QMS Inspections to Foreign Manufacturing Facilities and Utilization of MDSAP reports

FUJISAWA Hiroshi

Inspector

Office of Manufacturing Quality and Vigilance for Medical Devices, PMDA

QMS Inspections to Foreign Manufacturing Facilities

Authorities of QMS inspection

Products		Inspection Authorities (Based on application)
Medical Devices	• Class IV • New medical devices • Cell / Tissue-based medical devices • Reprocessed Single-use Device: R-SUD	PMDA
	• Class III and Class II (without CS*)	PMDA
	• Class III and Class II (with CS*)	Registered Certification Body
In-vitro diagnostics (IVDs)	• New IVDs • Radioactive IVDs	PMDA
	• Products without CS*	PMDA
	• Products with CS*	Registered Certification Body

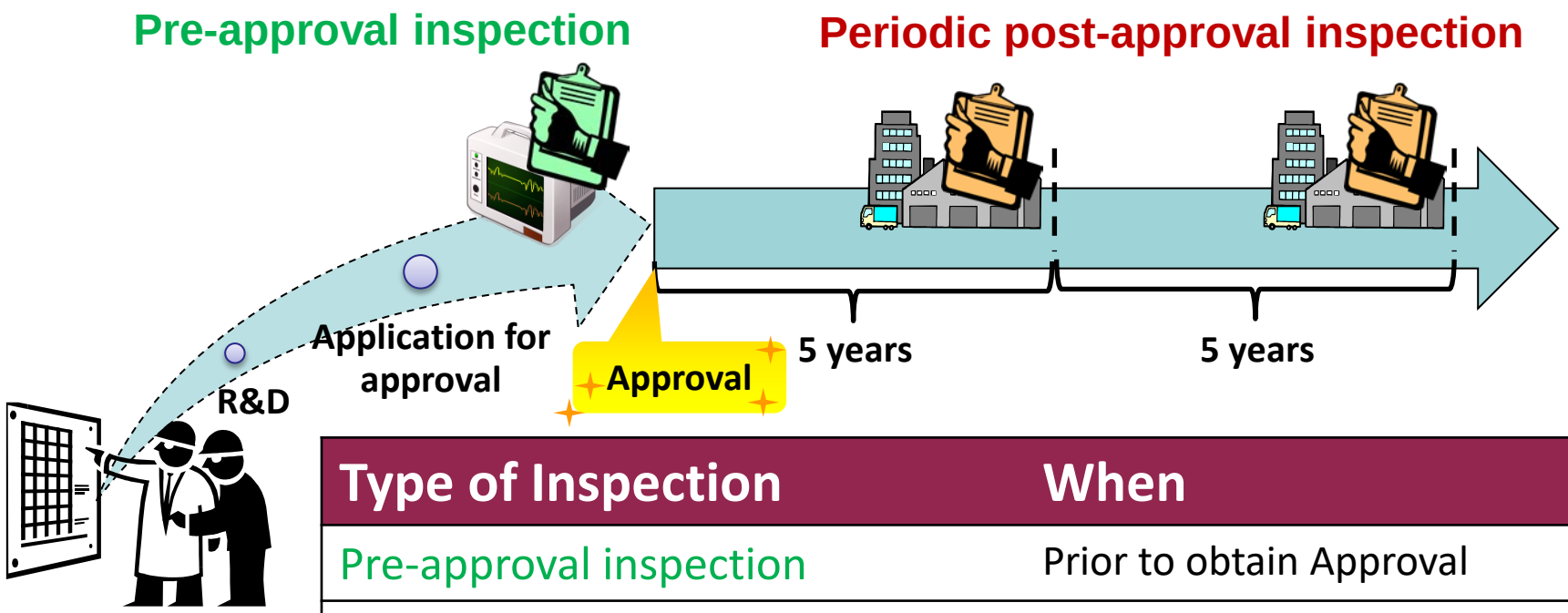
*CS : Certification Standards

Japanese Quality Management System regulation
(Ministerial Ordinance No. 169: "QMS Ordinance")

