

*Final*

**GLOBAL COOPERATION GROUP MEETING REPORT  
TUESDAY NOVEMBER 11, 2008**

*Brussels, Belgium  
(Radisson SAS Hotel Brussels)*

**PARTICIPANTS:**

**Ref: GCG 95F**

|                                 |   |
|---------------------------------|---|
| Dr. Peter Arlett                | EU (GCG Co-Chair)                                 |
| Mr. Kohei Wada                  | JPMA (GCG Co-Chair)                               |
| Mrs. Lenita Lindstrom-Rossi     | EU  |
| Dr. André W. Broekmans          | EFPIA   |
| Dr. Yves Juillet                | EFPIA   |
| Mr. Shinobu Uzu                 | MHLW  |
| Dr. Justina Molzon              | FDA   |
| Dr. Alice Till                  | PhRMA   |
| Dr. Lembit Rägo                 | WHO   |
| Mr. Mike Ward                   | Health Canada                                     |
| Dr. Petra Dörr                  | EFTA  |
| Dr. Odette Morin                | IFPMA   |
| Dr. Pavittranon Sumol           | APEC  |
| Dr. Yuppadee Javroongrit        | ASEAN   |
| Prof. Dr. Saleh Bawazir         | GCC   |
| Ms. Mandisa Hela                | SADC (Replacing Mr. Mthetwa for SADC Secretariat) |
| Dr. Jean-René Randriasamimanana | SADC (2nd Representative)                         |
| Dr. Leonie Hunt                 | DRA of Australia                                  |
| Dr. Ruth Lopert                 | DRA of Australia (2nd Representative)             |
| Mr. Chaoying Zhang              | Chinese Mission to the EU                         |
| Dr. Chi-Chou Liao               | DRA of Chinese Taipei                             |
| Dr. Peter Chang                 | DRA of Chinese Taipei (2nd Representative)        |
| Ms. Maria Churilova             | Russian Mission to the EU                         |
| Dr. Christina Lim               | DRA of Singapore                                  |
| Dr. Huei-Xin Lou                | DRA of Singapore (2nd Representative)             |

|                      |   |
|----------------------|---|
| Dr. Daibyoung Kim    | DRA of South Korea                      |
| Dr. KyungWon Jang    | DRA of South Korea (2nd Representative) |
| <i>Also Present:</i> |   |
| Dr. Thomas Salmonson | EU                                      |
| Dr. Matus Ferech     | EU                                      |
| Dr. Spiros Vamvakas  | EU                                      |
| Dr. Isabelle Clamou  | EFPIA                                   |
| Dr. Elisa Siviglia   | EFPIA                                   |
| Mr. Takayuki Okubo   | MHLW                                    |
| Dr. Yoshiaki Uyama   | MHLW                                    |
| Dr. Kurajiro Kishi   | JPMA                                    |
| Ms. Joan Blair       | FDA                                     |
| Ms. Tammie Bell      | FDA                                     |
| Dr. Michelle Limoli  | FDA                                     |
| Dr. Michael Garvin   | PhRMA                                   |
| Dr. Dawn Ronan       | ICH Secretariat                         |
| Dr. Sarah Adam       | ICH Secretariat                         |

## **1. Welcoming remarks and adoption of the agenda**

The Co-Chairs, Dr. Arlett (EU) and Mr. Wada (JPMA) welcomed all participants to the meeting of the ICH Global Cooperation Group (GCG). A special welcome was extended to representatives who were participating in the GCG for the first time.

The agenda was adopted with the following modifications: Under agenda item 4, Dr. Arlett will report on the Regulators Forum; under agenda item 18, the GCG will examine a proposed minor amendment in the GCG procedures and the members will discuss the future changes of the Co-chairmanship.

## **2. Review of current membership**

The GCG welcomed for the first time Ms. Mandisa Hela from South Africa as first representative of the SADC Secretariat replacing Mr. Joseph Mthetwa who was unable to join the meeting. Dr. Jean-René Randriasamimanana from Madagascar was also introduced as the second representative of the SADC. Apologies were received from Dr. José Luis Di Fabio of the PANDRH who was unable to attend.

