PMDA Perspective:
Recent Trends in the Regulation of Biopharmaceuticals

Daisaku Sato, PhD.
Director, Office of Cellular and Tissue-based Products
Pharmaceuticals and Medical Devices Agency (PMDA),
Japan

The contents of this presentation represent the view of this presenter only, and do not represent the views and/or policies of the PMDA
CONTENTS

• PMDA’s Structure, Policy and Trend
• Antibody Engineering Technologies and Products:
  (1) Current Status and Future Prospects
  (2) Recent Trends in the Regulation of Biopharmaceutical Products
• New Regulations for Cellular and Tissue-based Products (incl. quality evaluation)
• Accelerated Developing Programs (CMC Consideration)
• Lifecycle Approach to Process Validation
Pharmaceuticals and Medical Devices Agency

Major Services

- Scientific Review for Drugs & Medical Devices
- GCP, GMP Inspection
- Consultation on Clinical Trials
- Safety Measures
- Relief Services

Unique Three-pillar System Securing Nation’s Safety

Review

Japanese citizens

Safety

Relief

Kansai Branch
Organization of PMDA

Executive Director

Chief Executive

Director of Center for Product Evaluation

Deputy Center Director (for Medical Devices)

Associate Executive Director

Astrive Center Director

Office of Regulatory Science

Office of Standards and Guidelines Development

Office of Review Administration

Office of Review Management

Office of International Programs

International Coordination/Liaison Officers

Offices of New Drug I-V

Office of Cellular and Tissue-based Products

Office of Vaccines and Blood Products

Offices of OTC/Quasi-Drugs

Office of Generic Drugs

Offices of Medical Devices I-III

Office of Conformity Audit

Principal Senior Scientists

Senior Scientists

Advanced Review with Electric Data Promotion Group

Kansai Branch

Office of Manufacturing/Quality and Compliance

Offices of Safety I, II

Information Technology Promotion Group

Chief Actuary

Office of Relief Funds

Offices of General Affairs/Office of Financial Management/Office of Planning and Coordination

Chief Management Officer

Chief Relief Officer

Auditor

Deputy Executive Director

Audit Office

Senior Executive Director

Executive Director

Deputy Executive Director

As of November 1, 2014
3rd 5-year mid-term Plan of PMDA (FY2014-2018)

**Major challenges**

1. **Shortening the time to approval**
   - High quality review/consultation services

2. **Enhancing safety measures**

3. **Globalization**
   - Accelerated review process (Improvement of approval predictability)
   - Improvement of prior assessment (substantial acceleration of approval review process)
   - Readiness for introduction of RMP
   - Utilization of medical inf. database

**Specific measures**

- **Advanced Review/Consultation System**
  - Introduction of approval system with condition/period for Regenerative Medicines
  - Drastic improvement of consultation service
    - Improvement of pharmaceutical affairs consultation service on R&D strategy
    - Improvement of clinical trial consultation service
  - Improvement of prior assessment (substantial acceleration of approval review process)
  - Readiness for introduction of RMP
  - Utilization of medical inf. database

**Goal**

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

**Human Resources with excellent skills**

751 staffs → 1065 staffs

**3rd 5-year mid-term Plan of PMDA (FY2014-2018)**
### Accelerating Review Period

#### Total Review Period New Drug (Standard)

<table>
<thead>
<tr>
<th>Year</th>
<th>FY2008</th>
<th>FY2009</th>
<th>FY2010</th>
<th>FY2011</th>
<th>FY2012</th>
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<td>8.5</td>
<td>6.7</td>
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#### Total Review Period New Drug (Priority)

<table>
<thead>
<tr>
<th>Year</th>
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<th>FY2010</th>
<th>FY2011</th>
<th>FY2012</th>
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<td>9</td>
<td>8.1</td>
<td>7.7</td>
<td>5.3</td>
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</table>

#### Percentile

<table>
<thead>
<tr>
<th>Year</th>
<th>2013</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>2017</th>
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<tr>
<td>Standard</td>
<td>50</td>
<td>60</td>
<td>70</td>
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<tr>
<td>Priority</td>
<td>50</td>
<td>60</td>
<td>60</td>
<td>70</td>
<td>70</td>
<td>80</td>
</tr>
</tbody>
</table>

#### Total Review Period

- **Standard**: 12mo.
- **Priority**: 9 mo.

