

6 February 2014

MEETING REPORT
ICH Steering Committee
13-14 November 2013, Osaka, Japan

List of Participants

ICH Steering Committee:

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Dr. Hironobu Saito	JPMA	Japan
Dr. Kurajiro Kishi	JPMA	Japan
Dr. Theresa Mullin	FDA	USA
Dr. Justina Molzon	FDA	USA
Ms. Joan Wilmarth Blair	FDA	USA
Dr. Peter Honig	PhRMA	USA
Dr. Patrick Brady	PhRMA	USA
Ms. Lenita Lindström	EU	Europe
Dr. Tomas Salmonson	EU/EMA	Europe
Mr. Richard Bergström	EFPIA	Europe
Dr. Sabine Luik	EFPIA	Europe

ICH Observers:

Mr. Mike Ward	Health Canada	Canada
Mrs. Louise Déry	Health Canada	Canada
Dr. Petra Doerr	EFTA	Switzerland
Dr. Lembit Rägo	WHO	Switzerland

RHIs:

Dr. Jeong-Mi Kim	APEC	Republic of Korea
Dr. Yuppadee Javroongrit	ASEAN	Thailand
Ms. Jane Mashingia	EAC	Tanzania
Dr. Fred Siyoi	EAC	Republic of Kenya
Prof. Saleh Bawazir	GCC	Saudi Arabia
Dr. Analía Porrás	PANDRH	USA
Mr. Joseph Mthetwa	SADC	Botswana
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DRAs/DoH:

Ms. Patrícia Pereira	ANVISA	Brazil
Ms. Luciana Takara	ANVISA	Brazil
Ms. Dong Jiangping	CFDA	P.R. China
Ms. He Li	CFDA	P.R. China
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Dr. Christina Lim	HSA	Singapore
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ICH Coordinators:

Ms. Yasuko Inokuma	MHLW	Japan
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Dr. Michelle Limoli	FDA	USA
Dr. Michael Garvin	PhRMA	USA
Dr. Sébastien Goux	EU	Europe
Mr. Pär Tellner	EFPIA	Europe

Technical Coordinators:

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Others:

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Mr. Michiharu Abe	JPMA	Japan
Ms. Emer Cooke	EU/EMA	Europe
Ms. Cordula Landgraf	EFTA	Switzerland

ICH Secretariat:

Dr. Odette Morin	Switzerland
Dr. Dawn Ronan	Switzerland
Dr. Sarah Adam	Switzerland
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Opening Discussions

The ICH Steering Committee (SC) meeting in Osaka, Japan on 13-14 November 2013 was chaired by MHLW/PMDA.

Adoption of the Agenda

The agenda was adopted without modification.

