

**Final**

**GLOBAL COOPERATION GROUP MEETING REPORT  
TUESDAY OCTOBER 27, 2009**

*St. Louis, MO, USA  
(Renaissance Grand & Suites Hotel)*

**Ref: GCG 116F**

**PARTICIPANTS:**

Dr. Peter Honig	PhRMA (GCG Co-Chair)
Ms. Lenita Lindström-Rossi	EU (GCG Co-Chair)
Dr. André W. Broekmans	EFPIA
Dr. Justina Molzon	FDA
Mr. Shinobu Uzu	MHLW
Mr. Kohei Wada	JPMA
Dr. Lembit Rägo	WHO
Mr. Mike Ward	Health Canada
Dr. Petra Dörr	EFTA
Dr. Odette Morin	IFPMA
Dr. Sumol Pavittranon	APEC
Dr. Yuppadee Javroongrit	ASEAN
Prof. Dr. Saleh Bawazir	GCC
Dr. Maria Cortes	PANDRH
Dr. John Donohoe	DRA of Australia
Mr. Raposo de Mello	DRA of Brazil
Ms. Ana Soares Jucàs	DRA of Brazil
Dr. Jinhua Ding	DRA of China
Dr. Sun Hee Lee	DRA of Korea
Ms. Eun Hye Park	DRA of Korea
Dr. Elena Barmanova	DRA of Russia
Mr. Alex Terekhov	DRA of Russia
Dr. Christina Lim	DRA of Singapore
Dr. Huei-Xin Lou	DRA of Singapore

*Also Present:*

Ms. Joan Blair	FDA
Dr. Michelle Limoli	FDA
Ms. Mary Morrison	FDA
Dr. Michael Garvin	PhRMA
Dr. Thomas Salmonson	EU
Dr. Matus Ferech	EU
Dr. Spiros Vamvakas	EMA/EU
Mr. Takayuki Okubo	MHLW
Mr. Masaaki Tsukano	MHLW/PMDA
Dr. Kurajiro Kishi	JPMA
Dr. Sarah Adam	ICH Secretariat

### **1. Welcoming Remarks and Adoption of the Agenda**

The Co-Chairs, Dr. Honig (PhRMA) and Ms. Lindström-Rossi (EU) welcomed all participants to the meeting of the ICH Global Cooperation Group (GCG). A special welcome was extended to representatives of the Drug Regulatory Authority (DRA) of Brazil, China and Russia who were participating for the first time in the GCG meeting.

The agenda was adopted without any modification.

### **2. Review of Current Membership**

The GCG welcomed for the first time Mr. Raposo de Mello and Mrs. Soares Jucàs as representatives of the DRA of Brazil; Dr. Ding, representative of the DRA of China and Dr. Barmanova and Mr. Terekhov representatives of the DRA of Russia. Dr. Lee was introduced as the new representative of the DRA of South Korea, replacing Dr. Kang. Apologies were received from Dr. Lopert, DRA of Australia, Dr. Jang and Prof. Chang, Department of Health of Chinese Taipei and Mr. Mthetwa, representative of SADC.

Dr. Cortes (PANDRH) was introduced to the GCG as the representative of PANDRH replacing Dr. Fitzgerald in St. Louis.

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

### **3. Final Approval of the Report of the GCG Teleconference held on September 24, 2009 (Ref: GCG114R)**

*Action/Decision:*

- *The GCG approved as final the report of the GCG teleconference held on September 24, 2009.*

### **4. RHI pre-meeting Report**

Prof. Bawazir (GCC) reported on the Regional Harmonisation Initiative (RHI) pre-meeting.

