

# ICH STEERING COMMITTEE

November 6-11, 2010

Fukuoka, Japan

## SUMMARY

### 1. Opening Discussions

[The ICH Steering Committee \(SC\)](#) meeting in Fukuoka was chaired by MHLW. The meeting commenced with the provision of updates on the work of the ICH Secretariat, [ICH MedDRA Management Board](#) and the [ICH Global Cooperation Group \(GCG\)](#).

**ICH Secretariat:** The ICH Secretariat updated the SC on some of its recent activities, including work to revamp the [ICH website](#) to give it a more consistent look and feel and make it more user-friendly. The SC noted that the intention was to launch the new website in late 2010 to coincide with the 20<sup>th</sup> anniversary of ICH.

Also in celebration of the 20<sup>th</sup> anniversary of ICH, the SC welcomed the publication of a new brochure entitled [The Value & Benefits of ICH to Drug Regulatory Authorities-Advancing Harmonisation for Public Health](#). The Secretariat informed the SC that the brochure could be downloaded from the ICH website.

**ICH MedDRA Management Board:** The Chair of the ICH MedDRA Management Board reported on the decisions taken by the Board on behalf of the SC. The SC was updated on training activities undertaken by the [MSSO](#) (MedDRA Maintenance and Support Services Organization). The Chair informed the SC that as of the end of October 2010, over 600 subscribers, including many regulators, had received MedDRA training at different locations in Europe and the US. The SC noted that the MSSO was also offering training via web-conferencing and e-learning tools.

The SC was also updated on a meeting of the Board with Regional Harmonisation Initiative (RHI) and Drug Regulatory Authority (DRA)/Department of Health (DoH) representatives from the ICH GCG. The Chair informed the SC that RHIs in attendance included APEC, ASEAN, GCC and SADC, while DRAs/DoH in attendance included China, Chinese Taipei, Republic of Korea and Singapore. The SC noted that this was the second time a special session of the Board had been held with the GCG representatives to address their interest in [MedDRA](#).

The meeting included presentations on ICH's selection of MedDRA as its adverse event reporting terminology, Health Canada's experience with the recent implementation of MedDRA, and ICH efforts to help facilitate MedDRA's use in pharmacovigilance activities (e.g., development of ICH-endorsed Guidance on Coding and Data Retrieval & Analysis, provision of training and development of various web tools).

The SC also noted the Board's discussions in relation to: the scheduled release of a Hungarian translation of MedDRA in March 2011 (MedDRA v14.0), adding to the 10 languages already available (Chinese, Czech, Dutch, English, French, German, Italian, Japanese, Portuguese, and Spanish); Board approval of the 2011 subscription rates for

MSSO subscribers, with no increase in the rates for a sixth consecutive year; and potential future activities of the [CIOMS \(Council for International Organizations of Medical Sciences\)](#) Working Group on SMQs (Standardised MedDRA Queries) in relation to the promotion of SMQs utility in pharmacovigilance activities.

**ICH Global Cooperation Group:** The GCG Co-Chairs reported to the SC on the GCG meeting, which saw the participation of representatives from the RHIs of APEC, ASEAN, GCC, and SADC, and the DRAs of China, India, Republic of Korea and Singapore, in addition to the DoH of Chinese Taipei.

As part of the Fukuoka meeting RHI and DRA/DoH representatives provided updates on ICH-related matters in their regions. A presentation was also given by an ICH expert on the [ICH E2F Guideline](#) on *Development Safety Update Report (DSUR)* which reached [Step 4](#) in August 2010.

The GCG meeting also saw discussion of the considerations and criteria considered by the SC in relation to the opening-up of ICH technical working groups to participation from technical experts from the RHIs and DRAs/DoH.

## 2. Proposals for New Topics and Revisions/Maintenance of Guidelines

**Pharmacovigilance Brainstorming Session:** The SC was informed on the outcome of the 2-day brainstorming session held in Fukuoka to discuss safety reporting in view of the DSUR and PSUR (Periodic Safety Update Report), as well as benefit/risk approaches, and current legislative parameters and regional constraints.

