14 July 2021

FINAL MINUTES

ICH ASSEMBLY VIRTUAL MEETING

2 – 3 JUNE 2021

Please find hereafter the final minutes of the Assembly Virtual Meeting held on 2 and 3 June 2021.

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
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List of Assembly Participants

Chair: Ms Lenita Lindström-Gommers

Vice-Chair: Dr. Celia Lourenco

ICH Assembly Members Representatives

Mr. Gustavo Mendes Lima Santos	ANVISA, Brazil
Mr. Diogo Penha Soares	ANVISA, Brazil
Dr. Joseph Damond	BIO
Dt. Wassim Nashabeh	BIO
Dr. Georgios Balkamos	EC, Europe
Dr. Harald Enzmann	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. Hironobu Hiyoshi	JPMA
Dr. Masafumi Yokota	JPMA
Dr. Younjoo Park	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. Peter K. Honig	PhRMA
Ms. Janet Vessotskie	PhRMA
Dr. Adel Alharf	SFDA, Saudi Arabia[1]
Dr. Andreas Pfenninger	Swissmedic, Switzerland
Dr. Jo-Feng Chi	TFDA, Chinese Taipei
Mr. Kevin Ming-Hsun Liu	TFDA, Chinese Taipei
Ms. Nihan Burul Bozkurt	TITCK, Turkey
Mr. Oğuzhan Koyuncu	TITCK, Turkey

ICH Management Committee Member Representatives

Dr. Milton Bonelli	EC, Europe
Dr. Junko Sato	MHLW/PMDA, Japan

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

ICH Assembly Coordinators

Ms. Ana Carolina Moreira Marino Araujo	ANVISA, Brazil
Mr. David Dee	BIO
Dr. Georgios Balkamos	EC, Europe
Ms. Giovanna Rizzetto	EFPIA
Ms. Jill Adleberg	FDA, United States
Dr. Padmaja Kamath	Global Self-Care Federation
Mr. Nick Orphanos	Health Canada, Canada
Ms. Siew Wei Chua	HSA, Singapore
Dr. Shinchiro Hirose	IGBA
Dr. Manabu Yanagisawa	JPMA
Ms. Miyoung Hyun	MFDS, Republic of Korea
Mr. Hirooki Tanabe	MHLW/PMDA, Japan
Dr. Xiangyu Wang (Replacement)	NMPA, China
Ms. Amanda Roache	PhRMA
Dr. Gabriela Zenhaeusern	Swissmedic, Switzerland
Ms. Pao-Hsuan Huang	TFDA, Chinese Taipei

ICH Assembly Technical Coordinators

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

ICH Assembly Standing Observers Delegates

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

ICH Assembly Observer Delegates

Dr. Farid Hasanov	AEC, Azerbaijan[2]
Mr. Sebastien Duarte	ANMAT, Argentina
Dr. Rainer Fendt	APIC
Dr. Murray Lumpkin	Bill and Melinda Gates Foundation
Dr. Lembit Rago	CIOMS
Ms. Margarita Contreras	COFEPRIS, Mexico
Ms. Miriam Jackeline Loera Rosales	COFEPRIS, Mexico
Dr. Ofra Axelrod	CPED, Israel
Dr. Susanne Keitel	EDQM
Dr. Hajed M. Hashan	GHC
Ms. Yenny Marcela Suarez Gonzaléz	INVIMA, Colombia
Ms. Janeen Skutnik-Wilkinson	IPEC
Dr. Wesal Haqaish	JFDA, Jordan
Dr. Colette Raidy	MOPH, Lebanon

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

Mr. Jamie Convisser	MHRA, UK[3]
Dr. Roshayati Mohamad Sani	NPRA, Malaysia
Dr. Analia Porras	PANDRH
Mr. David Ward	PIC/S
Ms. Anastasia Nikitina	Roszdravnadzor, Russia
Ms. Fortunate Ntombi Bhembe	SADC
Ms. Portia Nkambule	SAHPRA, South Africa
Ms. Aida Malkhasyan	SCDMTE, Armenia
Mr. Avi Rebera	TGA, Australia
Dr. Kevin Moore	USP