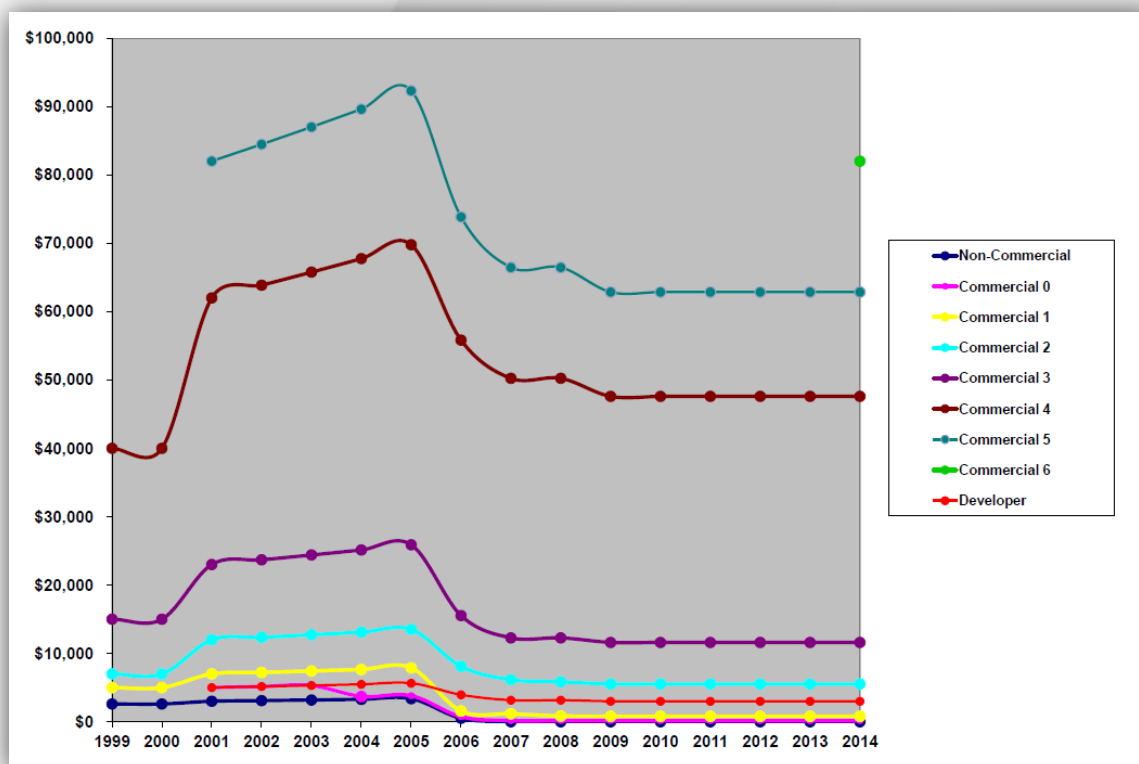
1. Membership Update

The SC noted the updated lists of the: ICH Steering Committee Members, Observers and Coordinators; ICH MedDRA Management Board Members and Observer; and RHIs/DRAs/DoH participating in the Global Cooperation session of the SC.

2. Update on MedDRA

The SC received a report on the ICH MedDRA Management Board meeting held on 9-10 November 2013.

The SC noted that the Board approved the 2014 subscription rates with the introduction of a new Commercial 6 level. Companies with revenue of \$20 Billion and over will be classified as Commercial 6, while the Commercial 5 level will be redefined as companies with revenue of between \$5 and \$20 Billion. There will be no change for Regulatory, Non-Commercial, Commercial 0-4 and Developer licenses. The last 8 years have seen these rates either decrease or remain flat.



MedDRA MSSO Subscription Rate Evolution from 1999 to 2014

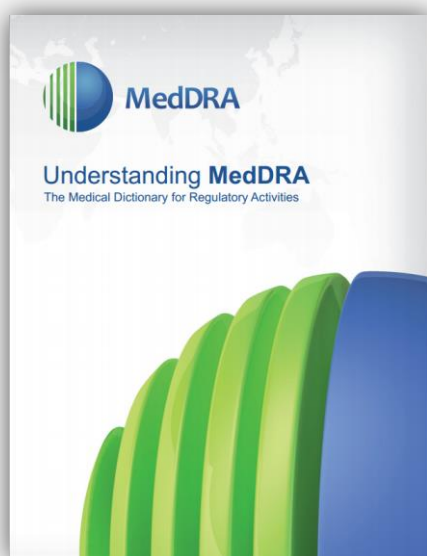
Training is key to helping facilitate the use of MedDRA. Free training is provided by the MSSO to regulators and other MedDRA subscribers in the form of classroom training, webconferences, and downloadable modules. The Board acknowledged the increase in interactive training scheduled by the MSSO in 2013 compared to 2012. This included 50 face-

to-face training courses and 13 webconferences. All training material is available on the MedDRA website (www.meddra.org) for subscribers and non-subscribers alike.

The SC noted that the MSSO has also been investing effort in the development of e-learning tools. A large number of training videos have already been developed and translated from English into several languages (Chinese, French, German and Spanish). All videocasts are available on the MedDRA website. A training curriculum will also be made available shortly to provide direction on the use of the videocasts. This is expected to be helpful for new MedDRA users to build knowledge before attending face-to-face training courses.

The SC was also updated on a meeting of the Board with Regional Harmonisation Initiative (RHI), Drug Regulatory Authority (DRA) and Department of Health (DoH) representatives participating in the ICH meeting. Presentations were made on: *Getting Started with MedDRA*; *Translations: Development & Maintenance*; *Accessing MedDRA*; and *Scope of MedDRA*.

The SC noted that in Osaka, Japan, the Board also met with the Singapore regulator Health Sciences Authority (HSA) and provided Board support for the granting of a Special License to HSA. This will allow HSA to use MedDRA (in non-downloadable format) within an E2B compliant web-based reporting system being developed for implementation in 2014. Small companies will be able to use the system without the need for a MedDRA subscription from the MSSO. Final confirmation on the financial threshold for small companies will be provided shortly by the Board. To-date Special Licences have also been granted to the EMA and Health Canada.



General MedDRA Brochure

The SC noted the work conducted to enhance communication about MedDRA. This included the launch of a revamped MedDRA website in July 2013, followed by the release of a General MedDRA Brochure in September 2013. The SC noted that factsheets on specific MedDRA topics were also under development.