The SC noted the group's vision to optimise the lifecycle benefit/risk of medicines for the promotion and protection of public health by establishing a modular and improved approach to the documentation of safety information, risk evaluation, risk minimisation and benefit/risk evaluation, including how these are evaluated and planned. To achieve this vision the SC was informed that an ICH Expert Working Group (EWG) would need to be established to evaluate the ICH pharmacovigilance documentation, conduct a gap and potential improvement analysis of ICH E2C, E2E and E2F Guidelines and also to draft a new ICH E2C(R2) Guideline to replace the current ICH E2C(R1) Guideline on *Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs*.

The SC supported that the EU revise the draft Concept Paper it had previously developed proposing a revision of the E2C(R1) Guideline to reflect the discussions from the pharmacovigilance brainstorming session. The SC agreed to consider approval of the draft Concept Paper and Business Plan at an *ad hoc* SC teleconference in December 2010.

## 3. Reports on Current Topics

### *EWGs/IWGs/Discussion Groups Meeting in Fukuoka*

**[M2/eCTD](#): Electronic Standards for the Transfer of Regulatory Information and the Electronic CTD:** The SC was updated on the outcome of the M2 meeting which was held in Fukuoka. At the meeting the restructuring of the M2 EWG was discussed. The SC noted that under the current M2 remit there was participation from M2 experts in a number of sub-groups: M2/E2B(R3); M2/M5; eCTD; SENTRI (Standards

Everyone Needs for the Transfer of Regulatory Information); and SDO (Standard Development Organisation) Relationship Management. Under the new structure, the M2 EWG would be responsible for SENTRI activities in addition to SDO relationship management, coordination and best practice. Work relating to the eCTD, E2B(R3) and M5 activities would be undertaken by extended EWGs. In support of this restructuring, the SC approved several documents developed by the group which included new Terms of Reference for M2 and an eCTD Concept Paper. The SC also agreed to assign the code M8 to the newly established eCTD EWG.

Regarding the eCTD Next Major Version (NMV), the SC approved an updated set of ICH Requirements to be fed into the [HL7 \(Health Level Seven\)](#) RPS (Regulated Product Submission) project. The SC noted that HL7 was currently targeting May 2011 for the DSTU (Draft Standard for Trial Use). In view of this timeline, the SC noted that the ICH and regional Implementation Guides would need to be drafted by May 2011, with ICH testing to be performed between June 2011 and February 2012. The expectation would be that the ICH Implementation Guide would then move to [Step 2](#) in August 2012.

The SC was also updated on the work being undertaken regarding ISO 32000 on the use of PDF versions, as well as an assessment of XML. The SC also approved M2 Recommendations for MD5 and EDI-INT (AS2).

**[E2B\(R3\): Revision of Electronic Submission in Individual Case Safety Reports:](#)** The Rapporteur reported to the SC on the outcome of the M2/E2B(R3) sub-group meeting in Fukuoka. Feedback was provided to the SC on the ICH and public comments generated by the *Feasibility Testing* carried out during the 2<sup>nd</sup> [ISO \(International Organization for Standardization\)](#) ICSR (Individual Case Safety Report) DIS (Draft International Standard) ballot. The SC noted that comments had then been identified for submission to ISO and the actions captured for updating the ICH Implementation Guide for the ICSR. The SC noted that the ICSR Part 2 standard had passed the ballots in both ISO and HL7, and also noted that ICH would only be using the ICSR Part 2 schemas for reports within the E2B(R3) scope.

The SC was also updated on the group's discussion concerning how to handle regional requirements. The Rapporteur informed the SC that at *Step 2* information on regional requirements would be provided separately from the ICH Implementation Guide, and for *Step 4* the Implementation Guide would set out the additional need to use regional guidance with links to these guidances to be provided on the ICH ESTRI (Electronic Standards for the Transfer of Regulatory Information) website.

**[M5: Data Elements and Standards for Drug Dictionaries:](#)** The SC was updated on the outcome of the M2/M5 sub-group meeting held in Fukuoka. The SC noted that the ISO IDMP (Identification of Medicinal Products) DIS ballot had been initiated on September 23, 2010 for a 5-month period. The Rapporteur informed the SC that ICH testing of the draft standard had already been initiated, with the first results from the ICH regions and Health Canada being reviewed at the Fukuoka meeting. The SC noted that testing would continue and that the final set of ICH comments for submission to ISO/HL7 would be agreed by the M5 EWG for endorsement by the SC in early 2011.