Dr. Daibyoung Kim was introduced to the GCG as the new first representative of the Drug Regulatory Authority (DRA) of South Korea replacing Dr. Dong Sup Kim. The GCG welcomed as well for the first time Dr. Ruth Lopert, Prof. Peter Chang, Dr. Huei-Xin Lou, and Dr. Kyung Won Jang as second representatives from the DRAs of Australia, Chinese Taipei, Singapore and South Korea, respectively.

Also, the GCG welcomed Mr. Chaoying Zhang and Ms. Maria Churilova attending for the first time the GCG meeting as mission to the EU on behalf of DRAs of China and Russia, respectively.

The Co-chairs also welcomed Dr. Sarah Adam as a new coordinator for the ICH Secretariat.

Dr. Ronan (ICH Secretariat) invited the GCG participants to communicate to the ICH Secretariat any current and future changes in the GCG membership.

### **3. Final approval of the report of the GCG teleconference held on October 15, 2008 (Ref: GCG93)**

*Action/Decision:*

- The GCG approved as final the report of the GCG teleconference held on October 15, 2008.

### **4. Regulators Forum report**

Dr. Arlett (EU) reported on the success and utility of the second ICH Regulators Forum held on November 10, 2008 in Brussels. The forum brought together regulators from EU, Japan, USA, Canada, Australia, China, Chinese Taipei, India, Russia, Singapore, South Korea and regulators representing APEC, ASEAN, GCC, and SADC. All participants provided a regulatory update on their respective region. The ICH E2C, E6 and Q7 guidelines were discussed and the limitations of current PSUR (Periodic Safety Update Report) format were raised.

The Forum highlighted the need for training for consistent ICH guideline implementation in both ICH and non-ICH regions and the importance of the development of training programs on specific key strategic areas (such as CTD, or Q7 and E6). Teleconferences and webinars on technical ICH topics were also suggested as important communication tools for trainings.

### **5. RHI pre-meeting report**

Prof. Bawazir (GCC) reported on the RHI pre-meeting. The RHIs discussed how to improve harmonisation in their respective regions. Prof. Bawazir discussed the value of training and how to maximize training efforts possibly with the use of webinars and e-learning tools.

The RHIs discussed the up-coming opening of the APEC Harmonisation Centre (AHC) in Seoul, South Korea (see also agenda item 12, *Training and capacity building*) and the feasibility of the creation of other Centres of Excellence for training in their respective regions.

Prof. Bawazir also mentioned that the RHIs discussed how to strengthen the capacity of stakeholders for the assessment of clinical trials. The RHIs encouraged the implementation of Q7 (*Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients*) in their regions and they also reported the need for sharing information on inspections.

### **6. RHI and DRA update on ICH-related matters**

RHIs and DRAs gave formal presentations to the GCG on their respective initiatives and current activities. The presentations will be posted on the ICH website.

*APEC*, Dr. Sumol provided an overview of APEC in terms of organisation, operations and funding. In addition, Dr. Sumol provided background information on the APEC Life Sciences Innovation Forum (LSIF) regarding the history, the structure, the operation and strategic plan of the forum. She reported on the sixth annual meeting (LSIF VI) that was held in Peru on August

14-15, 2008 and discussed the progress and challenges to date. Dr. Sumol highlighted the need for the development of greater synergies and coordination of efforts between industry and regulators. She also noted the necessity to develop mechanisms to sustain training & capacity building work and to better prioritize annual and long term plans and projects.

**ASEAN**, Dr. Yuppadee gave an overview of the ASEAN PPWG (Pharmaceutical Product Working Group) and its current activities. In addition, Dr. Yuppadee reported on the outcome of the 15<sup>th</sup> PPWG meeting held in Brunei Darussalam in July 2008. Progress was made at the meeting on the ASEAN MRA (Mutual Recognition Agreement) for Pharmaceuticals including MRA-BA/BE (Bioavailability/Bioequivalence) studies and MRA-GMP Inspection.