ICH Invited Participants

Mr. Jerry Stewart (for #7)	PhRMA
Mr. Mick Foy	MedDRA MC Chair; MHRA, UK

ICH Additional Participants

Dr. Agnès Saint-Raymond	EC, Europe
Mr. John Punzi	Global Self-Care Federation
Mr. Bruce Randall	Health Canada, Canada
Dr. Haruka Yoshimatsu	JPMA
Mr. Teruyoshi Ehara	MHLW/PMDA, Japan
Dr. Xiaoling Qin	NMPA, China
Dr. Michelle Rohrer	PhRMA

Other Participants

Ms. Aurélie Farfaro	Global Self-Care Federation
Ms. Lucy Teng	Health Canada, Canada

ICH Secretariat

Ms. Clarisse Bertherat
Mr. Masaki Fujita
Dr. Anne Latrive
Ms. Nikoleta Luludi
Dr. Dawn Ronan

[3] At the Assembly Virtual meeting under Agenda item 1, MHRA, UK was welcomed as a new ICH Observer.

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Opening of the ICH Assembly Meeting

The ICH Assembly Virtual Meeting, held on 2-3 June 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 AEC, Azerbaijan and MHRA, UK.

Adoption of the Agenda

Assembly Decision/Action:

- The Assembly adopted the agenda with addition of an item under Any Other Business regarding an award which ICH had been selected to receive.

1. 2020 Annual Report of the Association

The ICH Secretariat presented to the Assembly the 2020 Annual Report of the Association, developed by the Secretariat with the input of the ICH MC and MedDRA MC on the activities undertaken in 2020 on behalf of the ICH Association.

Assembly Decision/Action:

- The Assembly approved the 2020 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 2020 on behalf of the ICH Association.

2. 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 November 2020 and shared the ICH 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:
    - SFDA, Saudi Arabia;
- The Assembly approved the following applications for Observership under Article 17.1(a) of the ICH Articles of Association:
    - AEC, Azerbaijan;
    - MHRA, UK.

3. Update on MedDRA

The MedDRA MC Chair reported to the Assembly on MedDRA activities further to the MedDRA MC virtual meetings held on 18, 20 and 27 May 2021.

The Assembly was updated about the steady increase in the number of MedDRA subscribers, noting over 540 new subscribers in the last year, bringing the total number to 6,800 organisations in more than 127 countries, and noted the continuing efforts by the MedDRA MC to ensure support to the needs of MedDRA users. This included: ongoing translation development including initiation of a multiyear project of translating MedDRA into the remaining languages of the European Economic Area (EEA) in collaboration with EC, Europe and individual Member State Regulatory Authorities and support for development of an Arabic MedDRA translation; increasing the volume and types of MedDRA virtual training offerings available to users; continued work on targeted mappings with other terminologies; development of a new SMQ (Standardised MedDRA Query) on *Sexual dysfunction;* and approval of development of a Russian translation of the Points to Consider (PtC) documents on *MedDRA Term Selection* and *MedDRA Data Retrieval and Presentation*. The Assembly additionally noted ongoing IT activities including development of APIs (Application Programming Interfaces) to improve user experience of MedDRA and which are expected for official release to users towards end of 2021.

Assembly Decisions/Actions:

- The Assembly noted the decisions taken by the MedDRA MC during its meeting on 18, 20 and 27 May 2021, including the re-election of Mr. Mick Foy (MHRA, UK) as MedDRA MC Chair for a further one-year term;
- The Assembly gave its approval in principle for the MedDRA MC to authorize MSSO to proceed, prior to Assembly approval of the MedDRA Budget, of already contracting IT and local support staff needed for future years support, as well as an Arabic translation vendor;
- The Assembly supported the conduct of a study in 2021 to support ICH considerations on long-term MedDRA operations, and approved a revision to the 2021 MedDRA Budget to support this activity.