Chapters: Title	Contents
Chapter 1: General	Scope, Definition
Chapter 2: Basic requirements	**Requirements harmonized with ISO 13485**
Chapter 3: Additional Requirements	Additional Requirements
Chapter 4: Requirements for Biological Medical Devices etc.	Product specific requirements
Chapter 5: Requirements for Radioactive IVDs	
Chapter 5-2: Requirements for R-SUD	
Chapter 6: Provisions Applied Mutatis Mutandis for manufacturers etc.	Provisions applied mutatis mutandis

Type of QMS Inspection

QMS Inspection in Lifecycle of Medical Device



Type of Inspection	When
Pre-approval inspection	Prior to obtain Approval
Pre-partial change approval inspection	Prior to obtain Approval of partial change (Addition/ Change of Design sites, Main Assembly sites, or Sterilization sites)
Periodic post-approval inspection	Every 5 year since Initial Approval
Additional inspection	Required for notified cases

Inspection Unit

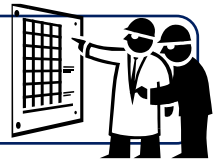
Example

Scope

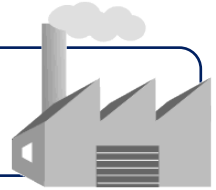
Product family

Marketing Authorization Holder （MAH）

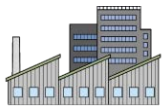
- **Manufacturing Site （Design Facility）**



- **Manufacturing Site （Main Assembling Plant）**



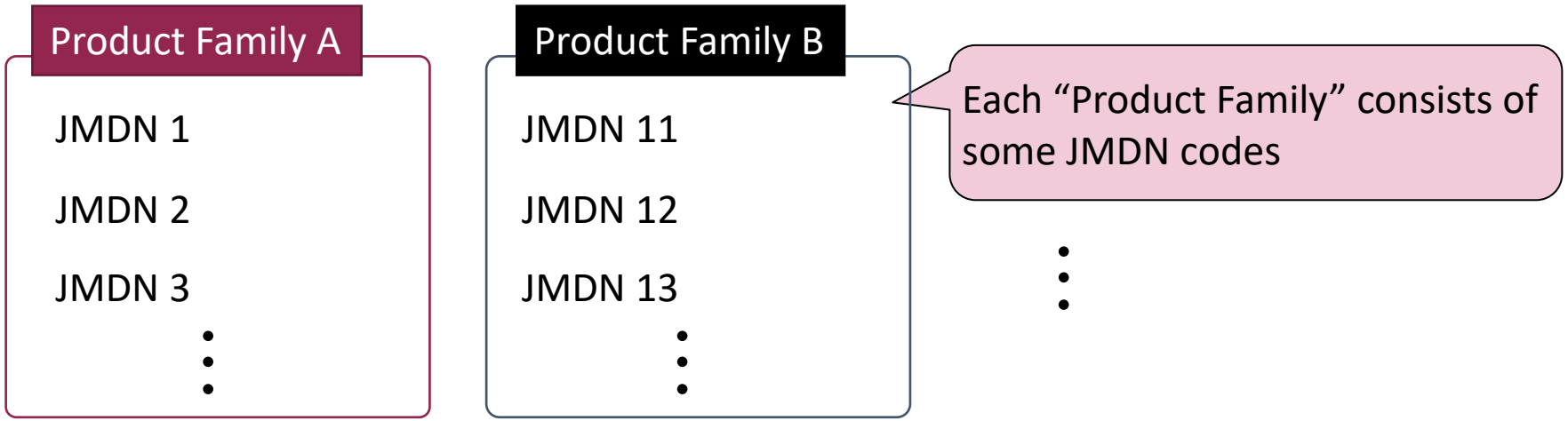
- **Manufacturing Site （Sterilizer）**



- **Manufacturing Site （Domestic Distribution Center）**

Product Family

- Japanese Medical Device Nomenclature (JMDN : Japanese version of Global Medical Device Nomenclature) codes are grouped into each **“Product Family”** depending on factors such as characteristics, usage method, risk etc.



