Asian Trends in Drug Development & Regulation

Competition, collaboration and Harmonization

Toshiyoshi Tominaga, Ph.D.
Associate Executive Director
Pharmaceuticals and Medical Devices Agency (PMDA)
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1. Competition Among Asian Countries

To become…

A) venue of early phase development

B) Authority approving innovative drugs as early as FDA & EMA
Promotion of Country - Taiwan -

**Why Taiwan? (1/2)**

*Continuous Improving Infrastructure*
- Regulatory Agency is continuously meeting international standards, and taking in new regulatory updates.
- Sites are taking initiatives to make the trial environment for clinical trials.

**Why Taiwan? (2/2)**

*Support Drug Registration*

<table>
<thead>
<tr>
<th>Drug Registration Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>#38-1 Phase I (n\geq 10) + Phase III (n\geq 80)</td>
</tr>
<tr>
<td>#38-2 Phase II (n\geq 20) + Phase III (n\geq 80)</td>
</tr>
</tbody>
</table>

- (a) Phase I (n\geq 10); or (b) Phase II (n\geq 20 or \geq 10%); or (c) Phase III (n\geq 80 or \geq 10%); or (d) Multinational Phase III, with participation of one of the 10 reference countries, and CSR submitted to FDA or EMA for NDA.

- For trial with total subject number \geq 200:
  - n\geq 30 or \geq 5%, for trial with total subject number \geq 200
  - n\geq 10, for trial with total subject number <200

*Benefit NHI Drug Price*

<table>
<thead>
<tr>
<th>NIH Drug Pricing Item and Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comply Drug Registration Guidance #38-1</td>
</tr>
<tr>
<td>Comply Drug Registration Guidance #38-2 (d)</td>
</tr>
</tbody>
</table>

NHI Price Mark-up

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Sarah Lin, DIA 12th Japan Annual Meeting 2015
MFDS’s Consultation & PHARM NAVI Project

Source: Ho-Jeong Kim, DIA 27th Annual EuroMeeting 2015
Japan’s Time-limited Conditional Approval of Regenerative Medical Products

Conventional Process

Clinical research

Clinical trial (efficacy & safety proven)

Approval

Marketing

CT

Approval

Time-limited Conditional

Marketing

Efficacy & Safety Validation

Approval

Marketing

Re-Application (or Expiration)

Efficacy predicted
Safety assured
…will launch a gene-therapy in Japan first in the world, taking advantage of de-regulation.
2. Collaboration

Un-met medical needs necessitate MRCTs

Drug’s Application Status  Satisfaction and Treatment Satisfaction  2005

Drug’s treatment contribution

Source: OPIR Views and actions No.31 (2010) issued by Office of Pharmaceutical Industry Research
Main Points of E17 (tentative)

- Conducting a MRCT is the preferred development option for investigating new drugs for simultaneous global development.
- To increase an acceptability of MRCT data in the review by multiple regulatory agencies for drug approval, a sponsor should carefully consider the planning and design of MRCTs in advance. – A major point for consideration is ethnic factors.
- Considering the impact of regional variability is important for patient selection, sample size allocation and assessment of degree of consistency between the populations.

Shuji Kamada (PMDA)  DIA Japan (2015)
Better cooperate with Asian Friends
Isolated Summit to Mountain Range

Taking advantage of:
- Asian common diseases
- Geographical proximity
- Similar ethnic backgrounds
- Regional Harmonization activities
- Similar cultures
- Growing population and economy

<table>
<thead>
<tr>
<th>Ranking</th>
<th>Country / Region</th>
<th>No. of Studies (Out of 37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>South Korea</td>
<td>32</td>
</tr>
<tr>
<td>2</td>
<td>Taiwan</td>
<td>22</td>
</tr>
<tr>
<td>3</td>
<td>Poland</td>
<td>15</td>
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<tr>
<td>4</td>
<td>Germany</td>
<td>14</td>
</tr>
<tr>
<td>5</td>
<td>U.S.</td>
<td>13</td>
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<tr>
<td>6</td>
<td>Australia</td>
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<td>6</td>
<td>UK</td>
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<td>6</td>
<td>Spain</td>
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<tr>
<td>6</td>
<td>France</td>
<td>12</td>
</tr>
<tr>
<td>6</td>
<td>Russia</td>
<td>12</td>
</tr>
</tbody>
</table>

Source: JPMA Website
http://www.jpma.or.jp/about/issue/gratis/newsletter/html/2014/162policy05.html
Anatomy of Mountain Range

Each Country’s Singularity or Competitive Edge

Common Operations Regulatory Harmonization
Meaningful harmonization (of operations) needs more than Guidelines

- Harmonized operations across countries
  - Regulatory practices
  - Competence to use GI
    - Competence to introduce GI (Regulators)
  - Harmonized Guidelines/ Regulations
  - Developer’s practices

Basic Regulatory System/Infrastructure
GCP is the same but operations are different.

**Japanese monitoring style**
CRAs work full-time for 1 study. They take care all activities not limited to monitoring (including Investigator’s role) with frequency visit.