- **Regulatory**
- **Applicant**
- **Number of application**
- **Target Period**
• PMDA’s Structure, Policy and Trend
• Antibody Engineering Technologies and Products:
  (1) Current Status and Future Prospects
  (2) Recent Trends in the Regulation of Biopharmaceutical Products
• New Regulations for Cellular and Tissue-based Products (incl. quality evaluation)
• Accelerated Developing Programs (CMC consideration and product life cycle)
mAbs & Fusion proteins account for more than 25%

As of September 1, 2013

No. of approved recombinant protein products

- Enzymes, 11
- Coagulation factors, Albumin, 6
- Hormones, 25
- Vaccines, 4
- Interferons, 7
- EPOs, 5
- Cytokines, 8
- mAbs & Fusion proteins, 28

As of September 1, 2013
Quality by Design (Q8(R2))

• Quality cannot be tested into products; i.e., quality should be built in by design.

• A systematic approach to development
• Begins with predefined objectives and emphasizes product and process understanding and process control
• Based on sound science and quality risk management.

QbD is useful tool for understanding quality of biotech products
Key Consideration of QbD Approach

QTPP → CQAs

Risk Management → Control Strategy

Continual improvement

Identify the critical quality attributes based on the potential risks

Linking material attributes and process parameters to CQAs, in this case, risk assessment is useful

Establishment and implementation of control strategy

Knowledge and understanding obtained could facilitate continual improvement
QbD Assessment Project

• In November 2011, PMDA launched a new project team to handle the participation in the EMA-FDA pilot program as an observer.
• The project team consists of reviewers, inspectors, etc.
What PMDA learned

- Although regulatory actions, especially post approval change procedure, might be a little different among regulatory agencies,
- post-approval changes will be well accommodated by QbD to minimize post-approval change application/notification process.
QbD gives more flexibility in Post-approval changes in Japan?
QbD gives more flexibility in Post-approval changes in Japan?
Regulatory History and Status of Biosimilars

- Application Category for biosimilars
- Guideline
- Nomenclature rules

2005-2009

2010

Somatropin BS [Sandoz]

Epoetin alfa BS [JCR]

2011

Filgrastim BS [F], [MOCHIDA]

2012

Filgrastim BS [NK], [TEVA]

2013

Revision of Nomenclature rules

2014

Filgrastim BS [Sandoz]

Infliximab BS [NK], [CTH]
## List of Approved Biosimilars in Japan

<table>
<thead>
<tr>
<th>Drug name</th>
<th>Japanese Accepted Name (JAN)</th>
<th>Manufacturer</th>
<th>Reference product</th>
<th>Approved year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatropin BS S.C. Injection 5mg [SANDOZ] etc.*</td>
<td>Somatropin (genetical recombination)</td>
<td>SANDOZ</td>
<td>Genotropin (Somatropin) (Pfizer)</td>
<td>2009.5</td>
</tr>
<tr>
<td>Epoetin alfa BS Injection 750 syringe [JCR] etc.*</td>
<td>Epoetin Kappa (genetical recombination) [Epoetin Alfa Biosimilar 1]</td>
<td>JCR Pharmaceuticals</td>
<td>Espo (Epoetin alfa) (Kyowa Hakko Kirin)</td>
<td>2010.1</td>
</tr>
<tr>
<td>Filgrastim BS Injection 75µg syringe [F] / [MOCHIDA] etc.*</td>
<td>Filgrastim (genetical recombination) [Filgrastim Biosimilar 1]</td>
<td>Fuji Pharma / Mochida Pharmaceutical</td>
<td>Gran (Filgrastim) (Kyowa Hakko Kirin)</td>
<td>2012.11</td>
</tr>
<tr>
<td>Filgrastim BS Injection 75µg syringe [NK] / [TEVA] etc.*</td>
<td>Filgrastim (genetical recombination) [Filgrastim Biosimilar 2]</td>
<td>NIPPON KAYAKU / Teva Pharma Japan</td>
<td>Gran (Filgrastim) (Kyowa Hakko Kirin)</td>
<td>2013.2</td>
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<tr>
<td>Filgrastim BS Injection 75µg syringe [SANDOZ] etc.*</td>
<td>Filgrastim (genetical recombination) [Filgrastim Biosimilar 3]</td>
<td>SANDOZ</td>
<td>Gran (Filgrastim) (Kyowa Hakko Kirin)</td>
<td>2014.3</td>
</tr>
<tr>
<td>Infliximab BS I.V. infusion 100mg [NK] / [CTH]</td>
<td>Infliximab (genetical recombination) [Infliximab Biosimilar 1]</td>
<td>NIPPON KAYAKU / Celltrion</td>
<td>Remicade (Infliximab) (Mitsubishi Tanabe Pharma)</td>
<td>2014.7</td>
</tr>
</tbody>
</table>

