9 August 2018

FINAL MINUTES
ICH Assembly
6-7 June 2018, Kobe, Japan

Please find hereafter the final minutes of the Assembly meeting held in Kobe, Japan on 6-7 June 2018.

List of Assembly Participants

ICH Assembly Member Representatives:

Ms. Tatiana Cambraia Sa Lowande	ANVISA, Brazil
Ms. Cammilla Horta Gomes	ANVISA, Brazil
Ms. Lila Feisee	BIO
Dr. Wassim Nashabeh	BIO
Mr. Siyuan Zhou	CFDA, China
Dr. Georgios Balkamos	EC, Europe
Ms. Lenita Lindström-Gommers (Chair)	EC, Europe
Dr. Tomas Salmonson	EC, Europe
Dr. Sabine Luik	EFPIA
Mr. Pär Tellner	EFPIA
Dr. Theresa Mullin	FDA, US
Dr. Celia Lourenco	Health Canada, Canada
Ms. Catherine Parker	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. Nakyung Kim	MFDS, Republic of Korea
Dr. WonSik Lee	MFDS, Republic of Korea
Dr. Nobumasa Nakashima	MHLW/PMDA, Japan
Dr. Toshiyoshi Tominaga (Vice-Chair)	MHLW/PMDA, Japan
Mr. Naoyuki Yasuda	MHLW/PMDA, Japan
Dr. Peter K. Honig	PhRMA
Mr. Rich Moscicki	PhRMA
Dr. Petra Doerr	Swissmedic, Switzerland
Ms. Cordula Landgraf	Swissmedic, Switzerland
Ms. Chao-Yi (Joyce) Wang	TFDA, Chinese Taipei[1]
Mr. Motohito Nishizawa	WSMI

ICH Management Committee Member Representatives:

Prof. Spiros Vamvakas	EC, Europe
Ms. Pujita Vaidya	FDA, US

ICH Assembly Standing Observer Delegates:

Dr. David Jefferys	IFPMA
Mr. Mike Ward	WHO

ICH Assembly Observer Delegates:

Dr. Eun Hee Kim	APEC
Mrs. Marieke van Dalen	APIC
Ms. Charunee Krisanaphan	ASEAN
Dr. David Mukanga	Bill and Melinda Gates Foundation
Dr. Celeste Sánchez González	CECMED, Cuba
Dr. Lembit Rägo	CIOMS
Mr. John Patrick Mwesigye	EAC
Dr. Susanne Keitel	EDQM
Dr. Hajed M. Hashan	GHC

[1] At the Assembly meeting in Kobe under Agenda 13, TFDA, Chinese Taipei was welcomed as a new ICH Member.

Ms. Janeen Skutnik Wilkinson	IPEC
Mrs. Aliya Kessikova	National Center, Kazakhstan
Dr. Ramli Zainal	NPRA, Malaysia[2]
Dr. Analía Porrás	PANDRH
Mr. David Churchward	PIC/S
Mr. Fortunate Ntombi Bhembe	SADC
Ms. Nihan Burul Bozkurt	TITCK, Turkey[3]
Dr. Kevin Moore	USP

ICH Assembly Coordinators:

Ms. Ana Carolina Moreira Marino Araujo	ANVISA, Brazil
Ms. Lila Feisee	BIO
Dr. Wei Zhou	CFDA, China
Dr. Georgios Balkamos	EC, Europe
Mr. Pär Tellner	EFPIA
Ms. Amanda Roache	FDA, US
Mr. Nick Orphanos	Health Canada, Canada
Ms. Siew Wei Chua	HSA, Singapore
Dr. Shinichiro Hirose	IGBA
Mr. Mitsuo Mihara	JPMA
Ms. Pan Soon Kim	MFDS, Republic of Korea
Mr. Fumihito Takanashi	MHLW/PMDA, Japan
Ms. Camille Jackson	PhRMA
Ms. Cordula Landgraf	Swissmedic, Switzerland

ICH Assembly Technical Coordinators:

Dr. Milton Bonelli	EC, Europe
Dr. Michelle Limoli	FDA, US
Ms. Chieko Hirose	MHLW/PMDA, Japan

ICH Additional Participants:

Mr. Xiangyu Wang	CFDA, China
Mr. Martin Harvey Allchurch	EC, Europe
Dr. Lei Zhang	FDA, US
Dr. Akira Kawahara	JPMA
Ms. Eunkyoung Lee	MFDS, Republic of Korea
Ms. Han Vit Yu	MFDS, Republic of Korea
Ms. Sayaka Kurihara	MHLW/PMDA, Japan
Ms. Hsiao-Han (Susan) Chiang	TFDA, Chinese Taipei
Dr. Churn-Shiouh Gau	TFDA, Chinese Taipei
Ms. Yi-Jing Kuo	TFDA, Chinese Taipei

ICH Secretariat:

Dr. Dawn Ronan (Director)	ICH Secretariat
Dr. Anne Latrive	ICH Secretariat
Ms. Nadia Gerweck	ICH Secretariat
Ms. Nikoleta Luludi	ICH Secretariat

[2] At the Assembly meeting in Kobe under Agenda 13, NPRA, Malaysia was welcomed as a new ICH Observer.
[3] At the Assembly meeting in Kobe under Agenda 13, TITCK, Turkey was welcomed as a new ICH Observer.

Table of Content

Opening of the ICH Assembly Meeting

The ICH Assembly meeting in Kobe, Japan held on 6-7 June 2018 was chaired by Mrs. Lindström-Gommers (Chair, EC, Europe) and Dr. Tominaga (Vice-Chair, MHLW/PMDA, Japan).

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

Assembly Decision/Action:

- The Assembly noted the Member Representatives and Observer Delegates participating in the Assembly meeting in Kobe, as well as the two invited Ad-Hoc Observer Delegates, one from NPRA, Malaysia and the other from TITCK, Turkey.

Adoption of the Agenda

Assembly Decision/Action:

- The Assembly adopted the agenda without any modification.

