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Overview of 2011 Activities

hosted/co-hosted 4 international workshops

- Asia Regulatory Conference
  - Asia’s Role in Global Drug Development
- AHC Workshop on Medical Devices:
  - Implementation of GHTF Documents
- AHC Quality by Design Workshop
- MRCT Tokyo Workshop

invited regulators (27 delegates, 7 economies)

AHC website updated and shared training materials & video recordings

worked in collaboration with other initiatives
### AHC Training Activities in 2011

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
<th>Title</th>
<th>Participation</th>
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<tr>
<td><strong>2011 1st Asia Regulatory Conference</strong></td>
<td>April 26~28, 2011</td>
<td>Asia Regulatory Conference - Asia's Role in Global Drug Development</td>
<td>About 730 Attendees including 55 speakers and 6 delegates</td>
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<tr>
<td><strong>2011 2nd AHC Workshop on Medical Devices</strong></td>
<td>June 4~5, 2011</td>
<td>AHC Workshop on Medical Device Workshop : Implementation of GHTF Documents</td>
<td>about 280 in attendance including 24 speakers and 8 delegates</td>
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<tr>
<td><strong>2011 3rd ICH Quality by Design Workshop</strong></td>
<td>October 4-5, 2011</td>
<td>ICH Quality by Design Workshop</td>
<td>About 510 Attendees including 9 speakers and 6 delegates</td>
</tr>
<tr>
<td><strong>2011 4th Multi-Regional Clinical Trials Tokyo Workshop</strong></td>
<td>November 1 ~ 2, 2011</td>
<td>Multi-Regional Clinical Trials Tokyo Workshop</td>
<td>about 400 in attendance including 23 speakers and 7 delegates</td>
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AHC MRCT  Tokyo Workshop in 2011

- **Date:** November 1 ~ 2, 2011
- **Title:** Multi-Regional Clinical Trials Tokyo Workshop
- **Participation:** about 400 in attendance including 23 speakers and 7 delegates
- **Co-sponsored by MHLW, PMDA, AHC & JPMA**
- 7 regulators invited by AHC
AHC MRCT Tokyo Workshop in 2011

Workshop Program

- Main Topics
  - Results from Korea-China-Japan Director General Meeting
  - Importance of Asia in Global Drug Development Strategy
  - Study Design
  - Case Study – Oncology
  - Session report
  - Panel Discussion
Discussions & Recommendations

- The importance of statistical analysis of intrinsic and extrinsic factors
- Require further studies to address issues associated with stability analysis depending on drug administration regimens
- Asian studies should be used for proof of concept and that more studies should be done in cooperation with academia
- Postmarketing data be used for conducting confirmatory studies for MRCTs
APEC Harmonization Center: Challenges and Issues Relating to Multiregional Clinical Trials in the APEC Region

KL Park¹, TG Kim¹, SK Seong¹, SY Lee¹ and SH Kim¹

The Asia-Pacific Economic Cooperation (APEC) Harmonization Center (AHC) was established in 2009 with the purpose of promoting harmonization of regulatory processes for drugs and medical devices. The AHC held three training workshops on multiregional clinical trials (MRCTs); these workshops provided forums for discussing the value and potential benefits of MRCTs. Participants from regulatory agencies, the pharmaceutical industry, and academia identified many issues and made recommendations for resolving major challenges with the aim of improving the capacity of the Asia–Pacific region to carry out MRCTs.

procedures and practices in the regulatory process so as to achieve convergence over time.

Data from large-scale MRCTs conducted on a global scale can be a basis for regulatory approval of new drugs. Given that MRCTs are performed in several geographical regions simultaneously under the same protocol, with the participation of a large number of patient groups, a variety of challenges can occur, such as assessing the quality of clinical trials, interpreting and translating clinical results, and estimating whether the clinical results are applicable to an entire patient group or only to a specific group. Therefore, MRCT results are important when considering the granting of marketing approval or the setting
AHC 2012 Workshop Plan

• Four International Workshops

- Biosimilars (Apr. 2012)
- RHSC Awareness Workshop (Aug. 2012)
- Combination Product or MRCT
- Pharmaco-Vigilance (Sep. 2012)
Overview of AHC Biosimilars Workshop

