Pharmacovigilance in Japan and Risk Management Plans（RMP）; Regulator Perspective

Kazuhiko Mori,
Chief Safety Officer
Pharmaceuticals and Medical Devices Agency (PMDA), Japan

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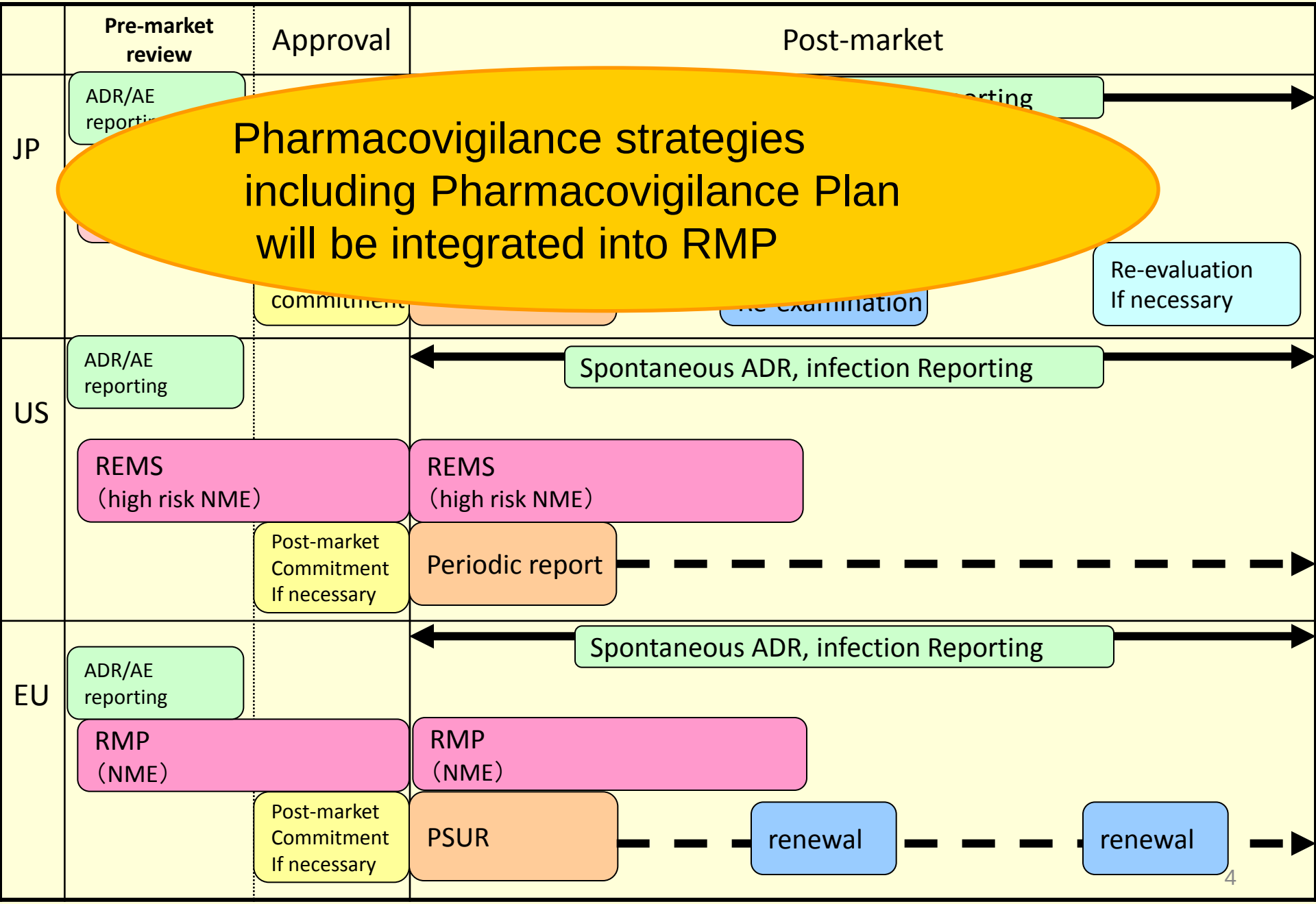
Agenda