The RHI discussed the need for flexibility due to differences in capacity and needs of the different authorities and regions, but also highlighted the importance of strengthening Good Review Practice for harmonization. Prof. Bawazir also emphasized the importance of developing training programs on key ICH topics such as *Quality* and *Good Clinical Practices* (ICH E6, GCP) to facilitate Guidelines implementation. Prof. Bawazir mentioned the usefulness of teleconferences /webinars on technical ICH topics and the importance to facilitate the participation of individual countries. The GCG noted also the RHI interest to have experts from their respective regions participating to the Expert Working Group (EWG) discussions. Prof. Bawazir referred to the importance of collaboration on clinical trials (e.g., encouraging clinical registries and inviting local DRA to inspections conducted by other agencies) and Good Manufacture Practices (GMP, Q7) for APIs (e.g., to obtain information of API inspection outcomes).

## **5. Regulators Forum Report**

Dr. Molzon (FDA) reported on the fourth ICH Regulators Forum held on October 26, 2009 in St. Louis. At the meeting, regulatory issues and regional experience on Good Review Practices was shared. The regulators initiated also discussions on Good Clinical Practices and Good Manufacturing Practice with Japan and EU as respective lead for future brainstorming in Europe in spring 2010. Considering the duplication of the topics, Mr Wada (JPMA) suggested the clarification of the role of Regulators Forum and GCG.

At the forum, the RHI and DRA/DoH expressed their interest to participate to EWGs discussion which would allow them to better understand the development process of a Guideline, and facilitate its implementation and training.

*Action/Decision:*

- *At the SC meeting, the GCG co-chairs will invite the SC to consider mechanism for the participation of RHI and DRA/DoH in the discussions/work of the EWGs.*

## **6. Finalization of RHI Profiles**

Dr. Pavittranon (APEC) informed the GCG that the APEC profile was under development and will be submitted to the APEC LSIF Forum for review and endorsement prior to submission to the GCG.

The ICH Secretariat will follow up with Mr. Mthetwa (SADC) on the progress made towards finalization of the SADC profile.

*Actions/Decisions:*

- *The ICH Secretariat will follow-up with APEC and SADC for the finalization of their regional profiles;*
- *The RHI will inform the ICH Secretariat of any changes in their regional profiles in order to maintain the GCG public website up-to-date.*

## **7. Drivers and Success Factors for Harmonisation**

In Commemoration of the 20<sup>th</sup> anniversary of ICH, Dr. Molzon (FDA) lead of a small working group (EU, FDA, EFTA, Health Canada and DRA of Australia) provided an overview to the GCG of the draft document describing *The value and benefits of ICH to Regulators*. As proposed in Yokohama, the document will be complementary of a report written ten years ago by Dr.

Caroline Nutley Loew of the PhRMA on *The value and Benefits of ICH to Industry*. In the overview of the document, Dr. Molzon explains where we stand ten years later and the particular impact of the incorporation of the Common Technical Document into regulatory processes in ICH and non-ICH countries. The GCG noted that Dr. Giaquinto (former PhRMA SC member) has provided historical perspectives on how this initiative had been started. The GCG document contains also sections on *ICH Guideline implementation* (Ms. Lindström-Rossi, GCG co-chair, EU), *GCG – a bridge between ICH and the world beyond* (Mr. Ward, HC), *Regulators Forum* (Dr. Dörr, EFTA), *Guideline information dissemination/uptake in non-ICH countries* (Dr. Hunt, TGA). Additional sections to the draft document proposed to be included are *increased access to Harmonisation efforts* (Dr. Rågo), *historical facts* (Ms. Cone, former ICH Secretariat Director) and *current Industry perspective*<sup>1</sup>. Dr. Molzon invited the GCG to provide their views and comments on the document by the end of December 2009. Once finalized, the document is expected to be presented at the time of the next ICH/GCG meeting in June 2010.