4. Financial Matters

ICH Finance Committee

The Assembly was informed by the ICH Finance Committee Chair on ongoing work by the recently established ICH Finance Committee, which includes representation from the ICH MC and MedDRA MC, on: alignment of ICH and MedDRA budget cycles with revision of ICH MC Rules of Procedure (RoP); approach of periodic 5-year cycle of adjustment of ICH Membership Fees and MedDRA Subscription Fees with revision of ICH MC and MedDRA MC RoP; strategy for ICH capital preservation; and review of the 2020 Closing Expenses and Income, including observation of significant underspend in 2020 largely attributable to the COVID-19 pandemic which resulted in lower than budgeted costs for items including Operating Costs (particularly travel), Meetings, Training and Communication (particularly 30th ICH Anniversary commemoration).

Assembly Decision/Action:

- The Assembly noted the report of the ICH Finance Committee and the ICH MC's recent approval of recommendations.

2020 Financial Statements

The Assembly was informed by the ICH Secretariat on ICH financial matters, including on the 2020 Audited Accounts and Financial Statements; and the 2020 ICH Closing Expense Report.

Assembly Decision/Action:

- The Assembly approved the 2020 Audited Accounts and Financial Statements of the ICH Association which will be filed with the 2020 tax return of the ICH Association.

5. Procedural Matters

Assembly Rules of Procedure, ICH Management Committee Rules of Procedure and MedDRA Management Committee Rules of Procedure

- ***Assembly Rules of Procedure***

The ICH Secretariat presented to the Assembly amendments proposed to the Assembly Rules of Procedure (RoP) related to: clarifying the rules on confidentiality and on additional participants at meetings.

Assembly Decision/Action:

- The Assembly noted the proposed changes to the ICH Assembly RoP v9.0, and approved the ICH Assembly RoP v10.0, which will be published on the ICH website.

- ***ICH Management Committee Rules of Procedure***

The ICH Secretariat presented to the Assembly updates to the ICH MC RoP related to: clarifying the rules on confidentiality and on additional participants at meetings; addition of a rule on the illustrative use of the ICH logo by third parties; and adjustment to the ICH budget approval cycle and periodic adjustment of ICH Membership Fees further to the recommendations of the ICH Finance Committee.

Assembly Decision/Action:

- The Assembly noted the proposed changes to the ICH MC RoP v10.0 and that the MC approved the ICH MC RoP v11.0 at its virtual meeting in May 2021, which will be published on the ICH website.

- ***MedDRA Management Committee Rules of Procedure***

The ICH Assembly noted updates to the MedDRA MC RoP related to: virtual meetings in extraordinary circumstances; removing outdated text; clarifying process for press releases; and addition of principles for 5-year budget planning and for periodic adjustment of the MedDRA subscription fees further to the recommendations of the ICH Finance Committee.

Assembly Decision/Action:

- The Assembly noted the proposed changes to the MedDRA MC RoP v5.0 and that the MedDRA MC approved the ICH MC RoP v6.0 at its virtual meeting in May 2021, which will be published on the ICH website.

- ***Application Forms for Expedited Membership Procedure***

Assembly Decision/Action:

- The Assembly noted the publication shortly on the ICH website of new application forms in view of the expedited procedure for ICH Membership approved in November 2020, and referred to in Article 11(1) and 11(2) third paragraph of the ICH Articles of Association.

6. New Topic Process & Strategic Discussions

2021 New Topics Proposals

The Assembly was informed by the ICH MC New Topic Subcommittee co-Lead on the New Topic proposals which were submitted by ICH Members and Observers in December 2020 as part of the limited call only for New Topics meeting need for high-impact and urgent regulatory harmonisation, and on the outcome of the review and assessment of proposals by the ICH MC.

