer Delegates:

Ms. Angelika Joos	IFPMA
Ms. Judith Macdonald	IFPMA
Dr. Samvel Azatyan	WHO

ICH Assembly Observer Delegates:

Ms. Yanina Rodriguez	ANMAT, Argentina
Dr. Amel Bensedira*	ANPP, Algeria
Mr. Sangyeon Oh	APEC
Dr. Rainer Fendt	APIC

* Virtual attendance
** Replacement for Vancouver meeting only

Mr. Pramote Akarapanon**	ASEAN
Dr. Murray Lumpkin*	Bill and Melinda Gates Foundation
Dr. Celeste Sanchez*	CECMED, Cuba
Dr. Lembit Ragö	CIOMS
Dr. Ofra Axelrod*	CPED, Israel
Mr. Felchism Apolnary*	EAC
Dr. Petra Doerr	EDQM
Dr. Hajed M. Hashan	GHC
Ms. Janeen Skutnik-Wilkinson	IPEC
Dr. Wesal Haqaish*	JFDA, Jordan
Mr. Moji Adeyeye	NAFDAC, Nigeria[4]
Dr. Hector Castro-Jaramillo	PANDRH
Mr. Paul Gustafson	PIC/S
Ms. Anastasia Nikitina*	Roszdravnadzor, Russia
Ms. Silverani Padayachee	SAHPRA, South Africa
Dr. Lilit Ghazaryan*	SCDMTE, Armenia
Dr. Kevin Moore	USP

ICH Additional Participants:

Dr. Varley Sousa	ANVISA, Brazil
Dr. Peter Bachmann	EC, Europe
Ms. Lidija Samardzic	IFPMA
Ms. Miyako Okayama	JPMA
Ms. Kaori Ogawa	MHLW/PMDA, Japan

ICH Secretariat:

Mr. Sivashen Cunden
Ms. Olga Frei
Ms. Nahimeh Jaffar
Ms. Nikoleta Luludi
Ms. Anca-Elena Matei
Dr. Dawn Ronan

[4] At the Assembly meeting under Agenda item 2, NAFDAC, Nigeria was welcomed as a new ICH Observer
* Virtual attendance
** Replacement for Vancouver meeting only

TABLE OF CONTENT

ICH ASSEMBLY MINUTES

Assembly Chair: Ms. Lenita Lindström, EC, Europe

Assembly Vice Chair: Dr. Gabriela Zenhäusern, Swissmedic, Switzerland

Opening of the ICH Assembly Meeting

The ICH Assembly Meeting, held on 12 – 13 June 2023 in Vancouver, Canada, was chaired by Ms. Lenita Lindström (Chair – EC, Europe) and Dr. Gabriela Zenhäusern (Vice-Chair – Swissmedic, Switzerland).

The Assembly noted the Member Representatives and Observer Delegates as well as the Ad hoc Observer delegate participating in the Assembly meeting.

Adoption of the Agenda

Assembly Decision/Action:

- The Assembly adopted the agenda without any modification.

1. Procedural Matters

Assembly Rules of Procedure

The ICH Secretariat presented to the Assembly amendments proposed to the Assembly Rules of Procedure (RoP) related to allowing Standing Observers to have a Coordinator position to support their work in relation to the ICH Assembly, MC and Working Groups (WGs).

Assembly Decision/Action:

- The Assembly noted the proposed changes to the ICH Assembly RoP v12.0, and approved the ICH Assembly RoP v13.0, which will be published on the ICH website.

ICH Management Committee Rules of Procedure

The ICH Secretariat presented to the Assembly updates made to the ICH Management Committee (MC) RoP related to allowing Standing Observers to have a Coordinator position to support their work in relation to the ICH Assembly, MC and WGs.

Assembly Decision/Action:

- The Assembly noted the proposed changes to the ICH MC RoP v12.0, and that the MC had approved the ICH MC RoP v13.0, pending Assembly approval of the related change in the Assembly RoP, which will now be published on the ICH website.

Standard Operating Procedures (SOPs) of the ICH WGs

The ICH Secretariat presented to the Assembly updates made to the SOPs of the WGs related to: allowing Standing Observers to have a Coordinator position to support their work in relation to the ICH Assembly, MC and WGs; addition of new templates for Concept Paper, Concept Paper Outline and New Topic Proposal; inclusion of a new minor revision procedure; addition and clarification of rules regarding Interim WGs Meetings; and clarification of rules regarding virtual participation to WGs in-person meetings.

Assembly Decision/Action:

- The Assembly noted the proposed changes to the SOPs of the WGs v12.0, and that the MC had approved the SOPs of the WGs v13.0, pending Assembly approval of a related change in the Assembly RoP, which will now be published on the ICH website.

2. Membership and Observership

The ICH Secretariat presented to the Assembly an overview of the applications for Membership and Observership processed by the ICH MC since the last ICH Assembly meeting in November 2022 and shared the ICH MC's recommendations on these applications in view of the eligibility criteria.

The applicants were invited to give a short presentation to introduce their organisations.

Assembly Decisions/Actions:

- The Assembly approved the following application for Membership under Article 11(1) of the ICH Articles of Association:
  - EDA, Egypt;
- The Assembly approved the following application for Observership under Article 17.1(a) of the ICH Articles of Association:
  - NAFDAC, Nigeria.

3. Update on MedDRA

A Representative of the MedDRA MC reported to the Assembly on MedDRA activities further to the MedDRA MC meeting held in Vancouver on 10 and 11 June 2023.

The Assembly was updated on the steady increase in the global uptake of MedDRA, with an 11% growth in new subscribing organisations in 2022 over the previous year, which brings the total number of subscribers to over 8,300 organisations in almost 134 countries.

