Japan Update

- Progress of measures to improve access to innovative MDs/IVDs -

March, 2016
Topics

1. Training center under international regulatory harmonization strategies by MHLW and PMDA

2. Designation of Sakigake products

3. Approval of regenerative medicine products for the first time after the implementation of PMD Act
1. Training Center for regulatory matters

PDMA is to set up Asia Training Center for Pharmaceuticals and Medical Devices Affairs and *promote understanding of Japan’s knowledge of regulatory science and Japan’s regulatory system* to mainly Asian regulatory authority staff, which would contribute to advancement of medical device regulations in Asia as a whole.

- Liaise with Asian countries to design and coordinate effective training in accordance with their needs and capabilities
- PMDA establishes professional organization
- (1) Provide training seminar attended by regulatory authority staff
- (2) Establish central training facility for APEC international collaborative clinical trials
- (2) Visit local site to lecture, carry out a case study, and conduct fieldwork
- Enables training tailored to local requirements to be offered to more personnel
3nd PMDA Medical Device Training Seminar for regulators in other jurisdictions

The seminar was held in cooperation with Japanese industries on 15 – 19 February, 2016 at PMDA (Tokyo, Japan).

- Topics such as pre-market review, QMS, PMS, training facility visit, collaboration among stakeholders and group works for review were provided in the 2016 seminar.
- 31 officials from the following jurisdictions participated:
  - Bahrain
  - Chinese Taipei
  - Ghana
  - Hong Kong SAR
  - India
  - Indonesia
  - Iran
  - Malaysia
  - Myanmar
  - Saudi Arabia
  - Singapore
(Reference) Establishment of new international regulatory harmonization strategies by MHLW and PMDA

*International Regulatory Harmonization Strategy by MHLW and PMDA International Strategic Plan 2015 by PMDA* have been published on 26 June 2015.

Based on the *mutually complementary* strategies, the following measures will be taken:

A) Promotion of Regulatory Science
   Guidelines related to medical device regulations in Japan will be prepared and internationally announced.

B) Establishment of Training Center for regulatory matters
   PMDA will provide regulators outside Japan with training for capacity building.

C) Active commitment to IMDRF as well as advancement of bilateral collaboration
   IMDRF has been reaffirmed as one of the most important activities.
### 2. Designation of Sakigake products

The following **5 products** under development have been designated as Sakigake products since 10 February 2016. If a pre-market application for the products is filed, a **priority review is applied**.

<table>
<thead>
<tr>
<th>No.</th>
<th>Product name</th>
<th>Expected performance/effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD1</td>
<td><strong>Titanium Bridge</strong> (Hinge-type plate with titanium)</td>
<td>Adduction-type spasmodic dysphonia</td>
</tr>
<tr>
<td>MD2</td>
<td><strong>Absorbing barrier for adhesion prevention</strong> (Trehalose solution)</td>
<td>Reduction of postoperative adhesion prevention by Intraperitoneal injection</td>
</tr>
<tr>
<td>RP1</td>
<td><strong>STR01</strong> (Autologous bone marrow-derived stem cells)</td>
<td>Improvement of neurological symptoms and functional impairment due to spinal cord injury</td>
</tr>
<tr>
<td>RP2</td>
<td><strong>G47Δ</strong> (Recombinant herpes virus)</td>
<td>Glioma</td>
</tr>
<tr>
<td>RP3</td>
<td><strong>Autologous intracardiac stem cells</strong></td>
<td>Improvement of heart function in children with congenital heart disease</td>
</tr>
</tbody>
</table>
An innovative MD/IVD for patients in urgent need of innovative therapy may be designated as a Sakigake Product if:

1) its premarket application will be filed in Japan firstly or simultaneously in some countries including Japan, AND
2) prominent effectiveness can be expected.

Once an MD/IVD is designated, its developer can enjoy such benefits as:

A) Prioritized Consultation by PMDA
B) Pre-application substantive review
C) Prioritized Review (12 months → 6 months [MD])
D) Review Concierge assigned by PMDA
3. Approval of regenerative medicine product (1/2)

<table>
<thead>
<tr>
<th>Brand name / General name</th>
<th>TEMCELL® / Human (allogeneic) bone marrow-derived mesenchymal stem cells</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marketing Authorization Holder</td>
<td>JCR Pharmaceuticals Co., Ltd.</td>
</tr>
<tr>
<td>Date of approval</td>
<td>18 September 2015</td>
</tr>
<tr>
<td>Date of pre-market application</td>
<td>26 September 2014</td>
</tr>
</tbody>
</table>

- The product is administered intravenously to patients that experienced immune response as a side effect after hematopoietic stem cell transplantation.
- Normal approval has been applied.
3. Approval of regenerative medicine product (2/2)

<table>
<thead>
<tr>
<th>Brand name / General name</th>
<th>HeartSheet / Autologous skeletal myoblast sheets</th>
</tr>
</thead>
<tbody>
<tr>
<td>Marketing Authorization Holder</td>
<td>Terumo Corporation</td>
</tr>
<tr>
<td>Date of approval</td>
<td>18 September 2015</td>
</tr>
<tr>
<td>Date of pre-market application</td>
<td>30 October 2014</td>
</tr>
</tbody>
</table>

- The product is attached to heart of patients with severe heart failure.
- Conditional and time-limited approval has been applied. The efficacy and safety of the product will be evaluated based on data from approximately 50 patients for 5 years.
Thank you