Assembly Decision/Action:

- The Assembly endorsed the proposal on *General principles on planning and designing pharmacoepidemiological studies that utilize real-world data for safety assessment of a medicine,* with an informal WG to be established to start in the second half of 2021. A Concept Paper outline will be provided for Assembly endorsement electronically in the June 2021 timeframe;
- The Assembly endorsed the proposal on *Stability Testing Guideline (ICH Q1) –Targeted revisions and additional issues in the ICH Q1 series/Q5C,* with an informal WG to be established with a delayed start, not earlier than Q1 2022. The starting time will be re-assessed by the MC ahead of the November 2021 meeting based on progress of other ICH activities in the Quality area. A Concept Paper outline will be provided for Assembly endorsement electronically in the June 2021 timeframe;
- The Assembly endorsed the proposal on *Proposal for a New Quality Topic on ICH Q6A and Q6B,* with an informal WG to be established with a delayed start following the above topic and to be re-assessed by the MC ahead of the November 2021 meeting based on progress of other ICH activities in the Quality area. A Concept Paper outline will be provided for Assembly endorsement electronically in the June 2021 timeframe;
- The Assembly noted ongoing efforts by Regulatory Members on collection of data on the topic of N-Nitrosamines, in order to further prioritise an appropriate ICH action related to N-Nitrosamines.

Reflection Paper on Patient-Focused Drug Development

The Assembly was updated on comments received during the public consultation on the ICH Reflection Paper on *Patient-Focused Drug Development* (PFDD), which was endorsed by the Assembly in November 2020 and published for public consultation until March 2021.

Assembly Decision/Action:

- The Assembly noted that a very good level of support had been received overall via the public consultation, with comments submitted by 38 stakeholders including in particular patient organisations, learned societies, and private companies;
- The Assembly endorsed the revised ICH Reflection Paper on PFDD, which integrates re-wording reflective of public feedback to clarify proposals compatible with ICH's scope, membership and nature;
- The Assembly noted that other comments received included recommendations for the development of the proposed guidance and recommendations on the use of existing tools / research / initiatives (and associated scientific references), which are considered relevant for future guideline work and are intended to be flagged in the upcoming activities for expert consideration;
- The Assembly supported the "Outcome of Public Consultation" document for publication on the ICH website.

7. 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.

Implementation Survey

The Assembly noted the implementation survey launched in December 2020 by CIRS (Center for Innovation in Regulatory Science), an independent third-party, to inform the elections for Elected MC Representatives and to provide an opportunity to ICH Observers interested in future ICH Membership to reference the survey findings in support of their application. The Assembly noted that this was the

second implementation survey performed to-date to support understanding of the level of implementation and adherence to ICH Guidelines within Regulatory Member and Observer countries/regions.

Representatives from CIRS joined the virtual meeting to present the Assembly the results of the phase 2b implementation survey. The Assembly was pleased to note that the survey results demonstrate good progress made by Regulatory Authorities in implementing ICH Guidelines since the first survey in 2019.

Assembly Decision/Action:

- The Assembly noted the outcome of the implementation survey.

8. Appointment of ICH Management Committee Elected Representatives

The Assembly was informed that in line with the ICH Articles of Association, up to eight Elected MC Representatives representing up to four Regulatory Members could be elected as MC Elected Representatives, and up to four Elected MC Representatives representing up to two Industry Members could be elected as MC Elected Representatives. The term for MC Elected Representatives is three years. The Assembly furthermore noted the eligibility criteria defined in Articles 30(1) and 31(1) of the ICH Articles of Association and ICH MC Rules of Procedure (RoP) Sections 2.2.1 and 2.3.1.

The Assembly noted that the following ICH Members had submitted an application: ANVISA, Brazil; MFDS, Republic of Korea; NMPA, China; BIO; Global Self-Care Federation and IGBA. The Applicants were each invited to say a few words to the Assembly to present their applications and interest in participation in the ICH MC. The ICH MC presented to the Assembly their considerations regarding the Applicants' eligibility.