The Assembly noted the continuing efforts by the MedDRA MC to ensure support of the needs of MedDRA users, including: ongoing translation development for new languages of the European Economic Area (EEA) in collaboration with EC, Europe and individual Member State Regulatory Authorities and a new Arabic MedDRA translation released in January 2023 which make MedDRA now available in 19 languages; the training of over 19,000 participants from 109 countries in 2022; the continuity of work on targeted mappings with other terminologies such as SNOMED-CT, IMDRF and ICD 10/11; the development of new SMQs (Standardised MedDRA Queries); and the ongoing IT activities including the release of the first MedDRA Application Programming Interfaces (APIs) in February 2023 and potential future use of Artificial Intelligence (AI) / Machine Learning (ML).

The Assembly was also updated on the progression of the planned MedDRA Business Continuity Assessment in the face of various scenarios to ensure the current high level of functionality which MedDRA users have come to expect.

Assembly Decision/Action:

- The Assembly noted the decisions taken by the MedDRA MC during its meeting on 10 and 11 June 2023.

4. Financial Matters

The ICH Finance Committee Chair updated the Assembly on the ongoing activities of the ICH Finance Committee, which includes representation from the ICH MC and MedDRA MC. This included an update

on the implementation of the asset preservation policy and the ongoing work to reduce the surplus funds (part of the 5-year budget plan). Information was further provided on: a new larger Secretariat office space; consideration on the approach and process for the funding of Regulatory Observers' travel to ICH meetings; and revisions made to the 2023 ICH Association budget and 5-Year budget plan to reflect recent discussions and decisions by the ICH MC including in relation to: organisation of interim meetings of the MC and WGs; provision of virtual support at ICH Biannual meetings and Q3E EWG project.

Assembly Decisions/Actions:

- The Assembly approved the revised 2023 ICH Association budget and supported the updated 5-Year budget plan, noting possible future revisions in view of ongoing discussions;
- The Assembly approved the 2022 Audited Accounts and Financial Statements of the ICH Association which will be filed with the 2022 tax return of the ICH Association.

5. 2022 Annual Report of the Association

The ICH Secretariat presented to the Assembly the 2022 ICH Annual Report on the activities of the Association which covered the activities undertaken by the ICH MC, the MedDRA MC and the ICH Secretariat on behalf of the ICH Association.

Assembly Decision/Action:

- The Assembly approved the 2022 Annual Report for publication on the ICH website and the discharge of the ICH MC, MedDRA MC and the ICH Secretariat for the activities undertaken by these bodies in 2022 on behalf of the ICH Association.

6. New Topics & Strategic Discussions

2023 New Topics Proposals

The Assembly was informed by the ICH MC New Topic Subcommittee Co-Leads on the New Topic proposals which were submitted by ICH Members and Observers in December 2022 as part of the call welcoming topics in Efficacy, Multidisciplinary and Safety topic areas where work could start immediately upon topic selection, and excluding Quality topics from the scope, in view of the number of currently approved / ongoing Quality topics; and on the outcome of the review and assessment of proposals by the ICH MC.

Assembly Decisions/Actions:

- The Assembly endorsed the proposal for a new Efficacy Topic on "General Considerations for Patient Preference Studies" and the related Concept Paper outline, with an informal WG to be established in early 2024 with a delayed start to initiate work in Q2 2024;
- The Assembly endorsed the proposal for a new Safety Topic on "Nonclinical safety studies for Oligonucleotide-based Therapeutics" and the related Concept Paper outline, with an informal WG to be established in June 2024 with a delayed start to initiate work;
- The Assembly endorsed the proposal for a new Multidisciplinary Topic on "Bioequivalence for Modified-Release Products" and the related Concept Paper outline, with an informal WG to be established with a delayed start to initiate work in June 2025 after the M13C EWG will have reached *Step 2*;
- The Assembly supported that a proposal on "General Considerations for Patient-Centric Product Information" is discussed at the International Pharmaceutical Regulators Programme (IPRP) Meeting as a possible IPRP topic.

Reflection Paper on Strategic Approach to International Harmonization of Cell and Gene Therapy (CGT) Product Regulation & Establishment of ICH Cell and Gene Therapies Discussion Group

The Assembly was informed on the development and endorsement by the MC of a remit document for the establishment of an ICH Cell and Gene Therapies Discussion Group (CGTDG), further to the BIO Reflection Paper on a *Strategic Approach to International Harmonization of Cell and Gene Therapy (CGT) Product Regulation*.

Assembly Decisions/Actions:

- The Assembly noted the remit of CGTDG which would focus on a narrow scope of work limited to high maturity modalities linked to broader global clinical development plans and existing approved products, with the DG to identify and recommend topics for potential harmonisation as part of a roadmap development including prioritisation, and with the DG to include experts with broad background in CGT;
- The Assembly noted that the CGTDG will operate with a 2-year term following the completion of the nomination process with a call for nominations to be launched after the meeting in Vancouver, in line with established ICH procedures, and should be comprised of a diverse group of strategically-oriented experts from Members and Observers of the ICH Assembly that collectively have extensive knowledge of the scientific and regulatory aspects of the selected CGT product modalities at all stages of development.

Reflection Paper on Harmonisation of Real-world Evidence Terminology, and Convergence of General Principles Regarding Planning and Reporting of Studies Using Real-world Data, with a Focus on Effectiveness of Medicines

The Assembly was updated on the Reflection Paper on *Harmonisation of Real-world Evidence Terminology, and convergence of General Principles Regarding Planning and Reporting of Studies Using Real-world Data, with a Focus on Effectiveness of Medicines* shared with the Assembly one month ahead of the Vancouver meeting for approval during the Vancouver meeting to be submitted for public consultation. The Assembly was provided with a high-level overview of how the comments received from MC Members ahead of the Vancouver meeting were addressed and incorporated into the Reflection Paper, as well as on the comments received from an Assembly Member just prior to the start of the meeting.

