18 January 2022

FINAL MINUTES

ICH ASSEMBLY VIRTUAL MEETING

17 – 18 NOVEMBER 2021

Please find hereafter the revised minutes of the Assembly Virtual Meeting held on 17 and 18 November 2021.

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List of Assembly Participants

Chair: Ms. Lenita Lindström-Gommers

Vice-Chair: Dr. Celia Lourenco

ICH Assembly Members Representatives

Mr. Diogo Penha Soares	ANVISA, Brazil
Dr. Wassim Nashabeh	BIO
Dr. Alejandro Ernesto Svarch Pérez	COFEPRIS, Mexico[1]
Dr. Bruno Sepodes	EC, Europe
Dr. Georgios Balkamos	EC, Europe
Dr. Sue Forda	EFPIA
Mr. Pär Tellner	EFPIA
Dr. Theresa Mullin	FDA, United States
Ms. Joan Wilmarth Blair	FDA, United States
Dr. Padmaja Kamath	Global Self-Care Federation
Dr. Celia Lourenco	Health Canada, Canada
Dr. Léo Bouthillier	Health Canada, Canada
Ms. Siew Wei Chua	HSA, Singapore
Dr. Dorothy Toh	HSA, Singapore
Dr. Nick Cappuccino	IGBA
Ms. Beata Stepniewska	IGBA
Dr. Manabu Yanagisawa	JPMA
Dr. Masafumi Yokota	JPMA
Dr. Younjoo Park	MFDS, Republic of Korea
Mr. Seogyoun Kang	MFDS, Republic of Korea
Dr. Nobumasa Nakashima	MHLW/PMDA, Japan
Mr. Naoyuki Yasuda	MHLW/PMDA, Japan
Dr. Sheng Yang	NMPA, China
Mr. Siyuan Zhou	NMPA, China
Dr. Michelle Rohrer	PhRMA
Ms. Janet Vessotskie	PhRMA
Dr. Abdullah Hamad Al Hatareshah	SFDA, Saudi Arabia
Dr. Adel Alharf	SFDA, Saudi Arabia
Dr. Andreas Pfenninger	Swissmedic, Switzerland
Mr. Kevin Ming-Hsun Liu	TFDA, Chinese Taipei
Dr. Jo-Feng Chi	TFDA, Chinese Taipei
Ms. Handan Öztunca	TITCK, Turkey
Dr. Elif İnci Ergönül	TITCK, Turkey

ICH Management Committee Member Representatives

Dr. Milton Bonelli	EC, Europe
Mr. Teruyoshi Ehara	MHLW/PMDA, Japan

[1] At the Assembly Virtual meeting under Agenda item 1, COFEPRIS, Mexico was welcomed as a new ICH Member.

ICH Assembly Coordinators

Mr. David Dee	BIO
Dr. Georgios Balkamos	EC, Europe
Ms. Andreea Iordache	EFPIA
Ms. Jill Adleberg	FDA, United States
Dr. Padmaja Kamath	Global Self-Care Federation
Mr. Nick Orphanos	Health Canada, Canada
Ms. Junhan Shang	HSA, Singapore
Dr. Shinichiro Hirose	IGBA
Dr. Hiroaki Hagiwara	JPMA
Ms. Miyoung Hyun	MFDS, Republic of Korea
Mr. Hirooki Tanabe	MHLW/PMDA, Japan
Mr. Baoshu Wen	NMPA, China
Ms. Amanda Roache	PhRMA
Mr. Yahya Al-Nujaym	SFDA, Saudi Arabia
Dr. Gabriela Zenhaeusern	Swissmedic, Switzerland
Ms. Pao-Hsuan Huang	TFDA, Chinese Taipei
Dr. Elif İnci Ergönül	TITCK, Turkey

ICH Assembly Technical Coordinators

Dr. Zahra Hanaizi	EC, Europe
Dr. Michelle Limoli	FDA, United States
Ms. Mami Ueda	MHLW/PMDA, Japan

ICH Assembly Standing Observer Delegates

Ms. Angelika Joos	IFPMA
Dr. Sharon Olmstead	IFPMA
Dr. Samvel Azatyan	WHO

ICH Assembly Observer Delegates

Dr. Farid Hasanov	AEC, Azerbaijan
Dr. Matias Gomez	ANMAT, Argentina
Dr. Youngju Choi	APEC
Dr. Rainer Fendt	APIC
Dr. Murray Lumpkin	Bill and Melinda Gates Foundation
Dr. Venugopal Girdharilal Somani	CDSCO, India
Dr. Celeste Sánchez González	CECMED, Cuba
Dr. Lembit Rägo	CIOMS
Dr. Ofra Axelrod	CPED, Israel
Dr. Asmaa Fouad Ismail	EDA, Egypt[2]

[2] At the Assembly Virtual meeting under Agenda item 1, EDA, Egypt was welcomed as a new ICH Observer.