- Outline of Japanese PhV
- PhV updates in Japan
  - Risk Manager system
  - Development Safety Update Report in Japan
  - Risk Management Plan in Japan

Phamacovigilance measures JP, US, EU



Risk Manager（RM）System in Japan

- For the continuous and comprehensive benefit-risk evaluation
  - Through life-cycle of product
    - From development stage to review period and post-approval stage
    - Integration of information of development and post-marketing stage.
- Enhancement of human resources in the safety department of PMDA began in fiscal 2009 (+100 person) → **RM was realized!!**

Risk Manager (RM)

- Advise to developing product
  - To clarify the safety issues
  - To make safety measure before approval
  - To identify issues to collect post-marketing data
  - To avoid misuse
  - To make user friendly information (incl. labeling)
- Liaison between clinical development and post-marketing safety measures
- **12 Risk Managers** in different disease areas

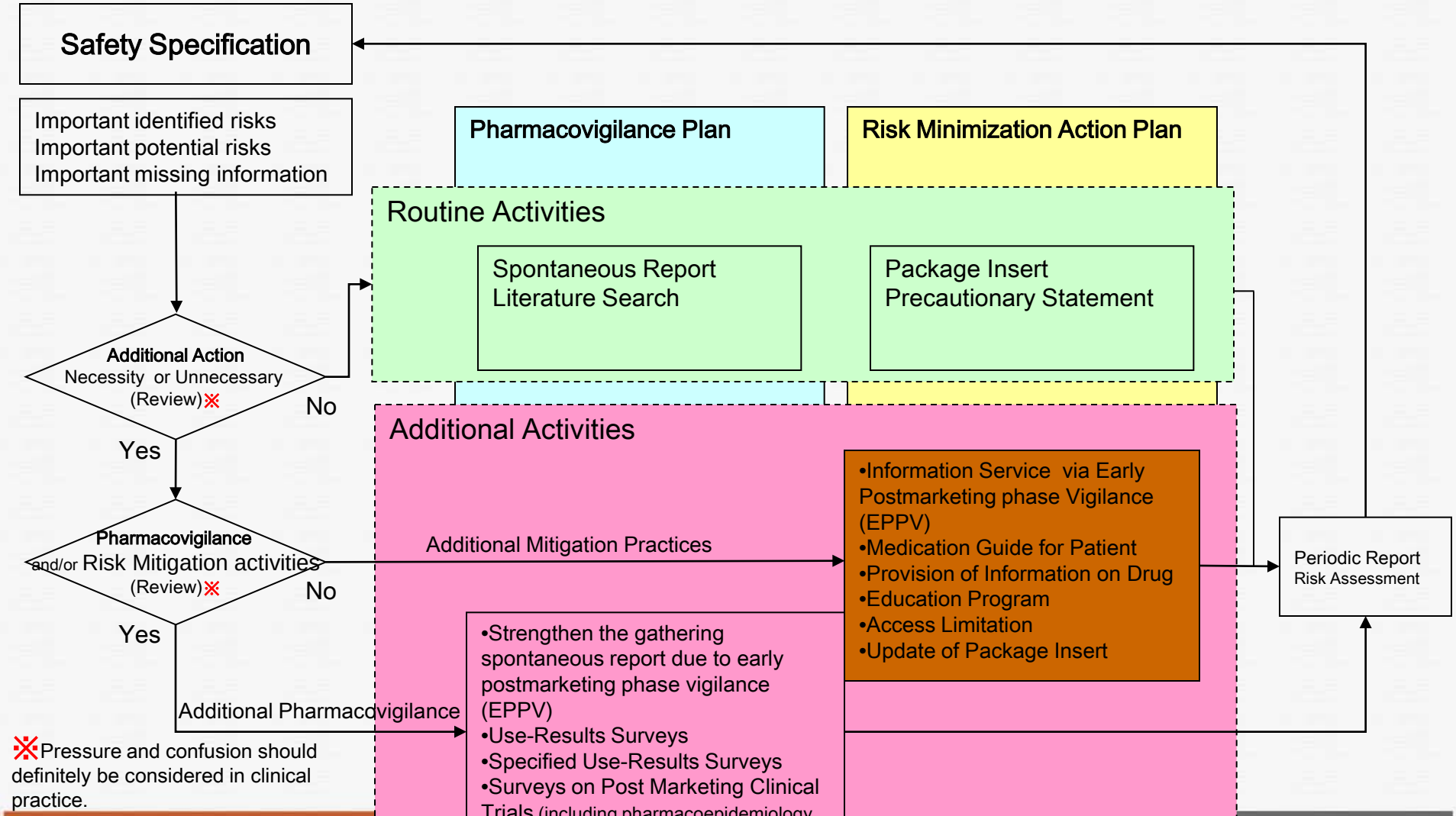
RMP in Japan

- Draft guidance
  - Public consultation; April 20th-October 31st ,2011
  - Pilot execution of RMP
    - Collaboration with applicants
  - Revision by public comments
- Notification
  - http://www.pmda.go.jp/english/service/pdf/mhlw/PFSB-SD_Notification120411-1.pdf
  - Preparing format and Q&A

Current RMP in Japan

- Discussion & Agreement of RMP between PMDA and MAH before approval
  - Are Healthcare professionals involved?
- Most of products are required PMS.
  - Are they sufficient and minimum?
- Is RMP made based product's character ?