In line with Assembly RoP Section 3.6.4, the Assembly Members were invited to vote via secret ballot.

Assembly Decisions/Actions:

- The Assembly elected the following Regulatory Member Applicants as ICH MC Elected Representatives:
    - Mr. Diogo Penha Soares and Mr. Gustavo Mendes Lima Santos from ANVISA, Brazil;
    - Dr. Seogyoun Kang and Dr. Youngjoo Park from MFDS, Republic of Korea;
    - Dr. Sheng Yang and Dr. Siyuan Zhou from NMPA, China;
- The Assembly elected the following Industry Member Applicants as ICH MC Elected Representatives:
    - Dr. Joseph Damond and Dr. Wassim Nashabeh from BIO;
    - Dr. Nicholas Cappuccino and Ms. Beata Stepniewska from IGBA.

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; S1B(R1) EWG; S12 EWG; Q13 EWG; GDG; MIDD DG; 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 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– EFPIA)

At the ICH meeting in November 2019, the MC endorsed the transition of the E2D(R1) informal WG to an EWG.

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

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.

Steps 1 and 2a/b are expected by November 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 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 Good Clinical Practice.

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 Decision/Action:

- The Assembly noted the work conducted by the E6(R3) EWG and progress towards *Steps 1/2*.

Steps 1 and 2 a/b for Annex 1 are expected by September 2022. The E6(R3) draft Technical document should be shared with the E6(R3) PWP ahead of Step 1 sign-off, and a virtual meeting between the E6(R3) EWG and PWP is planned in 2021/2022.

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 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) draft Guideline was in public regulatory consultation in the ICH Member regions until end of October 2019.

The Rapporteur and Regulatory Chair of the E8(R1) EWG provided an update to the Assembly on the EWG's activities on addressing the public comments received during the regional public consultation period which ended in October 2019, including the decision to remove two previous annexes on i) summary of ICH Efficacy guidance by E8(R1) topic area, which is considered for potential publication on the ICH website separately, and ii) table of critical to quality factors cross-referenced with ICH Efficacy guidance, which is considered for training materials.

Assembly Decision/Action:

- The Assembly noted the work conducted by the E8(R1) EWG and progress towards *Steps 3/4*.

Steps 3 and 4 are expected by July 2021. 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)

Step 4 was reached at the ICH meeting in November 2019.

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

The E9(R1) training materials are expected to be finalised by mid-2021.

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

In October 2017, the MC endorsed the E11A Concept Paper and Business Plan and the transition of the E11A informal WG to an EWG.

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

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

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

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 public meeting on the draft E14/S7B Q&As on 15 and 16 October 2020.

The E14/S7B IWG continues to address the comments received during the regional public consultation period which ended in December 2020.

Step 3 and 4 of the first stage of Q&As are expected by November 2021.

9.9. E19 EWG: Optimization of Safety Data Collection (Rapporteur: Dr. 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 June 2022.

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

At the ICH meeting in November 2019, the MC endorsed the E20 Concept Paper and Business Plan, and the transition of the E20 informal WG to an EWG.

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

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 2022.

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

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.

The M1 PtC WG continues its work on the revision of the Companion document, which is expected to be finalised by December 2021.

Release of v3.0 of the Companion document with a new section on manufacturing product quality issues is expected in December 2021.

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)

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 (further to the M2 WG's proposal which was presented to the MC at its biannual meeting in November 2020); 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(R1) IWG: (CTD-Quality) IWG: Addressing CTD-Q-Related Questions (Rapporteur: Dr. Schmuff – FDA, United States)

At the Virtual meeting in May 2020, the Assembly endorsed the proposal "Revision of M4Q(R1) CTD on Quality guidance", with an M4Q(R2) informal WG to be established with a delayed start once the Q13 EWG would reach Steps 1 and 2a/b.

