Experience Sharing on maintaining safety and quality of pharmaceuticals

Industry perspective
Post-approval change application

4th Joint Conference of Taiwan and Japan on Medical Products Regulation

Tomonori Nakagawa, Asia Project Leader,
GMP Sub Committee, Quality & Technology Committee,
JPMA

Post-Approval Change Reporting Categories

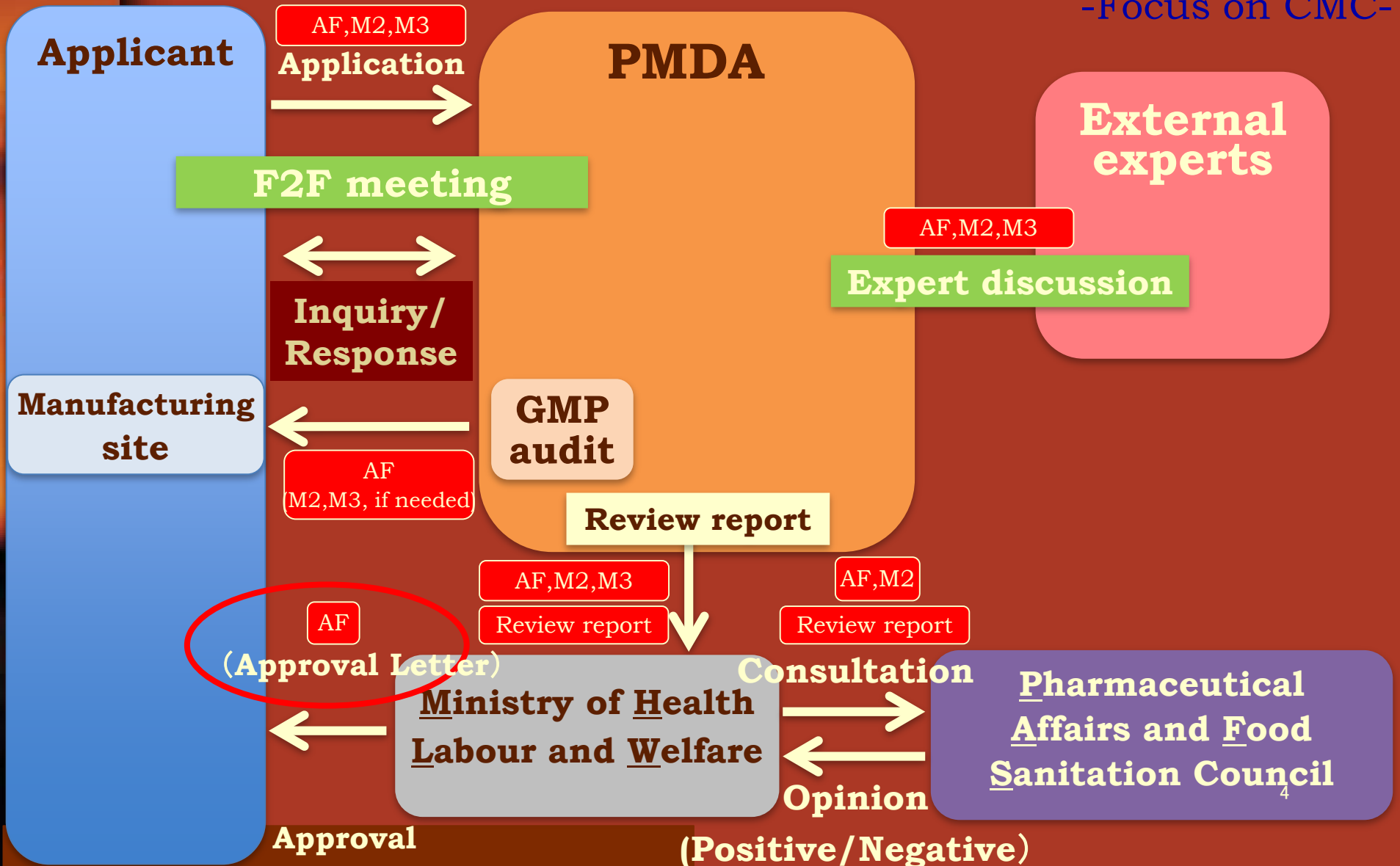
Impact on quality	Japan	US	EU
High	**Partial change Application** (approval of variation)	Major change (Prior approval supplement)	Type II variation (Application for approval of variation)
Moderate	**Minor change Notification** (within 30 days after implementation or shipping)	Moderate change 1) Supplement-changes being effected (CBE) in 30 days	Type IB variation (Notification before implementation and MAHs must wait a period of 30 days)
		2) Supplement-changes being effected (CBE)	Type IA_{IN} variation (Immediate notification)
Low	**SOP** (Under GMP change control)	Minor change (Annual report)	Type IA variation (Notification within 12 months after implementation)