Assembly Decisions/Actions:

- The Assembly noted that a revised Reflection Paper on *Harmonisation of Real-world Evidence Terminology, and convergence of General Principles Regarding Planning and Reporting of Studies Using Real-world Data, with a Focus on Effectiveness of Medicines* was endorsed by the MC at the meeting in Vancouver;
- The Assembly supported further revision of the Reflection Paper to include comments received from an Assembly Member, and approved the revised Reflection Paper and its release on the ICH website for a 3-months public consultation after the meeting in Vancouver, with a tentative date for finalisation of the Reflection Paper in June 2024 following the public consultation.

7. Implementation of ICH Guidelines

The Assembly was informed by the Co-Leads for the next Implementation Survey on the status of a preparatory work towards the development of the survey foreseen ahead of the June 2024 MC elections, with main goals to: (1) inform the MC elections; (2) support ICH training work; and (3) advance ICH's mission for regulatory harmonisation. The Assembly was also updated on the implementation status of ICH Guidelines by ICH Regulatory Members.

Assembly Decisions/Actions:

- The Assembly noted that information on the implementation status of ICH Guidelines by ICH Regulatory Members is made available on the ICH website and updated at least twice a year;
- The Assembly noted the timeline for the survey to be launched early December 2023 and high-level survey results to be available to the MC in March/April 2024, with a final report available in May 2024 at the latest in time for the MC Elections;
- The Assembly noted that the scope of the survey will be based on the 2021 survey, with the participation of all ICH non-Standing non-Founding Regulatory Members and strongly encouraged voluntary participation of ICH Regulatory Observers.

8. Training

The Lead of the Training Subcommittee of the ICH MC provided an update to the Assembly on recent ICH Training activities, including:

- ICH WG training materials, including: ICH Q9(R1), Q13, S12, ICH M7(R2) Guideline & Addendum and ICH M7(R2) Q&As *Step 4* Introductory Training Presentations and ICH M13A *Step 2* presentation recently published on the ICH website; as well as ICH E2B(R3) and ICH Q12 WG materials under development with FDA, United States Studios thanks to a grant it has provided for the development of ICH training materials, as well as the development of an ICH E19 video module by FDA, United States with FDA, United States Studios;
- Progress made by ICH's Training Associates to develop online training materials on ICH Q3 series, ICH M4, ICH E8(R1), ICH E17 and ICH Q8-12 Guidelines;
- Activities of 3 Training Subcommittee Sub-groups, focusing their work on the following key areas since their formation in December 2022: renovation and organisation of the ICH Training Website; development of a training evaluation process; and assessment of needs / benefits of the ICH Training Subcommittee outputs;
- ICH MC support of 2023 applications for ICH Funding of Regulatory Training from ICH Regulatory Members and Regulatory Observers: EDA, Egypt; Health Canada, Canada; MHLW/PMDA, Japan; NMPA, China and SFDA, Saudi Arabia.

Assembly Decisions/Actions:

- The Assembly noted the update and the ICH Training activities;
- The Assembly noted the work of Sub-group 1 focusing on the development of an interactive training web page and infographic for onboarding new ICH Members and Observers, which will be finalised after the meeting in Vancouver;
- The Assembly noted the work of Sub-group 2 focusing on developing evaluation measures and tools for materials developed by Training Associates, training funded by ICH, and other, as needed, with a planned conduct of a 2-phase evaluation pilot, with a first phase to be launched in 2023 for evaluation of ICH-funded Regulatory Trainings. The Assembly also noted that Sub-group 2 is currently exploring use of an E-learning platform to manage the evaluation process for online training;
- The Assembly noted the work of Sub-group 3 focusing on developing criteria and prioritising training needs related to content and/or implementation of ICH Guidelines with a more targeted approach, with a planned conduct of a simple questionnaire survey among the ICH Regulatory Members and Observers on training needs and implementation issues of all ICH Guidelines after the meeting in Vancouver, with the objective of informing the next Training Associates contracting and training development; with all Regulators being strongly encouraged to participate in the survey;

- The Assembly noted the 2023 Regulatory Training Funding applications approved by the MC at the interim MC meeting in March 2023, and that the criteria for ICH Regulatory Training Funding are being further elaborated by the Training Subcommittee to clarify expectations regarding what Guidelines should be considered for training in submitted requests for funding and the possible use of existing training materials, with an updated process document to be available for the 2024 Regulatory Training Funding Call for Expressions of Interest.

9. ICMRA PQ KMS

Representatives of the ICH participating on behalf of ICH in the activities of the International Coalition of Medicines Regulatory Authorities (ICMRA) Pharmaceutical Quality Knowledge Management System (PQ KMS) Working Group updated the Assembly on recent activities, including on the development of a Joint ICMRA-ICH-PICS-IPRP PQ KMS WG Work Plan detailing the work of each participating organisation, which will be shortly finalised; and the ongoing projects.

Assembly Decisions/Actions:

- The Assembly noted the update on the status of work with the ICMRA PQ KMS WG and a planned presentation at the DIA Global Annual Meeting at the end of June 2023 in Boston, the United States; the presentations of the DIA session will be shared with the Assembly after the Meeting.
- The Assembly noted a second representative for ICH from the MC joining a representative from the Assembly to participate in the ICMRA PQ KMS WG on behalf of ICH.

10. ICH Collaboration with PIC/S

The ICH MC and Assembly Chair informed the Assembly on the status of activities regarding collaboration pilot with PIC/S, including on the draft Memorandum of Understanding (MoU) with PIC/S put forward by the ICH MC, and a training funding request submitted by PIC/S.