*Actions/Decisions:*

- *The RHI and DRA/DoH will be invited to provide their comments on the draft GCG document by the end of December 2009;*
- *FDA will edit the document to ensure style consistency and publish booklets to be distributed by the time of the next ICH meeting in June 2010.*

## **8. Use of MedDRA in Pharmacovigilance**

The GCG, RHI and DRA received a presentation on the use of MedDRA in Pharmacovigilance. Dr. Brosch (M5 Co-Rapporteur, EU) provided background information on MedDRA structure, scope, maintenance and governance. She presented the objectives of MedDRA and the importance to develop an international medical terminology to standardize communication form to allow electronic exchange of information between regulators and industry/sponsors of clinical trials.

MedDRA is not only used for coding Adverse Effects in Individual Case Study Reports (ICSRs) but also could provide different level of medical information such as past medical History, report of Cause of Death, or parent past drug therapy indication. The GCG noted that the medical dictionary can also be used for new drug and biological product applications (using CTD/eCTD), and in Annual Safety Reports for Clinical Trials in the EU.

Dr. Brosch also presented the role of the European Pharmacovigilance Database, “EudraVigilance” which is a central data processing network and management system in the EU, which allows MedDRA to be implemented in different electronic tools to facilitate electronic adverse reaction reporting in clinical trials and post-authorisation for all medicinal products by small and medium size companies.

The GCG noted that MedDRA has been implemented in WHO Uppsala Monitoring Center (UMC) Adverse Event database (Vigibase) which allows WHO National Centres to input and review data and conduct analyses in both WHO-ART and MedDRA. It was noted that WHO receives the majority of ICSRs coded in MedDRA. Dr. Brosch informed the GCG that MSSO developed in conjunction with UMC a *bridge* or mapping from WHO-ART to MedDRA. The GCG noted that the *bridge* only works from WHO-ART to MedDRA since MedDRA is more

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<sup>1</sup> Post-meeting note: Following the GCG meeting, the document was updated with a section on *ICH and Domestic Regulations* from Mr. Tominaga (MHLW) and circulated for comments as version 2 dated October 29, 2009.

granular than WHO-ART. This mapping allows WHO-ART Users to convert their data into MedDRA and not the reverse.

She last presented on special licenses agreed by the MedDRA Management Board to provide free access to small and medium sized companies. Indeed, MedDRA is available at no charge to Academics, Healthcare providers and Regulatory authorities while commercial organizations pay an annual subscription fee based on annual turnover (Subscription rates have been reduced 4 consecutive years).

At the GCG meeting, the participants received also an Information Sheet on MedDRA (dated October 25, 2009), which provides basic information about MedDRA including the structure and content, relationship to other terminologies, access and support.

### **9. Step 2 Guidelines for Consultation**

The GCG noted that no comments had been received from the RHI and DRA on the following *Step 2* Guidelines: E16: *Genomic Biomarkers Related to Drug Response: Context, Structure and Format of Qualification Submissions*; Q4B Annex 9: *Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions on Tablet Friability General Chapter*; Q4B Annex 10: *Evaluation and Recommendation of Pharmacopoeial Texts for Use in the ICH Regions on Polyacrylamide Gel Electrophoresis General Chapter*.

The deadline for sending comments to the ICH Secretariat was by the end of September 2009 for E16 and October 13, 2009 for the Q4B Annexes.

### **10. Webinars on Step 2 / Step 4 Guidelines**

The GCG, RHI and DRA discussed the organisation of future webinars. It was proposed to organize webinars on ICH S6 Guideline on *Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals*<sup>2</sup>, ICH Q11 Guideline on *Development and Manufacture of Drug Substances* once *Step 2* of the ICH process is reached and ICH S9 Guideline on *Nonclinical Evaluation for Anticancer Pharmaceuticals* once *Step 4* is achieved<sup>3</sup>.

*Actions/Decisions:*

- *The GCG endorsed the organisation of webinars on S6 Step 2 and S9 Step 4;*
- *The ICH Secretariat to organise a webinar on Q11 once Step 2 will be achieved;*
- *The RHI and DRA/DoH will be invited to suggest any additional topics on which they would like a webinar.*

### **11. Presentation on ICH Topic – S9**

The GCG, RHI and DRA received a presentation on the ICH topic S9 on *Nonclinical Evaluation for Anticancer Pharmaceuticals* which was expected to reach *Step 4* in St. Louis<sup>4</sup>.