1. 2017 Annual Report of the Association

The ICH Secretariat presented to the Assembly the ICH 2017 Annual Report on the activities of the Association which covered the activities undertaken by the ICH Management Committee (MC), the MedDRA MC and the ICH Secretariat on behalf of the ICH Association.

Assembly Decision/Action:

- The Assembly approved the 2017 Annual Report and the discharge of the ICH MC, MedDRA MC and the ICH Secretariat for the activities undertaken by these bodies in 2017 on behalf of the ICH Association**,** which will be published on the ICH website.

2. Procedural Matters

- ***General***

The MC presented to the Assembly a process for enabling ICH Working Group (WG) consultation with ICH Members in situations where they are not permitted to appoint experts to a WG (despite being eligible), and a pilot of the process for the E8(R1) EWG.

Assembly Decisions/Actions:

- The Assembly acknowledged the pilot put in place by the ICH MC with a view to communicating on the draft Technical Document prior to *Step 1* with interested ICH Members not able to join the E8(R1) EWG, however the interest of Observers to participate in the pilot process was also acknowledged:
    - The process will involve the sharing of the draft for a 1-month period ahead of a teleconference with the experts to allow the presentation of the draft and the addressing of questions;
    - The process will be evaluated at the end for applicability to other ICH WGs.

- ***ICH Articles of Association and Assembly Rules of Procedure***

The MC proposed to the Assembly revisions to the ICH Articles of Association (AoA) and Assembly Rules of Procedure (RoP) related to: (1) overlapping ICH Membership/Observership of Regional Harmonisation Initiatives and their respective individual members with a view to avoiding double representation in ICH; and (2) management of the size of WGs by revising the process for appointing experts.

Assembly Decision/Action:

- The Assembly adopted the revised AoA and Assembly RoP, as well as the revised Membership/Observership application forms, which will be published on the ICH website.

- ***Standard Operating Procedures for WGs***

The MC presented to the Assembly revisions to the Standard Operating Procedures (SOP) for WGs for consistency with the changes to the AoA and Assembly RoPs regarding the management of the size of WGs by revising the process for appointing experts.

Assembly Decision/Action:

- The Assembly noted the proposed changes to the SOP v4.0 for WGs and that the MC approved the SOP v5.0 for WGs on 5 June 2018, which will be published on the ICH website.

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

Assembly Decision/Action:

- The Assembly noted that there were no changes at this time to the ICH MC RoP which were last updated in December 2017.

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

The MedDRA MC Chair's Delegate informed the Assembly on recent updates made by the MedDRA MC to the MedDRA MC RoP to: (1) align with the ICH Articles of Association, Assembly RoP and ICH MC RoP, and provide clarity regarding the roles of the ICH MC, MedDRA MC and Assembly with respect to MedDRA financial matters; and (2) clarify the policy regarding use of the MedDRA logo.

Assembly Decision/Action:

- The Assembly noted the proposed changes to the MedDRA MC RoP and that the MedDRA MC approved the revised MedDRA MC RoP at its meeting in Kobe on 2 June 2018, which will be published on the ICH website.

3. Financial Matters

The Assembly was updated by the ICH MC's Lead for ICH financial matters on items including the, financial situation following the transfer of assets from the former ICH trustee IFPMA to the new ICH Association which was completed on the 10 November 2017; the 2017 Financial Audit; 2018 cash flow; and the 2019 ICH budget, including financial considerations regarding the organisation of ICH meetings. The Assembly was also informed on MedDRA financial matters, including the 5-year MedDRA budget projection by the MedDRA MC Chair's delegate.

Assembly Decisions/Actions:

- The ICH Assembly approved the ICH MC proposal for the 2019 and future ICH meeting budgets to be increased to support meeting organisation, as well as to include a buffer for currency fluctuations; The ICH Assembly noted that this change will be reflected along with any others in the final 2019 budget which will be submitted ahead of the next ICH meeting;

- The Assembly approved the 2017 Audited Accounts and Financial Statements of the ICH Association which will be filed with the 2017 tax return of the ICH Association to be submitted following the Kobe meeting;
- The Assembly supported the ICH MC recommendation to appoint the same Auditor Moore Stephens for a further two years for the 2018 and 2019 financial audits;
- The Assembly supported a MedDRA MC proposal to proceed in 2018 with the recruitment of 7 new MSSO staff unbudgeted in the previously approved 2018 budget, but which could be covered in 2018 by current subscription collections and use of previous years' surplus.

4. New Topic Process & Strategic Discussions

- ***New Topic Proposals***

The ICH MC presented to the Assembly the New Topic proposals for the 2018 cycle as well as the ICH MC assessment submitted to the Assembly for its consideration.

Assembly Decisions/Actions:

- The Assembly adopted the Concept Paper outline on Analytical Procedure Development and Revision of Q2 (R1) (Quality topic) Analytical Validation and agreed on the establishment of an informal Working Group (WG) with the code Q2(R2)/Q14 to finalise the Concept Paper and develop a Business Plan ahead of the MC Teleconference to be held in September/October 2018;
- The Assembly adopted the Concept Paper outline on Continuous Manufacturing (Quality topic) and agreed on the establishment of an informal WG with the code Q13 to finalise the Concept Paper and develop a Business Plan ahead of the MC Teleconference to be held in September/October 2018;
- The Assembly adopted the Concept Paper outline on CeSHarP (Multidisciplinary topic) and agreed on the establishment of an informal WG with the code M11 to finalise the Concept Paper and develop a Business Plan ahead of the MC Teleconference to be held in September/October 2018;
- The Assembly supported that the ICH Secretariat proceed to launch the nomination process amongst ICH Members for the establishment of these 3 informal WGs and noted that in line with the revised procedures, ICH Members and Observers interested to participate in the activities of these new WGs would be invited to submit a nomination request within 3 weeks (from the date of the ICH Secretariat's call for nominations);
- The ICH Secretariat will solicit interest via email in the Rapporteurship and Regulatory Chairmanship of these informal WGs in line with the procedures;
- The Assembly adopted the Concept Paper outline on Adaptive Clinical Trials (Efficacy topic) with a delayed timeframe to start work to finalise the Concept Paper and develop a Business Plan, with the timeframe to establish an informal WG with the code E20 to be determined at a later point by the MC;
- The Assembly adopted the Concept Paper outline on Drug Interaction Studies (Multidisciplinary topic) with a delayed timeframe to start work to finalise the Concept Paper and develop a Business Plan, with the timeframe to establish an informal WG with the code M12 to be determined at a later point by the MC;
- The Assembly acknowledged the interest expressed by some ICH Members/Observers on the New Topic proposals on Nonclinical Safety Evaluation of Therapeutics for Severely-Debilitating or Life-Threatening Diseases (SDLTD) and Assessment and Control of Extractables and Leachables (E&L) and the possibility for these proposals to be further revised by the leading parties and re-submitted for the following ICH New Topic cycle to start in December 2018;