No questions were so far received following the implementation of the revised M4 Granularity Document which would need to be addressed by the M4Q(R1) IWG, and the M4Q(R1) IWG therefore remains in a dormant state until the establishment of the M4Q(R2) informal WG.

As agreed at the virtual ICH meeting in May 2020, the M4Q(R2) informal WG will be established further to the Q13 draft Guideline reaching *Step 2a/b*, which is currently expected for June 2021, and the MC supported that the M4Q(R1) IWG be disbanded upon establishment of the M4Q(R2) informal WG.

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. As part of Steps 2a/b, the Assembly Members / Regulatory Members of the Assembly pre-approved a change to be included in the future M7(R2) draft Guideline which is referenced in the Q&As, so that the change could be published alongside the M7 Q&As as a support document.

The M7(R2) Maintenance EWG/IWG continues its work on the finalisation of the M7(R2) Q&As and on the M7(R2) draft Guideline, which will include as revisions: the draft addendum, the pre-approved change in table 4, and the pre-approved error correction.

Steps 1 and 2a/b of the M7(R2) draft Guideline are expected in the first half of 2021.

Steps 3 and 4 of the M7(R2) Q&As are expected by December 2021.

Assembly Decisions/Actions:

- The Assembly noted that the MC supported the WG's proposal to divide the M7(R2) Guideline into two documents, with (1) the core Guideline and (2) one addendum document with all the monographs, and with both documents being interlinked via the URLs of the documents on the ICH webpage;
- The Assembly endorsed Dr. Aisar Atrakchi (FDA, United States) for 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, and supported the MC recommendation that the rotation of the Rapporteurship, initially planned for June 2021, would occur for continuity reasons only after the M7(R2) Q&As reach *Step 4*, which is currently expected by December 2021.

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 v4.0 Q&As v1.5 and Specification for Submission Format 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.

9.16. M10 EWG: Bioanalytical Method Validation (Rapporteur: Dr. Ishii-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 November 2021.

The M10 EWG will develop and finalise training materials within a 6-month timeframe 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 Specification document; 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, Basis of Requirements, and Technical Description are expected by September 2021.

Steps 1 and 2 a/b for the Full Technical Specification for Electronic Exchange are expected by February 2022.

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.

The M12 draft Technical Document should be shared with the M12 PWP ahead of Step 1 sign-off, and is expected to be shared by March 2022.

Steps 1 and 2a/b are expected by May 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 M13 draft Technical Document.

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

9.20. 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) and Q14 Technical Documents.

Steps 1 and 2a/b are expected by June 2021[4]

9.21. 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.

Assembly Decision/Action:

- The Assembly endorsed Dr. Akihiko Hirose (MHLW/PMDA, Japan) for the Rapporteurship of the Q3C(R9) Maintenance EWG, in line with Annex 4 of the SOP on rotation of Rapporteurship of the group amongst the Founding Regulatory Members, to be effective in June 2021.

9.22. 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 is currently undergoing public consultation in the ICH Member regions[5].

Steps 3 and 4 are expected by August 2021.

Assembly Decision/Action:

- 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 supported the MC recommendation that the rotation of Rapporteurship of the Q3D(R2) Maintenance EWG would be effective for continuity reasons only after *Steps 3* and *4* are reached, which is currently expected by August 2021.

9.23. 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.

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[4] Post-meeting note: following the meeting it was confirmed that *Steps 1* and *2a/b* are now expected by December 2021.

[5] Post-meeting note: following the meeting it was confirmed that the public consultation will be finalised by June 2021.

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

Additionally, as the Q9(R1) work on the Quality Risk Management Framework may have an impact on the Q3E Guideline, the MC supported that the Q3E EWG and the Q9(R1) EWGs identify a Q9(R1) liaison who will attend discussions of the Q3E EWG as needed to help both WGs coordinate their efforts.

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.

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

9.24. 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.

The Q5A(R2) draft Technical Document should be shared with the Q5A(R2) PWP ahead of Step 1 sign-off and is expected to be shared by September 2021.

