ICH STEERING COMMITTEE  
November 7-10, 2005, Chicago, USA  
SUMMARY

1. Opening Discussions

The ICH SC (Steering Committee) meeting was chaired by FDA’s Deputy Commissioner for International and Special Programs. 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 reported on the new codification system that has been developed for all ICH guidelines in accordance with the principles described in the revised ICH Procedures document. With the agreement of the SC, this new codification system, along with a history box for each guideline, will be implemented on the ICH public website and will allow users to verify more easily if they have the current version of a guideline. The SC also agreed to the ICH Coordinators’ proposal to implement the new coding system prospectively, rather than retrospectively, so as not to effect already implemented guidelines.

The SC also considered a number of proposals from the Coordinators that identified ways the ICH Secretariat could improve communications with ICH stakeholders. These proposals, agreed to by the SC, included the development of SOPs (Standard Operating Procedures) for handling Press inquiries, the drafting of improved Press Releases, the review of the user-friendliness of the ICH public website, and the creation of a version of the ICH SC Report for publication on the ICH public website.

MedDRA: The Chair of the MedDRA Management Board reported on the decisions taken by the MedDRA Management Board on behalf of the SC. Arising from contract renewal discussions with MSSO - Maintenance and Support Services Organisation - (the maintainer and distributor of MedDRA), and due to the significant increase in subscribers, was the decision to dramatically decrease the MedDRA subscription fee for 2006.

The Chair also reported on the agreement of the MedDRA Management Board to the organization of two Blue Ribbon Panels in 2006. One panel will be charged with reviewing the options for improving the terminology hierarchy (modifications at HLT/HLGT level), and the other will look at enhancing the utility of MedDRA for MedDRA oncology Users.

The Chair also reported that representatives of the Board had met with senior staff from WHO/WHO Uppsala Monitoring Centre to discuss ways by which the Board and WHO could work more closely together in order to contribute to enhanced public health protection. As a result of these discussions the Board endorsed formally the proposal for the WHO-ART (WHO Adverse Reaction Terminology) to be mapped to MedDRA. The
Board also supported the objective of integrating MedDRA into the WHO pharmacovigilance database. This would ensure that MedDRA coded data would be entered and retrieved in their original format. WHO UMC will develop a proposal with staged implementation options for Board consideration in early 2006.

The Board also supported the Points to Consider (PtC) Working Group’s proposal for the development of a third Points-to-Consider document describing common principles on MedDRA and listedness. The Rapporteur also reported directly to the SC on the development of the PtC WG’s second document on Data Retrieval and Presentation, which is now finalized and ready for public release. The first PtC document on MedDRA Term Selection was reviewed and amended in light of MedDRA Version 8.1. The ICH Secretariat/MSSO/JMO will post both of these PtC documents on their respective websites.

Global Cooperation Group (GCG): The GCG Co-Chairs reported on the activities of the GCG meeting. Participants in attendance from the regional harmonization initiatives (RHI) included representatives from APEC, ASEAN, GCC, PANDRH and SADC. The RHIs confirmed the value in meeting prior to the GCG meeting as it allows for brainstorming of views on GCG agenda items and information sharing on regional activities.

The GCG reviewed a draft discussion paper on Strategy on Training and Capacity-Building. This paper will be further discussed for finalization at the next meeting in Japan. The GCG chairs will also draft papers on Good Harmonization Practices, and on Structure, Organization and Processes of the RHI. These documents will also be considered for finalization in Japan.

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

GMP Quality Systems: At the opening of the SC meeting, the Discussion Leader of the Q10 Informal Working Group reported on the revised Business Plan. The revisions included an estimation of the costs for the industry to implement robust Quality Systems. The SC endorsed the revised Business Plan and the establishment in Chicago of the formal Expert Working Group (EWG) Q10.

Towards the close of the SC meeting, the EWG Q10 reported back on the progress made thus far. The group defined the scope, linkages to Q8 and Q9, the preliminary structure of the guideline (based on ISO), and the key topics in each section of the guideline. The key milestones in the development of the guideline will be the development of the first full draft (due at the next meeting in Japan), followed by the Step 2 document in spring 2007. Following discussions by the group on the membership of EWG Q10, the SC approved the invitation of a second representative from IGPA, and one representative from both the Indian and Chinese regulators. An invitation would also be extended to one representative from each RHI.
**Biotechnology Brainstorming Session:** The Co-Chairs reported on the outcome of the brainstorming session, at which the following topics were discussed: *Subsequent Entry Protein Products, Monoclonal Antibodies and Manufacturing Process Development and Validation.*

The SC approved the group’s recommendation to pursue the development of a Concept Paper on *Manufacturing Process Development and Validation.* The Concept Paper will be drafted under the rapporteurship of EFPIA and will be provided, along with a Business Plan, for SC consideration at the next meeting in Japan. ICH regulators will determine with their own regional Bio Associations, which interested parties/organizations to invite so as to best represent the views of their respective Bio Associations.