- The Assembly noted the process for the selection of New Topic proposals and that ICH Members and Observers are invited to submit New Topic proposals by December 2018 (date to be confirmed) to be assessed at the June 2019 meeting.

- ***Strategic Reflection Papers***

The ICH MC provided an update on the status of the PhRMA Quality Reflection Paper on Advancing Pharmaceutical Quality Standards, as well as on the draft FDA, US Reflection Paper on Generic Drugs Harmonisation and draft EC, Europe Reflection Paper on Vaccines.

Assembly Decisions/Actions:

- The Assembly endorsed as an ICH Reflection Paper the Quality Reflection Paper on Advancing Pharmaceutical Quality Standards;
- The Assembly noted that the MC approved the establishment of an Informal Quality Discussion Group (IQDG) under the remit of the MC;
- The Assembly acknowledged that the MC would further propose a revision to the Assembly RoP to give the possibility to the Assembly to establish informal Discussion Groups;
- The Assembly supported that as a next step the draft FDA, US Reflection Paper on Generic Drugs Harmonisation would be further revised to address comments received from the Assembly and to focus on areas identified as of most interest for harmonisation within ICH with an aim of providing a revised version by the end of 2018;
- The Assembly noted that interested ICH Members and Observers are invited to liaise directly with FDA, US through its ICH Coordinator to provide input for the revision of the draft FDA, US Reflection Paper on Generic Drugs Harmonisation;
- The Assembly noted that further to the feedback received, EC, Europe would not continue work on its draft Reflection Paper on Vaccines at this time.

- ***Strategic Discussions***

The ICH MC provided an update on the status of ongoing strategic discussions.

Assembly Decision/Action:

- The Assembly noted the ongoing preparation by PhRMA of a draft Reflection Paper on Model Informed Drug Development (MIDD) and ongoing MC Strategic discussions regarding a PhRMA proposal on Patient Focused Drug Development (PFDD).

5. Communication

The ICH MC provided the Assembly with an update on current communication activities including the transparency policy plan, the GCP renovation stakeholder engagement plan, recent and envisioned updates to the ICH website including a summary of the history of ICH, and development of the 2018-2019 communication and stakeholder engagement plan.

- ***Communication Activities***

Assembly Decisions/Actions:

- The Assembly noted the ICH MC's decision to disband its Communication Subcommittee and for activities to be continued by the ICH Secretariat. The Assembly thanked the Communication Subcommittee and its Lead Mr. Harvey (EC, Europe) for their work;
- The Assembly supported the way forward for the GCP renovation stakeholder engagement plan whereby this would be led by the E8(R1) EWG;

- The Assembly supported the communication orientations for the Secretariat for 2018-2019, including the way forward for the 'broadcasting alternative' and ICH history text proposals, acknowledging that these activities would be undertaken by the Secretariat with a prioritisation considering also current communication activities being undertaken in 2018-2019.

- ***ICH Regional Public Meetings***

The Assembly shared information on ICH Regional Public Meetings in their respective regions prior to and following the ICH meeting in Kobe in June 2018.

Assembly Decision/Action:

- The Assembly noted the following ICH Regional Public Meetings held prior to / following the ICH meeting in Kobe:
    - On 15 December 2017, JPMA and MHLW/PMDA, Japan held a joint meeting to report on the outcome of the Geneva ICH meeting;
    - On 6 April 2018, FDA, US and Health Canada, Canada held a joint Regional Public Meeting with presentations on ICH *Step 2* and *Step 4* Guidelines at FDA, US offices in Silver Spring, Maryland, USA and for which a recording is available online: https://www.fda.gov/Drugs/NewsEvents/ucm592065.htm;
    - On 17 May 2018, MFDS, Republic of Korea held a public meeting on ICH in Seoul, Republic of Korea;
    - On 23 May 2018, ANVISA, Brazil held a public regional consultation meeting regarding the ICH Q12 Lifecycle Management Guideline;
    - On 27 June 2018, FDA, US and PhRMA will co-host two sessions at the Annual DIA meeting in Boston, USA: Harmonizing Regulatory Science through ICH; and Harmonization beyond ICH;
    - On 18 July 2018, JPMA and MHLW/PMDA, Japan will organise a joint meeting to report on the outcome of the Kobe ICH meeting;
    - On 6-7 August 2018, ANVISA, Brazil will host the ICH Q1 Stability Training in partnership with the Noertheastern University open to Regulators from Latin Americaand Caribbean countries;
    - In October 2018, MFDS, Republic of Korea will hold a public meeting on ICH Guidelines.

- ***MHLW/PMDA, Japan and JPMA Publication***

Assembly Decision/Action:

- The Assembly noted a joint publication (in Japanese) from MHLW/PMDA, Japan and JPMA on the ICH reforms and introducing ICH Guidelines.