The SC was also informed of the organisation of the ICH Implementation Guide according to a new format, dividing the 5 modules into the ICH elements and the regional elements, and providing examples for both ICH and regional requirements.

**Pharmacopoeial Discussion Group:** On behalf of the Pharmacopoeial Discussion Group (PDG), the Japanese Pharmacopoeia reported on the current status of PDG harmonisation efforts. The SC noted that nine Q6A General Chapters had been signed-off as well as twelve other General Chapters, six methods for Biotech products and forty-one for excipients. It was noted that chromatography had also been added to the PDG work programme following a meeting of experts from the three ICH regions.

**Q4B: Evaluation and Recommendation of Pharmacopoeial Texts for use in the ICH Regions:** The Q4B Rapporteur reported to the SC on the progress made by the Q4B EWG in Fukuoka.

The Q4B EWG finalised Annex 13 on *Bulk Density and Tapped Density* and Annex 14 on *Bacterial Endotoxins*, and informed the SC that these were anticipated to be signed-off at *Step 4* once the relevant JP (Japanese Pharmacopoeia) test is official (expected in April 2011). The SC noted that Annex 6 on *Uniformity of Dosage Units* would be signed-off at *Step 4* subject to publication by USP (United States Pharmacopoeia). The Rapporteur informed the SC that the only remaining Q6A Chapter was *Colour* and this was not expected before 2013. The Q4B EWG also worked towards the finalization of training materials in Fukuoka.

The SC acknowledged that the Q4B work programme was largely complete and congratulated the group on its work. With regards to whether the scope of the work programme for Q4B should be expanded, the SC agreed that in line with ICH procedures any expansion of scope would require the development of a Concept Paper for its consideration. In recognition of the need to ensure that the Q4B Annexes are maintained should pharmacopoeial texts be updated, the Steering Committee approved a maintenance process which would allow for the establishment of an *ad hoc* EWG to undertake revisions as approved by the Steering Committee.

**Q11: Development and Manufacture of Drug Substances:** The Q11 Rapporteur provided an update on the activities of the Q11 EWG. The SC noted that good progress was made in Fukuoka towards reaching *Step 2* and that the next steps would be for each ICH Party to review the current draft and provide feedback. The Rapporteur commented that in the absence of significant comments from the ICH Parties it could be possible to reach *Step 2* early in 2011. However if significant comments are received *Step 2* would not be anticipated until the next meeting in Cincinnati in June 2011.

**Quality IWG:** The Rapporteur reported to the SC on the outcome of the Quality IWG (Implementation Working Group) meeting in Fukuoka and provided overall feedback from the three ICH regional workshops on the *Implementation of ICH Guidelines Q8, Q9 and Q10* which were held in Tallinn in June 2010, and in Washington D.C. and Tokyo in October 2010. The Rapporteur informed the SC that each of the workshops had been well attended with positive feedback received from the participants.

As part of its work plan, the SC noted that the Quality IWG would: develop further Questions & Answers (Q&As) to add to the 45 Q&As already published; finalise the

workshop summary report; continue collaboration with the ICH GCG to provide training outside of the ICH regions upon request; and work to address remaining technical and regulatory gaps through the development of implementation “Points to Consider” documents.

**Q3D: Guideline for Metal Impurities:** The Rapporteur reported to the SC on the outcome of the Q3D EWG meeting. In Fukuoka, the EWG worked to resolve the scope of the guideline, agreeing that the guideline would apply to new drug products, including biopharmaceuticals, but not to herbal products, radiopharmaceuticals, and metals that are intentionally part of the drug product.

The SC noted that the aim would be to reach *Step 2* by November 2011.

**S6(R1): Addendum to Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals:** The Rapporteur updated the SC on the outcome of the S6(R1) EWG meeting in Fukuoka and progress made to reach *Step 4* of the Addendum to the S6 Guideline. The EWG reviewed comments received from various regions on the *Step 2* document. The Rapporteur commented that good progress was made at the meeting with many of the remaining issues resolved. The SC noted that some discussion was still required.