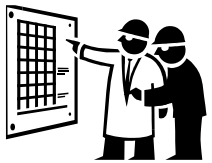
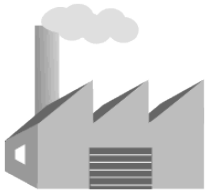
  - The relationship between each Product Family and JMDN code is specified by notifications.

Sites of QMS inspection

Example

※ Marketing Authorization Holder (MAH) obtains the marketing license and shall manage the manufacturer.

Manufacturing Site Registration

Site	Definition
 Design Facility	• maintains records of design and development • the responsible person should work at facility
 Main Assembling Plant	• substantially responsible for QMS or product realization of the product • operates assembling (filling) processes.
 Sterilizer	• operates sterilization process
 Domestic (Japan) Distribution Center	• stores products until final release to Japanese market.

Scope of QMS Inspection

Manufacturing Site Registration

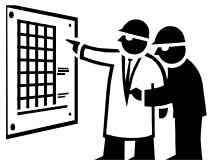
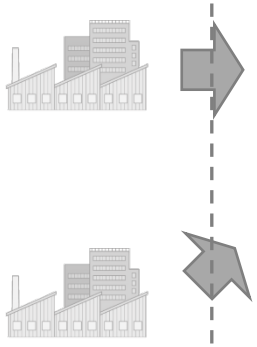
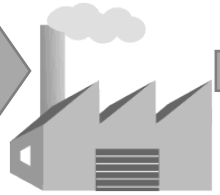
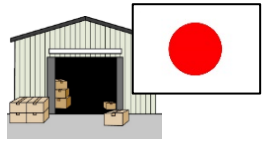
Example