**GCC**, Prof. Bawazir reported on the organization, the mission and the current activities of the GCC-DR. He reported on the outcome of the 39<sup>th</sup> GCC-DR meeting held in Riyadh, Saudi Arabia in October 2008. The meeting focussed on GMP inspections, requirements for registrations of manufacturers and pharmaceutical products, national drug code & barcoding and CTD training. Prof. Bawazir informed the GCG on the preparation of the up-coming 8<sup>th</sup> Middle East Regulatory Conference (MERC) to be held in Bahrain on January 20-21, 2009. The meeting will focus on counterfeit medicines, regulatory issues as well as current and future trends of the ICH quality topics including Q8 and Q9.

**SADC**, Ms. Hela presented on the organisation and objectives of the SADC Pharmaceutical Programme. She reviewed the harmonisation tasks accomplished to date including the development of a pharmaceutical business plan focusing on regulation, availability and access, with areas of priority for neglected diseases (such as Tuberculosis, Malaria and AIDS). Ms. Hela informed the GCG of the development and approval of 14 guidelines for the Registration and Control of Medicines. She also reported that with the assistance of the WHO Global Training Network, training had been conducted on basic requirements for GCP inspections and evaluation of Clinical Trial data for vaccine registration. The GCG also noted the future planned activities within SADC (such as the establishment of centre(s) of excellence), the challenges faced by SADC (capacity constraints, variable country priorities) and the lessons learnt.

**DRA of Australia**, Dr. Hunt provided background information on the objectives and activities of the TGA (Therapeutics Goods Administration). Dr. Hunt informed the GCG that since 1991, the Baume Review into medicine regulation recommended that there be no unique Australian guidelines or requirements, unless justified on public health grounds. It was recommended that the TGA should use globally harmonised guidelines and standards. Since then, the TGA has used European versions of ICH guidelines almost exclusively. Under Australian legislation, guidelines are not legally enforceable requirements, but instead set out best practice in demonstrating quality, safety and efficacy. The evaluation phases of a guideline were explained and guidelines can be consulted on the TGA website, <http://www.tga.gov.au>

**DRA of Singapore**, Dr. Lim provided an overview of the Singapore Health Science Authority's mission and activities. Dr. Lim informed the GCG that since the late 1990s relevant ICH Quality, Safety, and Efficacy guidelines have been used in drug evaluation. Dr. Lim presented to the GCG the development over the years of the Drug Registration System and Standards by HSA. The GCG noted that dossier submission in both the ICH CTD and ASEAN CTD format are accepted by Singapore (with 53% of dossiers currently submitted in ICH format). Dr. Lim informed the GCG on Singapore's future challenges.

## **7. Comments on Step 2 Guidelines**

The GCG noted that no comments had been received to date from the RHIs and DRAs on the following *Step 2* guidelines: E2F - *Development Safety Update Report*; M3(R2) - *Non Clinical Safety Studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceutical*; Q4B Annex 2 *Test for Extractable Volume of Parenteral Preparations General Chapter*; Q4B Annex 3 *Test for Particulate Contamination: Sub-Visible Particles General Chapter*; Q4B Annex 4A *Microbiological Examination of Non-sterile Products: Microbial Enumeration Tests General Chapter*; Q4B Annex 4B *Microbiological Examination of Non-sterile Products: Tests for Specified Micro-organisms General Chapter*; Q4B Annex 4C *Microbiological Examination of Non-sterile Products: Acceptance Criteria for Pharmaceutical Preparations and Substances for Pharmaceutical Use General Chapter* and Q4B Annex 5 *Disintegration Test General Chapter*.

Dr. Ronan (ICH Secretariat) informed the GCG that the deadline for sending comments to the Secretariat on the E2F guideline *Development Safety Update Report* was by the end of December 2008.

## **8. Webinars on Step 2 Guidelines**

Dr. Ronan (ICH Secretariat) reported on the organisation of the webinar on the E2F and M3(R2) *Step 2* guidelines that was held on September 16, 2008. She presented the webinar system to the GCG for those not familiar with the use of web-conferencing tools. Participants of the first webinar noted the usefulness and the intuitiveness of this new system. The ICH Secretariat will also consider in the future how to exploit the Voice over Internet Protocol communication technology (VoIP).