Dr. Petra Doerr	EDQM
Dr. Hajed M. Hashan	GHC
Ms. Yenny Marcela Suárez González	INVIMA, Colombia
Ms. Janeen Skutnik-Wilkinson	IPEC
Ms. L. Rizka Andalucia	Indonesian FDA, Indonesia[3]
Ms. Shatha Al-Quraan	JFDA, Jordan
Mr. Jamie Convisser	MHRA, UK
Dr. Analia Porras	PANDRH
Mr. David Churchward	PIC/S
Ms. Anastasia Nikitina	Roszdravnadzor, Russia
Ms. Fortunate Ntombi Bhembe	SADC
Ms. Aida Malkhasyan	SCDMTE, Armenia
Mr. Oleh Semeniuk	SECMOH, Ukraine[4]
Dr. Kevin Moore	USP

ICH Invited Participants

Mr. Mick Foy	MedDRA Management Committee Chair, MHRA, UK
Dr. Khair ElZarrad	Rapporteur, E6(R3) EWG, FDA, United States
Mr. Fergus Sweeney	Regulatory Chair, E6(R3) EWG, EC, Europe
Ms. Lisa Lavange	Rapporteur, E8(R1) EWG, FDA, United States
Mr. Andreas Kirisits	Regulatory Chair, E8(R1) EWG, EC, Europe
Ms. Lynne Yao	Rapporteur, E11A EWG, FDA, United States
Mr. Andrew Thomson	Invited Topic Leader, E11A EWG, EC, Europe
Mr. David Strauss	Rapporteur, E14/S7B, FDA, United States
Mr. Lawrence Yu	Rapporteur, M4Q(R2) EWG, FDA, United States
Mr. Roland Froetschl	Rapporteur M7(R2) Maintenance EWG/IWG, EC, Europe
Mr. Sau Lee	Rapporteur, Q13 EWG, FDA, United States
Mr. Matsuda Yoshihiro	Regulatory Chair, Q13 EWG, MHLW/PMDA, Japan
Mr. Roger Nosal	Rapporteur, QDG, PhRMA
Ms. Nanna Abby Kruse	Regulatory Chair, QDG, EC, Europe

ICH Additional Participants

Mr. Souha Mekary	Global Self-Care Federation
Dr. Bruce Randall	Health Canada, Canada
Dr. Haruka Yoshimatsu	JPMA
Mr. Eunkyoung Lee	MFDS, Republic of Korea
Dr. Risa Ishitani	MHLW/PMDA, Japan
Dr. Sean Curtis	PhRMA
Ms. Cindy Huang	TFDA, Chinese Taipei
Dr. Hiiti Silo	WHO

[3] At the Assembly Virtual meeting under Agenda item 1, Indonesian FDA, Indonesia was welcomed as a new ICH Observer.
[4] At the Assembly Virtual meeting under Agenda item 1, SECMOH, Ukraine was welcomed as a new ICH Observer.

ICH Other Participants

Dr. Rubina Bose	CDSCO, India
Ms. Margarita Contreras	COFEPRIS, Mexico
Ms. Lucy Teng	Health Canada, Canada
Mr. Jerry Stewart	PhRMA

ICH Secretariat

Mr. Masaki Fujita
Dr. Marine Lacroix
Dr. Anne Latrive
Ms. Nikoleta Luludi
Ms. Anca-Elena Matei
Dr. Dawn Ronan

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Opening of the ICH Assembly Meeting

The ICH Assembly Virtual Meeting, held on 17 – 18 November 2021, was chaired by Ms. Lenita Lindström-Gommers (Chair – EC, Europe) and Dr. Celia Lourenco (Vice-Chair – Health Canada, Canada).

The Assembly noted the Member Representatives and Observer Delegates as well as Ad hoc Observer delegates from EDA, Egypt; Indonesian FDA, Indonesia; and SECMOH, Ukraine.

Adoption of the Agenda

Assembly Decision/Action:

- The Assembly adopted the agenda without any modification.

1. Membership and Observership

The ICH Secretariat presented to the Assembly an overview of the applications for Membership and Observership processed since the last virtual ICH Assembly meeting in June 2021 and shared the ICH Management Committee's (MC's) recommendations on these applications in view of the eligibility criteria.

Assembly Decisions/Actions:

- The Assembly approved the following application for Membership under Article 11(1) of the ICH Articles of Association:
    - COFEPRIS, Mexico;
- The Assembly approved the following applications for Observership under Article 17.1(a) of the ICH Articles of Association:
    - EDA, Egypt;
    - Indonesian FDA, Indonesia;
    - SECMOH, Ukraine.

2. Procedural Matters

Standard Operating Procedures of ICH Working Groups

The ICH Secretariat informed the Assembly of three updates made by the ICH MC to the Standard Operating Procedures (SOPs) of ICH Working Groups (WGs) related to: publishing the names of Rapporteur Supporters on the ICH website in recognition of their work; clarifying the M2 recommendations approval process via a sign-off by M2 Topic Leaders followed by an approval by the Assembly Members; and ensuring more clarity on the matter for public comment on draft Guidelines undergoing a maintenance procedure by publishing under *Step 3* consultation a document listing only the changes to the core Guideline or Addendum.

Assembly Decisions/Action:

- The Assembly noted that the ICH MC had approved the SOPs of ICH WGs v11.0 at its Policy 3 TC on 18 October 2021, and that it will be published on the ICH website.

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

The Assembly was updated by the ICH Secretariat on the 2022 Work Plan and Multi-Annual Strategic Plan of the ICH Association.