Dr. Leighton, FDA Rapporteur for S9, provided background information on the development of S9 and described to the GCG the evolution of the guidance. The GCG noted the usefulness of the public consultation period once the Guideline reached *Step 2* of the ICH process. The Rapporteur

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<sup>2</sup> The S6 Guideline reached *Step 2* in St. Louis on October 29, 2009.

<sup>3</sup> The S9 Guideline reached *Step 4* in St. Louis on October 29, 2009.

highlighted the importance of the regional consultation at *Step 3* which can help revisit the language or identify the need for clarification of the draft Guideline.

The GCG noted that the ICH S9 guidance intends to facilitate and accelerate the development of anticancer pharmaceuticals and to protect patients from unnecessary adverse effects, while avoiding unnecessary use of animals, in accordance with the 3R principles (reduce/refine/replace), and other resources. The guidance provides recommendations on Nonclinical evaluations in pharmacology, toxicology and start dose of pharmaceuticals including specific consideration to specific issues (e.g., conjugated agents, liposomal products, evaluation of drug metabolites and impurities).

## **12. Training and Capacity Building**

### **❖ *GCG-Endorsed Training***

#### ***ASEAN Training***

Dr. Javroongrit (ASEAN) reported on the organisation of three GCG-endorsed regional training events hosted by the National Pharmaceutical Control Bureau (NPCB) to be held in Kuala Lumpur, Malaysia in 2010. The GCG noted that the MedDRA training program was almost finalized and ICH speakers will be soon nominated. Dr. Javroongrit informed the GCG that the training programmes on ICH Q5C and ICH Q8-Q10 Guidelines were currently under development in collaboration with the EU as the ICH lead for both events.

#### ***GCC Training***

Prof. Bawazir (GCC) informed the GCG that the organisation of the training on ICH Q5A-Q5E Guidelines will be held in the first quarter of 2010. He informed the GCG that work will continue to finalize the training programme with the EU as the ICH lead.

#### ***APEC Harmonisation Centre***

Dr. Lee (DRA, South Korea) provided background information on the structure of the APEC Harmonisation Centre (AHC) including scope and current activities. The GCG noted the success of the first AHC workshop on Multi-Regional Clinical Trials (MRCT) which was held on June 15-17, 2009 in Seoul, South Korea. Over six hundreds participants from the government, industry and academia attended the MRCT workshop. The programme included six plenary sessions and four breakout sessions and two onsite GMP and Clinical visits which were held on the last day of the workshop. The GCG noted the recommendations made during the workshop such as training, guidance development, creation of a repository of information for better understanding of the different regulations and the development of common templates for both reporting and reviewing to ensure acceptability of MRCT data.

Dr. Lee informed the GCG of the outcome of the second workshop on Biosimilars which was held in September 16-18, 2009, in Seoul, South Korea and with over 400 participants. The meeting highlighted the importance of training, dialogue and information sharing.

Future AHC activities in 2010 included the continuation of education and training, the conduct of survey and research to assess training needs, the development of e-publication and website and the promotion of international Cooperation with APEC and non-APEC government, industry and academia. In conclusion, Dr. Lee invited the GCG to provide its support and suggestions for future training and capacity building activities, and welcomed other interested governments, institutions, cooperations and foundations to work cooperatively with AHC.

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

Dr. Cortes (PANDRH) expressed the interest of PANDRH to have future training(s) in Pharmacovigilance conducted in Spanish which would facilitate communication with native Spanish speakers.

Mr. Ward (HC and chair of the Regulatory Harmonisation Steering Committee, RHSC) also informed the GCG that any training proposal submitted to AHC and related to ICH and Harmonisation would be directed to the ICH Secretariat for GCG consideration.