- Is purpose of RM/data collection clear ?

Risk Management Program (RMP) Workflow Process



※Pressure and confusion should definitely be considered in clinical practice.

PMDA website (http://www.pmda.go.jp/)

Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare

Translated by Office of Safety I,
Pharmaceuticals and Medical Devices Agency

This English version is intended to be a reference material to provide convenience for users. In the event of inconsistency between the Japanese original and this English translation, the former shall prevail.

PFSB/SD Notification No. 0411-1
PFSB/ELD Notification No. 0411-2
April 11, 2012

To: Directors of Prefectural Health Departments (Bureaus)

From: Directors of Safety Division
Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare

Director of Evaluation and Licensing Division,
Pharmaceutical and Food Safety Bureau,
Ministry of Health, Labour and Welfare

Risk Management Plan Guidance

To ensure the safety of drugs, it is important to consider the ways to manage the risk

Table of Contents of RMP Guidance

1. Introduction
2. Risk Management Plan
3. Safety Specification
4. Pharmacovigilance Plan
5. Plan for Survey/Study on Efficacy
6. Risk Minimization Plan
7. Evaluation of Risk Management Plan and Report to PMDA

2. Risk Management Plan

- Development of Risk Management Plan
- Points to Consider in Development of Risk Management Plan
- Setting of Milestones in Risk Management Plan
- Review of Risk Management Plan
- Safety Specification
- Identification of Safety Specification