Assembly Decision/Action:

- The Assembly approved the 2022 Work Plan and Multi-Annual Strategic Plan of the Association, which will be published on the ICH website.

4. Update on MedDRA

The MedDRA MC Chair reported to the Assembly on MedDRA activities and items for approval further to the MedDRA MC virtual meetings held on 25, 28 October and 4 November 2021.

The Assembly was updated on the steady increase in the global uptake of MedDRA, noting over 600 new subscribers in 2021 to-date, bringing the total number to over 7,400 organisations in more than 130 countries. The Assembly noted the continuing efforts by the MedDRA MC to ensure support to 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 preparation for initiating work for an Arabic MedDRA translation in 2022 in coordination with SFDA, Saudi Arabia; increasing the volume and types of MedDRA virtual trainings available to users; continued work on targeted mappings with other terminologies; development of new SMQs (Standardised MedDRA Queries) on *Sexual dysfunction, Neurodevelopmental delay,* and *Noninfectious myocarditis;* and development of a Russian translation of the Points to Consider (PtC) documents on *MedDRA Term Selection* and *MedDRA Data Retrieval and Presentation*. The Assembly was furthermore informed on ongoing IT activities including development of tools such as APIs (Application Programming Interfaces) to improve user experience of MedDRA which are expected for official release to users in early 2022.

Assembly Decision/Action:

- The Assembly approved the MedDRA MC Work Plan for 2022, which will be published on the ICH website.

5. Training

The Training Subcommittee Co-Lead updated the Assembly on ICH Training activities, including:

- Activities related to ICH Recognised Training Programmes, which are published on the ICH website;
- ICH WG training materials, including: Q13, S12, S1B(R1) and M7(R2) *Step 2* presentations recently published on the ICH website; as well as E9(R1), E2B(R3) and Q12 WG materials under development with FDA, United States Studios thanks to a grant it had provided for the development of ICH training materials, with the development of materials with other WGs also under discussion;
- Progress made by ICH's two Training Associates to develop online training materials on ICH Q1 Stability Guidelines (Introductory Overview Video already published on ICH website, to be shortly followed by additional Online Training Modules), in addition to materials on ICH M4 Common Technical Document Guidelines and ICH E2 Pharmacovigilance Guidelines (with ongoing work on development of Introductory Overview Videos for both);
- Considerations related to: short-term and long-term training goals; and planning on the use of ICH Training Budget based on goals; and resulting proposal to use the ICH Training Associate approach

to develop online training materials for more guidelines, as well as for the offering of tailored training.

Assembly Decisions/Actions:

- The Assembly noted the update and the Training Subcommittee's activities;
- The Assembly endorsed the proposed multi-year training approach including: general concept of ICH training on specific Guidelines and crosscutting training approach; working with three organisations as ICH Training Associates on developing online training materials, as well as offering of tailored training for regulatory authorities; proposed 5-year cost estimates and utilising a monitored approach with adjustments to be made annually based upon actual cost estimates;
- The Assembly supported entering into cooperation (with agreements to be put in place) with three proposed future Training Associates, in consideration of: the scope of work, duration of work; expected resource (human and financial), and any obligations or risks for the ICH Association;
- The Assembly supported monitoring the use of training materials developed by Training Associates to try to understand numbers of users undertaking training and user feedback on materials, with the Training Subcommittee to further consider the approach which might include seeking Training Associate support with this, as well as applying analytics to the new ICH Training Library being developed for the ICH website.

6. Financial Matters

ICH Finance Committee and 2022 Budget and 5-Year Projection Plan

The ICH Finance Committee Chair updated the Assembly on ongoing activities of the ICH Finance Committee, which includes representation from the ICH MC and MedDRA MC, and on ICH and MedDRA financial matters, including revisions to the 2022 ICH and MedDRA budget and 5-Year ICH and MedDRA budget projection for 2022-2026, including the 2023 ICH Membership fees and 2022 MedDRA subscription fees, as well as development of an asset preservation policy.

Assembly Decisions/Actions:

- The Assembly approved the multi-year training project to enter into cooperation with three organisations as ICH Training Associates, and its associated estimated costs (see also item #5);
- The Assembly approved the 2022 ICH and MedDRA budgets and supported the 5-Year ICH and MedDRA budget projection for 2022-2026, including 1 additional Secretariat staff from 2022 in view of increased training projects, along with continued expansion of ICH;
- The Assembly approved the 2023 ICH Membership fees, which are kept at the same stable level from 2016 for Founding and Standing Members, and increased to CHF 45 000 for non-Founding/non-Standing Members, and the 2022 MedDRA subscription fees kept at the same level as 2021 fees;
- The Assembly noted that the proposal for implementation of meeting participation fees for Observers, which had been discussed at the November 2020 meeting, was now postponed until 2024;
- The Assembly supported to launch a new call for expressions of interest from ICH Regulatory Members and Observers interested in being considered for ICH funding of training on ICH Guidelines in 2022, and confirmed this call as a standing yearly process, subject to yearly confirmation of budget.

7. New Topics & Strategic Discussions

The Assembly was informed by the Leads of the ICH MC New Topics Subcommittee on the status of and considerations for New Topics adopted by ICH which have not yet started, and on the conduct of the New Topics process for the 2022 cycle in view of ICH capacity.