- **Date:** April 3 ~ 5, 2012
- **Title:** AHC Biosimilars Workshop
- **410 participants** from APEC and Non-APEC region, including
  - More than 30 experts invited as speakers and panelists
  - 8 delegates from APEC travel-eligible economies
2012 1st AHC Biosimilars Workshop

- Current Status of Biosimilar Global Regulatory Framework
- Biosimilar Regulation & Guideline Update
- Issues and Challenges in Developing Biosimilars (Case-study)
- Regulatory Harmonization on Biosimilar
- Regulators’ Meeting (Closed) and Manufacturing Site Tour
The workshop covered the following topics:

- Overview and current status of the global biosimilar regulatory landscape
- Agency perspectives on regulating biosimilars, challenges faced to date, and expectations for the future
  - 7 Regulatory authorities (EU, Canada, Korea, Singapore, China, Japan, Chinese Taipei)
- Review of FDA draft biosimilar guidelines by US FDA
- Challenges to developing biosimilars (quality, clinical, extrapolation of indications, interchangeability and substitution)
- Areas for harmonization, including challenges and strategies to effectively developing biosimilars globally (registration considerations, regulatory environment changes, future role of pharmacopoeias, CMC content considerations and agency expectations, and role of pharmacovigilance)
**Key points discussed:**

- **Biosimilars are not generic medicines**
- Due to the insufficient experience on the biosimilars development, **stepwise approach** are necessary with regulators
- **Different flexibility** among regulatory agencies on Reference Product
- Importance to **build regulatory capacity** and regulators experience to be able to evaluate biological and biosimilar products
- **The QbD principles** as described in ICH Q8 and Q11 (step 4) are equally applicable to Biosimilar and reference products
- **Extrapolation of indications** is possible if the following two assumptions are met:
  - Mechanism(s) of action of a protein is (are) the same to the studied indication
  - Clinical testing to exclude differences done in the most sensitive setting to detect such differences
- **Safety / Pharmacovigilance** must be part of any biosimilar process
2012 1st AHC Biosimilars Workshop

Discussion & Recommendation

- **Stepwise Approach**
  - Due to the insufficient experience on the biosimilars development, stepwise approach are necessary with regulators.

- **Flexible Assessment**
  - Comprehensive information is needed to prove the similarity of reference drug.
  - Regulators need to have the flexibility when assessing similarity with the reference drug.

- **Regulatory Harmonization**
  - Regulatory harmonization on the reference product, clinical trial and the scope of biosimilars is required.
Regulators’ Meeting: Summary
Chaired by Drs Yeowon Sohn (KFDA) and Kwasi Nyarko (Health Canada)

26 regulators from 15 national regulatory agencies (NRAs)
Thailand 1, Canada 1, Australia 1, Malaysia 1, Singapore 6, Republic of Korea 4, Philippines 1, Indonesia 2, Chinese Taipei 1, Japan 1, Peru 2, Chile 1, Mexico 1, China 2, Finland 1

Share insights on the preceding workshop

Identify areas for enhancing the regulatory harmonization and/or convergence

Need for enhanced cooperation among regulators

Ensure access to affordable high quality products (biosimilars) in the marketplace

Report ‘AHC Biosimilars Workshop & Regulators’ Meeting Results’ to WHO Meeting (May 28, 2012)
Harmonization of terminology and definitions within the biosimilar lexicon and regulatory language would be essential as it provides a basis for communication at the same level.

Regulators should not lose sight of the overall purpose of the development of biosimilars, which is the availability of affordable alternatives to biologics drugs.

- Without regulatory harmonization this goal will not be achieved.

Harmonization of the reference product would enhance global development of biosimilars, which should ultimately help in the cost reductions needed.
The need for more interactions amongst regulatory agencies, ranging from exchange of information on reviews to performance joint reviews was suggested as a means for attaining regulatory harmonization and/or convergence.

- The need for ongoing avenues such as regular meetings among regulators for information sharing, capacity building, and further collaboration initiatives was highlighted.

Scientific issues such as how similarity should be established at the quality, non-clinical, and clinical level was raised.
Regulators’ Meeting: Priority Issues

Reference product

- The idea of a ‘declaration’ and use of a global reference product or agreement on a reference product was thought as one that could facilitate global biosimilar development.
- Scientific issues around the use of a foreign reference product, bridging data, and the role of reference product in the extrapolation of indications was raised by a number of attendees.