The SC was informed that in Osaka the Board had agreed to the organisation of a Blue Ribbon Panel (BRP) in early 2014 on the Scope of MedDRA. The SC noted that recently the MSSO had received requests for terms which it considered push the boundaries of MedDRA's scope. The Board considered it would be helpful to receive recommendations from a BRP on whether such terms should be included in MedDRA. Further information on the BRP will be available shortly on the MedDRA website.

The SC was updated on activities related to mapping ICD-10 and SNOMED to MedDRA. It was noted that the MSSO was continuing to investigate the feasibility of an ICD-10 to MedDRA mapping, while the UK MHRA had completed its initial mapping to MedDRA of a subset of SNOMED (with input from the MSSO).

SC Decisions/Actions:

- *The SC noted the decisions taken by the MedDRA Management Board on its behalf;*
- *The SC agreed the following communication as part of the post-meeting public press release:*

“In 1999, ICH released MedDRA as its standardized medical terminology. The maintenance and support of MedDRA is contracted to a Maintenance and Support Services Organisation (MSSO). ICH has decided that a new Call for

Tender should be undertaken. This decision represents the interest of the ICH to conform with good business practices and does not reflect on the performance of the current contractor. Therefore, ICH will publish in early 2014 a request for information/call for expression of interest in order to identify interest from potential service providers.”

3. Global Cooperation

In Osaka, Japan, the Global Cooperation (GC) session saw the participation of representatives from the RHIs of ASEAN (Association of Southeast Asian Nations), EAC (East African Community), GCC (Gulf Cooperation Council), PANDRH (Pan American Drug Regulatory Harmonisation) and SADC (Southern African Development Community), and the DRAs of Brazil, China, the Republic of Korea, Russia and Singapore, in addition to the DoH of Chinese Taipei. Participants continued their discussions on the main focuses of this session which are the implementation of ICH Guidelines in the ICH regions and beyond, and training.

The RHIs and DRAs/DoH reported on the outcome of their respective discussions during their pre-meetings where the strategy for ICH global training and experiences/challenges in implementing Quality systems in regions and countries were discussed. The GC members noted the status of implementation of ICH Guidelines in regions and countries and also received presentations on Quality by Design and on the conclusions of the first EMA/FDA Parallel Assessment Pilot.

The GC members noted the outcome of the third ICH/DIA training course on the ICH E2 Series of Pharmacovigilance Guidelines which was held in Muscat, Sultanate of Oman on 22-23 September 2013 and which preceded the DIA Middle East Regulatory Conference (MERC). They also noted the organisation of the next training on the Pharmacovigilance Guidelines in collaboration with DIA in Zagreb, Croatia on 28-29 November 2013.



Recent ICH/DIA training course

Interest was expressed from SADC, EAC and Chinese Taipei on training on the ICH Q8/Q9/Q10/Q11 Guidelines and from Brazil on the ICH Q7 and Q11 Guidelines.

At the GC session, the SC noted the need to develop a strategic plan for ICH global training and a proposal to convene a global summit of key interested parties with a view to defining needs/services and vision to more effectively respond to regional/global training and capacity building needs. The results of an assessment on e-learning tools were presented to GC members. The SC supported continuing research on costs, modalities and services providers. Lastly, the GC members noted the progress made on the development of an ICH training schematic for the ICH website aimed at broadening the outreach to ICH stakeholders and including more the general public.

SC Decisions/Actions:

- *The SC agreed that a small drafting working group should further progress the development of the ICH training schematic for the ICH website;*

- *The SC agreed that the ICH Secretariat with support from the Training Working Group should conduct an assessment of required resources with different training service providers for the development and conduct of e-learning courses on ICH Guidelines;*
- *The SC tasked the informal Quality Discussion Group to consider the training requests of EAC, SADC, Brazil and Chinese Taipei and make a recommendation to the SC prior to the next ICH meeting in Minneapolis, USA in June 2014.*



4. Status Report on Topics

At the start of the meeting in Osaka, Japan, the SC noted the current status of draft ICH Guidelines and predictions for progress towards *Step 2* and *Step 4*. Updated information was provided during the SC meeting by the ICH Rapporteurs of the EWGs/IWG meeting in Osaka.