Post-Approval Change Reporting Categories case in Japan

- Change category and contents are agreed between the agency and the company prior to approval
- On-site/document inspection is conducted on product basis, rather than site base
- GMP assessments are evaluated by the inspectors (PMDA QC Department). Contact window for GMP and Review process are separated
- (Pros) “Do and Tell” contents are clearly defined and PQS are thoroughly assessed
- (Cons) Reporting items need to be agreed prior to approval and it is difficult to change after approval

Review Process of Marketing Authorization Applicant with document flow

-Focus on CMC-



Review Process of Marketing Authorization Applicant

Reviewer

Science base

Frequent Communication

GMP

Risk base inspection

Product and PQS

Application Form and Review/Inspection

inspection

-Focus on post-approval change-

Development / Co-Development Report

Product / Process Performance Review

Other ...

Management review

Past Changes Implemented

PQR / APR

CAPA

Scientific Knowledge / Knowledge Management

AF

review

Regulatory notification (if required)

Stimulus
Driving to Change Request

Change- Management Process

Implement PAC & Strategy

Regulatory approval (if required)

Change Evaluation
- Science & Risk-based evaluation
- Evaluate the PAC against EC/ non-EC
- Determine the data needed
- Design & review PAC strategy

Change Approval

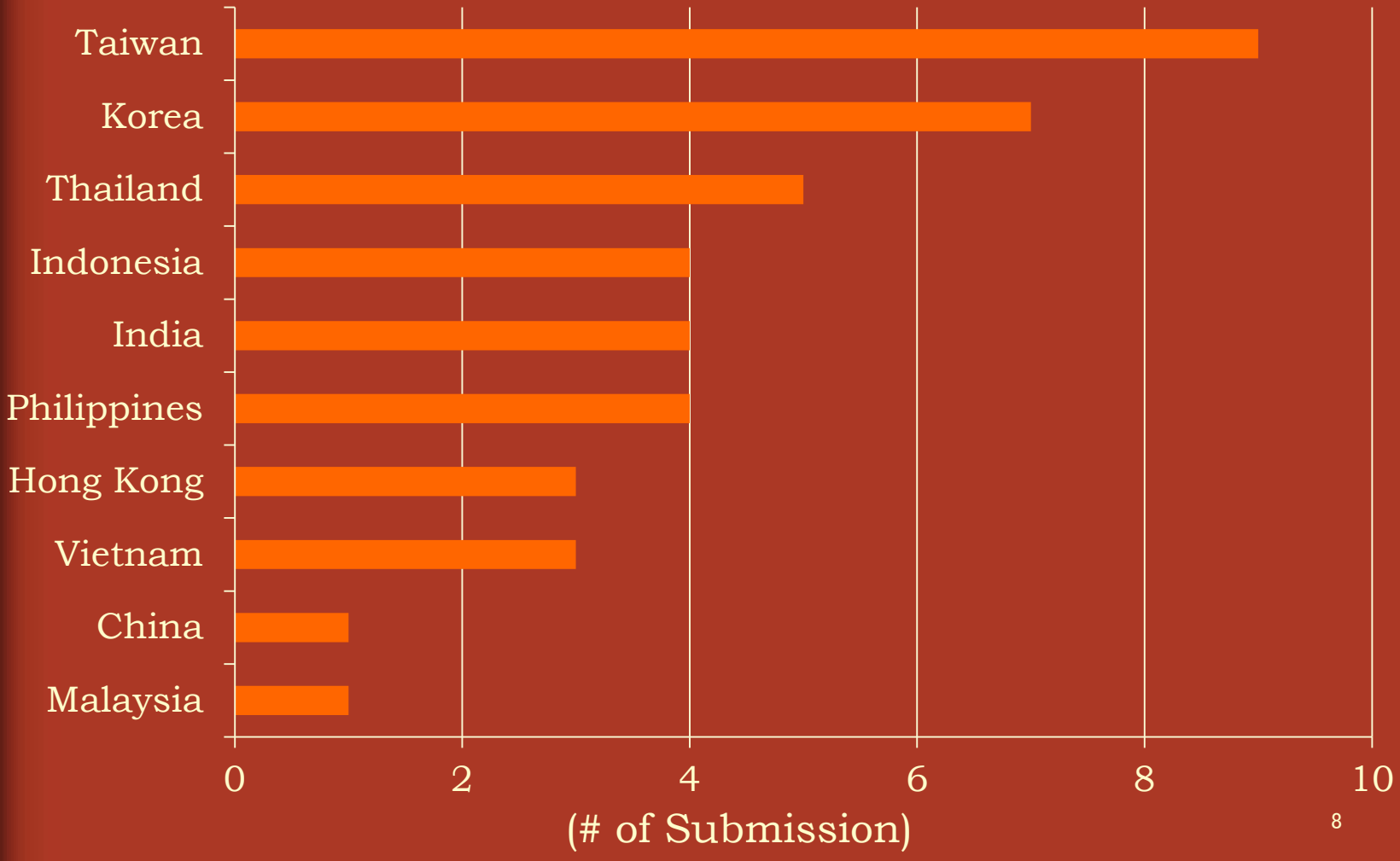
Internal Company Process

Modified from draft Q12 document

Application Form (AF) and Pharmaceutical Quality System (PQS)

- Approved Matter (AM) in application reflect one portion of the product
- Company gain trust from the agency through inspections on how PQS is operated, including change management
- Confirmation of PQS system and consistent alignment with AF will secure the robust change management
- Consistent alignment with AF will engage to transparency between company and the agency to engage in better post-approval managements