Ms. Lindström-Rossi (GCG Co-chair, EU) informed the GCG on the clarifications made on the ICH/GCG 2009 Procedures with regards to funding aspects of GCG-endorsed training activities. The GCG noted that GCG training endorsement does not necessary mean that ICH party pays its own travel expenses.

#### ❖ *Evaluation of GCG training events*

Dr. Adam (ICH Secretariat) circulated to the GCG an updated version of the training evaluation form which has been developed to monitor, evaluate and help refine future GCG-endorsed training events. The GCG noted the changes made on the document and approved as final the training evaluation form.

#### *Actions/Decisions:*

- *The ICH Secretariat will circulate the revised 2009 GCG procedures;*
- *The GCG endorsed as final the training event evaluation form.*

### **13. Hurdles to Simultaneous Product Development and Registrations**

Dr. Taglieber, Chair of PhRMA Simultaneous Global Development Committee provided an overview on Simultaneous Global Development, describing its benefits and practical national and regional issues to overcome. Dr. Taglieber described the multifactorial reasons why drug development and Clinical Trials (CT) are nowadays more *Global*. The GCG noted that CT ultimate goal is to simultaneously conduct CT, develop a single dossier and support product registration. Dr. Taglieber discussed the benefits of the Simultaneous Global Development such as reduction of drug lag, communication enhancement among regulators and files harmonisation. He presented as an example, Japan's basic principles on Global CTs. The GCG noted the barriers in the regulatory environment which includes the lack of harmonisation for regional/local requirements, the lack of formal mechanism for agency consultation the inefficient review processes and resources within the agency. Dr. Taglieber provided an overview of the ideal regulatory expectations from CT application, review and acceptance. He provided examples of progress made through interactions between regulators and industry towards Simultaneous Global Development. Last, the GCG noted the importance of harmonisation beyond ICH and among GCG regions and the need of continuous constructive dialogue between industry and regulators will help forward the goal of conducting Simultaneous Global Development based on science, logic and practicability.

### **14. RHI and DRA Update on ICH-related Matters**

RHI and DRA provided formal presentations to the GCG on their respective initiatives and current activities. The presentations will be made available on the ICH website.

*China*, Dr. Ding provided background information on the new structure and responsibility of the Chinese State Food and Drug Administration (SFDA) including its internal structure. He

presented an overview of the affiliated organisations of SFDA such as the National Institute for the control of Pharmaceuticals and Biological Products, the Center for Drug Evaluation, and the Center for Drug Certification. Dr. Ding informed the GCG on the local organisation and structure of the SFDA which includes over 60,000 staff to support wide function at each level. The GCG noted ICH-related activities at the SFDA such as the organisation of the Q8/Q9/Q10 workshop in Beijing in December 2008, the translation of all ICH Guidelines in Chinese, the organisation of a training course on ICH Guidelines at the SFDA Training Center and the recent establishment of an ICH study group to do gap analysis between ICH and Chinese Guidelines.

**APEC**, Dr. Pavitranon provided background information on the APEC Life Sciences Innovation Forum (LSIF) including its mission and regulatory performance. She highlighted the efforts of regulators, industry and academia in promoting greater synergies and coordination, to optimise benefits derived from interactions with international harmonization initiatives; and to develop mechanisms to sustain training and capacity-building work. She reported on the seventh annual meeting (LSIF VII) held in Singapore on August 3-4, 2009 and informed the GCG that the next LSIF meeting will be held in Hiroshima, Japan, in 2010.

Dr. Pavitranon summarized the outcomes of the inauguration of the AHC, the creation of the RHSC and the first workshop on MRCT. Last, she presented the operational model of LSIF with RHSC and AHC.

