

# ICH STEERING COMMITTEE

**June 5-10, 2010**

**Tallinn, Estonia**

## **SUMMARY**

### **1. Opening Discussions**

The ICH Steering Committee (SC) meeting was chaired by the EU. The meeting commenced with the provision of updates on the work of the ICH Secretariat, MedDRA and the Global Cooperation Group (GCG).

**ICH Secretariat:** The ICH Secretariat updated the SC on some of its recent activities, which included the posting of all Final Concept Papers and Business Plans on the ICH website, and work to revamp the ICH website.

**MedDRA:** The Chair of the ICH MedDRA Management Board reported on the decisions taken by the Board on behalf of the ICH Steering Committee. The SC was updated on training activities undertaken by the MSSO (MedDRA Maintenance and Support Services Organization). The Chair informed the SC that in May 2010 the first free training for MedDRA users in China had been offered. In addition, the SC noted the establishment of a Chinese MedDRA User Group.

The Chair also reported on the successful organisation of a 3-day workshop on *MedDRA and its Application in Safety Drug Monitoring* which was held in Kuala Lumpur, Malaysia in March 2010. The training was requested by ASEAN through the ICH GCG and was supported by the National Pharmaceutical Control Bureau of the Malaysian Ministry of Health. The workshop was well-received, being attended by 22 ASEAN Regulators from Brunei, Cambodia, Indonesia, Laos, Malaysia, Philippines, Singapore and Vietnam, in addition to 26 representatives of local pharmaceutical and multinational companies.

The SC was also updated on a meeting of the Board with Regional Harmonisation Initiative (RHI) and Drug Regulatory Authority (DRA) representatives of the GCG. The meeting was organised in response to interest expressed in the use of MedDRA, and was attended by representatives of the RHIs of APEC, ASEAN, GCC and SADC, and the DRAs of Singapore and South Korea.

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); the renewal by the Board of the Memorandum of Understanding with CIOMS (Council for International Organizations of Medical Sciences) to continue the developmental activities of Standardised MedDRA Queries (SMQs); the decision to use MedDRA to support toxicity monitoring in the EU's Alerting System for Chemical Health Threats (ASHT Phase II); and agreement by the Board for MSSO to proceed with the development of a MedDRA Versioning Analysis

Tool (MVAT) to support user understanding of the impact of MedDRA releases on their coded data.

**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 Drug Regulatory Authorities (DRAs) of Brazil, China, Singapore, and South Korea.

The report included an update on the finalisation of a paper describing the *Value and Benefits of ICH to Regulators*. The SC noted that the paper would be published shortly to commemorate the 20<sup>th</sup> anniversary of ICH and would be distributed at the next ICH meeting in Fukuoka in November 2010.

As part of the Tallinn meeting RHI and DRA representatives provided updates on ICH-related matters in their regions. Presentations were also given by ICH experts on *ICH's Work with Standard Development Organisations (SDOs)*, the development of the ICH Q11 Guideline on *Development and Manufacture of Drug Substances*, and the organisation in Tallinn on June 2-4, 2010 of the first ICH regional workshop on the *Implementation of ICH Guidelines Q8, Q9 and Q10*. A presentation was also provided on the *Evolution of the EU System for the Authorisation of Medicinal Products*.

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

**Proposal for New Safety Topics: Genotoxic Impurities, Photosafety Evaluation, & Non-Clinical Aspects of Vaccine Testing:** Following review of Concept Papers and Business Plans on *Genotoxic Impurities* and *Photosafety Evaluation* developed by the Safety Brainstorming Discussion Group, the SC endorsed these new topics and approved the establishment of two new Expert Working Groups (EWGs). The M7 EWG will work to develop an ICH Guideline on *Genotoxic Impurities*, and the S10 EWG a Guideline on *Photosafety Evaluation*.

The SC also discussed the draft Concept Paper which had been developed on *Non-Clinical Aspects of Vaccine Testing*. The SC agreed that before considering this topic further it would await the outcome of both the international scientific workshop convened by IABS (International Association for Biologicals) (April 29-30, 2010) and a WHO Expert Consultation to be held on September 1-2, 2010. Based on the outcomes of both events the SC will decide at its teleconference (to be held in preparation for the next ICH meeting) whether there is a need to organise a brainstorming session with vaccine experts to discuss the next steps.

**In Vitro Models for Reproduction Toxicity Workshop:** The SC received feedback from a half-day workshop which was held in Tallinn to discuss *In Vitro Models for Reproduction Toxicity*. The workshop was held as part of an assessment of whether the S5(R2) Guideline on *Detection of Toxicity to Reproduction for Medicinal Products and Toxicity to Male Fertility* needed to be revised. The SC agreed that no further work needed to be undertaken on the topic at the current time, and that each party should consider the outcome of the workshop in relation to any of their own internal projects.