List of countries requested to submit SMF and/or PMF as a part of GMP assessment

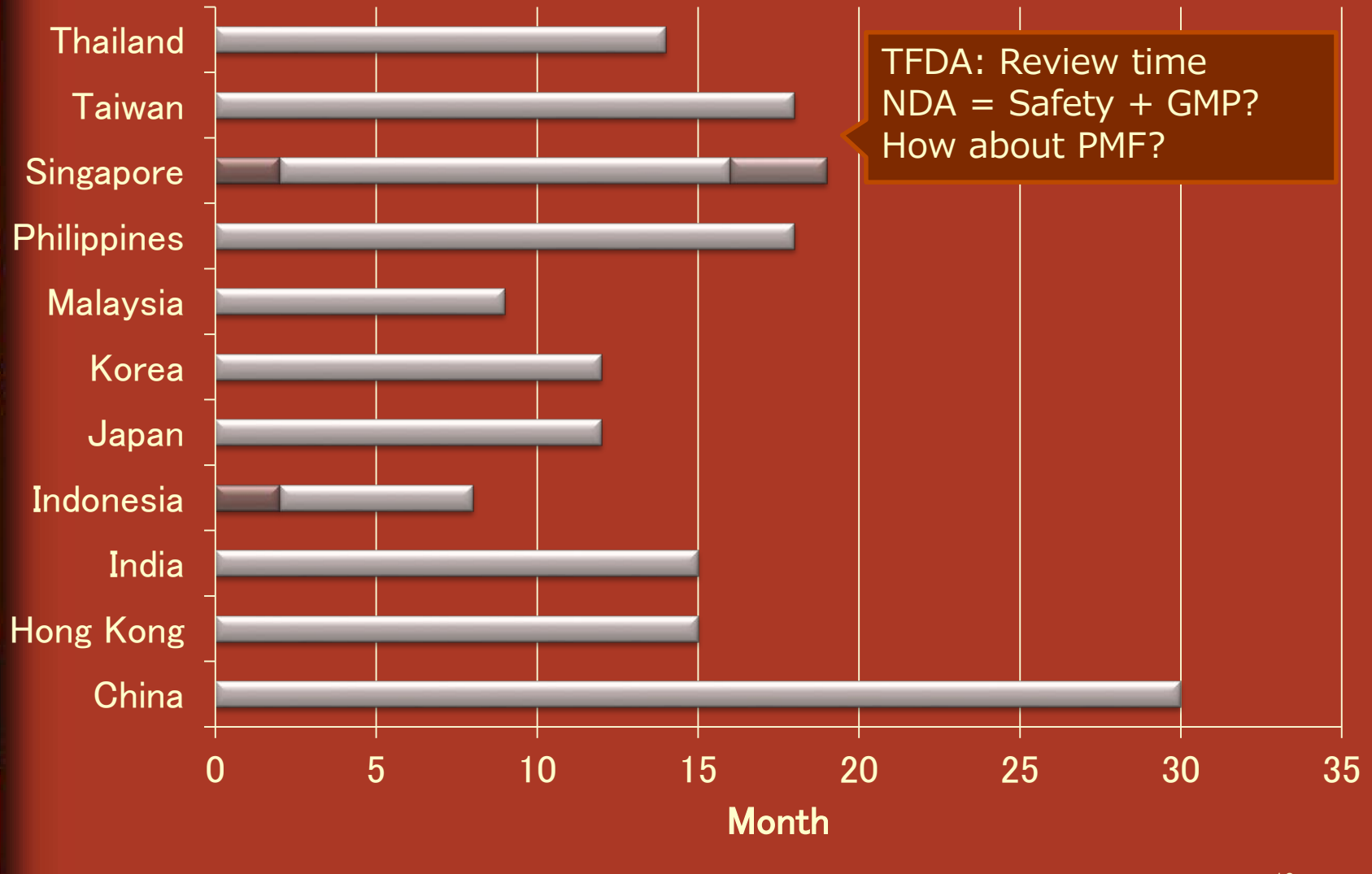


base on JPMA questionnaire response from 17 companies

Current Situation on Submission to Taiwan

- For GMP assessment, the company submits Plant Master File (PMF) and periodically submitting SMF, Inspection reports from other PIC/S members, Annual Quality Reports, major change history and such
- The documents are reviewed by the assessors and seldom on-site GMP inspection is conducted to the company
- PMF review may take as long as 1 year for new submission and this is an unique requirement for Taiwan submission.
- For routine renewal, detail technical document request for major changes requested

NDA Review Period



TFDA: Review time
NDA = Safety + GMP?
How about PMF?

Reference: 2015 APAC Analysis Review

NDA and Post-approval review process

- NDA review timeframe and GMP assessment is not aligned
- GMP assessment through PMF may take longer than safety evaluation
- How PMF GMP assessment and SMF submission at the time of GMP renewal of the site is not clearly seen
- How could we use this scheme at the time of post-approval changes?

Industry Perspective

- Maximize existing scheme, such as PIC/S and inspection training
- Convergence of regulatory flame work through new discussion, ie. ICH Q12 Product Lifecycle to have transparency between the company and the agency
- Common understanding of intended purpose, content and interpretation of SMF
- Seek alternative ways of reviewing GMP other than Plan Master File process in long term engagement for the smooth post-approval changes