Assembly Decisions/Actions:

- The Assembly noted that ICH Assembly express approval is needed to enter into cooperation with PIC/S in line with the ICH procedures, which will be sought after the meeting in Vancouver electronically, with the MoU to also be formally approved by PIC/S in parallel;
- The Assembly noted the MC's approval of a training budget to PIC/S for 2023 in line with its proposal on training deliverables.

11. Communication

ICH Regional Public Meetings

The Assembly shared information on ICH Regional Public Meetings in their respective regions prior to and following the ICH meeting in Vancouver in June 2023, including meetings organised by: COFEPRIS, Mexico; EDA, Egypt; FDA, United States and Health Canada, Canada; and JPMA.

Assembly Decision/Action:

- The Assembly noted that ICH Regional Public Meetings taking place prior to/following the ICH meeting in Vancouver communicated to the Secretariat will be published on the ICH website.

Approaches for Patient Stakeholder Engagement in ICH

The ICH MC Chair provided an update on the status of activities regarding ICH Patient Engagement, including organisation of an ICH session at the DIA Global Annual Meeting at the end of June 2023, in Boston, the United States

Assembly Decision/Action:

- The MC noted the planned ICH session lead by the ICH MC Chair and ICH Assembly Vice Chair at the DIA Global Annual Meeting at the end of June.

12. General Operational Matters

ICH Operational Efficiency

The Assembly was updated on the status of activities related to operational efficiency, including on the following items: (i) accomplishments to-date and future opportunities; (ii) feedback on the work of technical writers for M14 and M15 WGs, and the possibility to leverage technical writers going forward; and (iii) proposal for enhancements to the Plenary Working Party (PWP) process.

Assembly Decisions/Actions:

- The Assembly noted the update and accomplishments to-date further to a few pilot projects launched in 2022, including: revision of the New Topic Proposal Template; revision of the Concept Paper Template which is merged with the Business Plan; improvement of informal WG and MC exchanges; development of an open document in ICH SharePoint for populating informal WGs; introduction of a new approach for expert sign-off and Assembly endorsement of guidelines; and development of supportive materials for Rapporteurs and Regulatory Chairs;
- The Assembly noted the update on pilot use of technical writers to assist the M14 and M15 WGs with guideline drafting, as well as MC recommendations to issue a Request for Proposals (RFP) to identify a vendor to provide a technical writer to support a further ICH WG, noting that technical writers may not be provided for all WGs, but will be considered as a potential resource for new WGs established going forward (e.g., E21);
- The Assembly noted the proposal for enhancements to the PWP process by providing PWP participants additional opportunities to observe the activities of the WGs in order to give PWP Members greater understanding of discussions and decisions made in developing guidelines, with MC agreement in Vancouver to develop a pilot process on enhancements to the PWP process.

ICH Secretariat Report

The ICH Secretariat informed the Assembly on general operational matters and the current level of participation of ICH Members and Observers in the ICH Assembly and WGs.

Assembly Decision/Action:

- The Assembly noted as of the start of the meeting, the participation in 31 ongoing WGs of 741 experts from amongst the 20 ICH Members and 36 ICH Observers.

13. Q4B Maintenance

A Representative from the Pharmacopeial Discussion Group (PDG) provided an update on the proposal made in Incheon 2022 for the maintenance of the Q4B process, noting challenges with the implementation of the ICH Q4B, and the recommended PDG option ("Option 2") of a parallel implementation approach for ICH Q4B where additional pharmacopoeias harmonise their text with PDG text and ICH Regulatory Members accept reference to any pharmacopoeia if declared as harmonised

according to the respective Q4B Annex, with acknowledgement that ICH Member Pharmacopoeias may still publish their local chapter in parallel to the Q4B text/PDG harmonised chapter.

Assembly Decisions/Actions:

- The Assembly supported the PDG's recommendation to use "Option 2" – harmonisation with PDG, with possibility for parallel publication of Q4B text with local chapter(s) allowing for a declaration of interchangeability;
- The PDG will submit for ICH consideration at the Prague meeting in October/November 2023, a proposed revision in view of the new maintenance approach to both the ICH Q4B Guideline and Annex 5 of the ICH SOPs for WGs (on the Q4B maintenance process). The PDG will subsequently submit an update to a first three Q4B Annexes by the ICH meeting in November 2024.

14. WGs Meeting in Vancouver

The Assembly received reports from each of the 14 WGs meeting in Vancouver. The Assembly was informed that requests from the ICH WGs to meet at the next ICH meeting in Prague, Czech Republic on Saturday, 28 October – Wednesday, 1 November 2023 would be taken under consideration by the ICH MC at the end of its meeting in Vancouver, and that the list of WGs agreed by the ICH MC to have interim meetings and/or to meet face-to-face in Prague will be made available to the Assembly in due course.

14.1. E2D(R1) EWG: Post-Approval Safety Data Management: Definitions and Standards for Expedited Reporting (Rapporteur: Ms. Edwards – EFPIA)

The E2D(R1) Rapporteur reported to the Assembly on the outcome of the meeting of the E2D(R1) EWG. The E2D(R1) EWG identified that practical examples are needed to facilitate implementation and consensus was reached on the following areas: reporting terminology, timelines for reporting, digital platforms, and literature. The E2D(R1) EWG is on track to deliver the revised guideline for PWP consultation by July and is actively planning to reach *Step 2* by October 2023 in line with its work plan.

Assembly Actions/Decisions:

- The Assembly noted the work plan of the E2D(R1) EWG which is expected to reach *Steps 1* and *2a/b* in October 2023;
- The Assembly noted that if the E2B(R3) EWG/IWG is to meet in Prague, October-November 2023, the E2D(R1) EWG would like to meet virtually with the E2B(R3) EWG/IWG.