*: etc. means different presentations.
Regulations for Biosimilars in Japan

- Guideline for the Quality, Safety and Efficacy Assurance of Follow-on Biologics (FOBs)*
  (PFSB/ELD Notification No. 0304007 / March 4, 2009)
  http://www.pmda.go.jp/english/service/pdf/notifications/PFSB-ELD-0304007.pdf (GL in English)
  with Overview of comments on Guideline

  *: “Follow-on Biologics” in this guideline is a synonym for “Biosimilars”.

- Marketing Approval Application for FOBs
  (PFSB Notification 0304004 / March 4, 2009)

- Nonproprietary Name and Drug Name of FOBs
  (PFSB/ELD Notification No. 0214-1, Administrative Notice / February 14, 2013)

- Questions & Answers regarding Guideline

- Risk management plan (RMP) guidance
  PFSB/ELD Notification No. 0411-1, 0411-2 Administrative Notice / April 11, 2012
  • RMP should be considered at the time of submission of approval application for biosimilar
Number of Consultation for Biosimilars

<table>
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<th>Fiscal year</th>
<th>No. of consultations</th>
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<tr>
<td>2012</td>
<td>20</td>
</tr>
<tr>
<td>2013</td>
<td>20</td>
</tr>
</tbody>
</table>

Based on date of application (from April 1 to March 31)
Consultation on Clinical Trial

Trend of Clinical Trial Consultation

Fiscal Year; Start from April

*: Currently calculating

Number of Clinical Trial Consultation

% of Global Clinical Trials

281     315     336     359     411     361     312

27.0  32.1  29.5  28.4  23.8  29.9 (*)&
Clinical Trial

- The acceptability of foreign clinical data
  - Ref. to ICH guideline E5 (R1)

- Global clinical trial
  - It is important that the consistency between entire population and the Japanese population could be explained from the results.

- Requirement of Japanese data
Global Issues to be addressed

i. Can a sponsor use non-XXX sourced reference product in comparability exercise?

ii. Is toxicity study (repeat-dose toxicity study) required for biosimilar development?

iii. What should a sponsor consider when designing the efficacy trials?

iv. Is regional data required for biosimilar development?

v. What should a sponsor consider when designing global clinical trial?

vi. Is extrapolation of indications acceptable?

vii. What is the rule of biosimilar naming?
Reference Product (1)

Guideline: The reference product (RP) should be already approved in Japan.

- PMDA thinks the sponsor should confirm the comparability to the RP which is approved (and used by healthcare providers and patients) in Japan.
However, if a sponsor needs to use non Japan-sourced RP in comparability exercise, it is required to explain that the non-Japan sourced RP is the representative of the Japan sourced RP by analytical assays and publicly available information.
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• Accelerated Developing Programs (CMC consideration and product life cycle)
New Legislative Framework

These two acts were promulgated in November 2013 by the Japanese Diet (Parliament) in line with the Regenerative Medicine Promotion Act, in order to reform the pharmaceutical and medical regulation related to regenerative medicine.

- Revision of the Pharmaceutical Affaires Law: The Pharmaceuticals, Medical Devices, and Other Therapeutic Products Act (PMD. Act)
- The Act on the Safety of Regenerative Medicine

These two acts are scheduled to be enacted on 25 November 2014.