The GCG discussed how to maximize the usefulness of webinars for facilitating *Step 2* comments and agreed to the organisation of webinars for the S9 guideline (once it reaches *Step 2*), the Annex to Q8 and the M3(R2) guideline (once finalised). It was noted that webinars could also be valuable to see the evolution of a guideline from *Step 2* to *Step 4*.

*Actions/Decisions:*

- The ICH Secretariat will subscribe for a web-conferencing system in 2009.
- The ICH Secretariat will investigate the use of the VoIP technology.
- The ICH Secretariat will organize webinars on the S9 guideline (once it reaches *Step 2*), the Annex to Q8 and the M3(R2) guideline (once finalised).
- The GCG supported the development and the use of webinars not only to facilitate *Step 2* comments and to enable RHIs and DRAs to follow the progression of the guideline from *Step 2* to *Step 4*.

## **9. Stability Guideline developments**

Dr. Rágo (WHO) noted that the WHO Expert Committee on Specifications for Pharmaceutical Preparations received numerous comments and feedback on the draft Stability Guideline. Comments were reviewed and changes made and the Guideline was adopted during the WHO meeting in Geneva on October 13-17, 2008. The WHO Expert Committee is planning to execute the guideline at the timeframe of the World Health Assembly meeting in May 2009. Dr. Rágo proposed to develop a cross link to the finalized Stability Guideline in the ICH website.

## **10. RHI Survey update: Review of RHI Profiles**

Dr. Adam (ICH Secretariat) informed the GCG that the RHI profiles for the ASEAN, GCC and PANDRH were completed and that the ICH Secretariat was working with the SADC for the finalisation of its profile.

Dr. Adam presented “mock-up” webpages of the GCC profile for GCG comments. The profile highlighted the geographical situation, the organisation and function of the RHI. A list of current harmonisation topics for the RHI is available and each completed topic has been linked to the final guideline. The GCG noted the usefulness of the webpages and the value of developing the RHI profile.

### *Actions/Decisions:*

- The GCG supported the publication of the completed ASEAN, GCC and PANDRH profiles on the GCG public website following the Brussels meeting.
- The GCG noted that the information contained within the profiles should be reviewed biannually.
- The GCG agreed that the RHIs should inform the ICH Secretariat of any changes in their regional profiles in order to maintain the GCG public website up to date.

## **11. Benefit of Harmonisation**

In view to discuss benefits of harmonisation outside the ICH regions the GCG agreed to discuss the success factors for harmonisation.

### *Action/Decision:*

- The GCG supported the establishment of a working group for the writing of a paper describing the drivers and the success factors necessary for harmonisation.

## **12. Training and capacity building**

### ***APEC LSIF Workshops***

Dr. Yuppadee (ASEAN) reported on the organisation of the two ICH GCG-endorsed APEC LSIF sponsored workshops for regulators to be organised in 2009. The “Review of Drug Development in Clinical Trials” advanced workshop will be held from February 2-6, 2009 in Bangkok, Thailand. The event is a continuation of the first workshop that was held in March 2008 with the participation of many of the same trainers and trainees from the previous training. PhRMA, MHLW and Health Canada were participating in the organisation and the development of the agenda. Regarding the “GCP Inspections” advanced workshop that would be held from March 2-6, 2009 in Bangkok, Thailand, the program is under development with the participation of Health Canada, FDA and PhRMA. This event is a continuation of the preliminary workshop on GCP & Clinical research Inspection that was held in Bangkok, Thailand on May 2008.

### ***China Quality Workshop***

Dr. Till (PhRMA) provided an update on the organisation of the quality workshop on Q8, Q9 and Q10 to be held in Beijing, China on December 3-5, 2008. Mr. Ward (Health Canada) informed the GCG that the workshop was being organised by PhRMA, US Government and Chinese Government on behalf of APEC-LSIF. The workshop is primarily focussing on the interpretation

and application of ICH Q8-Q10, with a synopsis on the Q1 to Q7 guidelines and an introduction of the new Q11 ICH guideline. Dr. Molzon (FDA) noted that this workshop will involve about 250 participants from industries and regulatory agencies.