14.2. E6(R3) EWG: Good Clinical Practice (Rapporteur: Dr. M. El Zarrad – FDA, United States; Regulatory Chair: Dr. Twomey – EC, Europe; E6(R3) Annex 2 Sub-group Regulatory Chair: Dr. Thompson – EC, Europe)

The E6(R3) Rapporteur and Annex 2 Sub-group Regulatory Chair reported to the Assembly on the status of work before the meeting with the E6(R3) draft Guideline (Principles and Annex 1) reaching *Step 1* and *2* sign-off and currently in public consultation, and progress of the meeting of the E6(R3) EWG Annex 2 Sub-group during the Vancouver meeting. The Sub-group have begun to draft Annex 2 and will include guidance on the conduct of interventional clinical trials with specific fit-for-purpose design elements and RWD sources and the challenges of clinical trials with unique designs. The Assembly noted that the Annex 2 Sub-group is considering approaches for the appropriate engagement with stakeholders.

Assembly Actions/Decisions:

- The Assembly noted the work plan of the E6(R3) EWG, and that the E6(R3) draft Guideline (Principles and Annex 1) is expected to reach *Steps 3* and *4* for by September – October 2024 and the E6(R3) draft Annex 2 is expected to reach *Steps 1* and *2a/b* by April 2024;
- The Assembly noted the E6(R3) EWG request for a targeted updates mechanism, previously discussed in Incheon 2022, which would allow for agile updates to annexes in a 6–12-month period with the E6(R3) EWG to put forward a proposal to be discussed by the ICH MC.

14.3. E11A EWG: Paediatric Extrapolation (Rapporteur: Dr. Yao – FDA, United States; Regulatory Chair: Dr. Thomson – EC, Europe)

The E11A Rapporteur reported to the Assembly on the progress of the E11A EWG meeting wherein the E11A EWG reviewed all collected comments received during the *Step 3* public regulatory consultation period by prioritising the comments within E11A EWG sub-groups (Similarity of Disease, Statistics, and Modelling and Simulation) which were formed after triaging the comments.

Assembly Actions/Decisions:

- The Assembly noted the work plan of the E11A EWG with the importance to meet in Prague, Czech Republic to reach *Steps 3* and *4* of the E11A ICH Guideline by first quarter of 2024;
- The Assembly noted the E11A EWG will develop training materials within 6 months after the publication of the final ICH E11A Guideline and the necessity to maintain full E11A EWG participation due to relevant expertise to complete the training materials;
- The Assembly noted the E11A EWG is in the process of identifying a new Regulatory Chair with a nomination to be shared with the Secretariat;
- The Assembly supported the request of the E11A EWG to continue to use currently appointed Subject Matter Experts (SMEs) to address the collected comments and consideration to add additional statistical SMEs, if needed.

14.4. E20 EWG: Adaptive Clinical Trials (Rapporteur: Dr. Zhong – PhRMA; Regulatory Chair: Dr. Levin – FDA, United States)

The E20 Rapporteur reported to the Assembly on the progress of the E20 EWG meeting. The E20 EWG continues to work on the E20 draft Technical Document. The Assembly noted the concerns of the E20 EWG to be able to reach the originally foreseen timeline of *Steps* 1 and *2a/b* by December 2023 and the EWG's request for an extension by several months in the timeline. The Assembly noted that this was in view of the need to additionally consider learnings arising out of the COVID-19 pandemic.

Assembly Action/Decision:

- The Assembly noted the work plan of the E20 EWG, and while the new timeline for the draft Technical Document to reach *Steps 1* and *2 a/b* in May 2024 was supported, the EWG was urged to try to deliver sooner if possible.

14.5. E21 EWG: Inclusion of Pregnant and Breastfeeding Individuals in Clinical Trials (Rapporteur: Dr. Bischof – EFPIA; Regulatory Chair: TBC)

The E21 Rapporteur reported to the Assembly on the progress of the E21 EWG meeting wherein the E21 EWG have begun outlining the overall topics to be included within the draft Technical Document to acknowledge the need to generate data for medicinal products in pregnant and breast-feeding individuals with the guideline objective to provide a globally accepted framework and best practices to

enable inclusion and/or retention of pregnant and breast-feeding individuals in clinical trials. The Assembly noted the transition of the E21 informal WG to an EWG in Vancouver with the MC's approval of the Final E21 Concept Paper.

Assembly Actions/Decisions:

- The Assembly noted the preliminary work plan of the E21 EWG, and that the EWG currently aims to reach *Steps 1* and *2a/b* for the E21 Technical Document by Q1 2025 with the EWG's first work plan to be provided in July 2023;
- The Assembly noted the interest of the E21 EWG to consult with other EWG (M15, E6(R3), E11A) to incorporate cross guideline considerations to the drafting of the Technical Document;
- The Assembly noted the request for the appointment of a Regulatory Chair for which the procedure will be carried out by the ICH Secretariat;
- The Assembly noted the request to appoint a Technical Writer to assist drafting of the Technical Document which was being considered by the MC which was working on the process for addressing Technical Writer requests going forward.

14.6. M4Q(R2) EWG: Revision of M4Q(R1) CTD on Quality guidance (Rapporteur: Dr. Yu – FDA, United States; Regulatory Chair: Mr. van der Stappen – EC, Europe)

The M4Q(R2) Rapporteur reported to the Assembly on the progress of the M4Q(R2) EWG meeting and work progressed on the M4Q(R2) draft Technical Document, including framing Module 2 as the basis for Regulatory Assessment supported by Module 3, which is to be structured to be flexible and modular, with optional section fit for all types of medicinal products. The M4Q(R2) EWG have begun discussion on how to accommodate within Module 2 initial registration and lifecycle management and have begun drafting mock examples to support M4Q(R2) design development and reach consensus on language and communication.

Assembly Action/Decision:

- The Assembly noted the M4Q(R2) EWG work plan and that *Steps 1* and *2a/b* are expected by June 2024.

