“Revision of Pharmaceutical Affairs Law (PAL) ”

- Japan Update -
Revision of Pharmaceutical Affairs Law (PAL) was adopted by the Diet, and announced on 27 November 2013.

- The amendment law will be enforced in November 2014.
- Ordinance and notification (detail of the new regulations) will be announced in advance to the new law enforcement.
Brief overview of revision of PAL

- Points of the amendment are to:
  1. Strengthen safety measures regarding drugs and medical devices
  2. Revise medical device regulations based on its characteristics
  3. Introduce Regenerative and Cellular Therapy Products (RCTP) & Gene Therapy Products (GTP) regulations based on their characteristics

- Name of PAL will be changed to
  “Act on Securing Quality, Efficacy and Safety of Pharmaceuticals, Medical Devices, Regenerative and Cellular Therapy Products, Gene Therapy Products, and Cosmetics”.

- The chapter for “Medical Device” will be prepared.
Scope of *Third Party Certification* will be expanded

<table>
<thead>
<tr>
<th>GHTF Classification</th>
<th>PAL classification</th>
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<tbody>
<tr>
<td><strong>Class A</strong></td>
<td></td>
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<tr>
<td>extremely low risk</td>
<td>General MDs (Class I)</td>
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<tr>
<td>X-Ray film</td>
<td>Self declaration</td>
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<tr>
<td><strong>Class B</strong></td>
<td>Controlled MDs (class II)</td>
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<tr>
<td>low risk</td>
<td>Third party Certification</td>
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<tr>
<td>MRI, digestive catheters</td>
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<tr>
<td><strong>Class C</strong></td>
<td>Specially Controlled MDs (class III &amp; IV)</td>
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<tr>
<td>medium risk</td>
<td>Minister’s Approval (Review by PMDA)</td>
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<tr>
<td>artificial bones, dialyzer</td>
<td></td>
</tr>
<tr>
<td><strong>Class D</strong></td>
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<tr>
<td>high risk</td>
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Framework of Approval Review and QMS Inspection

Pre-approval:
- Application Form
- Review by Review Divisions
- Market Approval
- Design transfer to manufacturing site
- Actual production
- QMS inspection before approval

Post-approval:
- Partial Change Application
- Minor Change Notification
- Market Release
- QMS inspection every 5 years after approval
QMS regulation change under the revision of PAL

- QMS inspection applied to Market Authorization Holder (MAH)
- Foreign manufacturer’s Accreditation to Registration
- QMS inspection per product family
QMS inspection will be applied to MAH, not each manufacturer

[Current QMS inspection]

Marketing Authorization Holder (MAH)

GQP

Plant A in USA

QMS

PMDA

Plant B in Tokyo

QMS

Tokyo

Plant C in Osaka

QMS

Osaka

[New QMS inspection]

Marketing Authorization Holder (MAH)

QMS

Plant A in USA

PMDA or Third Party

Plant B in Tokyo

Plant C in Osaka
Registration of Foreign Manufacturer

Foreign manufacturer need to register until the QMS inspection is conducted.

Accreditation of foreign manufacturer would change to Registration.

Accreditation → Registration

Manufacturing License would change to Registration.

License for inland manufacturing → Registration
QMS inspection per product family

Ex) Product A, B, C are Product family XXX

Now

QMS Inspection per Product A, B and C

After the revision of PAL

QMS Inspection per Product family XXX

※ QMS inspection per product family manufactured by the same establishments.
Standalone Medical Device Software (SMDS) will be regulated by the revised PAL

**Current PAL**

*Image Diagnostic Apparatus*

It processes, stores and displays image data from CT, MRI etc.

**Hardware**

**Software (program)**

Only combination of hardware and software is regulated.

**Future**

**SMDS**

Software (program)

Standalone Software will also be regulated.
Outcome examination system, instead of re-examination system, will be introduced

Outcome examination system

Outcomes (efficacy and safety) of a designated medical device under a post-marketing surveillance for an appropriate period will be examined.

Current

[Scope]
All brand-new medical devices

Review

Approval

Re-examination period

Orphan ···················· 7 years
New structure ·········· 4 years
Others ······················· 3 years

Annual report

Post-marketing surveillance

Application for re-examination

Future

[Scope]
Designated medical devices
ex) Implantable medical devices like stent

Outcome examination period

[Designated Period]
Not necessary to start the period just after approval

Annual report
1. Contents of package insert of class IV medical device should be notified to MHLW in advance.

2. Package insert notified will be uploaded on web-site.

3. Draft of package insert will be required as a material in a new medical device application.

4. Paper package insert of any medical devices can be omitted under certain conditions.
Regenerative and Cellular Therapy Products (RCTP), and Gene Therapy Products (GTP) will be newly categorized.
Thank you

MHLW

PMDA