### ***PANDRH Training Request***

Dr. Molzon (FDA) proposed to follow-up on the PANDRH request for training on Q8, Q9, Q10 approved by GCG in 2007. The GCG noted that the programme for the China Quality workshop could serve as a template.

### ***APEC Harmonisation Centre (AHC)***

Dr. Kim (DRA, South Korea) provided information regarding the establishment of the APEC Harmonisation Centre (AHC) located in Seoul, South Korea. The concept of establishing an AHC was introduced by Korea at the APEC LSIF VI, in August 2008. The objective of the AHC is to create international cooperative networks for harmonisation between regulators, industry experts, institutions, investors and policy makers to develop and disseminate harmonisation models across the Asia-Pacific region. The AHC mission is to conduct surveys and research to define harmonisation challenges and opportunities, to provide education programs, and to develop a website for posting AHC reports and publications. The AHC inauguration ceremony will be held in June 2009.

#### ***Action/Decision:***

- The GCG expressed its support for the AHC agreeing when appropriate to offer collaboration on specific topics, where harmonisation would be required.

### ***Anticipating Future Training Needs***

***ASEAN Request***, Dr. Yuppadee presented to the GCG three requests for training in 2009 proposed by Malaysia: 1) Q9, Quality Risk Management; 2) Q5C, Stability Test of Biotechnology Products; and 3) MedDRA for Clinical Trials.

The GCG endorsed the three training requests, with the suggestion that the Q9 training should be expanded to cover Q8 and Q10 guidelines. The EU agreed to be the lead ICH Party for the Q9 and Q5C training events, while the ICH MedDRA Management Board was confirmed as the lead for the MedDRA training.

***GCC Request***, Prof. Bawazir presented a request for a 2-3 days didactic workshop in 2009 on the Quality of Biotechnological Products, focussing on the interpretation and application of ICH Q5A-Q5E. The GCG endorsed the request and the EU agreed to be the lead ICH Party.

***SADC Request***, Ms. Hela presented the SADC training request for an ICH Quality expert to participate in a workshop on the Manufacturing of Medicines, Harmonisation of Regulatory Guidelines, Safety and Quality Matters to take place in Zambia on November 18-20, 2008. Unfortunately due to the short timeframe the GCG was unable to provide an expert for the event. However, the GCG expressed its commitment to support a future quality workshop if the request was submitted with sufficient time to allow the identification of experts to participate.

#### ***Actions/Decisions:***

- The GCG endorsed the ASEAN training requests on Q9 (to be expanded to cover Q8 to Q10) & Q5C with the EU as the ICH lead party, and the training request on MedDRA with the MedDRA Management Board as the lead.

- The GCG endorsed the GCC training request on Q5A-Q5E guidelines with the EU as the ICH lead party.
- The GCG expressed its commitment to support a future quality workshop in the SADC region.

### **13. Training-Related procedural matters**

#### ***Publication of Training Materials/Presentations on the ICH Website***

Dr. Adam (ICH Secretariat) presented the speaker authorization form developed by the Secretariat to authorize the posting of all training materials and presentations from ICH GCG-endorsed events on the ICH public website. The GCG agreed on the new form which invites the speakers/trainers to sign a simple document granting ICH and the host RHI permission to publish their training materials/presentations on their respective websites.

#### ***Development of an assessment tool for GCG-endorsed events***

With regards to the evaluation of trainings, Dr. Ronan (ICH Secretariat) informed the GCG of the development of a generic standard form based on the WHO training evaluation tool recently provided by Dr. Rågo (WHO). This valuable tool would be sent to organisers in order to collect feedback information and help to refine further trainings.

#### ***Actions/Decisions:***

- The GCG approved the Speaker Authorization subject to minor amendments.
- The GCG supported the development of a generic assessment tool to gather feedback from ICH GCG-endorsed training events.

### **14. ICH update report**

Dr. Ronan (ICH Secretariat) gave an update on the organisation of the Brussels ICH meeting and the status of the Quality, Safety and Efficacy ICH topics:

***Annex to Q8:*** The annex to the Q8 Guideline *Pharmaceutical Development* focuses on quality by design and design space throughout the life-cycle of a pharmaceutical product. Together with Q8, Q9 and Q10 guidelines forms the foundation for a modern risk-based approach to pharmaceutical quality and manufacturing. The Annex reached *Step 4* of the ICH process at the Brussels meeting.