14.7. M13 EWG: Bioequivalence for Immediate-Release Solid Oral Dosage Forms (Rapporteur: Dr. Zhang – FDA, United States; Regulatory Chair: Dr. Welink – EC, Europe)

The M13 EWG Rapporteur reported to the Assembly on the progress of the M13 EWG who are developing a series of guidelines M13A, M13B and M13C. Work on M13A and M13B is currently ongoing and work on M13C is only foreseen to commence when M13B reaches *Steps 1* and *2a/b*. Currently the M13 EWG are working on M13A and M13B in parallel having triaged comments received from public consultation for the M13A draft Guideline which reached *Step 2* in December 2022. The Assembly also noted initial considerations to develop Questions and Answers (Q&As) to provide additional clarification.

Assembly Actions/Decisions:

- The Assembly noted the work plan of the M13 EWG, with priority to progress the finalisation of the M13A Guideline, which is expected to reach *Steps 3* and *4* in June-July 2024;
- The Assembly approved the request for a 6-month extension for the M13B draft Technical Document work plan which is now expected to reach *Steps 1* and *2a/b* by June-July 2024 to enable finalisation of M13A.

14.8. M15 EWG: General Principles for Model-Informed Drug Development (Rapporteur: Dr. Marshall – PhRMA; Regulatory Chair: Dr. Karlsson – EC, Europe)

The M15 Rapporteur reported to the Assembly on the progress of the M15 EWG meeting and progress to date on the structuring of the draft Technical Document, integrating across sections "Regulatory Assessment of MIDD Evidence" concepts and adding an "MIDD-Related Regulatory Interaction" section to position MIDD giving clarity with respect to the scope of the M15 Guideline.

The Assembly was also informed on the use of "Credibility Framework for MIDD Evidence", which the Assembly expressed interest to receive additional information on at the next meeting.

The Assembly additionally noted the positive benefit of the Technical Writer in supporting the M15 EWG drafting the Technical Document

Assembly Action/Decision:

- The Assembly noted the work plan of the M15 EWG and that the draft Technical Document is expected to reach *Steps 1* and *2a/b* by March-April 2024.

14.9. Q1/Q5C EWG: Targeted revisions of the ICH Stability Guideline Series (Rapporteur: Ms. McMahon – PhRMA; Regulatory Chair: Dr. Rao – FDA, United States)

The Q1/Q5C Rapporteur reported to the Assembly on the progress of the Q1/Q5C EWG meeting wherein the Q1/Q5C EWG further worked on the development of the draft Technical Document. In addition, the EWG has begun development of examples to reach common understanding of stability variations and drafted an Advanced Therapy Medicinal Product (ATMP) Annex.

Assembly Actions/Decisions:

- The Assembly noted the work plan of the Q1/Q5C EWG and that the draft Technical document is expected to reach *Steps 1* and *2a/b* by Q3/4 2024;
- The Assembly noted the Q1/Q5C EWG would like to leverage and engage ATMP experts from the CGTDG (see item #6 above), after it is established to assist in the review of the ATMP Annex, with it noted that it would likely be possible for the two WGs to connect in the September 2023 timeframe.

14.10. Q2(R2)/Q14 EWG: Analytical Procedure Development and Revision of Q2(R1) Validation of Analytical Procedures (Rapporteur: Dr. Hiyama – MHLW/PMDA, Japan; Regulatory Chair: Dr. Keire – FDA, United States)

The Q2(R2)/Q14 Rapporteur reported to the Assembly on the progress of the Q2(R2)/Q14 EWG meeting in which the Q2(R2)/Q14 EWG reviewed the changes made since the interim meeting in Tokyo, February 2023 and identified topics for further discussion. The Assembly noted that the EWG had been discussing an appropriate title for Q14 and have also begun discussion on the development of training materials to address specific comments received and request to transition to an IWG after reaching of *Step 4*.

Assembly Actions/Decisions:

- The Assembly noted the work plan of the Q2(R2)/Q14 EWG and that the draft Guidelines are expected to reach *Steps 3* and *4* by November 2023;

- The Assembly supported the transition of the Q2(R2)/Q14 EWG to an IWG, pending MC approval of a Concept Paper, and that the EWG would begin development of training material after the Q2(R2)/Q14 Guidelines have reached *Step 4* and deliver the training material within a 12-month timeframe at longest.

14.11. Q3E EWG: Impurity: Assessment and Control of Extractables and Leachables for Pharmaceuticals and Biologics (Rapporteur: Dr. Li – PhRMA; Regulatory Chair: Dr. Rodriguez – FDA, United States)

The Q3E EWG Rapporteur reported to the Assembly on the progress of the Q3E EWG meeting wherein the Q3E EWG finalised the selection of 3 vendors to be approached to support the Threshold Project and have proposed a 3-part plan consisting of: Chemical space analysis; PDE generation and secondary review; and Data integration and analysis. The Q3E EWG would leverage internal and external sources, to generate the PDEs ensuring consistency by providing a common template for all providers to use which will be reviewed by the Q3E EWG for integration into the ICH Q3E draft Technical Document.

Assembly Actions/Decisions:

- The Assembly supported the Q3E EWG Threshold project and approved the required funding as part of the revised 2023 ICH Association budget (see item #4 above);
- The Assembly supported the 1-year extension to the work plan to enable completion of the Threshold Project with *Steps 1* and *2a/b* now expected by October 2024;
- The Assembly endorsed the nomination of a new Rapporteur, Ms. Patricia Parris (PhRMA), for the Q3E EWG in line with Assembly RoP Section 4.2.