6. Implementation of ICH Guidelines

The ICH MC provided to the Assembly an update on recent activities undertaken by its Implementation Subcommittee including on: defining the terminology to be used with respect to the degrees of implementation of and adherence to ICH Guidelines; and developing a Phase 2a Study to assess the level of implementation of ICH Guidelines by the new ICH Regulatory Members and the level of adherence to ICH Guidelines within the Founding and Standing Regulatory Member countries/regions. MHLW/PMDA, Japan, and FDA, US also presented case studies on the implementation of the ICH E2D and M8 Guidelines respectively.

The Assembly was also updated on an analysis recently undertaken by IFPMA and DCVMN (Developing Countries Vaccine Manufacturers Network) regarding challenges associated with registration of vaccines in emerging countries and sources of divergence in the registration.

The ICH Secretariat presented to the Assembly the implementation table which reflects the current state of implementation of ICH Guidelines, based on the information provided by ICH Regulatory Members to the ICH Secretariat.

Assembly Decisions/Actions:

- The Assembly noted that, in preparation of the next ICH meeting in November 2018, ICH Members and Observers are invited to submit to the ICH Secretariat suggestions for ICH Guidelines or topics which could be a focus for discussion under the Assembly meeting's agenda item on implementation;
- The Assembly provided general support on the proposal for a new terminology to be used with respect to the degrees of implementation of ICH Guidelines, including the steps "not implemented", "in the process of implementation", and "implemented (self-declaration of regulator)" which would be further assessed as "(confirmed) adequate implementation" or "not adequately implemented";
- The Assembly noted it was invited to provide comments on the draft terminology and definitions by the end of June 2018 via the ICH Secretariat, with the aim of approving a final terminology at the November 2018 meeting;
- The Assembly acknowledged that the new terminology is intended to be further introduced into the Assembly RoP and MC RoP, with the current term "partial implementation" to be modified to "in the process of implementation" and "full implementation" to "implemented (self-declaration of regulator)";
- The Assembly supported the project proposal Phase 2a Study for the ICH-driven survey led by an independent third party on ICH Guideline Implementation in new ICH Regulatory Member countries/regions and ICH Guideline Adherence in ICH Founding/Standing Regulatory Member countries/regions with the aim of providing the results to the Assembly at the June 2019 ICH meeting;
- The Assembly supported that following the completion of the survey, a high level "white paper" would be produced and published on the ICH website to enable a transparent dialogue on ICH Guideline implementation;
- The Assembly acknowledged that the financial support for the survey would be within the allocated budget for 2018 and 2019;
- The Assembly acknowledged that the MC Implementation Subcommittee membership would be open for nomination requests from new Elected MC Representatives.

7. Training

The ICH MC updated the Assembly on activities undertaken by the Training Subcommittee, including the status of work with training partners; development of online training programmes; conduct of a gap analysis for Tier 3 ICH Guideline training; support to WGs in developing training materials in 2018; establishment of quality control mechanisms to review and assess existing and new trainings; and the establishment of procedures to develop trainings for newly completed ICH Guidelines.

Assembly Decisions/Actions:

- The Assembly noted the report of the Training Subcommittee and supported the next steps for the work of the Training Subcommittee;

- The Assembly supported the ICH WG templates for *Step 2* informational materials and *Step 4* online slide presentations which will be made available to ICH WGs.

8. Update on MedDRA

The Assembly received a report from the MedDRA MC Chair's Delegate on the ICH MedDRA MC meeting held on 2-3 June 2018. The report included the following matters: appointment of a new MedDRA MC Chair at the Kobe meeting; expansion of MedDRA use worldwide; the current MedDRA 5-year strategic plan to facilitate the use of MedDRA, including through MedDRA translations, MedDRA training, and the maintenance and development of tools by the Maintenance and Support Services Organisation (MSSO).

The Assembly was informed that Ms. Sommerer (Health Canada, Canada), who had been appointed in November 2017 as MedDRA MC Chair, had stepped down in early 2018, and that the role was filled on an interim basis by Ms. Morrison (Health Canada, Canada) until the Kobe meeting, at which time Mr. Foy (MHRA, UK) was appointed as MedDRA MC Chair with the unanimous support of the MedDRA MC to serve until June 2019.

The Assembly was updated on the continued growth of MedDRA users throughout the world, which went from over 4,000 organisations in 111 countries as reported during the November 2017 meeting in Geneva, to currently over 5,000 MedDRA subscribing organisations in 119 countries, reflecting the successful adoption of MedDRA as a worldwide standard in the protection of public health. The Assembly noted the reduction in MSSO subscription fees granted in 2017 and 2018 in view of the ability to share costs across more subscribers.

The Assembly was informed on the current MedDRA 5-year strategic work plan which includes a focus on the facilitation of the use of MedDRA in a broader set of countries/regions with new translations and expanded training and support services; further development of software tools; and exploring interoperability with other terminologies. The Assembly also took note of the 5-year budget projection regarding how costs are expected to evolve and considerations on new areas of work to be financed from the use of surplus funds.

The Assembly noted that the translations of MedDRA into Korean and Russian are due for release by end of 2018 to early 2019. Furthermore, the Assembly noted that in line with MedDRA MC's policy that all translations should be accessible as part of a standard MedDRA subscription, the MedDRA MC in coordination with the Japanese Management Board (JMB) supported the removal of a fee for MSSO Subscribers to access the Japanese translation of MedDRA maintained by the Japanese Maintenance Organisation (JMO).

The Assembly was also informed on MedDRA implementation training conducted by MSSO in Beijing, China in April 2018 for CFDA, China, which took place over 2 days, followed by 2 additional days for both CFDA, China and Chinese Industry. The training in Beijing involved close to 400 participants and included the participation of the MedDRA MC Chair at the time, Ms. Morrison who shared an ICH Regulator's experience with MedDRA. The Assembly was also informed on the MedDRA implementation training conducted by MSSO in May 2018 for MFDS, Republic of Korea and Korean Industry and involving close to 300 participants. The Assembly noted the increase of training support planned for 2019, both through face-to-face meetings and webinars.