**Asian style (Global style)**
“Monitoring activities” should be defined and visit frequency & timing should be specified. Sponsor should check the important process for study success.
On Asian Regulatory Harmonization

1. Opportunity created by ICH Reform
2. APEC RHSC
3. APAC
4. PMDA’s Asian Training Center
5. Expectation on Asia New drug Conference
NEW ICH (2015 - )

Ich Association

Management Committee

4 Regulators

2 Industries

Report & Recommendation

ICH Association

Assembly

Founding Members

Standing Members

Standing Observers

Members

Observer

Secretariat

EWG/IWG

Founding Members: FDA, EC, MHLW/PMDA, PhRMA, EFPIA, JPMA

Standing Members: HC, SM,

Standing Observer: WHO, IFPMA

Non-members

Application & Review & Admission

MedDRA Mgmt Board

FM, SM, MHRA

EWG/IWG

Application & Review & Admission
ICH and Future

Expectation on new Members

• Active participation in EWG
• Voting right to endorse Guidelines in Assembly
• Surer Implementation

Member eligibility: Application of ICH Guidelines

- **Q1**: Stability Testing guidelines
- **Q7**: GMP Guideline for Active Pharmaceutical Ingredients
- **E6**: Good Clinical Practice guideline

APEC (ASIA-PACIFIC ECONOMIC COOPERATION)

Leaders’ Meeting

APEC Business Advisory Council

Ministerial Meeting

Sectoral Ministerial Meetings

Senior Officials’ M.

Finance Deputies’ Meeting

Committee on Trade & Investment

Budget and Management Committee

Economic Committee

SOM Steering Committee on ECOTECH

Senior Finance Officials’ Meeting

Life Sciences Innovation Forum

Committee on Trade & Investment

FoTC

Sub-Forum

Special Task Force

Steering Council

Policy Partnerships

Working Groups

Regulatory Harmonization Steering Committee (RHSC)
The Goal of RHSC:
to promote a strategic and coordinated approach to regulatory convergence and capacity building efforts within the APEC region.

RHSC Member Economy:
Canada, China, Chinese Taipei, Indonesia, Japan, Korea, Malaysia, Mexico, Peru, Philippines, Russia, Singapore, Thailand, U.S.

Industry Member:
JPMA, JIRA, PhRMA, BIO, IGPA
Priority Work Area (PWAs) of APEC LSIF-RHSC

- Pharmaco-vigilance: Champion: Korea
- Combination Products: Champion: Taiwan
- Global Supply Chain Integrity: Champion: USA
- Biotherapeutics: Champion: Korea
- Cell and Tissue Based Therapeutic Products: Champion: Singapore
- Good Review Practice/Good Submission Practice: Champion: Taiwan and Japan
- Multi-Regional Clinical Trials/GCP Inspection: Champion: Japan and Thailand
Concept of Good Registration Management

GRevP: Documented best practices for a medical product review.

GSubP: An industry practice for submission for registration of medical products.

Good Registration Management: A concept to promote efficient registration process by GRevP and GSubP.
Promote Implementation of GRM through Trainings

Proposed Structure of GRM Training

- **Common Training**
  1. Basic Concept of GRM
  2. Outline of GRevP Guideline
  3. Outline of GSubP Guideline

- **Reviewer Specific GRevP Training**
  - To be developed in each review authority

- **Applicant Specific GSubP Training**
  - To be developed in each country/area by industry

- The main activity after Step 2, starting from 2015
- Common Training for both reviewers and applicants
- “Train-the-Trainer” model
- **GRM CoE Pilot:**
  - Planned for late 2016
  - Training curriculum and materials will be developed.
  - Outcome assessment
- The trainings will be initially applied to new pharmaceutical products, and subsequently applied to other medical products stepwise.

LSIF-RHSC, APEC 2016
Lima, Peru
February 24, 2016
Center of Excellence
Training Seminar
on MRCT/GCP
Mission:
To expedite the launch of innovative medicines for the peoples in Asia
APAC Members
1. Philosophy

PMDA International Strategy 2015

Vision III: To share the wisdom with other countries/regions

Strategy 5: Provision of information and training programs that are essential for building regulatory capacity in partner countries

1) Launch of “Asian Training Center for Pharmaceuticals and Medical Devices Regulatory Affairs”

2. Expectation

1. Capacity level-up and harmonization
2. Cooperation with APEC, PIC/S
3. Coordination with regional capacity building activities
Providers of Trainings in East Asia

- PMDA Training Seminar
- APEC CoE (MRCT/GCP)
- APEC CoE (PVg)
- APEC CoE (GRM)
- APEC CoE (BioPharm)
- APEC Harmonization Ctr
- Regulatory Authority
- WPRO
For Future

1. Science/Technology and harmonization
   1. Personalized medicine, big data and ethnic factors
   2. Quality approach and clinical data quality
2. Asia New Drug Conference to discuss Asian Regulatory Harmonization
Ask