***Q4B:*** The Q4B *Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions* EWG would continue its work to develop topic-specific annexes to the Q4B Guideline. The following annexes are currently undergoing regulatory public consultation in the ICH regions and are expected to reach *Step 4* in Brussels: Annex 4A on *Microbial Enumeration Tests*, Annex 4B on *Tests for Specified Micro-organisms*, Annex 4C on *Acceptance Criteria for Pharmaceutical Preparations and Substances for Pharmaceutical Use*, and Annex 5 on *Disintegration Test*. The Q4B EWG would continue its work towards reaching *Step 2* in Brussels on Annex 6 on *Uniformity of Dosage Units*, Annex 7 on *Dissolution Test* and Annex 8 on *Sterility Test*.

***Quality IWG:*** The IWG focusing on the implementation of the Q8, Q9, Q10 ICH Guidelines would work in Brussels to develop a Q&As document.

**Q11:** The Q11 *Development and Manufacture of Drug Substances* EWG was meeting in Brussels to work towards *Step 2* which is currently expected in autumn 2009.

**M3(R2):** In Brussels, the M3(R2) *Revision of Non-Clinical Safety Studies for the Conduct of Human Clinical Trials for Pharmaceuticals* EWG would be reviewing the comments received from regulatory consultation and working towards reaching *Step 4*.

**S6(R1):** The S6(R1) *Revision of Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals* EWG held its first meeting in Brussels. The EWG would be working to develop an *addendum* to the S6 Guideline.

**S9:** In Brussels, the S9 *Oncology Therapeutics* EWG would be working towards reaching *Step 2*.

**E16:** In Brussels, the E16 would continue its work towards *Step 2* of the guideline on *Genomic Biomarkers Related to Drug Response: Context, Structure and Format of Qualification Submissions*. *Step 2* is expected in 2009.

**GTDG:** The Gene Therapy Discussion Group has been working to finalise the ICH Considerations document on *Oncolytic Viruses*. In Brussels, the GTDG would be discussing the development of an ICH Guideline for *Viral/Vector Shedding* based on an ICH Considerations document currently under development.

**MedDRA PtC:** The MedDRA Points to Consider Working Group would work in Brussels to finalise the extension of the guidance on SMQs within the *Data Retrieval and Presentation PtC* document.

## **15. Presentations on ICH Topics**

The GCG, RHIs and DRAs received a presentation on the ICH quality topics Q8, Q9 and Q10, including the Annex to Q8 (which reached *Step 4* in Brussels and will be added to the parent guideline Q8 which will be subsequently renamed Q8(R1)).

Dr. Robert, EU Rapporteur for the Annex to Q8 and the Quality IWG, presented to the GCG an overview and the objectives of the Q8, Q9, Q10 guidelines that are the essence of the new quality paradigm. Dr. Robert also reported on the work of the Quality IWG in the implementation of the quality guidelines Q8, Q9, Q10. Dr. Robert introduced the new Q11 guideline on *Development and Manufacture of Drug Substances* which is currently in the early stage of development.

## **16. Any Other Business**

### ***Revised GCG Principles and Procedures***

*Action/Decision:*

- The GCG endorsed a change in the GCG Principles and Procedures to clarify that DRAs may nominate one or two representatives to attend the biannual GCG meeting.

### ***GCG Co-Chairmanship***

The GCG was informed that Dr. Arlett would stand down from ICH activities following the Brussels meeting and would be replaced by Mrs. Lenita Lindström-Rossi (EU). In order to have continuity, it was also suggested that Mr. Wada (JPMA) will continue as Industry Co-Chair until

the Yokohama meeting in June 2009, and then the Industry Co-Chairmanship would rotate to PhRMA.

*Action/Decision:*

- The SC confirmed that Mrs. Lindstrom-Rossi will take over the EU Co-chairmanship after the Brussels meeting and that Mr. Wada will continue until the Yokohama meeting, then the Industry Co-Chairmanship will be transferred to PhRMA.