In Japan

MAH

Registration is not needed but
the license of marketing is required

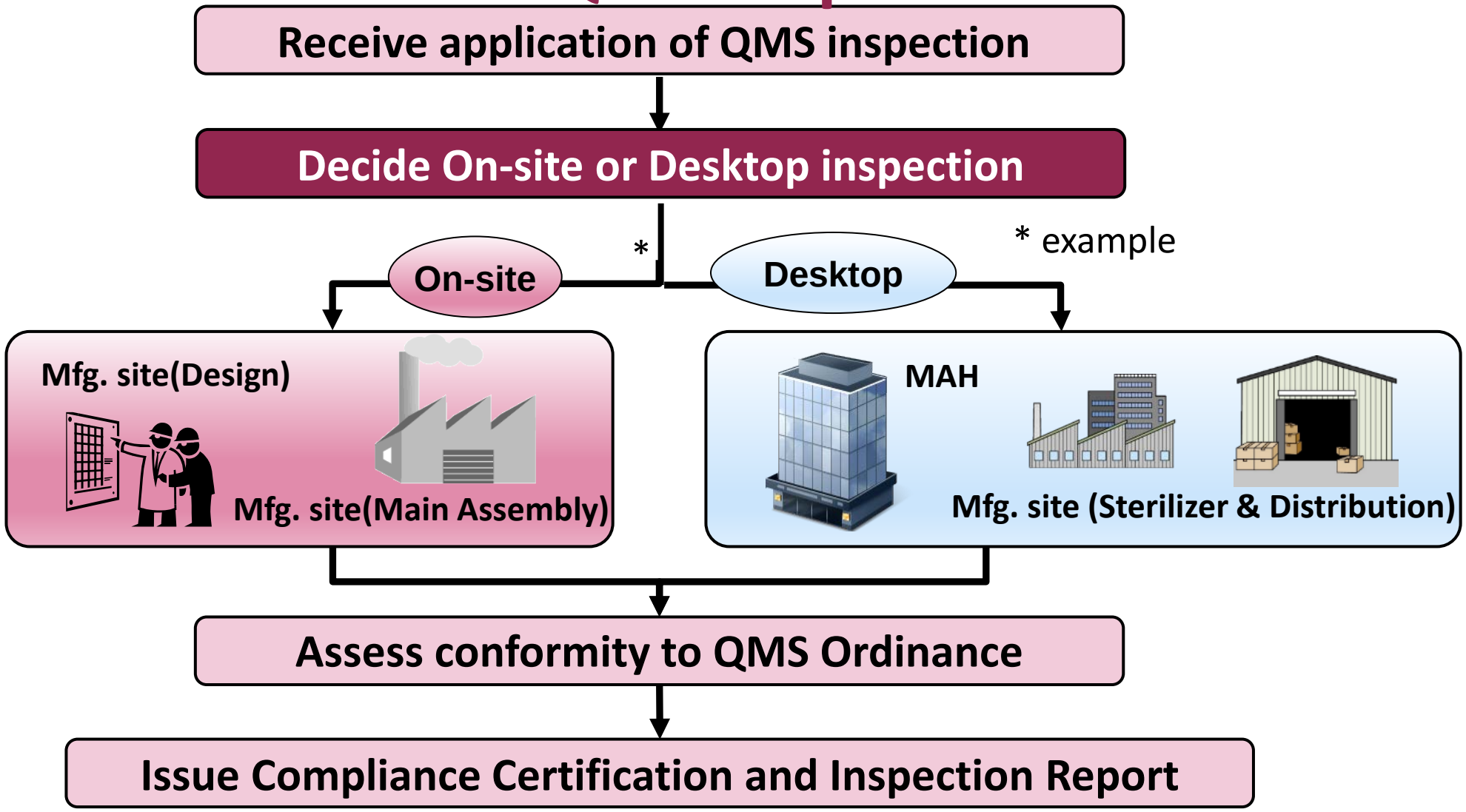
In foreign country

Design & Development	Supplier	Sub-Assembly	Main Assembly	Sterilizer	Packing	Distribution
						
Required	N/A	N/A	Required	Required	N/A	Required

market

Registration

Overview of QMS Inspection Flow



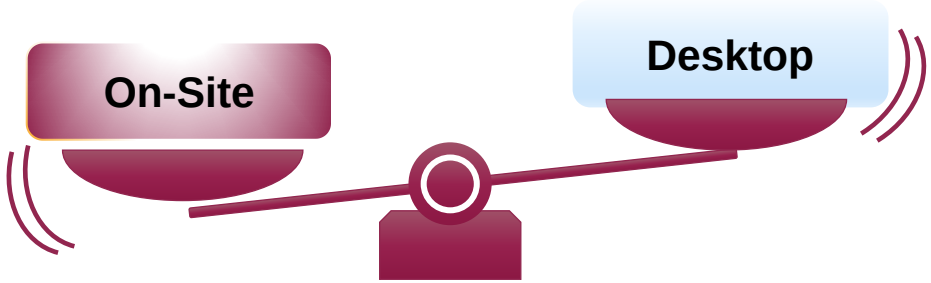
MAH: Marketing Authorization Holder

Decision of On-site / Desktop inspection

Input Information

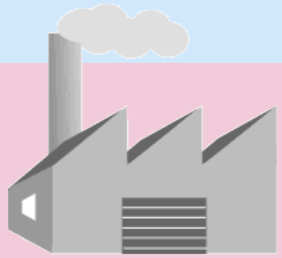
- Submitted documents
- **Reported adverse events**
- **Reported recalls**
- **Complexity of manufacturing processes**
- **Risks associated with the use of products**
- Results and nonconformities of the previous inspections
- Audit results by other regulatory authorities/organization
- MDSAP reports inspection(Pilot phase in Japan) etc.