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

9.25. Q9(R1) EWG: Quality Risk Management (acting 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 Q9(R1) EWG continues its work on the development of the Q9(R1) draft Technical Document.

Additionally, as the Q9(R1) work on the Quality Risk Management Framework may have an impact on the Q3E Guideline, the MC supported that the Q3E EWG and the Q9(R1) EWGs identify a Q9(R1) liaison who will attend discussions of the Q3E EWG as needed to help both WGs coordinate their efforts.

Steps 1 and 2a/b are expected by September 2021, further to which the WG is expected to begin development of training materials to be finalised by May 2022.

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

Steps 3 and 4 for the Q12 Guideline were reached at the ICH meeting in November 2019.

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 IWG is working on the finalisation of Training Material Module 8 and case studies.

The Q12 Training Material Module 8 and case studies are expected to be finalised by November 2021.

Assembly Decision/Action:

- The Assembly noted that the Q12 IWG experts had signed-off on the Q12 Training Materials Modules 0-7, which will be shortly published on the ICH website.

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

The Rapporteur and Regulatory Chair of the Q13 EWG provided an update to the Assembly on the EWG's activities on the finalisation of the Q13 draft Technical Document, which consists of a core document focusing on fundamentals of Continuous Manufacturing, and of five annexes focusing on specific continuous manufacturing technologies.

Assembly Decision/Action:

- The Assembly noted that the Q13 EWG had completed the draft Technical Document and that *Step 1* sign-off by experts would be initiated shortly, further to which the Assembly would be invited electronically to endorse the draft Guideline under *Step 2a/b* and the draft Q13 Guideline would be released for public consultation.

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

9.28. 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 Rapporteur and Regulatory Chair of the S1B(R1) EWG provided an update to the Assembly on the EWG's activities further to the finalisation of the S1B(R1) draft Technical Document in April, including on finalisation of the 4th Status Report from Regulatory Authorities and planning for a scientific publication in 2021.

Assembly Decision/Action:

- The Assembly noted the update on S1B(R1) EWG activities.

The 4th Status Report from Regulatory Authorities is expected to be finalised for publication in June 2021.

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

9.29. 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.

As per the maintenance process endorsed in March 2019, the S5(R4) Maintenance EWG will stay in a dormant state for at least 1 year after Step 4, i.e. until March 2021, and would become active if needed if proposals for revisions of Annex 1 or 2 are received. No proposals were received at this time.

Assembly Decisions/Actions:

- The Assembly endorsed the acting Rapporteur Dr. Guenter Waxenecker (EC, Europe), who was the Rapporteur of the S5(R3) Maintenance EWG, for the Rapporteurship of the S5(R4) Maintenance EWG;
- The Assembly noted that no proposals for revisions of Annex 1 or 2 have been received at this time and that therefore the group remains in a dormant state.

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

At the ICH meeting in November 2019, the MC endorsed the S12 Concept Paper and Business Plan, and the transition of the S12 informal WG to an EWG.

The Rapporteur and Regulatory Chair of the S12 EWG provided an update to the Assembly on the EWG's finalisation of the draft S12 Technical Document which had been signed off by experts at *Step 1* in May 2021.

Assembly Decision/Action:

- The Assembly endorsed under *Step 2a* the S12 draft Guideline, further to which the Regulatory Members of the Assembly endorsed under *Step 2b* the S12 draft Guideline which will be released for public consultation.

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

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

At the Virtual meeting in May 2020, the MC supported that the term of the GDG be extended by up to one year until June 2021, with a view to disbanding the group earlier if it would finalise its activities sooner, and with the frequency of its TCs to be reduced.

The Rapporteur and Regulatory Chair of the GDG provided an update to the Assembly on the DG's activities as per its remit on i) information sharing and prioritisation, ii) identification of New Topic(s) for future Guideline(s), and iii) development of a New Topic proposal.

