Overview of PACMP* pilot program in Japan

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* Post-Approval Change Management Protocol
Approved Matters in Application Forms in Japan

Module 1 (Approved Matters are described in Application Forms)

- Approved Matters in Module 1 is the target of regulatory process in Japan
- Change categories for approved matters:
  ① Partial change Application
  ② Minor change Notification

Reference: ICH M4
### Post-Approval Change Procedures

<table>
<thead>
<tr>
<th>Risk of Changes</th>
<th>Japan</th>
<th>US</th>
<th>EU</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High</strong></td>
<td>Partial change Application (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><strong>Moderate</strong></td>
<td>Minor change Notification (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><strong>Low</strong></td>
<td>(Non-approved matters)</td>
<td>Minor change (Annual report)</td>
<td>Type IA variation (Notification within 12 months after implementation)</td>
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</table>
This guideline provides a framework to facilitate the management of post-approval CMC changes in a more predictable and efficient manner.

**Definition of a PACMP:**
A PACMP is a regulatory tool that provides predictability and transparency in terms of the requirements and studies needed to implement a change as the approved protocol provides an agreement between the MAH and the regulatory authority.
Regulatory tool that provides predictability and transparency in terms of the requirements and studies needed to implement a CMC change as the approved protocol provides an agreement between the MAH and the regulatory authority.

A protocol describes the CMC change an MAH intends to implement during the commercial phase of a product, how the change would be prepared and verified, including assessment of the impact of the proposed change, and the suggested reporting category in line with regional requirements, i.e., a lower reporting category and/or shortened review period.

PACMP enables planning and implementation of future changes to approved matters in an efficient and predictable manner.

Already implemented in US (2003-) and EU (2010-)

In Japan, PACMP pilot program has started since April 2018
PACMP pilot program in Japan

- PACMP pilot program provides predictability and transparency of post-approval CMC change.
- PACMP pilot program provides the type of change categories (PCA / MCN) based on prior agreement between the MAH and PMDA.
- Conditions and acceptance criteria outlined in the PACMP must be met in order to implement the change(s).
- Partial Change Application ⇔ Approval: 3 months (median).

User restrictions and general instructions:

- The MAH is responsible for ensuring that whenever a CMC change is to be introduced under a PACMP.
- The use of a PACMP is enabled through an effective PQS (ICH Q10).
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Step 1

- Confirm draft PACMP (incl. draft application form)
- Agree PACMP between PMDA and MAH

Step 2

- If PACMP (incl. draft application form) is changed, follow-up meeting is used to confirm revised PACMP and agree between PMDA and MAH

Pre-meeting

- Share draft PACMP Documents and schedule
- Determine the necessity of GMP consultation

PACMP Quality Consultation

PACMP GMP Consultation

Follow-up Meeting (Optional)

Minor Change Notification

Partial Change Application

GMP Inspection Application

Approval

- Judge the GMP status (Compliance / Non-compliance)

- Check the detail operations under GMP control and PQS at the manufacturing site

3 months (median)

4 months

- Step 1
- Step 2