Assembly Decisions/Actions:

<u>New Topics adopted with a delayed start</u>

- The Assembly endorsed the revised New Topic proposal and associated Concept Paper Outline on *General Considerations for Model-Informed Drug Development*, developed by the MIDD DG, for establishment of a M15 informal WG in the June 2022 timeframe;
- The Assembly noted the New Topics previously adopted with a delayed start of work and the expected timelines:
    - *Targeted revisions and additional issues in the ICH Q1 series/Q5C*: start date in June 2022, when the ICH Secretariat will send the call to ICH Members and Observers for nominations of experts [5];
    - *New Quality Topic on ICH Q6A and Q6B*: start date to be confirmed, no sooner than initiation of the above topic;
    - *Structured Product Quality Submissions*: start date when the M4Q(R2) EWG reaches *Step 2*, which is currently expected for end of 2022;
    - *Proposal for E4 on Dose Response Information to Support Drug Registration*: proposal to be re-evaluated after further MIDD DG discussions.

<u>2022 New Topics Process</u>

- The Assembly noted that, in view of the high number of topics already progressing in parallel, ICH has limited capacity to develop new topics for technical harmonisation in 2022, especially in some technical areas which are resource constrained such as quality, pharmacovigilance, and bioequivalence;
- The Assembly supported that the 2022 New Topic selection process would focus on a narrow scope, excluding the aforementioned areas, with Members and Observers invited to submit any proposals for New Topics in specific areas (e.g., safety/non-clinical) where these three criteria are met:
    - there is resource capacity;
    - the work can start immediately upon adoption of the topic;
    - the topic is considered of high public health impact;
- The Assembly noted that the deadline to submit proposals meeting these criteria to the ICH Secretariat is 10 December 2021.

[5] Post-Meeting Note: In line with the SOP for WGs Section 1.2.1, it is noted that the call for expression of interest to eligible ICH Members and Observers to nominate experts will be initiated several weeks prior to the intended start of WG activity, with the timeframe for the launch of the call to be confirmed by the ICH MC at its Technical Teleconference.

8. Election of ICH Assembly Chair and Vice Chair

Assembly Action/Decision:

- The Assembly re-elected Ms. Lenita Lindström-Gommers (EC, Europe) as Assembly Chair and elected Dr. Gabriela Zenhaeusern (Swissmedic, Switzerland) as Assembly Vice-Chair and noted that they would serve for a two-year mandate.

9. Status Update of Working Groups

The Assembly was invited to note the Work Plans and the written status (noted below) of the WGs. Furthermore, an oral update was provided by the Rapporteurs and Regulatory Chairs of the E6(R3) EWG; E8(R1) EWG; E11A EWG; E14/S7B IWG; M4Q(R2) EWG; M7(R2) Maintenance EWG/IWG; Q13 EWG; and QDG.

9.1. 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 providing guidance to WGs charged with developing new or revised guidance which may be of relevance to paediatric drug development.

9.2. 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)

Steps 3 and 4 for v1.1. of the Dose Forms and Routes of Administration for Individual Case Safety Reports in the E2B(R3) message were finalised in July 2020.

The Information Paper regarding the Use of ISO IDMP Standards in ICH E2B(R3) Messages was finalised in June 2021.

The E2B(R3) EWG/IWG continues its work, including on the development of Training Module III and the voice over for Training Module I, and on the update of the ICSR BFC (Backwards and Forwards Compatibility) Specification document (in view of an error correction and updates needed further to the revision of the EDQM User Guide).

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

The E2D(R1) EWG was established at the ICH meeting in November 2019.

The E2D(R1) EWG continues its work on the development of the E2D(R1) draft Technical Document.

Steps 1 and 2a/b are expected by November 2022. The E2D(R1) draft Technical document should be shared with the E2D(R1) Plenary Working Party (PWP) ahead of Step 1 sign-off, and is expected to be shared by August 2022.

9.4. E6(R3) EWG: Good Clinical Practice (Rapporteur: Dr. M. El Zarrad – FDA, United States; Regulatory Chair: Dr. Sweeney – EC, Europe)

The EWG published the draft principles of Good Clinical Practice (GCP) on the ICH website on 19 April 2021 and has organised a global web conference on 18 and 19 May 2021 to facilitate broad dissemination of and public engagement on the principles of GCP.

The Rapporteur and Regulatory Chair of the E6(R3) EWG provided an update to the Assembly on the EWG's activities on the E6(R3) draft Technical Document, including revisions to the overarching general principles guideline, with Annex 1 on traditional interventional trials being developed in parallel, and continues engaging with stakeholder representatives and EWG members during guideline development to ensure that stakeholders' perspectives on and experiences with clinical trials, specifically with GCP guidelines, are considered in developing ICH E6(R3).

Assembly Decisions/Actions:

- The Assembly noted the update on E6(R3) EWG activities;
- The Assembly noted that the report on the global web conference held on 18 and 19 May 2021 by the ICH E6(R3) EWG was published on the ICH website.

Steps 1 and 2 a/b for Principles and Annex 1 are expected by October 2022. The E6(R3) draft Technical document should be shared with the E6(R3) PWP ahead of Step 1 sign-off, and is expected by August 2022.