**S10: Photosafety Evaluation:** The S10 Rapporteur updated the SC on the discussions of the S10 EWG at its first meeting. In Fukuoka, the EWG confirmed the objectives and scope of the guideline. The Rapporteur highlighted the key objectives of the guideline which would be to recommend international standards for photosafety assessment, and to promote harmonisation of such assessments to support human clinical trials and marketing authorization for pharmaceuticals. The guideline would contain additional information to that provided in ICH M3(R2) Section 14 on Photosafety Testing, including criteria for initiation of and triggers for additional photosafety testing.

Consideration would also be given in the guideline to the use of *in vitro* alternative methods for photosafety assessment, with the consequence of reducing the use of animals in accordance with the 3R (reduce/refine/replace) principles.

The SC noted that the timeframe for reaching *Step 2*, and subsequently *Step 4*, would be dependent on whether the group conducts a data survey. With the conduct of a data survey, the Rapporteur informed the SC that *Step 2* would be expected by June 2012. Without the data survey *Step 2* would be possible six months earlier than this.

**M7: Genotoxic Impurities:** The Rapporteur reported to the SC on the outcome of the first meeting of the M7 EWG. In Fukuoka, the EWG agreed that the guidance should focus on carcinogenic risk of mutagenic impurities. The group identified the areas that need to be addressed, started to identify general principles, and assigned parties for the drafting of the various topic sections. The scope of the M7 Guideline was also discussed, including alignment with the scopes of the Q3D and Q11 Guidelines currently under development.

The SC approved the new title for the M7 Guideline proposed by the group: *Assessment and Control of DNA Reactive (Mutagenic) Impurities in Pharmaceuticals to Limit Potential Carcinogenic Risk*.

The SC noted that *Step 2* was expected in either June or November 2012.

***EWGs/IWGs/Discussion Groups Meeting in Fukuoka***

**Q3C(R5): Impurities: Guideline for Residual Solvents:** The Q3C(R5) EWG did not meet in Fukuoka. The SC noted that the revision to the Q3C(R4) guideline (to take account of new toxicity data related to cumene) was expected to reach *Step 4* in early 2011.

**CTD-Quality: Q&As:** The CTD-Quality IWG did not meet in Fukuoka. The SC noted the ongoing work of the group to address Quality Change Request issues identified by the M2 EWG. With a first set of Q&As already finalised, the SC supported the request of the group to meet face-to-face in Cincinnati in June 2011 to further progress the development of a second and third set.

**S2(R1): Guidance on Genotoxicity Testing and Data Interpretation for Pharmaceuticals Intended for Human Use:** The S2(R1) EWG did not meet in Fukuoka. The SC noted that further to the FDA advisory committee meeting held in January 2010, discussion was still ongoing within the FDA in relation to the S2(R1) draft Guideline which had reached *Step 2* in March 2008.

**E14: Q&As: The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs:** The E14 IWG did not meet in Fukuoka. The SC approved a detailed work plan produced by the group for the development of the additional E14 Q&As, and the group's request for a face-to-face meeting. The SC noted that the aim of the group would be to finalise its Q&A document by autumn 2011 and to initiate Phase 2 of its work in June 2013 which would involve addressing topics that required extensive data analysis including those arising from tQT studies, scientific developments and regulatory requirements. The outcome of Phase 2 could either be an enhancement of the current guideline, either by re-opening it or by developing an additional set of Q&As.

**M1 PtC: MedDRA Points to Consider (PtC):** The MedDRA PtC Working Group did not meet in Fukuoka. The SC noted the ongoing work of the group in relation to the development and maintenance of the MedDRA PtC guidance documents on *Term Selection* and *Data Retrieval and Presentation*.

**M3(R2): Q&As: Guidance on Nonclinical Safety Studies For the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals:** The M3(R2) IWG did not meet in Fukuoka. The SC noted the work being undertaken by the M3(R2) EWG to develop Q&As.

**M6: Guideline on Virus and Gene Therapy Vector Shedding and Transmission /GTDG: Gene Therapy Discussion Group:** The M6 EWG/GTDG did not meet in Fukuoka. The SC noted the status of the groups' activities.

**4. Dates of Next Meetings for 2011 & 2012:**

June 11-16, 2011	Cincinnati, Ohio, USA
November 5-10, 2011	Europe – location to be confirmed
June 2-7, 2012	Japan – location to be confirmed