14.12. Q5A(R2) EWG: Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin (Rapporteur: Dr. Welch – FDA, United States; Regulatory Chair: Dr. Blumel – EC, Europe)

The Q5A(R2) EWG Rapporteur reported to the Assembly on the progress of the Q5A(R2) EWG meeting wherein the Q5A(R2) EWG continued to address comments from public consultation, further to the reaching of *Step 2* in September 2022. The EWG made good progress in Vancouver to resolve scientific/technical issues and comments related to "Continuous Manufacturing" and "Prior Knowledge/Alternative validation approaches", discussed consistency with other regulatory guidance, and clarified language to describe use of Next Generation Sequencing (NGS) and included description on terminology. The Assembly also noted provisional Q5A(R2) considerations on the development of training materials.

Assembly Action/Decision:

- The Assembly noted the work plan of the Q5A(R2) EWG for activities to be undertaken and the Guideline which is expected to reach *Steps 3* and *4* by September – October 2023.

14.13. Q9(R1) EWG: Quality Risk Management (Rapporteur: Mr. O'Donnell – EC, Europe; Regulatory Chair: Mr. Viehmann – FDA, United States)

The Q9(R1) EWG Rapporteur reported to the Assembly on the progress of the Q9(R1) EWG meeting and work on six training material topics, including: Hazard Identification; Product Availability Risks;

and Risk Review, drafts of which were finalised by the EWG end of March, with work progressed in Vancouver on the remaining three topics: Risk-based Decision-making; Formality in Quality Risk Management (QRM); and Subjectivity in QRM, with all finalised in Vancouver and expected to be published by July 2023.

In addition, the Assembly noted the planned Q9(R1) EWG transition into an IWG by September 2023, to work on the old 2006-2010 Q8/Q9/Q10 training materials currently published on the ICH website. The Assembly however noted that an extension in the timeline for this work may be needed since a need was now also foreseen for the IWG to provide input into ICH Q9(R1) training materials under development by an ICH Training Associate.

Assembly Action/Decision:

- The Assembly noted and endorsed the Q9(R1) EWG work plan, with the Q9(R1) EWG to transition in September 2023 to an IWG.

14.14. Q13 IWG: Continuous Manufacturing of Drug Substances and Drug Products (Rapporteur: Dr. Lee – FDA, United States; Regulatory Chair: Dr. Matsuda – MHLW/PMDA, Japan)

The Q13 Rapporteur reported to the Assembly on the outcome of the Q13 IWG meeting, including the progress made on determining the topics and format of Q13 IWG training materials, which will be developed by Q13 IWG. The topics will include those not captured within the ICH Q13 Guideline but likely to be used in Continuing Manufacturing such as "Use of models" and "Continuous Process Verification". The training materials would also consider some of the potential challenges for global implementation of the ICH Q13 Guideline.

Assembly Action/Decision:

- The Assembly noted the Q13 IWG work plan with the training materials consisting of presentations and video expected to be finalised by June 2024.

15. WGs not Meeting in Vancouver

15.1. E2B(R3) EWG/IWG: Revision of the Electronic Submission of Individual Case Safety Reports (Rapporteur: Dr. Misu – MHLW/PMDA, Japan; Regulatory Chair: Mr. Chen – FDA, United States)

The E2B(R3) EWG/IWG continues to work, considering updates to Q&As as needed. Training Module III is expected shortly.

15.2. E14/S7B DG: The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs (Rapporteur: Dr. Strauss – FDA, United States)

The E14/S7B DG continues its work, and at the conclusion of a one-year term the DG will recommend next steps including returning to an EWG to develop second stage Q&As, disbanding the group, or providing a limited extension.

15.3. M1 PtC WG: MedDRA Points to Consider (Rapporteur: Dr. Winter – EFPIA; Regulatory Chair: Dr. Brajovic – FDA, United States)

The M1 PtC WG continues to work on the annual updating with the March MedDRA release of the MedDRA Term Selection: Points to Consider and MedDRA Data Retrieval and Presentation: Points to Consider documents, having most recently released translations in English, Japanese, Chinese, Korean, Russian and Spanish in March 2023. The M1 PtC WG has also resumed work on a new section of the companion document on product quality issues during manufacturing and is in the process of identifying manufacturing experts.

15.4. M2 EWG: Electronic Standards for the Transfer of Regulatory Information (ESTRI) (Co-Rapporteurs: Ms. Slack – FDA, United States / Dr. Okada – MHLW/PMDA, Japan; Regulatory Chair: Dr. Jaermann – Swissmedic, Switzerland)

The M2 EWG continues its work on: exploring/identifying technological risks or opportunities by discussing with ICH WGs at *Step 1* and reviewing *Step 3-4* documents; development of a report on the potential to innovate regulatory process through technology; considering the need to update recommendations for streamlining ICH standards development process; and working on the technical specification document for CeSHarP with the M11 EWG.

The Assembly noted that the M2 EWG was holding an interim meeting on 13-16 June 2023 in Berlin, Germany.

15.4.1. M8 Sub-group of M2: The Electronic Common Technical Document (eCTD) Ms. Slack – FDA, United States / Dr. Okada – MHLW/PMDA, Japan; Regulatory Chair: Ms. Puusaari – EC, Europe)

The M8 Sub-group of the M2 EWG continues its work to monitor the status of implementation of eCTD v4.0. The Assembly noted the M8 Sub-group would virtually join the M2 EWG interim meeting on 13-14 June 2023 in Berlin, Germany.

15.5. M7(R2) Maintenance EWG/IWG: Addendum to Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk (Rapporteur: Dr. Atrakchi – FDA, United States)

Steps 3 and 4 for the M7(R2) Guideline and Addendum were reached in April 2023. At *Step 4*, the M7(R2) Guideline and Addendum, along with the Q&As which reached *Step 4* in May 2022, were published on the ICH website and the Rapporteurship rotated to Dr. Aisar Atrakchi (FDA, United States).