Endorsement of the revised E6(R3) Concept Paper updated in regards to Annex 2 is expected by September 2022. Timeline for Steps 1 and 2 a/b for Annex 2 is to be determined (work to be undertaken following reaching of Steps 1 and 2 a/b for Annex 1).

9.5. E8(R1) EWG: Revision on General Considerations for Clinical Studies (Rapporteur: Dr. LaVange – FDA, United States; Regulatory Chair: Dr. Kirisits – EC, Europe)

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

The E8(R1) EWG held a global public stakeholder meeting as per the GCP renovation plan on 31 October 2019 at the FDA, United States headquarters, and a report was published on the ICH website summarising the discussion from the global public stakeholder meeting on E8(R1).

The Rapporteur and Regulatory Chair of the E8(R1) EWG provided an update to the Assembly on the EWG's activities further to *Step 4* adoption in October 2021; including developing a training/change management plan in collaboration with the E6(R3) Rapporteur and Regulatory Chair to ensure new approaches are understood and implemented, in addition to the development of training materials.

Assembly Decision/Action:

- The Assembly noted the update on E8(R1) EWG activities.

Training materials are expected by December 2021.

9.6. E9(R1) EWG: Addendum to Defining the Appropriate Estimand for a Clinical Trial/Sensitivity Analyses (Rapporteur: Dr. Petavy – EC, Europe; Regulatory Chair: Dr. Ando – MHLW/PMDA, Japan)

Steps 3 and 4 were reached at the ICH meeting in November 2019.

The E9(R1) EWG is working on the development of training materials and videos.

The E9(R1) training materials and videos are expected to be finalised in 2021, further to which the E9(R1) EWG will be disbanded.

9.7. E11A EWG: Paediatric Extrapolation (Rapporteur: Dr. Yao – FDA, United States)

The E11A EWG was established in October 2017.

The E11A EWG continues its work on the E11A draft Technical Document and the development of examples to be included in training materials.

Steps 1 and 2a/b are expected by January 2022.

Assembly Decision/Action:

- The Assembly noted the update on E11A EWG activities, including the development of training materials after the E11A draft Guideline reaches *Step 2* to provide case examples (in replacement of an Annex), and supported that the EWG further considers to already make available a couple of examples during public consultation.

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

Steps 1 and 2a/b of the first stage of Q&As were reached electronically in August 2020 and the document underwent public consultation until end of December 2020. The E14/S7B IWG held a virtual meeting on the draft E14/S7B Q&As on 15 and 16 October 2020.

The Rapporteur of the E14/S7B EWG provided an update to the Assembly on the EWG's activities on the recent finalisation of the draft ICH E14/S7B Q&As; and the plan to develop additional technical trainings materials.

Assembly Decisions/Actions:

- The Assembly noted that the E14/S7B EWG had completed the draft ICH E14/S7B Q&As and that *Step 3* sign-off by Regulatory Topic Leaders will be initiated shortly, following which the Regulatory Members of the Assembly will be invited to adopt the Q&As under *Step 4*;
- The Assembly noted the plan for the *Step 4* Training Presentation to be posted simultaneously with the *Step 4* ICH E14/S7B Q&As document on the ICH website in January 2022, with further Training Materials to follow in June 2022.

9.9. E19 EWG: Optimization of Safety Data Collection (Rapporteur: Dr. Thanh Hai – FDA, United States; Regulatory Chair: Dr. Mol - EC, Europe)

The E19 draft Guideline was in public regulatory consultation in the ICH Member regions until end of September 2019.

The E19 EWG continues to address the comments received during the regional public consultation period which ended in September 2019.

Steps 3 and 4 are expected by April 2022.

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

The E20 EWG was established at the ICH meeting in November 2019.

The E20 EWG continues its work on the E20 draft Technical Document.

Steps 1 and 2a/b are expected by June 2023. The E20 draft Technical document should be shared with the E20 PWP ahead of Step 1 sign-off, and is expected to be shared by March 2023.

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

In October 2020, the MedDRA MC approved the development of an additional section of the Companion document on manufacturing quality issues.

V2.0 of the Companion document with a new section on product quality issues was released in October 2020.

Updated "MedDRA Term Selection: Points to Consider" and "MedDRA Data Retrieval and Presentation: Points to Consider" documents (based on MedDRA Version 24.0) in English, Japanese, Chinese, Korean, and Spanish translations were released in March 2021, and followed more recently by a new Russian translation of these documents. Updated versions of these documents will be made available in these languages in March 2022.

The M1 PtC WG continues its work on the revision of the Companion document and on the Points to Consider documents.

Release of v3.0 of the Companion document with a new section on manufacturing product quality issues in English and Japanese is expected in Q2 2022.

9.12. 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)

In October 2021, the Assembly endorsed the revised M2 Recommendation documents, further to which they were published on the ICH website.

The M2 EWG continues to work on: exploring/identifying technological risks or opportunities by discussing with ICH WGs at *Step 1* and reviewing *Step 3-4* documents; the development of 1-2 detailed process pilots for streamlining the ICH process for developing technical standards which would be submitted for ICH MC consideration; the development of a technical specification document for CeSHarP with the M11 EWG; and monitoring FHIR development and maturity progress that is relevant to ICH.