Other related governmental policy:
- Healthcare and Medical Strategy Promotion Act (2014.5)
- Japan Medical Research Development Institution Act (2014.5)
Revising of Pharmaceutical Affairs Law

**Revisions of Drugs and Medical Devices Articles**
- Relevant party’s obligations are specified to ensure quality, safety, and efficacy of drugs and medical devices.
- MAH’s obligation to notify labeling and its revision, reflecting the latest findings

**Revisions of Medical Devices Articles**
- Independent Chapter for “Medical Devices”
- Expansion of Third party certification system to higher risk devices
- Quality Management System (QMS) adherent to ISO 13485
- Other revisions related to medical devices

**Additions for Regenerative Medical Products**
- Definition and independent chapter for Regenerative Medical Products
- Introduction of conditional/time limited approval system
Definition of “Regenerative Medical Products” in Japanese Legislation

- **Regenerative medical products** are defined as processed human/annimal cells that are intended to be used 1) for either (1) the reconstruction, repair, or formation of structures or functions of the human body or (2) the treatment or prevention of human diseases, or 2) for gene therapy.

Under the Revised PAL (=Pharmaceuticals and Medical Devices Act. (PMD Act.)

Cellular and Tissue based Products and Gene therapy Products

Advanced-therapy medicinal products (ATMPs)

Regulation (EC) No 1394/2007
Two Authorized Products under PAL
Ref. Japan Tissue Engineering Co., Ltd. (J-TEC), HP

**Autologous Culture Epidermis  
**JACE**

- **Indication:** Relief of symptoms of traumatic cartilage defects and osteochondritis dissecans (exclude osteoarthritis) for knee joints.
  - Limited to a defect area of over 4cm² with no alternative therapy.

Marketing authorization for medical device on 29 October 2007  
(submission: 6 October 2004)

**Autologous Cultured Cartilage **JACC**

- **Indication:** Serious burns treatment (limited to the burns of more than 30% of the body surface area)

Marketing authorization for medical device on 27 July 2012  
(submission: 24 August 2009)
Two of the New Products Application under the New Regulation during grace period

- According to the news released by the sponsor companies, in September and in October 2014, two new product applications for marketing authorization were filed by PMDA

1. Bone marrow mesenchymal stem cells for GVHD
2. Skeletal myoblast sheet for serious heart failure due to ischemic heart disease

Note: Figures quoted from the company press release docs
## Early Access Schemes of ICH 3 parties

<table>
<thead>
<tr>
<th>US</th>
<th>EU</th>
<th>JAPAN</th>
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</thead>
<tbody>
<tr>
<td>Priority Review</td>
<td>Priority review</td>
<td>Priority review</td>
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<tr>
<td>Accelerated approval for</td>
<td>Conditional MA</td>
<td>Conditional Approval for Oncology drug, Orphan drug</td>
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<tr>
<td>serious or life-threatening</td>
<td>MA under exceptional circumstances</td>
<td>Conditional &amp; Time-limited approval for regenerative medicine</td>
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<tr>
<td>illnesses</td>
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<tr>
<td>Break through therapy</td>
<td>Forerunner Review Assignment</td>
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<tr>
<td>&amp; Fast Track designation</td>
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</table>

Various agencies have various approaches to accommodate patient access though they have certain similarity.
How to expedite R&D and review for cellular and tissue based product

• Designed for unmet needs under the present treatment: limited number of patients available for CT
• Difficult to conduct controlled study to demonstrate “true end point” of clinical benefit
• Heterogeneity of Quality affected by source materials

Would it take long time for CTs and review if regulator pursues the conventional drug pathway too much?
The Pharmaceuticals and Medical Devices Act (PMD Act)

- Separate category and definition of "regenerative medical products"

Difficult to gather and evaluate the data for efficacy of regenerative medical products in a short time due to heterogeneity of cells.

To secure timely provision of safe regenerative medicines, a new regulatory framework is needed.

