Progress of International Collaboration among Asian Countries

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Pharmaceuticals and Medical Devices Agency

Date of Establishment: April 2004

PMDA’s Safety Triangle

Unique Three-pillar System Securing Nation’s Safety

- Review Risk reduction
- Japanese Citizens
- Safety Mitigation efforts to continuing risk
- Relief Relief measures for health damage caused by risk factors

Kansai Branch
Guest speakers: Prof. Guido Rasi (EMA); Mr. Jüng H. Schnetzer (Swissmedic); A/Prof. John C W Lim (HSA); Dr. Chung Seung (MFDS); Dr. M. Hayatie Amal (NADFC); Mr. Kees de Joncheere (WHO); Dr. Margaret A. Hamburg (FDA, video presentation)
Rapid Paradigm Shift Surrounds The International Regulatory Community

To cope with rapid paradigm shift, Regulatory Science (RS) and medical ethics are becoming more important.
Today’s agenda

1. Recent Trend of Pharmaceutical Affairs in Japan
2. Role of Japanese Regulators in Asia
3rd 5-year mid-term plan of PMDA (FY2014-2018)

Major challenges

- Shortening the time to approval & High quality review/consultation services
- Enhancing safety measures
- Globalization

Specific measures

- Accelerated review process (Improvement of approval predictability)
- Improvement of prior assessment (substantial acceleration of approval review process)
- Readiness for introduction of risk management plan
- Drastic improvement of consultation service
  - Improvement of pharmaceutical affairs consultation service on R&D strategy
  - Improvement of clinical trial consultation service
- Utilization of medical information database
- Advanced Review/Consultation System

Human Resources with excellent skills 【751 staffs → 1065 staffs】

Goal

- Development of Japan’s original innovative drugs and medical devices
- Marketing of cellular and tissue-based products
- Activation of the industry
- Extending health and life span of Japanese people
- Contribution to global medicine

Advanced Review/Consultation System

Readiness for introduction of risk management plan

Improvement of prior assessment (substantial acceleration of approval review process)

Drastic improvement of consultation service

Utilization of medical information database

Accelerated review process (Improvement of approval predictability)
Activities of PMDA

1. Science Board

2. Advanced Review System
Establishment of the Science Board

The Science Board was established in May 2012 to discuss how PMDA can better cope with products with advanced science & technology, in each developmental stage such as basic research, development support, product review, and post market safety measures.
Outcome of the Science Board

Cellular & Tissue-based Products

➢ Current Perspective on Evaluation of Tumorigenicity of Cellular and Tissue-based Products Derived from iPSCs and iPSCs as Their Starting Materials (Aug. 21, 2013)

Pharmaceuticals, Bio-based Products

➢ Summary of Discussion on Non-clinical Pharmacology Studies of Anticancer Drugs (Dec. 10, 2013)

➢ Summary of the discussion on assessment of the current status of personalized medicine relating to drug development and review (Mar. 11, 2014)
Innovative evaluation methods
Active utilization of Modeling & Simulation
- Disease model
- Objective B/R assessment
- Identifying AE-related factors etc.

Cross-Products Analysis

Sophisticated NDA review
- Each reviewer utilizes innovative assessment techniques

Sophisticated Consultation
- More evidence-based consultation

Database

Data Accumulation
e-Submission of study data

Analysis by PMDA
- Giving additional scientific value to submitted data

Cooperation with Academia

Practical use of Innovative Medical Products
- A rational & effective evaluation process for regulatory decision

Effective and High Quality Review
- More predictable efficacy/safety after approval
- Reduction of applicant’s work load
- More scientific regulatory decision

Effective and Successful Development
- Epoch-making proposal leading the world
- Proactive publication of guideline
## Utilization of study data and expected outcomes

Clinical: evaluation of data from Japanese subjects, comparison with those from non-Japanese subjects, etc.

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<tr>
<th>Subject</th>
<th>Outcome</th>
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| Prediction of drug interaction using a model (eg. in vitro and in vivo PK prediction) | • Increase of study success rate  
• Avoidance of unnecessary studies  
• Confirmation of model appropriateness in the review process, decrease of regulatory inquiries |
| Development of a dose-response model and prediction of optimal dose (Eg. optimal pediatric dose, optimal dose for Japanese patients in a global clinical trial) |  |
| Development of a new evaluation indicator for disorders with no appropriate indicator (Eg. Alzheimer’s disease) |  |
| Identification of factors affecting efficacy or safety (Eg. placebo reaction of antidepressant users) |  |
| Evaluation of class effect in rare adverse events (Eg. heart failure, suicide) | • Enhanced safety prediction, etc. |
| Prediction of QT prolongation based on simulated blood concentration-QT relationship |  |
Strengthen Safety Measures regarding Drugs, Medical Devices

- Specify relevant party’s obligation to ensure quality, safety, and efficacy of drugs and medical devices.
- MAH’s obligation to notify revised Package insert reflecting the latest findings

Regulation considering Medical Devices Character

- Independent Chapter for “Medical Devices”
- Third party certification system
- Quality Management System (QMS)
- Other revisions related to medical devices
- Regenerative and Cellular Therapy Products, and Gene Therapy Products

Regulation considering Regenerative Medicines Character

- Creation for Regenerative Medicines regulations
- Introduction of approval system with condition/period
Today’s agenda

1. Recent Move of Pharmaceutical Affairs in Japan

2. Role of Japanese Regulators in Asia
MHLW/PMDA have been working as a steering committee member for ICH to harmonize guidelines across different countries and regions to built up the global standard for regulatory administration.