**E2C(R1): Clinical Safety Data Management: Periodic Safety Update Reports for Marketed Drugs:** The SC shared views on a Concept Paper which had been

developed to propose a revision of the E2C(R1) Guideline. The SC agreed that the Concept Paper would need to be redrafted, but as a first step a brainstorming session would be organized at the next meeting in Fukuoka in November 2010 to allow an overarching discussion on safety update reporting in view of the DSUR and PSUR, as well as benefit/risk approaches, and current legislative parameters and regional constraints.

### 3. Reports on Current Topics

**Electronic Standards for the Transfer of Regulatory Information and the Electronic CTD (Topic M2/eCTD):** The SC was updated on the outcome of the M2 meeting which was held in Tallinn. The report included feedback from the M2 SDO Relationship Management sub-group, the eCTD sub-group, and the SENTRI sub-group.

The Rapporteur updated the SC on discussions concerning the future of the M2 EWG and a proposal to restructure the group, which would include the current M2 eCTD sub-group becoming an EWG for the duration of the work to develop the next major version of the eCTD. The SC agreed that the group should work to develop detailed terms of reference and working practices for the new M2 EWG, in addition to a Concept Paper for the new eCTD EWG.

Concerning the next major version of the eCTD, the Rapporteur informed the SC that a request for further definition of ICH requirements had been received from HL7 (Health Level Seven). Based on this the requirements were further refined and approved by the SC for provision to HL7. The SC noted that the group would work to develop ICH and Regional Test Cases and the ICH Test Plans. Work would also be initiated for the development of the ICH Implementation Guide.

The SC was also updated on the activities of the SENTRI sub-group, and approved a plan for the conduct of an evaluation programme for the use of XML, which would consider its potential applicability within the eCTD and potential future projects.

**E2B(R3): Revision of Electronic Submission in Individual Case Safety Reports:** The Rapporteur reported to the SC on the outcome of the E2B(R3) EWG meeting in Tallinn, including joint meetings held with the M2 EWG and the M5/M2 sub-group. The SC was informed that the 2<sup>nd</sup> ISO ICSR DIS (Draft International Standard) was expected to be published shortly by ISO and the ISO ballot initiated. Once published, the SC noted that *Feasibility Testing* for the ICSR would be initiated via the ICH website for a period of one-month during which time comments would be collected from the public.

The Rapporteur also updated the SC on discussions held in relation to how to manage regional information for the ICSR and ensure that such requirements are not in conflict with ICH's requirements.

The SC was also informed of the groups' recommendation to conduct ICH *Step 3* using the 2<sup>nd</sup> DIS document as a basis. The target timeframe for this would be November 2010 – May 2010, with *Step 4* targeted for November 2011.

**M5: Data Elements and Standards for Drug Dictionaries:** The SC was updated on the outcome of the M5 EWG meeting held in Tallinn, including joint meetings held with the M2 EWG and the E2B(R3)/M2 sub-group.

The SC was informed that the ISO IDMP (Identification of Medicinal Products) DIS ballot was expected to be initiated in August 2010. The Rapporteur presented the SC with a recommendation from the group that *Feasibility Testing* not be carried out by ICH until *Step 2* is reached. Instead testing of the DIS would remain within ICH.

The SC noted that in Tallinn the group had worked to outline ICH's Test Plan, as well as a plan for completion of the Implementation Guide. In addition, the group worked to resolve a number of issues, including how to manage regional information for the IDMP whilst ensuring that regional requirements are not in conflict with ICH requirements.

**Pharmacopoeial Discussion Group:** On behalf of the Pharmacopoeial Discussion Group (PDG), the European Pharmacopoeia reported on the current status of PDG harmonisation efforts.

It was noted that eight out of the original ten Q6A General Chapters submitted to Q4B had been completed. Work was continuing on the *Bulk and Tapped Density* and the *Colour* General Chapters.

**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 Tallinn.

*Step 4* was reached for Q4B Annex 11 on *Capillary Electrophoresis* and Annex 12 on *Analytical Sieving*. *Step 2* was reached for Annex 13 on *Bulk Density and Tapped Density* and Annex 14 on *Bacterial Endotoxins*.

The SC was also informed that the group had made progress on the development of a PowerPoint presentation and Q&As on the implementation of the interchangeable texts.

The SC was also gave its support to further discussion by the Q4B EWG on future options for the interchangeability of pharmacopoeial texts.

**Q11: Development and Manufacture of Drug Substances:** The Q11 Rapporteur provided an update on the activities of the Q11 EWG and progress made in Tallinn in the development of the Q11 *Step 2* Guideline.