The other topics discussed by the group will be a future priority.

**Maintenance of ICH Controlled Terminology Lists:** The Rapporteur reported on the outcome of the meeting of the Pilot Working Group for Testing the Draft SOPs (Standard Operating Procedures). Based on the experience from the two pilot testings, the group proposed a revised simplified structured process for the maintenance of the terminology lists included in *Step 4/5 ICH guidelines.*

The process defines the composition of the ICH Implementation Working Group (IWG) and the roles and responsibilities of its members. The process includes the basic steps including collecting change requests, evaluating change requests, decision making process and maintaining terminology lists and codes. It involves the endorsement by the SC of the recommendation to accept a change request.

The group proposed that the following lists should be maintained using the new procedure:

**ICH Quality Guidelines:**
- Q3A(R1) – Table of thresholds
- Q3B(R) – Table of thresholds
- Q3C(R3) – List of solvents and PDE
- Q5A(R1) – Virus detected in antibody tests

**ICH Safety Guidelines:**
- S2A – listing of base set of bacterial strains to be used for routine testing

**ICH Efficacy Guidelines:**
- E3 - Data elements to be included in clinical study reports
- E6 – List of essential documents
- E2A – list of key data elements for inclusion in expedited reports of serious adverse drug reactions

**ICH Multidisciplinary Guidelines:**
– M5
  • Active ingredient
  • Pharmaceutical dose form
  • Route of administration
  • Units of measure
  • Pharmaceutical Product Identifiers

The group suggested outsourcing the maintenance of complex terminology such as the M5 vocabulary.
The SC approved the revised SOPs for the maintenance process with the caveat that a report will be provided at the next meeting in Japan on how it operated. In addition, the SC endorsed the establishment of a formal IWG with the current membership. The SC requested that the group work closely with M5 to develop an Options Paper that would describe the various options for outsourcing, including the benefits, risks and costs.

**New Proposal on Efficacy: Development of Efficacy Q&As/Multiregional Trials:** The Rapporteur reported on the outcome of the informal working group discussion on E5. The group evaluated JPMA’s Question & Answer (Q&A) proposal on the use of multi-regional trials in global development. Consensus was reached that resulted in a new proposed question #11 that will be added to the current ten E5 Q&As. The Q&A #11 clarifies that the bridging study does not need to occur after completion of development in the original region. It also provides points to consider in design, analysis and evaluations of a multi-regional trial used for the purposes of bridging.
The SC endorsed the establishment of an IWG. Should no issues be raised following circulation of Q&A #11 amongst the parties, the ICH Secretariat will organise a postal sign-off for regulator experts and then for SC regulators, following which Q&A #11 will be posted on the ICH website with the existing E5 Q&As.

**New Proposal on Efficacy: Pharmacogenomics:**
The Co-Chair presented on the outcome of the informal working group discussion. The report included the group’s recommendation for the development of an ICH guideline on terminology and definitions in Pharmacogenomics, for SC consideration. The group will revise their Concept Paper on terminology and definitions in Pharmacogenomics to provide a clearer definition of the scope. The SC requested that the group also develop a Business Plan. Both documents will be considered at the next SC Teleconference.

**New Proposals on Pharmacovigilance: Risk Communication:** The Co-Rapporteurs reported on the outcome of the informal working group meeting. Having presented a revised Concept Paper and a Business Plan for Dear Healthcare Professional Letter (DHPL), the group underlined the importance of harmonization of risk communication
tools. The SC requested that the group develop a more focused Concept Paper which would be more explicit on what would be in and out of the scope, and also a more detailed Business Plan. Both the revised Concept Paper and Business Plan will be presented at the next SC Teleconference.

3. Reports on Current Topics

Reports from Expert/Implementation Working Groups were made.

**Common Technical Document (Topic M4): Quality Overall Summary (QOS):** The Quality Rapporteur reported on the outcome of the 2 hour discussion on QOS. The content of QOS, that is part of Module 2, is similar in the EU and US, and does not form the basis for the assessment of the application file for marketing authorization. In Japan, the review process is driven by QOS. The group supports the use of QOS as the principal assessment tool, and foresees benefits in having one global QOS for both regulators and industry. It was also proposed to apply a concept similar to the non-clinical and clinical part.