The Assembly noted that in addition to the MSSO working on recruitment of MSSO local support in the Republic of Korea and Latin America as agreed in November 2017, the MedDRA MC supported during the Kobe meeting providing local MSSO support in China already from 2018. The Assembly noted that this could be accommodated within the 2018 MedDRA budget.

The Assembly noted the continued cooperating effort with the WHO and its Collaborating Centre, the Uppsala Monitoring Centre (UMC), which resulted in a further joint MSSO MedDRA and UMC WHO-Drug user group meeting in Bengaluru, India (February 2018).

Assembly Decision/Action:

- The Assembly noted the decisions taken by the MedDRA MC at its meeting in Kobe on 2-3 June 2018 including the 5-year strategic work plan with activities to be funded from the use of surplus funds and supported the MedDRA MC's proposal to proceed in 2018 with the recruitment of 7 new MSSO staff (see also item #3 above).

9. General Operational Matters

- ***ICH General Operational Matters***

The ICH Secretariat updated the Assembly on general operational matters including its activities to establish fully independent operations following the finalisation of the transfer of assets of the former ICH (International Conference on Harmonisation) from IFPMA to the new ICH Association in November 2017; an overview of the participation of current ICH Members and Observers in ICH; and the implementation of recent Assembly/MC decisions.

Assembly Decisions/Actions:

- The Assembly noted the full operationalisation of the ICH Secretariat following the completion of the asset transfer in November 2017 which had included relocation to a new office as of April 2018;
- The Assembly noted the implementation by the ICH Secretariat of the Transparency Policy, including the publication on the ICH website of the photographs and short biographies of all ICH Member Coordinators and ICH MedDRA MC Representatives, as well as the list of experts' names for active WGs.

- ***IFPMA Role***

The IFPMA delegate updated the Assembly on IFPMA's work to facilitate the participation of IFPMA National Association experts in ICH WGs. There has been involvement of 6 IFPMA National Associations, with 30 experts contributing to 6 ICH topics. Five of the experts are attending WGs meetings in Kobe. The system put in place by IFPMA also operates as a form of training. Feedback is that the process is working well.

Assembly Decision/Action:

- The Assembly noted the current level of participation by 5 IFPMA National Association experts in 6 ICH WGs.

- ***IPRP Cooperation***

The Chair of the International Pharmaceutical Regulators Programme (IPRP) updated the Assembly on IPRP activities.

Assembly Decisions/Actions:

- The Assembly noted that the consolidated IPRF-IGDRP initiative had taken effect as of 1 January 2018 under the new name IPRP (International Pharmaceutical Regulators Programme);
- The Assembly noted that the ICH Secretariat had begun providing support services to IPRP from 1 January 2018 under a yearly Memorandum of Understanding (MoU) between ICH and IPRP, and that the renewal of the MoU for the year 2019 had been signed by the IPRP Chair and ICH Assembly Chair and Vice-Chair in Kobe.

10. WGs Meeting in Kobe

Regarding requests from EWGs/IWGs to meet at the next ICH meeting in Charlotte, North Carolina, USA on 10-15 November 2018, the Assembly noted that any such requests would be taken under consideration by the MC. A list of EWG/IWGs agreed by the MC to meet face-to-face in Charlotte will be made available to the Assembly, and also on the ICH website, following the MC teleconference to be held at least 8 weeks ahead of the meeting. It was also agreed that in order to facilitate logistics and organisation, confirmation of face-to-face meeting of EWGs/IWGs may occur sooner via mailing.

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

The Rapporteur reported to the Assembly on the outcome of the E2B(R3) EWG/IWG meeting and the joint meeting with the M2 EWG, including the progress made on the development with the M2 EWG of a Standard Operation Procedure (SOP) for data extraction and publication of EDQM Dose Form (DF) and Routes of Administration (RoA) terms, and the development of a mapping table for RoA between E2B(R2) and EDQM terms.

Assembly Decisions/Actions:

- The Assembly approved the work plan of the E2B(R3) EWG/IWG for activities to be undertaken;
- The Assembly noted that the Regulatory Topic Leaders of the E2B(R3) EWG/IWG signed-off under *Step 3* the ICSR Q&A, further to which the Regulatory Members of the Assembly adopted under *Step 4* the final updated ICSR Q&As;
- The Assembly noted that the experts had signed-off a common template for E2B data element and business requirements;
- The Assembly noted the completion of the SOP for data extraction and publication of EDQM terms with the M2 EWG;
- The Assembly noted the plan of the E2B(R3) EWG/IWG to develop further training materials, in liaison with the MC Training Subcommittee.

10.2. E8(R1) EWG: Revision on General Considerations for Clinical Trials *(Rapporteur: Dr. LaVange – FDA, US; Regulatory Chair: Dr. Sweeney – EC, Europe)*

The Rapporteur reported to the Assembly on the outcome of the E8(R1) EWG meeting and the progress made on the development of the draft E8(R1) Technical Document.

Assembly Decisions/Actions:

- The Assembly approved the work plan of the E8(R1) EWG for activities to be undertaken;
- The Assembly supported the proposal of the E8(R1) EWG to develop two documents that would go for Assembly endorsement under *Step 2a/b*: the E8(R1) Technical Document and an E8(R1) Annex that could in the future be revised separately from the E8(R1) Guideline;
- The Assembly noted that the draft Technical Document will be completed by November 2018, and that *Steps 1* and *2a/*b are expected to be reached electronically between January and February 2019;
- The Assembly approved that as per the communication pilot (see also item #2 above), the E8(R1) EWG will share the draft Technical Document with interested ICH internal stakeholders one month prior to *Step 1*, and that a teleconference will be organized with the E8(R1) EWG and interested ICH internal stakeholders to answer questions regarding the draft Technical Document. The

timeframe to share the Technical Document and organise a teleconference will be dependent on the progress of the EWG in finalising the draft;

- The Assembly acknowledged that the intent of the pilot was to communicate with the internal ICH stakeholders rather than to revise the draft Technical Document and noted that the ICH Secretariat would make a call for interest in the process;
- The Assembly noted that an ICH public stakeholder meeting to take place after the closure of the public consultation phase is expected in 2019, as per the GCP renovation plan.