ICH has developed 80 harmonized guidelines including Common Technical Document (CTD) and their electrical submission system. ICH also directed the development of the Medical Dictionary for Regulatory Activities (MedDRA) Terminology.
Outcomes of ICH

ICH have harmonized over 80 guidelines regarding technical elements about the evaluation of quality, efficacy and safety, as well as the format of application form and the post-market safety measures.

- Preventing duplication of clinical trials and reducing research resources (E6 Guidelines, etc.)
- Reducing International barriers
- Facilitating the dissemination and communication of information on harmonized guidelines and their use for non-member countries

Examples of guidelines harmonized by Japan’s Initiative

M8: Electronic Common Technical Document (eCTD)
E2B (R3) IWG: Implementation: Electronic Transmission of Individual Case Safety Reports
S10: Photo Safety Evaluation of Pharmaceuticals
Q3C(R5): Impurities: Guideline for Residual Solvents (from 2014 June)
International Pharmaceutical Regulators Forum (IPRF)

Former Regulators Forum

- Voluntary party of regulators participating ICH
- Updating each activity, sharing domestic issues, discussing common topics.
- Paperwork regarding GCP inspection for E6 Discussion Group

IPRF

- No big changes of activity per se from the former RF
- Assigned the chair, Co-chair and secretariat
- Enhancement the management system by Terms of Reference (ToR)
- Will publish manuals for the establishment of Working/Discussion group
# Implementation of Outcomes of Global Clinical Study Project to APEC LSIF RHSC

APEC LSIF RHSC is established to promote a strategic and coordinated approach to regulatory harmonization and capacity building efforts within the APEC region. Japan takes a leadership of MRCT project and cooperates other 7 on-going priority work area projects.

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<th>Project Theme</th>
<th>Achievements</th>
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| **Multi-Regional Clinical Trials (led by Japan)** | Roadmap approved  
Workshop held in Seoul and Tokyo  
Joint workshop held in Tsingtao                                  |
| Supply chain integrity                     | Established the expert working group                               |
| Good Review Practices                      | Roadmap approved  
Workshop will be held in November                                 |
| Good Clinical Practices                    | Preparing questionnaire to compare the member economies’ status of implementation |
| Combination Products                       | Roadmap approved  
Workshop will be held in November                                 |
| Biosimilars                                | Workshop held in April  
Discuss definition of terms                                         |
| Pharmacovigilance                          | Roadmap approved  
Discussion focused on pharmaceuticals                               |
| Advanced Therapies                         | Roadmap approved                                                  |
APEC/RHSC MRCT-GCP inspection Workshop

Date: 8-10 May, 2014
Venue: Qingtao, PR of China
Participants: c.a.150 People (including c.a. 100 Chinese Regulators and Industries)

- **[Purpose]**
  - To deepen understanding of regulatory/scientific aspect of MRCT
  - To understand GCP inspection issue from good practice
  - To make clear gap analysis amongst participant Economies
  - **Last stage of STEP 1 of MRCT and GCP inspection project**

- **[Result]**
  - MRCT and GCP inspection issues are close link to implement
  - Scientific evaluation MRCT based on the data is significant apart from country’s requirement
  - Need to make convergence of difference raised by GAP

Progress at the next stage (for making curriculum)
Training Opportunities: Seminars

2014 February 3-7: Reviewing Generic Drugs
17 participants (Korea 3, Saudi Arabia 3, Taiwan 2, Indonesia 2, Yemen 1, Russia 1, WHO 1, Vietnam 4*) *WHO Fellows

2014 March 3-7: 1st Medical Devices Training Seminar
19 participants (Taiwan 4, Malaysia 4, Korea 3, Singapore 3, Saudi Arabia 2, Hong Kong 1, Switzerland 1, Uganda 1)

Website: http://www.pmda.go.jp/english/seminar/
Training Opportunities: Individual Training (including OJT)

NADFC (Indonesia) officials: 5 days, March 2013
FDA (US) analyst: 6 months, September 2013- February 2014
NPBC (Malaysia) officials: 1 month, 2014
Thai FDA (Thailand) officials: 5 days, 2014

Dr. Kondo with Trainees from Indonesia NADFC

Presentation by the Trainees from US FDA
Dissemination of Information

English translations of review reports

- 64 reports (59 drugs and 5 medical devices) have been available in English through PMDA website since 2007
- Aim for the publication of 40 reports in FY2014, and more in the future

![Image of Votrient Tablet 200mg, issued on 28 August 2012](http://www.pmda.go.jp/english/service/review.html)

◆A review report is around 100 pages and consists of
  ✓ Review Result,
  ✓ Review Report (1) and
  ✓ Review Report (2).
◆The contents are
  Summary of study results and PMDA evaluation.
◆Reports without confidential information are available on PMDA web.

PMDA has chosen review reports for translation, taking into account the following nature of the products:
1) Japan is the first approval country,
2) approved based on multi-national clinical trials (particularly Asian trials),
3) the dose is different from that of western countries due to ethnic difference
PMDA will continue active cooperation with the regulators in the world.
Thank you for your attention

大谢谢了

ご清聴ありがとうございました