Expedited approval system for regenerative medical products

After the safety is confirmed and the results predict likely efficacy, the product will be given conditional, time-limited marketing authorization in order to enable timely provision of the products to patients.
Expedited approval system under PMD Act

[Traditional approval process]

Clinical study

Phased clinical trials
  (confirmation of efficacy and safety)

Marketing authorization

< Drawback of traditional PAL approval system >

Long-term data collection and evaluation in clinical trials, due to the characteristics of cellular/tissue-based products, such as non-uniform quality reflecting individual heterogeneity of autologous donor patients

[New scheme for regenerative medical products]

Clinical study

Clinical trials
  (likely to predict efficacy, confirming safety)

Conditional / term-limited authorization

Marketing (Further confirmation of efficacy and safety)

Re-application within a period (max. 7 yrs)

Marketing authorization or Revocation

Marketing continues

Post-marketing safety measures must be taken, including prior informed consent of risk to patients
Likely to predict efficacy (clinical benefit)

- To approve products based on the limited data, such as surrogate endpoints in exploratory study.
- Similarity to **accelerated approval of** USFDA * The product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit (ref.)
- We have experiences in the orphan drug area.

Ref.) USFDA--Accelerated Approval of New Drugs for Serious or Life-Threatening Illnesses (57 FR 58958, Dec. 11, 1992)

- It applies to certain new drug products in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit to patients over existing treatments.
- Approval based on a surrogate endpoint or on an effect on a clinical endpoint other than survival or irreversible morbidity.
- The drug product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity.
- Approval will be subject to the requirement that the applicant study the drug further, to verify and describe its clinical benefit (such as OS).
- Postmarketing studies would usually be studies already underway.
- FDA may withdraw approval, if a postmarketing clinical study fails to verify clinical benefit; .............
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)
The Science board discussion, further

• Further to the discussion in the last term, in the present term following immediate discussion is on-going to support scientific consultations and reviews of PMDA:

1. Drugs
   - Necessity and condition of placebo-controlled trials for diseases under unmet medical needs
   - Effective utilization animal models for non-clinical testing to demonstrate POCs

2. Medical Devices
   - Application of numerical analysis for non-clinical testing
   - Evaluation of medical devices for pediatric use (including application of non-clinical testing)

3. Cellular & tissue-based products
   - Manufacturing and quality of cellular products during the early development in cell processing centers
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Forerunner Package Strategy

The Ministry of Health, Labour and Welfare (MHLW) has formed the "Strategy of SAKIGAKE" by Ministry Project Team to lead the world in the practical application of innovative medical products (Press release in Japanese). This PT has been launched to plan strategies as a package covering from basic research to the practical application with related divisions within the MHLW.

The Strategy of SAKIGAKE consists of two measurements as follows and covers from basic research to clinical research/trials, approval reviews, safety measures, insurance coverage, improvement of infrastructure and the environment for corporate activities, and global expansion.

- SAKIGAKE Designation System: promoting R&D in Japan aiming at early practical application for innovative pharmaceutical products, medical devices, and regenerative medicines.
- Scheme for Rapid Authorization of Unapproved Drugs: accelerating the practical application of unapproved/off-label use of drugs for serious and life-threatening diseases by expanding the scope of the Council on Unapproved Drugs/Off-label Use to include unapproved in Western countries if it satisfies certain conditions and by improving the environment for companies to undertake development of such drugs.

The MHLW will implement these policies during the budgetary request process in FY2015, but some of them which are ready will be executed in 2014 ahead of schedule.

<Materials>
- Strategy of SAKIGAKE (PDF:379KB)
- Summary of Strategy of SAKIGAKE (PDF:587KB)

Forerunner Review Assignment System

Forerunner Review Assignment System is a system to put innovative medicines/medical devices/regenerative medicines originated from Japan into practice.

Designation Criteria

Medical products for diseases in dire need of innovative therapy and satisfies the following two conditions:

1. Having developed firstly in Japan and anticipating an application for approvals (desirable to have PMDA consultation from the beginning of R&D)

2. Prominent effectiveness (i.e. radical improvement compared to existing therapy), can be expected based on the data of mechanism of action from non-clinical study and early phase of clinical trials (phase I to II)

Not limited to life-threatening and regenerative medicine
• Shorten review time, using rolling submission of data as “prior review” during P-III
• Similar to breakthrough therapy designation of USFDA
• Come into effect in early 2015
CMC Challenges for Consideration on Early Approval (much relies on post-approval change)

• Experience of manufacturing is limited with small number of batches for clinical trial in terms of specification
  ✓ Considering number of batches to be tested for CMC development?
  ✓ Look at the product life cycle management in post-approval change control.