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

The Rapporteur reported to the Assembly on the outcome of the E9(R1) EWG meeting and the progress made on analysing and addressing the comments received from the regional public consultations which ended in April 2018, and on developing an extensive training slide deck including examples and case studies, as well as a video explaining the Estimand concept.

Assembly Decisions/Actions:

- The Assembly approved the work plan of the E9(R1) EWG for activities to be undertaken;
- The Assembly noted that the training material slide decks on the *Step 2* draft ICH Guideline are expected to be published on the ICH website within one month of the ICH meeting in Kobe;
- The Assembly noted that *Steps 3* and *4* are expected by June 2019.

10.4. E11A EWG: Paediatric Extrapolation *(Rapporteur: Dr. Yao – FDA, US)*

The EC, Europe, standing in for the Rapporteur reported to the Assembly on the outcome of the E11A EWG meeting and progress made on the development of the E11A draft Technical Document on Paediatric Extrapolation, and activities with respect to reviewing literature on paediatric extrapolation and discussing comments compiled by the E11(R1) EWG regarding paediatric extrapolation and use of existing knowledge.

Assembly Decisions/Actions:

- The Assembly approved the work plan of the E11A EWG for activities to be undertaken;
- The Assembly noted the progress made on the draft Technical Document and that *Steps 1* and *2a/b* are expected by November 2020.

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

The Rapporteur reported to the Assembly on the outcome of the meeting of the E19 EWG and the progress made on the development of the E19 draft Technical Document on Optimization of Safety Data Collection.

Assembly Decisions/Actions:

- The Assembly approved the work plan of the E19 EWG for activities to be undertaken;
- The Assembly noted the progress made on the draft Technical Document and that *Steps 1* and *2a/b* are expected by November 2018.

10.6. M2 EWG: Electronic Standards for the Transfer of Regulatory Information (ESTRI) *(Co-Rapporteurs: Dr. Okada – MHLW/PMDA, Japan; Ms. Slack – FDA, US; Regulatory Chair: Mr. Srivastava – Health Canada, Canada)*

The Co-Rapporteur reported to the Assembly on the outcome of the M2 EWG meeting and joint meetings with the E2B(R3) EWG/IWG, and the group's current activities with respect to the project opportunity proposals including on eCCTS – electronic Common Clinical Trial Submission and on Trial Master File metadata harmonization (TMF); the development of a revised ESTRI recommendation; and the development of a Service Level Understanding (SLU) with E2B(R3) EWG/IWG for terminology list management.

Assembly Decisions/Actions:

- The Assembly noted that the M2 EWG had completed its work on the project opportunity related to eCCTS – electronic Common Clinical Trial Submission, and that this topic would be submitted as an ICH New Topic proposal by ICH Member WSMI in the 2019 New Topic cycle;
- The Assembly noted the progress made on the TMF- Trial Master File and supported that the M2 EWG further engage with subject matter experts to clarify or refine the project scope;
- The Assembly noted that the M2 EWG finalised in Kobe an ESTRI recommendation signed-off by the M2 experts and supported its publication on the ESTRI section of the ICH website;
- The Assembly noted the development by the M2 EWG of a white paper on FIHR (Fast Healthcare Interoperability Resources) with consideration on implications for ICH;
- The Assembly noted the progress made on Terminology list management and that this topic would be put forward for endorsement at the November 2018 meeting;
- The Assembly supported the work plan of the M2 EWG for activities to be undertaken.

10.7. M8 EWG/IWG: The Electronic Common Technical Document (eCTD) *(Acting Rapporteur: Mr. Gray – FDA, US; Regulatory Chair: Dr. Menges – EC, Europe)*

The Rapporteur reported to the Assembly on the outcome of the M8 EWG/IWG meeting, and progress made on the finalisation of the eCTD v4.0 Implementation Package v1.3 addressing change requests received.

Assembly Decisions/Actions:

- The Assembly noted that the Regulatory Topic Leaders of the M8 EWG/IWG signed-off under *Step 3* the eCTD v4.0 Implementation Package v1.3, Q&As and Specification Change Request Document v1.2, as well as the eCTD v3.2.2 Q&As and Specification Change Request Document v1.31 and the Specification for Submission Formats for CTD v1.2, further to which the Regulatory Members of the Assembly adopted these documents under *Step 4*;
- The Assembly noted that interest in eCTD training should be communicated to the ICH MC's Training Subcommittee via the ICH Secretariat;
- The Assembly approved the work plan of the M8 EWG for activities to be undertaken;
- The Assembly endorsed the nomination of the current Acting Rapporteur as the formal Rapporteur for the M8 EWG/IWG in line with the SOP Section 1.5.2.

10.8. M9 EWG: Biopharmaceutics Classification System-based Biowaivers *(Rapporteur: Dr. Welink – EC, Europe; Regulatory Chair: Dr. Seo – FDA, US)*

The Rapporteur reported to the Assembly on the outcome of the M9 EWG meeting and progress made towards finalising the M9 draft Technical Document on Biopharmaceutics Classification System-based Biowaivers.

Assembly Decisions/Actions:

- The Assembly noted that the Topic Leaders of the M9 EWG signed-off *Step 1* of the M9 draft Technical Document, further to which the Members of the Assembly endorsed the M9 draft Technical Document under *Step 2a* and the Regulatory Members of the Assembly endorsed the M9 draft Guideline under *Step 2b*;
- The Assembly approved the work plan of the M9 EWG for activities to be undertaken;
- The Assembly noted that *Steps 3* and *4* are expected by June 2019.