The SC endorsed the establishment of an informal working group for the development of a Concept Paper on the future role/utility of QOS. The Concept Paper will be considered at the next SC Teleconference and a decision will be made on how to proceed.

**Electronic Standards for the Transfer of Regulatory Information and the Electronic CTD (Topic M2 and eCTD):** The Rapporteur reported on the progress made by the eCTD IWG and M2 EWG at the September interim meeting and at the Chicago meeting. He presented on the regional implementation of eCTD in EU (numbers increasing slowly), USA (1000 eCTD submissions at CDER and 421 submissions at CBER), Japan (started to recently accept eCTD submissions) and Health Canada (18 eCTD applications).

A report was made on the interactions of M2 with both the M5 and E2B working groups. Their objectives are to develop ICH specifications for Medicinal Product Identifier (MedID), Controlled Vocabulary (CV) and E2B(R3) messages by June 2006. They also intend to develop, for SC consideration in Japan, a PtC (Points to Consider) Document on the implementation of Data Elements and Standards for Drug Dictionaries.

With the ever-increasing number of activities for the M2 EWG, the SC requested that the group develop an Options Paper outlining the various options for the M2 process, including the possible interfacing with SDOs (Standard Development Organizations) and the associated benefits and risks. This Options Paper will be considered at the next SC Teleconference.

Following news of the departure of the group’s current Rapporteur, the SC concurred with the group’s proposal to rotate the Rapporteurship across all six-ICH parties, including Health Canada. All parties will be invited to confirm the Rapporteurship at the next SC Teleconference.
Pharmacopoeial Discussion Group (PDG): The US Pharmacopoeia reported on the current status of Pharmacopoeial Harmonization and the progress made during their meeting. A report was also made on the joint meeting with Q4B that was held during the ICH SC week. The PDG submitted packages to Q4B on Residue on Ignition / Sulphated Ash, Sterility Test, Extractable Volume, Particulate Matter in Injectables, and Dissolution Test. Packages are being prepared on Uniformity of Dosage Units, Disintegration Test and Bacterial Endotoxins.

With regards to Q6A General Chapters, the PDG signed-off the Microbial Contamination Chapter in Chicago. It contains three chapters: microbial enumeration tests, tests for specified micro-organisms and acceptance criteria for pharmaceutical preparations and substances for pharmaceutical use. Dr. Sheinin reiterated that USP has agreed to continue to work on the Colour General Chapter due to its importance to the ICH Q6A Guideline. Implementation of any of the General Chapters is expected to occur in 2007.

Q4B: Regulatory Acceptance of Pharmacopoeial Interchangeability: The Rapporteur reported on the progress made by the Q4B EWG at its meeting. New concepts have been added in the form of ICH style topic Annexes (similar to Q3C process – Category 4 Maintenance Procedure) and will be used to convey the Q4B EWG evaluations and outcomes for the individual General Monographs/Chapters. Step 2 on Q4B should be reached in or before the next meeting in Japan. Agreement should be reached on the Annex on Residue on Ignition/Sulphated Ash to be used as a template for the first draft annex proposal. This will be provided in Japan for SC consideration. A second Annex on Extractable Volume should be completed and presented in Japan.

Q8: Pharmaceutical Development: The SC adopted the Step 4 Document on the core Q8 Guideline. In addition, the Rapporteur reported on the progress achieved on the addendum to Q8 on specific dosage forms (solid oral, liquid oral and parenterals). It was noted that the addendum would be added to the core Guideline that will be then renamed Q8(R1) Guideline, as per the new codification procedure.

Q9: Quality Risk Management: The SC signed-off the Step 4 document and supported the EWG’s proposal for the development of a standard set of training slides.

E2B(R3): Revision of the Data Elements for Electronic Submission in Individual Case Safety Reports: The Co-Rapporteurs reported on the progress made by the E2B EWG at its meeting in Chicago. Following the Step 3 public consultation, the group reviewed the 361 comments received (EU: 44, Japan: 307 and US: 10) and addressed all major comments. Based on this feedback, the EWG identified 22 additional requirements to M2. Step 4 of the E2B(R3) Guideline is expected by November 2006.
The E2B(R3) EWG will develop test plans in consultation with M2 and M5 EWGs. Step 4 of the M2 E2B(R3) specification including the M2 change control process is expected by May 2007.