• Stability testing may not meet the conventional requirements
  ✓ consider robustness of severe test and acceleration test data for acceptance

• When process validation should be conducted during the review, would be time limiting. validation vs. verification
  ✓ Consider similarity to the transfer from investigational drug batches to commercial butches (continuous process verification)
  ✓ Knowledge management in the lifecycle
Overall picture of CMC activities through the product life cycle

- Product Quality Review
- Process Validation
- Commercial Production
- Technical Transfer
- Development
- Knowledge
- Quality Improvement
- Post-approval change
- Report of Research and Development

Cycle that connects development and commercial production
# Post-Approval Change Procedure

<table>
<thead>
<tr>
<th>Risk of Changes</th>
<th>Japan</th>
<th>US</th>
<th>EU</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td><strong>Partial change</strong> (Application for approval of variation)</td>
<td>Major change (Prior approval supplement)</td>
<td>Type II variation (Application for approval of variation)</td>
</tr>
<tr>
<td>Moderate</td>
<td><strong>Minor change</strong> (Notification within 30 days after implementation or shipping)</td>
<td>Moderate change 1) Supplement - changes being effected (CBE) in 30 days</td>
<td>Type IB variation (Notification before implementation and MAHs must wait a period of 30 days)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2) Supplement - changes being effected (CBE)</td>
<td>Type IA\textsubscript{IN} variation (Immediate notification)</td>
</tr>
<tr>
<td>Low</td>
<td><strong>SOP</strong> (Under GMP change control)</td>
<td>Minor change (Annual report)</td>
<td>Type IA variation (Notification within 12 months after implementation)</td>
</tr>
</tbody>
</table>
Further international arrangement would be needed?

- Timeframe and regulatory actions for post-approval change would be coordinated
- Consultation between regulators and sponsors would be encouraged in a timely manner.

Then, international cooperation, including among regulatory authorities, will be more vital in the biologics area.
Japan Approved Member at the 38th PIC/S Committee Meeting

- Japan (MHLW, PMDA, 47 prefectures) GMP Inspectors applied for PIC/S membership on March 2012
- On-site examination on September 9-13, 2013
- Decided to become official membership on July 1st 2014 at the committee meeting on May 15-16, 2014 (Rome)
- 45th member

Basic requirements of Validation Internationally to respond to global biologics quality
## Global Activities

<table>
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<tr>
<th>Abbreviation</th>
<th>Official Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Summit</td>
<td>International Summit of Heads of Medicines Regulatory Agencies</td>
</tr>
<tr>
<td>ICH</td>
<td>International Conference on Harmonization</td>
</tr>
<tr>
<td>IMDRF</td>
<td>International Medical Device Regulators Forum</td>
</tr>
<tr>
<td>PIC/S</td>
<td>Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme</td>
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<tr>
<td>HBD</td>
<td>Harmonization By Doing</td>
</tr>
<tr>
<td>APEC LSIF RHSC</td>
<td>APEC Life Science Innovation Forum Regulatory Harmonization Steering Committee</td>
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<tr>
<td>OECD MAD</td>
<td>OECD Mutual Acceptance of Data</td>
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<td>PDG</td>
<td>Pharmacopoeial Discussion Group</td>
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<tr>
<td>IGDRP</td>
<td>International Generic Drug Regulators Pilot</td>
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MOU between the Chinese SFDA (present CFDA) and the Japanese MHLW, under which PMDA supports cooperative activities.

**MOU concluded between Interchange Association and East Asia Relations Commission, but is being implemented through cooperation of related organizations.**
Thank you for your attention

Daisaku Sato, PhD.
Director, Office of Cellular and Tissue-based Products Pharmaceuticals and Medical Devices Agency (PMDA), Japan

sato-daisaku@pmda.go.jp

Regenerative medicine literature available in English