5. M2: Electronic Standards for the Transfer of Regulatory Information

The Rapporteur reported to the SC on the outcome of the M2 EWG meeting held in Osaka, Japan. The report included an update on:

- M2 Management activity in relation to ICH's electronic standards with the revision and finalisation of five documents (Best Practice Maintenance, SDO Monitoring Process, SDO Monitoring Inventory, File Format Criteria and Revised M2 Glossary) that are included in the information repository;
- Outcome of a SDO survey with the E2B(R3) EWG conducted in April 2013;
- ESTRi recommendation on file format requirements with each region having to confirm the business usability of ".docx" for the exchange of regulatory information;
- Investigation of ".docx" capability for tagging commercial and/or personal information to enable redaction from dossier files;
- Benefits and challenges of moving from unstructured to structured regulatory data.

A work plan was also proposed for activities to be undertaken between the Osaka meeting and the next meeting in Minneapolis, USA, in June 2014. This included: continuing SDO monitoring activities; drafting a Technology Watch document; providing the information repository to ICH EWGs/IWG; and proceeding with ESTRi action items.

SC Decisions/Actions:

- *The SC approved the work plan and major activities between the Osaka and Minneapolis meetings;*
- *The SC endorsed the work plan of the M2 EWG for activity to be undertaken at the Minneapolis meeting in June 2014;*
- *The SC agreed that the M2 EWG should consult on an appropriate candidate to assume the Rapporteurship of the EWG, for endorsement by the SC as soon as possible.*

6. M8 EWG/IWG: The Electronic Common Technical Document: eCTD

The Rapporteur reported to the SC on the outcome of the M8 EWG/IWG meeting held in Osaka, Japan.

The report included an update on the work of the M8 IWG with respect to current eCTD specification, for which one new Change Request was processed. The regulatory expert members of the M8 IWG subsequently signed-off *Step 4* of Version 1.25 of the Change Request/Q&A document.

The M8 IWG invited the SC to consider reconvening the CTD-Q IWG to address questions the M8 IWG receives related to CTD-Q by updating the M4 Annex Granularity Document or by developing Q&As.

The status of the ongoing *Step 2 for Testing* of the next major version of the eCTD, Version 4.0 was reported. The SC supported the proposed timeframe for reaching *Step 2* in November 2014 and *Step 4* in November 2015.

The M8 EWG also presented the SC with its work plan for activity to be undertaken between the Osaka meeting and the next ICH meeting in Minneapolis in June 2014. It included work related to completion of *Step 2 for Testing* and preparation for *Step 2*.

The group also informed the SC of its discussion regarding the compound document. The SC noted that the group aimed to reach consensus by January 2014 on a proposal regarding the approach.

SC Decisions/Actions:

- *The regulatory SC members signed-off Step 4 of Version 1.25 of the eCTD Change Request/Q&A document;*
- *The SC agreed to reconvene the CTD-Q IWG to work by email and teleconference to address questions from the M8 IWG;*
- *The ICH Secretariat will confirm the nominations for the CTD-Q IWG;*
- *The ICH Secretariat will follow-up with the ICH Parties to confirm the Rapporteurship of the CTD-Q IWG;*
- *The SC supported the updated milestones set for the progression of eCTD v4.0 with Step 2 to be reached in November 2014 and Step 4 in November 2015;*
- *The SC endorsed the work plan of the M8 EWG/IWG for work to be undertaken between the Osaka and Minneapolis meetings;*
- *The SC endorsed the work plan of the M8 EWG/IWG for activity to be undertaken at the Minneapolis meeting in June 2014.*

7. Q7 IWG: Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients

The Rapporteur reported to the SC on the outcome of the Q7 IWG meeting held in Osaka, Japan and progress made in the development of the ICH Q7 Q&A document.

Based on feedback received from a survey conducted in late 2012, 114 questions on technical issues were divided amongst the three regions. The SC noted that the Q7 IWG reviewed regionally drafted Q&As with agreement reached on 24 Q&As with the three regional sub-groups.

The SC noted that the Q7 IWG would discuss and revise 32 outstanding drafted Q&As between now and Minneapolis.

The SC noted the recommendation of the Q7 IWG to wait for the finalisation of all the ICH Q7 Q&As before publication.

SC Decisions/Actions:

- *The SC supported the work plan of the Q7 IWG for activity to be undertaken between the Osaka and Minneapolis meetings;*

- *The SC supported the work plan of the Q7 IWG for activity to be undertaken at the Minneapolis meeting in June 2014.*

8. S10 EWG: Photosafety Evaluation

The Rapporteur reported to the SC on the outcome of the S10 EWG meeting held in Osaka, Japan.