10.9. M10 EWG: Bioanalytical Method Validation *(Rapporteur/Regulatory Chair: Dr. Ishii-Watabe – MHLW/PMDA, Japan)*

The Rapporteur reported to the Assembly on the outcome of the M10 EWG meeting and progress made towards developing the M10 draft Technical Document on Bioanalytical Method Validation.

Assembly Decisions/Actions:

- The Assembly approved the work plan of the M10 EWG for activities to be undertaken.
- The Assembly noted the progress made on the draft Technical Document and that *Steps 1* and *2a/b* are currently planned by November 2018.

10.10. S5(R3) EWG: Revision on Detection of Toxicity to Reproduction for Human Pharmaceuticals *(Rapporteur/Regulatory Chair: Dr. Waxenecker – EC, Europe)*

The Rapporteur reported to the Assembly on the outcome of the S5(R3) EWG meeting and progress made on analysing and addressing the comments received from the regional public consultations which ended in March 2018.

Assembly Decisions/Actions:

- The Assembly approved the work plan of the S5(R3) EWG for activities to be undertaken;
- The Assembly noted the preliminary considerations from the S5(R3) EWG on the need for a maintenance procedure to be applied to the annexes of the Guideline (Annex 1: In Vivo Studies, Annex 2: Alternative Assays) and supported that the S5(R3) EWG would further develop a detailed plan for maintenance of the two Annexes for MC's further clarification;
- The Assembly noted that *Steps 3* and *4* are expected by November 2019.

10.11. S11 EWG: Nonclinical Safety Testing in Support of Development of Paediatric Medicines *(Rapporteur: Dr. Keller – PhRMA; Regulatory Chair: Dr. van der Laan – EC, Europe)*

The Rapporteur reported to the Assembly on the outcome of the S11 EWG meeting, and the progress made on data collection activities and towards developing the S11 draft Technical Document on Nonclinical Safety Testing in Support of Development of Paediatric Medicines.

Assembly Decisions/Actions:

- The Assembly approved the work plan of the S11 EWG for activities to be undertaken;
- The Assembly noted the progress made at the meeting on the finalisation of the draft Technical Document and that *Steps 1* and *Steps 2a/b* are expected electronically by August 2018.

11. WGs/DGs Not Meeting in Kobe

11.1. Standing Paediatric EWG *(Rapporteur: Dr. Hirata – MHLW/PMDA, Japan; Regulatory Chair: Dr. Yao – FDA, US)*

Following its establishment in February 2018, the Standing Paediatric EWG did not receive any requests for paediatric advice at this time. The Technical Coordinator of MHLW/PMDA, Japan informed the Assembly that Concept Papers are required to include paediatric considerations, that the Standing Paediatric EWG is at the disposal of WGs to provide recommendations on specific paediatric aspects of their work; and that requests for paediatric expertise should be sent to the ICH Secretariat.

11.2. E14/S7B DG: The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs *(Rapporteur: Dr. Leishman – PhRMA; Regulatory Chair: Dr. Prasad – EC, Europe)*

The E14/S7B Discussion Group (DG) has been actively monitoring the non-clinical Comprehensive *in vitro* Proarrhythmic Assay (CiPA) initiative to inform a recommendation as to whether, and what sort of revision or update is needed on the E14 and S7B ICH Guidelines and/or Q&A documents to reflect the current advancements in cardiovascular safety pharmacology that predict risk of arrhythmia from drug-induced cardiac repolarization.

Assembly Decision/Action:

- The Assembly noted that in light of new data from the CiPA initiative, the E14/S7B DG would provide a revised Concept Paper to the MC for its consideration in advance of the November 2018 meeting.

11.3. E17 IWG Multi-Regional Clinical Trials *(Rapporteur: Dr. Dunder – EC, Europe; Regulatory Chair: Dr. Otubo – MHLW/PMDA, Japan)*

The E17 IWG was established in February 2018 and is finalising its work plan for the development of case studies supportive of harmonised implementation activities of the recently released E17 ICH Guideline on General Principles for Planning and Design of Multi-Regional Clinical Trials.

Assembly Decision/Action:

- The Assembly endorsed the nomination of the current Acting Rapporteur as the formal Rapporteur for the E17 IWG in line with the SOP Section 1.5.2.

11.4. M1 PtC WG: MedDRA Points to Consider *(Rapporteur: Dr. Winter – EFPIA; Regulatory Chair: Dr. Brajovic – FDA, US)*

The Assembly noted that the M1 PtC WG continues its work on the update of the two Points to Consider (PtC) documents on Term Selection and Data Retrieval and Presentation for the MedDRA version 21.1 release on 1 September 2018; as well as on the translation of the condensed versions of the PtC documents into all MedDRA languages, to be released by end of 2018.

Assembly Decision/Action:

- The Assembly noted that the Companion Document to the PtC Document was endorsed by the MedDRA MC at the meeting in Kobe.

11.5. M4Q(R1) IWG: (CTD-Quality) IWG: Addressing CTD-Q-Related Questions *(Rapporteur: Dr. Schmuff – FDA, US; Regulatory Chair: N/A)*

The M4Q(R1) IWG remains in a dormant state in case any questions are received while the eCTD 4.0 Implementation Guide, including the Granularity document, is being implemented in the ICH Regions.

11.6. M7(R2) Maintenance EWG: Addendum to Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk *(Rapporteur: Dr. Honma – MHLW/PMDA, Japan; Regulatory Chair: N/A)*

The M7(R2) Maintenance EWG continues its work on finalising the Concept Paper with the list of the new set of compounds to be evaluated in the second Addendum and developing a Q&A on the control of impurity in the M7 Guideline. *Steps 1* and *2a/b* of the second Addendum and Q&A are expected by June 2019.