Harmonization of Definitions

- The need for common definitions to enhance communication and consistency in interpretation was raised by a number of respondents.
- The need for standard or same definitions and consistency in terminology such as “interchangeability/substitutability” and “comparability/similarity” were raised.
Regulators’ Meeting: Priority Issues

3. Capacity building

- The lack of a regular platform for regulatory agencies to communicate/share ideas with each other, be able to participate in training workshops such as discussion of case studies, interpretation of data was raised.
- Seeking avenues such as projects for joint review of dossiers by NRAs or between an experienced and non-experienced NRAs were suggested as potential avenues for capacity building.

4. Other issues

- The evaluation of clinical studies for biosimilar products was also considered important by many regulators.
- The extrapolation of indications and clinical study design for proving similarity seemed to need some guidance to regulators.
- It was understood that the practices of interchangeability for biosimilar products varied from country to country. These were other issues identified for further discussion.
AHC Advisory Board

Countries of members of the AHC Advisory Board (As of April. 2012)
<table>
<thead>
<tr>
<th>Name</th>
<th>Organization/Position</th>
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<tbody>
<tr>
<td>Kwang-Ho Lee</td>
<td>Director General, National Institute of Food and Drug Safety Evaluation, KFDA</td>
</tr>
<tr>
<td>Yves Juillet</td>
<td>Senior Advisor, LEEM/Chair of Regulatory Policy and Technical Steering Committee, IFPMA</td>
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<tr>
<td>Michael B. Gropp</td>
<td>Vice President, Global Regulatory Strategy, Medtronic Co.</td>
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<tr>
<td>Hiroshi Ishikawa</td>
<td>Assistant to President, Toshiba Medical Systems Co./ GHTF Steering Committee</td>
</tr>
<tr>
<td>Kian Ming Lam</td>
<td>Division Director, Strategic Planning, Operations &amp; Communications Division, HSA</td>
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<td>Mark Paxton</td>
<td>Advisory Board, RHI Associate VP, PhRMA</td>
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<tr>
<td>Nancy S. Travis</td>
<td>Vice President, Global Strategy and Analysis, AdvaMed</td>
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<tr>
<td>William Wang</td>
<td>Head of Asia Pacific Operations, Department of Biostatistics and Research Decision Sciences(BARDS), Merck &amp; Co, Inc</td>
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<tr>
<td>Herng-Der Chern</td>
<td>Executive Director, Center for Drug Evaluation, Chinese Taipei</td>
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<td>Florence Houn</td>
<td>Vice President, Regulatory Policy and Strategy, Celgene Co.</td>
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<tr>
<td>Rae Yuan</td>
<td>A.P. Head of PhRMA Development, Roche PhaRMA</td>
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<tr>
<td>Stuart Walker</td>
<td>Founder of Center for Medical Research(CMR)</td>
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<tr>
<td>Heng Siew</td>
<td>Celgene Co.</td>
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<td>Marie Vodicka</td>
<td>Assistant Vice President, International Regulatory Affairs, PhRMA</td>
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<tr>
<td>Toshiyoshi Tominaga</td>
<td>PMDA, Japan</td>
</tr>
<tr>
<td>Patrice Pineda</td>
<td>COFEPRIS (Mexico)</td>
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<tr>
<td>Hans Vasquez Solpopuco</td>
<td>DGEMID (Peru)</td>
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<tr>
<td>Lembit Rago</td>
<td>WHO</td>
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<tr>
<td>Jacques Morenas</td>
<td>Agency for the Safety of Health Products, France (AFSSAPS)</td>
</tr>
<tr>
<td>Odette Morin</td>
<td>IFPMA (Switzerland) Director, Regulatory and Scientific Affairs, Director of ICH Secretariat</td>
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<tr>
<td>Andre Broekmans</td>
<td>MSD Co. (Netherlands) Vice President, Most of World Regulatory Policy &amp; Regulatory Affairs</td>
</tr>
<tr>
<td>Romi Singh</td>
<td>Amgen (USA) Executive Director, Global Regulatory Affairs &amp; Safety</td>
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AHC Activities: Linkages & Outreach

- Importance of synergy effect made through close cooperation

- Expanding the opportunities to work together with other initiatives
Thank You for your attention!

Send your additional comments or questions at parkkl@korea.kr or ahckorea@khidi.or.kr

Please visit our website at www.apec-ahc.org