9.13. M4Q(R2) EWG: Revision of M4Q(R1) CTD on Quality guidance (Rapporteur: Dr. Yu - FDA, United States)

At the Virtual meeting in May 2020, the Assembly endorsed the proposal "Revision of M4Q(R1) CTD on Quality guidance". The M4Q(R2) informal WG was established further to the Q13 draft Guideline reaching Step 2a/b in July 2021, and the M4Q(R1) IWG was disbanded upon establishment of the M4Q(R2) informal WG with the support of the MC.

The informal WG Leader of the M4Q(R2) EWG provided an update to the Assembly on the EWG's activities and the Work Plan.

Assembly Decisions/Actions:

- The Assembly noted that the M4Q(R2) Concept Paper and Business Plan have been finalised and endorsed by the MC and the establishment of the M4Q(R2) EWG;
- The Assembly endorsed the appointment of the informal WG Leader as EWG Rapporteur.

Step 2 is expected by the end of 2022.

9.14. M7(R2) Maintenance EWG/IWG: Addendum to Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk (Rapporteur: Dr. Froetschl – EC, Europe)

Steps 1 and 2 a/b for the M7(R2) Q&As were reached in June 2020. Step 2 of the M7(R2) draft Guideline was reached in October 2021.

At the Virtual meeting in June 2021, the Assembly endorsed the Rapporteurship of the M7(R2) Maintenance EWG/IWG, in line with Annex 4 of the SOP on rotation of Rapporteurship of the group amongst the Founding Regulatory Members, to rotate to Dr. Aisar Atrakchi (FDA, United States), but for continuity reasons only after the M7(R2) Q&As reach Step 4, which is now expected by June 2022.

The Rapporteur of the M7(R2) EWG provided an update to the Assembly on the EWG's activities on the finalisation of the M7(R2) Q&As.

Assembly Decisions/Actions:

- *Steps 3* and *4* of the M7(R2) Q&As are expected by June 2022. The Assembly noted that, further to a recommendation from the WG supported by the MC, the publication format of the M7(R2) Guideline and Addendum for public consultation under *Step 3* includes for clarity only a document with a list of the revisions to the M7(R1) Guideline and the new monographs for the 7 new compounds;
- The Assembly noted that, further to MC support, the same publication format will also apply to all Maintenance WGs' draft Guidelines which would undergo public consultation under *Step 3*, for consistency.

9.15. M8 EWG/IWG: The Electronic Common Technical Document (eCTD) (Rapporteur: Mr. Gray – FDA, United States; Regulatory Chair: Ms. Puusaari – EC, Europe)

Step 4 of the eCTD v3.2.2 Q&As and Specification Change Request Document v1.31 was reached in June 2018.

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

The M8 EWG/IWG continues its work to monitor the status of implementation of eCTD v4.0.

Assembly Decision/Action:

- The Regulatory Members of the Assembly adopted under *Step 4* the eCTD v4.0 Q&A Document v1.6 and eCTD v3.2.2 Q&A Document v1.32.

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

The M10 draft Guideline was undergoing public regulatory consultation in the ICH Member regions until end of September 2019.

The M10 EWG continues to address the comments received during the regional public consultation period.

Steps 3 and 4 are expected by May 2022.

The M10 EWG will develop and finalise training materials shortly after completion of the M10 Guideline.

9.17. M11 EWG: Clinical electronic Structured Harmonized Protocol (CeSHarP) (Rapporteur: Ms. Combs – PhRMA; Regulatory Chair: Dr. Fitzmartin – FDA, United States)

The M11 EWG continues its work on the development of 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.

Steps 1 and 2 a/b for the Guideline, Template, and Technical Implementation Guide are expected by May 2022.

Steps 3 and 4 for Guideline, Template, and Technical Implementation Guide are expected by May 2023.

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

At the ICH meeting in November 2019, the MC endorsed the M12 Concept Paper and Business Plan, and the transition of the M12 informal WG to an EWG.

The M12 EWG continues its work on the development of the M12 draft Technical Document.

*Steps 1 and 2a/b are expected by May 2022. The M12 draft Technical Document should be shared with the M12 PWP ahead of Step 1 sign-off, and i**s** expected to be shared by March 2022.*

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

In July 2020, the MC approved the M13 Concept Paper and Business Plan, and the transition of the M13 informal WG to an EWG.

The M13 EWG continues its work on the development of the first M13 draft guideline in the series (M13A).

Steps 1 and 2a/b are expected by June 2022.

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

Assembly Decision/Action:

- The Assembly noted that the M14 informal WG will be established shortly after the meeting.

9.21. 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)

As noted at the Assembly meeting in November 2019, the group is working on two separate draft documents (i.e. for Q2(R2) and Q14), with the group to consider at a later stage whether they should be combined into a single draft Technical Document.

The Q2(R2)/Q14 EWG continues its work on the development of the two draft Q2(R2)/Q14 Technical Documents.

Steps 1 and 2a/b are expected by December 2021.

9.22. Q3C(R9) Maintenance EWG: Maintenance of the Guideline for Residual Solvents (Rapporteur: Dr. Hirose – MHLW/PMDA, Japan)

Steps 3 and 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 were reached in April 2021.