**M5: Data Elements and Standards for Drug Dictionaries:** The Rapporteur presented an update on the work of the M5 EWG. The joint ICH M5/M2/E2B(R3) EWGs met in Chicago to finalize the Proof of Concept (POC) Plan. The detailed POC protocol should be elaborated by June 2006. The M5 EWG reviewed comments on the M5 Step 2 document from EU, EFPIA, MHLW and Health Canada, and revised the M5 data model accordingly. The draft Step 4 document will be discussed at the next meeting in Japan and aligned based on the POC results. The Step 4 Guideline is planned for November 2006. The M5 EWG also defined the mapping and hierarchy structure for chemical substances, herbal substances & herbal preparations, and substances used in vaccines. Mapping should be completed in February 2006 for chemical substances, May 2006 for herbal and vaccine substances, and in August 2006 for herbal preparations.

**Gene Therapy Discussion Group (GTDG):** The Co-Rapporteurs reported on the Public Workshop on Oncolytic Viruses held in Chicago. The workshop was well attended (80 participants) and achieved its objectives of identifying and discussing issues relevant to the clinical development of oncolytic viruses, as well as of increasing awareness of ICH GTDG activities. The SC approved the group’s proposal to post the full-length report on the Workshop on the ICH website.

An update was provided on the progress made at the GTDG meeting on the Considerations document on Inadvertent Germline Transmission. With the second draft of the document completed in Chicago, the objective is to finalize the document by the fourth quarter of 2006 or first quarter of 2007, and will require to group to meet in Japan.

**4. Future of ICH**

**Proposals for New Operating Principles for ICH:** The SC commented on the FDA’s *ICH Reflections Paper*. This paper proposes new operating principles for the ICH to adopt and describes topics such as the Greater Inclusion of Non-ICH Organizations, Increased Transparency and Leveraging ICH Efforts.

The SC agreed on the basic principles of the document. To increase transparency, the SC agreed to the development of a framework for ICH EWGs to outreach to organisations, whether professional, consumer, patient or other within the ICH regions. The Reflections Paper also proposed to publish Concept Papers on the ICH web site. The SC agreed to discuss this proposal at the next meeting in Japan.

The SC also discussed the development of a communications strategy in the context of the GCG, and a proposal to work with accredited SDOs (Standards Development Organisations) to leverage the development of technical standards for ICH e-Initiatives.
The revised document will be considered at the next meeting in Japan, when the FDA will make a proposal on how this paper might be further disseminated.

**ICH7:** The SC considered proposals for the organization of ICH7. It was agreed that in order to maximize attendance and minimize financial risk the meeting should be organized with DIA (a non-profit organization) and, as such, will follow the DIA EURO meeting in Vienna in March 2007.

5. Any Other Business

**Q3B(R): Impurities in New Drug Products:** The Rapporteur reported on the revision for clarification purposes of Q3B(R) attachment 2 on *Illustration of Reporting Degradation Product Results for Identification and Qualification in an Application*. The SC endorsed the establishment of an IWG so as to give the group the status to officially give the agreement to the revised document. It is proposed to carry out a similar exercise for Q3A, for SC consideration at the next SC Teleconference.

**Q1F: Stability Data Package for Registration Applications in Climatic Zones III/IV:** The Rapporteur reported on the outcome of the informal discussion on how to resolve this issue at a global level and its possible impact on the future of Q1F. She reported on the recent decision made by the WHO Expert Committee Meeting on *Specifications for Pharmaceutical Preparations*. The decision is to split Climatic Zone IV into:

- Climatic Zone IV a: 30°C / 65 % RH
- Climatic Zone IV b: 30°C / 75 % RH

After much discussion and in the light of this decision, the informal working group proposed the complete withdrawal of ICH Q1F. The SC endorsed the formation of an EWG. The Q1F EWG will develop a formal proposal and draft an explanatory note for consideration by the SC at the next SC Teleconference. Once endorsed by the SC, the Q1F Guideline will be withdrawn from the ICH/regulatory websites, with an explanatory note posted on the sites.

6. Dates of Next Steering Committee Meetings:

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<tr>
<th>Date</th>
<th>Location</th>
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<tbody>
<tr>
<td>June 5-8, 2006</td>
<td>Yokohama, Japan</td>
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<tr>
<td>October 23-26, 2006</td>
<td>Chicago, USA</td>
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* Post-meeting note – this decision was revoked at the June 2006 Steering Committee meeting in Japan.