15.6. M10 EWG: Bioanalytical Method Validation (Rapporteur: Dr. Ishii-Watabe – MHLW/PMDA, Japan; Regulatory Chair: Dr. Booth – FDA, United States)

The M10 EWG continues its work to finalise training materials which are to be expected shortly.

15.7. M11 EWG: Clinical electronic Structured Harmonised Protocol (CeSHarP) (Rapporteur: Dr. Fitzmartin – FDA, United States; Regulatory Chair: Dr. Manent– EC, Europe)

The M11 EWG continues to work to review comments collected during the *Step 3* public consultation to update the M11 draft Technical Document, the clinical protocol template and the Technical Implementation Guide; as well as on the strategic engagement with other key WGs including: E6(R3) EWG, E9(R1) EWG, E20 EWG, and M2 EWG. The M11 draft Technical Document is expected to reach *Steps 3 and 4* by November 2024.

The Assembly noted that the M11 EWG was holding an interim meeting on 12-15 June 2023 in Berlin, Germany.

15.8. M12 EWG: Drug Interaction Studies (Rapporteur: Dr. Madabushi – FDA, United States; Regulatory Chair: Dr. Ishiguro – MHLW/PMDA, Japan)

The M12 EWG continues its work to address comments from public regulatory consultation in the ICH Member regions. The M12 Guideline is expected to reach *Steps 3* and *4* by Q1 2024.

15.9. M14 EWG: General principles on planning and designing pharmacoepidemiological studies that utilize real-world data for safety assessment of a medicine (Rapporteur: Dr. Moeny – FDA, United States; Regulatory Chair: Dr. Kajiyama – MHLW/PMDA, Japan)

The M14 EWG continues to work on the M14 draft Technical Document, with the support of a technical writer as part of a piloting of the use of technical writers by ICH WGs. The M14 draft Technical Document is expected to reach *Steps 1* and *2 a/b* by August 2023.

15.10. Q3C(R9) Maintenance EWG: Maintenance of the Guideline for Residual Solvents (Acting Rapporteur: Dr. Froetschl – EC, Europe)

Step 4 of the Q3C(R8) Guideline including the Permitted Daily Exposure (PDE) levels for the solvents 2-2-Methyltetrahydrofuran, Cyclopentyl methyl ether and Tertiary butyl alcohol was reached in April 2021.

The Q3C(R9) Maintenance EWG remains in a dormant state until proposals for revisions are received.

Assembly Action/Decision:

- The Assembly endorsed the nomination of Dr. Roland Froetschl (EC, Europe), as the formal Rapporteur for the Q3C(R9) Maintenance EWG in line with Assembly RoP Section 4.2.

15.11. Q3D(R3) Maintenance EWG: Maintenance of the Guideline for Elemental Impurities (Rapporteur: Dr. Froetschl – EC, Europe)

Steps 3 and *4* of the Q3D(R2) revision for the cutaneous and transdermal products were reached in April 2022.

The Q3D(R3) Maintenance EWG remains in a dormant state until proposals for revisions are received.

15.12. Q12 IWG: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management (Rapporteur: Ms. Boam – FDA, United States; Regulatory Chair: Ms. Kruse – EC, Europe)

The Q12 Training Materials Modules 0-7 were finalised in June 2021. The Q12 Training Material Module 8 (case studies) is expected to be finalised shortly. The Q12 IWG is working on the finalisation of a broad-audience video with the support of the FDA, United States studios.

15.13. S1B(R1) EWG: Revision of the Rodent Carcinogenicity Studies for Human Pharmaceuticals Guideline (Rapporteur: Dr. McGovern – FDA; Regulatory Chair: Dr. Van der Laan – EC, Europe)

The Regulatory S1B(R1) EWG experts continue to write a final evaluative paper of the complete dataset as the result of the Prospective Evaluation Period.

15.14. S5(R4) Maintenance EWG: Revision on Detection of Toxicity to Reproduction for Human Pharmaceuticals (Rapporteur: Dr. Waxenecker – EC, Europe)

No proposals for revisions of Annex 1 or 2 have been received at this time and therefore the S5(R4) Maintenance EWG remains in a dormant state.

15.15. Generic drug Discussion Group (GDG) (Rapporteur: Dr. Tampal – FDA, United States; Regulatory Chair: Dr. Welink – EC, Europe)

The GDG is dormant until the ICH MC requests or directs them to resume work.

15.16. Standing Paediatric EWG (Rapporteur: Dr. Hirata – MHLW/PMDA, Japan; Regulatory Chair: Dr. Yao – FDA, United States)

The Standing Paediatric EWG did not receive any request for paediatric advice from WGs and the group remains available for expert consultation and guidance to WGs charged with developing new or revised guidance which may be of relevance to paediatric drug development.

15.17. Quality Discussion Group (QDG) (Acting Rapporteur: Dr. Miksinski – PhRMA; Regulatory Chair: Dr. Barry – EC, Europe)

The QDG continues as a DG with low activity.

Assembly Action/Decision:

- The Assembly endorsed the nomination of a new Rapporteur, Dr. Sarah Pope Miksinski (PhRMA), for the QDG in line with Assembly RoP Section 4.2.

16. Organisation of Next Meetings

The Assembly was updated by the ICH Secretariat on the organisation of next ICH biannual meetings.

Assembly Decision/Action:

- The Assembly noted the dates and locations of the next ICH meetings as per the below:

- 28 October - 1 November 2023 in Prague, Czech Republic
- 1 - 5 June 2024, Fukuoka, Japan
- 2 - 6 November or 16 - 20 November 2024 in the Americas (dates & location to be confirmed)
- 10 - 14 May 2025 in Europe (location to be confirmed)

17. **Press Release**

Assembly Action/Decision:

- The Assembly noted the development of a Press Release to be issued shortly after the close of the virtual meeting in line with the usual process, with the aim being to publish on the ICH website within a week of the end of the meeting.