11.7. Q3C(R7) Maintenance EWG: Maintenance of the Guideline for Residual Solvents *(Rapporteur: Dr. McGovern – FDA, US; Regulatory Chair: N/A)*

The Q3C(R7) Maintenance EWG is working on developing Permitted Daily Exposure (PDE) levels for the 3 solvents agreed on at the meeting in Montreal, Canada, in May/June 2017, which include 2-methyltetrahydrofuran, cyclopentylmethylether and tert-butanol. *Steps 1* and *2a/b* are anticipated in the fourth quarter of 2018. The Q3C(R7) Maintenance EWG is also undertaking an error correction for the PDE for ethyleneglycol.

11.8. Q3D(R1) Maintenance EWG: Maintenance of the Guideline for Elemental Impurities *(Rapporteur: Dr. McGovern – FDA, US; Regulatory Chair: N/A)*

The Q3D(R1) Maintenance EWG is working on an addendum to the Q3D Guideline to include PDEs for the cutaneous and transdermal routes of administration. The Assembly noted that the Q3D(R1) revision of the Cadmium inhalation PDE recently reached *Steps 1* and *2a/b* and was published on the ICH website for public comment and will also be issued for public comment in the ICH Regions. The updated Cadmium inhalation PDE of 3 micrograms (µg) per day is based on a modifying factor approach like that used for calculating the PDEs for the cadmium oral and parenteral routes of exposure. *Steps 3* and *4* of the Q3D(R1) revision of the Cadmium inhalation PDE are expected by end 2018. *Steps 1* and *2a/b* of the Q3D(R2) revision for the cutaneous and transdermal routes of administration are expected by end of 2018.

11.9. Q11 IWG: Q&As on Selection and Justification of Starting Materials for the Manufacture of Drug Substances *(Rapporteur: Mr. McDonald – EC, Europe; Regulatory Chair: Dr. Condran – Health Canada, Canada)*

The Q11 IWG continues its work on finalising the training materials to be disseminated in the ICH regions. A first supportive slide deck will be published shortly on the ICH website. The Q11 IWG is also developing training material in the form of a video with voice-over narration and expects to finalize the training material before the ICH November 2018 meeting.

11.10. Q12 EWG: Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management *(Rapporteur: Ms. Boam – FDA, US; Regulatory Chair: Ms. Kruse – EC, Europe)*

The Q12 draft Guideline reached *Step 2b* in November 2017 and was subsequently issued for up to a one-year comment period ending in December of 2018. Furthermore, the Q12 EWG will hold an interim meeting in early 2019 to initiate review of the comments received. *Steps 3* and *4* are expected by the second half of 2019.

11.11. S1(R1) EWG: Revision of the Rodent Carcinogenicity Studies for Human Pharmaceuticals Guideline *(Rapporteur: Dr. Sistare – PhRMA; Regulatory Chair: Dr. van der Laan – EC, Europe)*

The S1(R1) EWG is conducting a prospective evaluation period involving the submission of Carcinogenicity Assessment Documents (CADs) waiver proposals by industry sponsors and related carcinogenicity study summaries or final study reports. The assessment of these proposals by drug regulatory authorities will inform the potential revision of the S1B ICH Guideline with the goal to introduce a more comprehensive and integrated approach to addressing the risk of human carcinogenicity of pharmaceuticals. The S1(R1) EWG continues to review data submissions. Currently 22 carcinogenicity study reports have been submitted. *Steps 1* and *2a/b* are expected by June/November 2019.

11.12. S9 IWG: Q&As on Nonclinical Evaluation for Anticancer Pharmaceuticals *(Rapporteur/Regulatory Chair: Dr. Leighton – FDA, US)*

The Regulatory Members of the Assembly adopted *Step 4* on the S9 Q&As on Nonclinical Evaluation for Anticancer Pharmaceuticals electronically in April 2018.

Assembly Decision/Action:

- The Assembly noted the disbandment of the S9 IWG.

12. 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. Furthermore, it was noted that as per Article 26 (9) of the ICH AoA the election should be conducted by secret ballot.

The Assembly noted that the following ICH Members had submitted an application: CFDA, China; MFDS, Republic of Korea; HSA, Singapore; BIO; IGBA and WSMI. The Applicants for ICH MC Elected Representatives provided the Assembly a brief introduction and presented their interest in joining the ICH MC. The ICH MC presented to the Assembly their considerations regarding the Applicants' eligibility.

Assembly Decisions/Actions:

- The Assembly elected the following Regulatory Member Applicants as ICH MC Elected Representatives:
    - Mr. Xiaoling Qin and Mr. Siyuan Zhou from CFDA, China;
    - Dr. Nakyung Kim and Dr. Won Sik Lee from MFDS, Republic of Korea;

- Ms. Siew Wei Chua and Dr. Dorothy Toh from HSA, Singapore.

- The Assembly elected the following Industry Member Applicants as ICH MC Elected Representatives:
  - Ms. Lila Feisee and Dr. Wassim Nashabeh from BIO;
  - Dr. Nick Cappuccino and Ms. Beata Stepniewska from IGBA;
- The Assembly noted that the new elected MC Representatives would be given the opportunity to also participate in any Subcommittees and Discussion Groups set-up under the MC.

13. Membership and Observership

The ICH MC presented to the Assembly an overview of applications for Membership/Observership processed since the meeting in Geneva in November 2017 and its recommendation on these applications in view of the eligibility criteria.

Assembly Decisions/Actions:

- The Assembly approved the following Membership application:
  - TFDA, Chinese Taipei.

- The Assembly approved the following Observership applications :
  - TITCK, Turkey;
  - NPRA, Malaysia;
  - SCDMTE, Armenia;
  - MMDA, Moldova.
- The Assembly did not approve the following Observership application:
  - EEC, Eurasian Economic Commission.

14. Organisation of Next Meetings

Assembly Actions/Decisions:

- The Assembly noted the next ICH Assembly meeting will be held in Charlotte, North Carolina, USA, on 15-16 November 2018;
- The Assembly noted that the following ICH Assembly meetings will be held in Europe (location to be confirmed) on 5-6 June 2019 and in Asia (location to be confirmed) on 20-21 November 2019.