The SC noted that the EWG reached agreement on all public comments which were received from regional consultation. The regulatory S10 experts signed-off the *Step 4* S10 Guideline. The SC noted that a set of slides on the final ICH S10 Guideline will be developed by the S10 EWG ahead of the organisation of a webinar by the ICH Secretariat which will also be made available on the ICH website.

SC Decisions/Actions:

- *The regulatory members of the SC signed-off Step 4 of the S10 Guideline;*
- *The ICH Secretariat will organise a webinar on ICH S10 Guideline in Q1 2014;*
- *The SC acknowledged that this completed the S10 EWG's work.*

9. Safety Brainstorming Session

The Chair reported to the SC on the outcome of the two-day brainstorming session held in Osaka, Japan. Sixteen topics were discussed by the group with the following four ranked as priority topics by the SC:

- Development of Q&A for ICH S9 on *Evaluation of Anti-Cancer Drugs* to facilitate S9 implementation;
- Revision of ICH S5(R2) on *Reprotoxicity* to evaluate new data collected;
- Development of Q&A for ICH S3A on *Toxicokinetics* to address the use of microsampling techniques that would lead to saving of animals;
- Development of a new ICH Guideline on *Non-Clinical Safety Assessment for Pediatric Drugs*.

Apart from these topics, there was general agreement among the safety experts to propose an approach to further enhancing implementation of Safety topics.

SC Decisions/Actions:

- *The SC agreed that Concept Paper should be developed and provided to the SC for its consideration prior the SC webconference in spring 2014. The SC will decide at its webconference on which working groups would meet in Minneapolis in June 2014 ;*
- *The SC supported the proposed approach to further enhance implementation of Safety topics by setting-up an e-mail box on the ICH website to collect any safety-related questions.*

10. M7 EWG: Assessment and Control of DNA Reactive (mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk

The Rapporteur reported to the SC on the outcome of the M7 EWG meeting held in Osaka, Japan.

The SC noted that the group had progress to review the comments received from the regulatory public consultation conducted in the three ICH regions on the *Step 2* M7 draft Guideline. The SC noted that the M7 EWG would recommend that for combination products,

each active ingredient should be regulated separately. Consensus was also reached within the M7 EWG that only actual data from a well performed bacterial mutation assay should trigger regulatory action on an impurity in a marketed product. The SC noted that the table describing the relationship of the duration of treatment and its application to LTL-TTC for actual clinical use can generate confusion among stakeholders and pointed out that a feedback from clinicians working for each party should be necessary.

Progress was also made on the development of an addendum table on known mutagenic impurities commonly found or used in drug synthesis. The Rapporteur suggested that a proposed list of monographs and limits could be submitted for public comment (*Step 2b*) after the next ICH meeting in Minneapolis in June 2014. The SC also noted that monograph additions to the addendum could be made following a procedure similar to that used for ICH Q3C.

The M7 EWG will continue to work by e-mail and teleconference with the aim of reaching *Step 4* in June 2014 on the core ICH M7 Guideline.

SC Decisions/Actions:

- *The SC supported the work plan of the M7 EWG with the aim of reaching Step 4 in June 2014;*
- *The SC tasked M7 EWG to have a feedback from clinicians on the table describing the duration of treatments to apply LTL-TTC for actual clinical use.*
- *The SC agreed that the addendum should go out for public comment (Step 2b) prior to its finalisation;*
- *The SC agreed that additional monographs could be added to the addendum following a similar procedure to that used for the ICH Q3C Guideline;*
- *Each Party approved the inclusion of the addendum chart.*

11. E2C(R2) IWG: Periodic Benefit-Risk Evaluation Report (PBRER)

The Rapporteur reported to the SC on the outcome of the first E2C(R2) IWG face-to-face meeting held in Osaka, Japan.

The SC noted that a stakeholder survey was conducted with all interested parties from April to October 2013 to support implementation of the new PBRER. Key themes were identified by the IWG including: the prevention of overlapping/repetition of data for signals and risks across different PBRER sections that would lead to expanded guidance on signal and risk sections; the clarification on: (1) how to present benefit-risk evaluation; (2) how to transition information from the PSUR to the new PBRER; (3) how to present exposure data; and lastly, (4) how to manage different periodicities of PBRER submission.

The SC also noted the progress made by the E2C(R2) IWG in Osaka on the development of the E2C(R2) Q&A document which is expected to reach *Step 4* of the ICH process by the end of 2013.