The SC was informed of the issues that were discussed by the Q11 EWG in Tallinn. As a next step it was agreed that draft 4 would be completed and circulated within the group for internal comments from the ICH Parties on issues such as the application of the definition of Critical Quality Attribute. Feedback from this internal consultation would be provided to the SC ahead of its teleconference which will be held to prepare for the next ICH meeting.

**Quality IWG:** The Rapporteur reported to the SC on the outcome of the Quality IWG meeting and provided feedback from the first ICH regional workshop on the *Implementation of ICH Guidelines Q8, Q9 and Q10* which was held in Tallinn on June 2-4, 2010. The SC noted that the workshop was very well attended with more than 240

participants, who included over 100 regulators. The US training will take place in Washington, D.C. on October 6-8, 2010 and the Japanese training in Tokyo, on October 25-27, 2010.

Regarding the IWG's evaluation of existing ICH Quality Guidelines in view of the new quality paradigm created by Q8, Q9, and Q10, the Rapporteur informed the SC that the initial finding of the group was that there was currently no need to revise the existing Guidelines. Gaps would be further addressed after the completion of the three workshops.

**Q3D EWG: Guideline for Metal Impurities:** The Rapporteur updated the SC on the outcome of the first meeting of the newly established Q3D EWG. The SC noted that the EWG was working to establish a complete definition of the scope. The EWG recommended that herbals be excluded while new drug substances and new drug products resultant from chemically synthesized new drug substances and excipients should be in scope. The EWG was still debating whether biotechnology products, biologics, existing products, and clinical phase of development should be in the scope.

The Rapporteur informed the SC that the ICH Q3C Guideline would be used as the template for the guideline. The Rapporteur also proposed to have two categories of metal impurities with PDE limits (significant & moderate safety concerns).

**S6(R1): Revision of Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals:** The Rapporteur updated the SC on the outcome of the S6(R1) EWG meeting in Tallinn and progress made to reach *Step 4* of the Addendum to the S6 Guideline.

The SC noted that in Tallinn the group had worked to address comments received from regulatory consultation. The Rapporteur informed the SC that in addition to input from the ICH parties, input was also received from scientific parties (STP, ESTP), public organisations on animal use (ICAPP, NC3R's) and other regulatory authorities (e.g., Health Canada, Singapore, Korea and China). The SC also noted the positive impact that the Guideline will have for the 3Rs agenda which is related to the reduction, refinement and replacement of animal testing.

The Rapporteur informed the SC that it may be possible to reach *Step 4* ahead of the next ICH meeting in Fukuoka in November 2010.

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

**M1 PtC: MedDRA Points to Consider Working Group:** The SC was updated on the outcome of the MedDRA PtC WG meeting in Tallinn, including the work of the group to: provide guidance on new topics such as product quality versus medication error terms and device related terms; to include text on the extent of versioning practices into a PtC document in an Appendix; to provide timing of version change; and, efforts to reformat the Term Selection and Data Retrieval & Presentation PtC documents for ease of use and streamlining.

In Tallinn, the PtC WG finalised the revision of both PtC documents (Term Selection and Data Retrieval & Presentation) with an anticipated release of both documents in October 2010, in line with the next scheduled release of MedDRA version 13.1.

**GTDG: Gene Therapy Discussion Group:** The Co-Rapporteurs reported on the outcome of the GTDG meeting, and progress made in the development of the ICH Considerations document on *General Principles to Address in Preparation for First-in-Human Gene Therapy Studies*.

**M6: Guideline on Virus and Gene Therapy Vector Shedding and Transmission:** The Rapporteur provided a report on the outcome of the M6 EWG meeting in Tallinn, and progress made towards reaching *Step 2* in spring 2011.

**E2F: Development Safety Update Report:** The E2F EWG did not meet in Tallinn. The SC was updated on efforts by the Group to reach *Step 4* which was expected shortly. It was noted that the group would continue its work through e-mail, teleconferences, and web conferences.

**E7: Studies in Support of Special Populations: Geriatrics:** The E7 EWG did not meet in Tallinn, but the SC was informed that the group had finalised its *E7 Step 4* Q&As (Questions & Answers) document which would be signed-off by a postal procedure.

**E16: Genomic Biomarkers Related to Drug Response: Context, Structure and Format of Qualification Submissions:** The E16 EWG did not meet in Tallinn. The SC noted that the group was working by e-mail and teleconference and expected to reach *Step 4* shortly.

**E14 IWG: The Clinical Evaluation of QT/QTc Interval Prolongation and Proarrhythmic Potential for Non-Antiarrhythmic Drugs:** The E14 IWG did not meet in Tallinn. The SC approved a detailed work plan which was presented by the group for the development of the additional E14 Q&As.

#### **4. Dates of Next Meetings for 2010 & 2011:**

November 6-11, 2010

Fukuoka, Japan

June 11-16, 2011

Cincinnati, Ohio, USA