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

9.23. Q3D(R2) Maintenance EWG: Maintenance of the Guideline for Elemental Impurities (Rapporteur: Dr. Hirose – MHLW/PMDA, Japan)

Steps 1 and 2a/b of the Q3D(R2) revision for the cutaneous and transdermal products were reached in September 2020, and the Q3D(R2) Guideline underwent public consultation in the ICH Member regions until June 2021.

At the Virtual meeting in June 2021, the Assembly endorsed Dr. Roland Froetschl (EC, Europe) for the Rapporteurship of the group in line with Annex 4 of the SOP on rotation of Rapporteurship of the group amongst the Founding Regulatory Members, and that this rotation would be effective for continuity reasons only after Steps 3 and 4 are reached, which is now expected by January 2022.

The Q3D(R2) Maintenance EWG continues to address the comments received during the public regulatory consultation period.

Steps 3 and 4 of the Q3D(R2) revision for the cutaneous and transdermal products are expected by January 2022.

9.24. 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 MC approved the Q3E Concept Paper and Business Plan in July 2020, and the transition of the Q3E informal WG to an EWG.

The Q3E EWG and the Q9(R1) EWGs have identified a Q9(R1) liaison who is attending discussions of the Q3E EWG as needed to help both WGs coordinate their efforts, as the Q9(R1) work on the Quality Risk Management Framework may have an impact on the Q3E Guideline.

The Q3E EWG continues its work on the development of the Q3E draft Technical Document.

Steps 1 and 2a/b are expected by November 2022. The Q3E draft Technical Document should be shared with the Q3E PWP ahead of Step 1 sign-off and is expected to be shared by September 2022.

9.25. 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)

At the ICH meeting in November 2019, the MC endorsed the Q5A(R2) Concept Paper and Business Plan, and the transition of the Q5A(R2) informal WG to an EWG.

The Q5A(R2) EWG continues its work on the development of the Q5A(R2) draft Technical Document.

Steps 1 and 2a/b are expected by May 2022. The Q5A(R2) draft Technical Document should be shared with the Q5A(R2) PWP ahead of Step 1 sign-off.

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

In October 2020, the MC endorsed the Q9(R1) Concept Paper and Business Plan and the transition of the Q9(R1) informal WG to an EWG.

The Q3E EWG and the Q9(R1) EWGs have identified a Q9(R1) liaison who is attending discussions of the Q3E EWG as needed to help both WGs coordinate their efforts, as the Q9(R1) work on the Quality Risk Management Framework may have an impact on the Q3E Guideline.

Assembly Decision/Action:

- The Members of the Assembly endorsed under *Step 2a* the Q9(R1) Technical Document, further to which the Regulatory Members of the Assembly endorsed under *Step 2b* the Q9(R1) Draft Guideline which will now be released for public consultation.

Training materials are expected by August 2022.

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

At the ICH meeting in November 2019, the Assembly approved the development of training material on the Q12 Guideline, and further to the MC endorsement of the Q12 IWG Concept Paper in March 2020, the Q12 IWG was established in May 2020.

The Q12 Training Materials Modules 0-7 were finalised in June 2021.

The Q12 IWG is working on the finalisation of Training Material Module 8 and case studies as well as on a broad-audience video with the support of the FDA, United States studios.

The Q12 Training Materials are expected to be finalised by November 2021.

Assembly Decision/Action:

- The Assembly noted that the MC may consider the disbandment of the Q12 IWG following the finalisation of the broad-audience video, which is the last deliverable by the WG.

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

Steps 1 and 2a/b on the Q13 draft Guideline were reached in July 2021, further to which the draft Guideline was published for public consultation.

The Rapporteur of the Q13 EWG provided an update to the Assembly on the EWG's activities: the Q13 EWG continues to receive comments during the public regulatory consultation period and is working on the development of training materials.

Assembly Decisions/Actions:

- The Assembly noted the update on Q13 EWG activities;
- The Assembly noted that the Q13 EWG will be the first WG to use the new public consultation template; a feedback on its use is expected afterwards from the EWG.

Steps 3 and 4 are expected by November 2022.

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

Steps 1 and 2a/b on the S1B(R1) draft Guideline were reached in May 2021, further to which the draft Guideline was published for public consultation.

The 4th Status Report from Regulatory Authorities was finalised and published in August 2021.

The S1B(R1) EWG continues to collect comments during its public consultation period.

Steps 3 and 4 on the S1B(R1) Guideline are expected by May 2022.

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

Steps 3 and 4 for the S5(R3) Guideline were reached electronically in February 2020, and the S5(R3) Step 4 training presentation was published on the ICH website in June 2020.

No proposals for revisions of Annex 1 or 2 have been received at this time and therefore the group remains in a dormant state.

9.31. S12 EWG: Biodistribution Studies for Gene Therapy Products (Rapporteur: Dr. Hirata – MHLW/PMDA, Japan; Regulatory Chair: Dr. Serabian – FDA, United States)

Steps 1 and 2a/b on the S12 draft Guideline were reached in June 2021, further to which the draft Guideline was published for public consultation.

The S12 EWG continues to collect comments during the public consultation period.

Steps 3 and 4 on the S12 Guideline are expected by May 2023.