6. Risk Minimization Plan

6.1 Routine Risk Minimization Practices

6.2 Additional Risk Minimization Activities

6.2.1 Provision of Additional Information to Healthcare Professionals

6.2.2 Provision of Information to Patients

6.2.3. Establishment of Conditions of the Use of the Drug

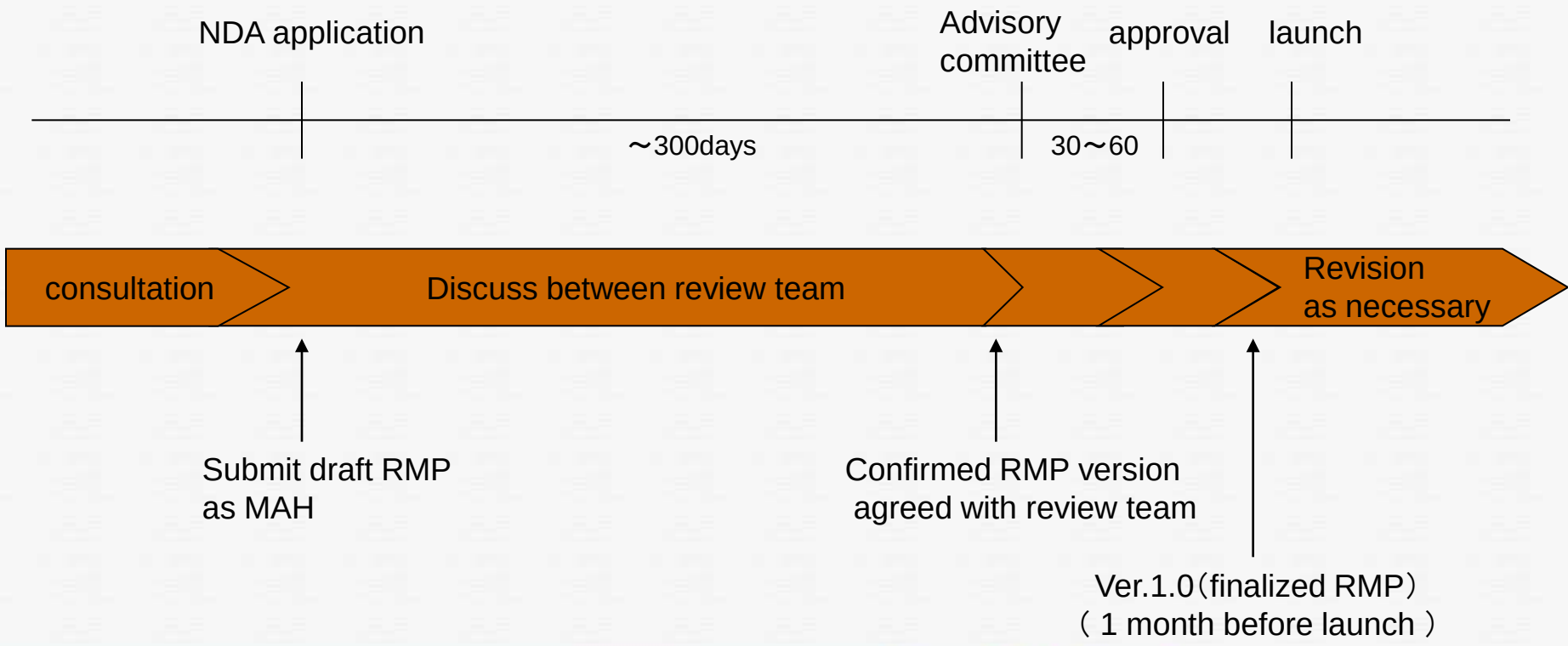
6.2.4 Other Activities

6.3 Implementation Plan for Additional Risk Minimization Activities

Characteristics of Japanese RMP

- Optimal risk management and data collection
  - Incl. generic drug
- Start to discussion at the submission of NDA
- Set up milestones
  - Obvious goal of surveillance
  - Revision of RMP by new information, if ecessary.
- Transparency among stakeholders
  - Comprehensive information collection & risk management thorough life-cycle of the product

Development and revision of RMP



Development Safety Update Report

- ICH-E2F
  - *Step4*; August, 2010
  - *Step 5;*
    - EU:Adopted by CHMP, September 2010, issued as EMA/CHMP/ICH/309348/2008
    - MHLW:To be notified
    - FDA:Published in the Federal Register, 23 August 2011, Vol. 76, No. 163, p. 52667-8

http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html

Implementation of DSUR in Japan

- Still ongoing…..

Safety report begins with development stage and next stage

- Safety report throughout from development phase to post-marketing phase
  - ICH-E2C(PSUR)
  - ICH-E2F(DSUR)
- **The NEXT STAGE ⇒ ICH-E2C(R2)**
  - Benefit / Risk evaluation **PBRER**

Summary

- Comprehensive Risk Management
  - Through life-cycle of products
  - Involve all related stakeholders
  - Transparency
- Data collection based on available data
  - Based on character of product
- Utilization of existing data
  - Safer, more beneficial, and more optimal