Assembly Decision/Action:

- The Assembly noted the update on the GDG activities.

Finalisation of recommendations for a draft new Topic Proposal is expected by July 2021.

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

The QDG developed 2 New Topic proposals, which have been submitted as part of the 2021 ICH New Topics cycle.

The Rapporteur and Regulatory Chair of the QDG provided an update to the Assembly on the DG's completion activities as per its remit on recommendation and prioritisation on assessment of ICH Q and relevant M Guidelines that warrant revision, updates, annexures, clarifications, Q&A, a new potential guideline, implementation plans and/or training. The QDG plans to submit its roadmap by August 2021 to provide a perspective of the future Quality landscape of scientific innovations, patient need and associated regulatory expectations and convey recommendations for the prioritization of future modernization of the remaining ICH Quality Guidelines.

Assembly Decision/Action:

- The Assembly noted the update on the QDG activities and planned completion of activities by August 2021.

The MC approved the QDG to operate for a 2-year term beginning on the date of MC approval of the QDG Remit (i.e. November 2018), and, further to the MC approving an extension of its term, the QDG is now expected to finalise its work in August 2021.

9.33. 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.

The PEpiDG continues its work on prioritisation of proposed topics based on feasibility, needs and importance for harmonisation.

The MC approved the PEpiDG to operate for a 2-year term. The PEpiDG is expected to have completed its work by early 2022.

9.34. 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 Rapporteur and Regulatory Chair of the MIDD DG provided an update to the Assembly on the DG's activities as per its remit to finalise the scope of a Guideline on Model-Informed Drug Development (MIDD), make a recommendation for 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 noted the update on the MIDD DG activities.

The proposal for the scope of a Guideline on MIDD is expected by October 2021 or earlier. The MIDD DG is expected to complete its activities by December 2021.

10. General Operational Matters

Assembly Decision/Action:

- The Assembly noted the written 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.

11. Training

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

- Activities related to ICH Recognised Training Programmes, which are published on the ICH website;
- ICH WG training materials, including: a Q3C(R8) *Step 4* introductory training presentation recently published on the ICH website and Q12 Training Materials (Modules 0-7) expected to be published shortly; 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;

- Work to collect from ICH Regulatory Members web links for the ICH website to make available translations of ICH Guidelines;
- 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 followed by additional Online Training Modules), ICH M4 Common Technical Document Guidelines, and ICH E2 Pharmacovigilance Guidelines (work being initiated on Introductory Overview Videos);
- ICH MC support of 2021 applications for ICH Funding of Regulatory Training from ICH Regulatory Members and Regulatory Observers: ANVISA, Brazil; Health Canada, Canada; JFDA, Jordan; MHLW/PMDA, Japan; and NMPA, China;
- Considerations related to: short-term and long-term training goals; planning on the use of ICH Training Budget based on goals; and finding efficiencies in process.

Assembly Decision/Action:

- The Assembly noted the update and the Training Subcommittee's activities.

12. Communication

ICH 30th Anniversary

Assembly Decision/Action:

- The Assembly noted an upcoming publication to be made available on the ICH website to celebrate ICH's important 30th Anniversary milestone reached in 2020 and the significant support being generously provided to coordinate the development of the publication by three individuals formally involved closely with ICH activities.

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.

13. Organisation of Next Meetings

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

Assembly Decisions/Actions:

- The Assembly noted that, due to the COVID-19 pandemic, the ICH MC had considered necessary to cancel the next face-to-face meeting planned to be held in November 2021. The meeting will be held in a virtual format instead;
- The Assembly noted the dates and locations of its next meetings as per the below:
    - Wednesday 17 – Thursday 18 November 2021 in a virtual setting
    - 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);
- May/June 2023 in the Americas (location and dates to be confirmed).

14. Any Other Business

Award to ICH

Assembly Decision/Action:

- The Assembly welcomed news that ICH had been selected by DIA to receive the 2021 DIA Global Award for Outstanding Contribution to Health.