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

Assembly Decisions/Actions:

- The Assembly noted that the GDG has submitted its report to the MC on finalisation of its activities;

- The Assembly noted and supported the MC's decision to keep the GDG dormant until the MC requests or directs them to resume work.

9.33. Quality Discussion Group (QDG) (Rapporteur: Mr. Nosal – PhRMA; Regulatory Chair: Ms. Kruse – EC, Europe)

The Rapporteur and the Regulatory Chair of the QDG provided an update to the Assembly on the DG's activities: the QDG presented a summary of the QDG roadmap report and the reasons for extending the duration of the remit of the DG.

Assembly Decisions/Actions:

- The Assembly noted that the QDG has submitted its report to the MC on finalisation of its activities;
- The Assembly noted and supported the MC's decision to keep the QDG as a DG with low activity;
- The Assembly noted that the MC supported and approved the QDG roadmap report to be published on the ICH website.

9.34. Pharmacoepidemiology Discussion Group (PEpiDG) (Rapporteur: Dr. Uyama – MHLW/PMDA, Japan; Regulatory Chair: Dr. Ball – FDA, United States)

The PEpiDG developed a New Topic proposal, which has been submitted as part of the 2021 ICH New Topics cycle. At the Virtual meeting in June 2021, the Assembly supported the New Topic proposal and submission of the Concept Paper Outline.

Assembly Decision/Action:

- The Assembly noted that the PEpiDG has finalised its activities and that the MC has therefore confirmed its disbandment.

9.35. Model-Informed Drug Development Discussion Group (MIDD DG) (Rapporteur: Dr. Marshall – PhRMA; Regulatory Chair: Dr. Karlsson – EC, Europe

The MIDD DG was established in January 2021.

The MIDD DG continues its work to make a recommendation of a "roadmap", including appropriate sequencing and format for incorporating MIDD concepts into a proposal on ICH E4 (i.e., Revision, Addendum, Q&A).

Assembly Decision/Action:

- The Assembly endorsed the revised New Topic proposal and associated Concept Paper Outline on *General Considerations for Model-Informed Drug Development*, developed by the MIDD DG, for establishment of a M15 informal WG in the June 2022 timeframe (see item #7).

MIDD DG is expected to complete its activities by December 2021.

10. Q4B Maintenance

The ICH Representative for EDQM, on behalf of the Pharmacopoeial Discussion Group (PDG), presented to the Assembly an update regarding the progress of the pilot for the maintenance of Q4B Annexes and on PDG ongoing work regarding the engagement of other Pharmacopeias.

Assembly Decision/Action:

- The Assembly noted the update and that a complete evaluation and report on the pilot will be delivered to ICH in 2022.

11. Implementation of ICH Guidelines

Implementation by ICH Regulatory Members

Assembly Decision/Action:

- 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.

12. General Operational Matters

Assembly Decision/Action:

- The Assembly noted the report of the ICH Secretariat on general operational matters, including on the continuing expansion of ICH and level of participation of ICH Members and Observers in ICH WGs.

13. Communication

ICH 30th Anniversary Publication and Leaflet

Assembly Decision/Action:

- The Assembly noted the written update on the communication activities, including on: the publication of the ICH 30th Anniversary Publication on the ICH website in October 2021; the ongoing work on the development of an informative leaflet on ICH,; and the request to confirm how many printed copies of the publication and leaflet the ICH Members and Observers would like to receive to be sent shortly by the ICH Secretariat.

Press Release

Assembly Decision/Action:

- 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.

14. Organisation of Next Meetings

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

Assembly Decisions/Actions:

- The Assembly noted that the ICH MC agreed on the importance of ICH face-to-face meetings to efficiently progress ICH work and noted that the absence of meetings in 2020 and 2021 had delayed the work of some WGs and the reaching of consensus;
- The Assembly noted that the MC agreed to maintain planning for its next biannual meeting in Athens, Greece in May 2022 in a face-to-face setting, with planning to be made for hybrid in-person/virtual formats as needed, with this need to be further determined depending on the status of the COVID-19 pandemic;

- The Assembly noted that the MC had also agreed to maintain for the moment the biannual meeting in Incheon, Republic of Korea, in November 2022 in a face-to-face setting;
- The Assembly noted the dates and locations of its next meetings as per the below:
    - Tuesday 24 - Wednesday 25 May 2022 in Athens, Greece (final confirmation pending);
    - Tuesday 15 - Wednesday 16 November 2022 in Incheon, Republic of Korea (final confirmation pending);
    - Monday 12 – Tuesday 13 June 2023 in Vancouver, Canada (final confirmation pending);
    - Tuesday 31 October - Wednesday 1 November or Tuesday 14 - Wednesday 15 November 2023 in Europe (dates & location do be confirmed)
    - Tuesday 4 – Wednesday 5 June 2024 or Tuesday 21 – Wednesday 22 May 2024 in Asia (dates & location to be confirmed)

15. Any Other Business

ICH Award

The ICH MC informed the Assembly on a proposal for an ICH Award, intended to show recognition to those ICH WG experts meeting the criteria of a sustained participation in ICH over multiple years, having served in leadership role(s) and made outstanding contributions to ICH work.

Assembly Decision/Action:

- The Assembly supported the proposal for the ICH Award and noted that it would be further informed on details of the process in 2022.