**ASEAN**, Dr. Javroongrit provided information on the activities of the Pharmaceutical Product Working Group (PPWG). The GCG noted that the PPWG organised a workshop on *Ethical and Regulatory Issues in Global Paediatric Trials* in Maryland, USA on September 20-22, 2009. Dr. Javroongrit reported also on the outcome of the *Regulatory Pathways for Clinical Trials of Dengue Vaccines* held in Bangkok, Thailand on October 1-2, 2009 and of the regional training on *ACTD* held in the Philippines on October 26-30, 2009. The GCG noted the organisation of three workshops in the ASEAN region with the participation of the ASEAN-EU program for Regional Integration Support early December 2009, in addition to the three GCG-endorsed workshops on *ICH Quality by Design*, *Q5C* and *MedDRA* topics to be held in 2010. Last, Dr. Javroongrit presented the draft programme of the 17<sup>th</sup> ACCSQ/PPWG meeting to be held in Bangkok in the spring 2010.

**GCC**, Prof. Bawazir provided background information on the structure of the Gulf Central Committee for Drug Registration (GCC-DR) including current activities. He informed the GCG about the transfer of Drug Regulations from the Ministry of Health to Saudi Food and Drug Authority. Prof. Bawazir reported on the outcome of the GCC-DR 44<sup>th</sup> Meeting in Riyadh held on October 12-14, 2009. It was noted that the GCG-endorsed workshop on Biosimilars will be planned for 2010.

**PANDRH**, Dr. Cortes provided background information on PANDRH including its mission, structure and regional organisation. Dr. Cortes reported on the outcome of the V<sup>th</sup> PANDRH conference held in Buenos Aires on November 17-19, 2008 where over 250 participants from National Drug Regulatory Authorities (NRAs), Industry and Academia were welcomed. She highlighted the principle themes and conclusions of the V<sup>th</sup> Conference and future planned activities of the PANDRH Steering Committee. The GCG noted the conclusions of the PANDRH Steering Committee meeting held in July 2009 in PAHO offices, Washington D.C., USA including the proposal of improving communication using virtual tools and the creation of a Biotechnology Products Working Group (Biosimilars). Dr. Cortes informed the GCG that the next PANDRH SC meeting will be held in December 2010 using web-teleconferencing system.

Suggestion was made to provide explanation on the relationship between PANDRH and MERCOSUR in the next GCG in Europe.

## **15. Any Other Business**

### ***African Initiative***

Dr. Rágo (WHO) provided an overview on a new project on harmonisation of medicines registration in Africa. The initiative comes from Africa's regional economic communities and the national medicines regulatory authorities. The GCG noted that the project is supported by a consortium of partners which includes WHO, NEPAD (New Partnership for African Development), BMGF (Bill and Melinda Gates Foundation) and UK DFID (UK Department for International Development ) which agreed an approach in mobilizing technical and financial resources to support Drug Harmonisation efforts in Africa. Dr. Rágo informed the GCG about the organisation of a NEPAD/WHO African Medicines Registration Harmonisation (AMRH) meeting in London, UK on November 19-20, 2009 to seek the financial interest of other donors. The GCG noted that to date three African regional blocks had submitted their project proposal for consideration and funding and the most advanced projects will start in the second quarter of 2010.

### ***GCG Members Only Website***

Dr. Adam (ICH Secretariat) informed the GCG of the update made on the GCG Member's only website on the GCG Calendar and the GCG Reference documents. The GCG Calendar presents the major regional events of interest to and open to RHI, DRA/DoH. In addition, the page also provides an overview on the main organizers of the events (EMEA, FDA CBER/CDER, Health Canada, AHC Center and DIA). Major changes have been recently implemented to improve the user-friendliness of the GCG Reference documents, where all GCG-related working and reference documents can be accessed (Agenda and Reports, Presentations to SC, GCG Procedures, Final RHIs Profile, etc.).

Dr. Adam informed the GCG that new representatives for RHI and DRA/DoH were provided with instructions, login and password to enter the Member's only website.

### ***Date of the Next GCG Meeting***

June 8, 2010

made in February 2010.

Europe (location to be confirmed) Official announcement will be