SC Decision/Action:

- *The SC supported the work plan of the E2C(R2) IWG and the proposed timeframe for reaching Step 4 of the ICH E2C(R2) Q&As by the end of 2013.*

12. EWGs/IWGs not Meeting in Osaka, Japan

❖ **Q3D EWG: Guideline for Elemental Impurities**

The Q3D EWG did not meet in Osaka, Japan.

The SC noted the deadline for regulatory consultation in the three regions as follows:

- ✧ Japan: November 29, 2013;
- ✧ USA: December 23, 2013; and,
- ✧ EU: December 21, 2013.

The SC noted that the ICH Q3D Guideline was expected to reach *Step 4* in June 2014.

SC Decision/Action:

- *The SC endorsed the work plan of the Q3D EWG for activity to be undertaken up to the Minneapolis meeting in June 2014.*

❖ Q4B EWG: Evaluation and Recommendation of Pharmacopoeial Texts for use in the ICH Regions

The Q4B EWG did not meet in Osaka, Japan.

The SC noted that the Q4B EWG had completed its overall work with the finalisation of Annex 6 on *Uniformity of Dosage Units*.

SC Decisions/Actions:

- *The regulatory SC members signed-off Step 4 of the Q4B Annex 6 on Uniformity of Dosage Units General Chapter;*
- *The SC acknowledged that this completed the Q4B EWG's work.*

❖ S1 EWG: Rodent Carcinogenicity Studies for Human Pharmaceuticals

The S1 EWG did not meet in Osaka, Japan.

The SC noted the current activities of the S1 EWG including the publication of the Final Regulatory Notice Document on the ICH website and the launch of confidential submissions of Carcinogenicity Assessment Documents (CADs) by sponsors to the regulatory authority within each ICH region which formally marks the beginning of the Prospective Evaluation Period.

SC Decision/Action:

- *The SC endorsed the work plan of the S1 EWG for activity to be undertaken up to the Minneapolis meeting in June 2014.*

❖ E14 IWG: Q&As on Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs

The E14 IWG did not meet in Osaka, Japan.

The SC noted that the group was expecting to finalise shortly the two remaining Q&As on *Guidance for Collecting ECG Data in Drugs that are not Amenable to TQT Studies*, and on *Combination Products*.

SC Decisions/Actions:

- *Once the two E14 Q&As have been finalised by the E14 IWG, the regulatory members of the SC will be invited to sign-off the Step 4 document;*
- *The SC acknowledged that this would complete the E14 IWG's work.*

❖ M1 PtC: MedDRA Points to Consider (PtC) Working Group

The MedDRA PtC Working Group (WG) did not meet in Osaka, Japan.

The SC noted the ongoing activities of the group with respect to the updating with each MedDRA release of the two PtC documents on *Term Selection* and *Data Retrieval and Presentation* to facilitate consistent use of MedDRA. The documents for MedDRA Version 16.1 were released on 1 October 2013.

SC Decision/Action:

- *The SC endorsed the work plan of the M1 PtC WG for activity to be undertaken up to the Minneapolis meeting in June 2014.*

13. Future ICH Topics

The ICH SC reviewed proposals for new topics provided by all parties and agreed on the development of Concept Papers for potential items such as providing further harmonisation on requirements for clinical trials. The SC will discuss draft Concept Papers at its spring webconference with a view to approving the establishment of new ICH working groups to already progress some of the new topics. The SC will also further discuss and prioritise potential new quality topics before the next face-to-face meeting. In order to improve the strategic oversight on ICH work, future topics will be integrated in a 5-year plan.

14. Communication about ICH

ICH Regional Public Meetings

The SC received a report from MHLW/PMDA and JPMA on the workshop held with DIA Japan at the 10th Japan Annual Meeting on 6 - 8 November 2013 in Tokyo, Japan. This was very well received with over 1,000 attendees.

The SC received an update on the regional ICH public meeting that would be organised by JPMA in collaboration with MHLW/PMDA in Japan on 10 December 2013, in Tokyo.

The SC noted the organisation by EFPIA of a Regional Public Meeting to be held with DIA Europe in Vienna on 28 March 2014, following the DIA Euro Annual Meeting.

Dates of Next Meetings for 2014

31 May - 5 June 2014 in Minneapolis, MN, USA

8 - 13 November 2014 in Europe (location to be confirmed)

EWG/IWGs Meeting in Minneapolis, MN, USA

A list of EWG/IWGs which will meet face-to-face at the next ICH meeting in Minneapolis, MN, USA on 31 May - 5 June 2014 will be made available on the ICH public website following the SC webconference to be held in spring 2014.