Risk-based Assessment



On-site Inspection Flow

MAH: support



Manufacturing site

Notification of Inspection

About 6 weeks

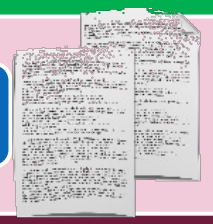
Submit documents PMDA requests

2-4 days

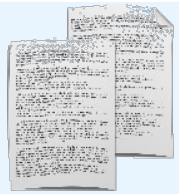
On-site QMS Inspection (Two inspectors in general)

within 2 weeks

Issue Finding Reports



About 4 weeks



Submit improvement report or plan

Accept improvement report or plan

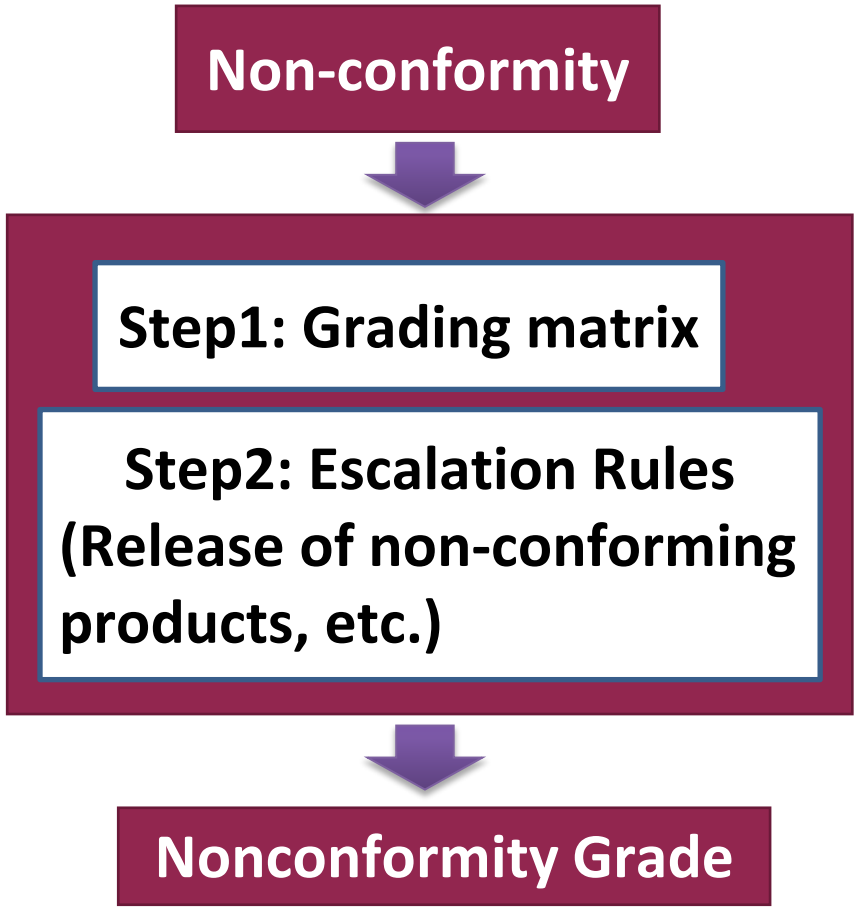
Required Documents for On-site Inspection （Example）

Documents	Outline of Documents	Subject
Layout of all mfg. site building	・Bird's eye-view photograph or location map of mfg. site	Mfg. sites (except for Design facility)
Floor plan	・Clean room grade, Differential pressure ・List or layout of representative manufacturing and test equipment	Mfg. sites (except for Design facility)
Organization chart	・Responsible persons and departments under QMS	Mfg. sites
Quality management system	・Quality Manual	Mfg. sites
QC flow chart	・Process name, # of SOP, equipment name, parameter of process control etc.	Mfg. sites
Medical Device File	・All the related documents to the product under QMS. (Design history file would be fine)	Product subject to Inspection
Validation of mfg. process	・Validation procedure ・Validation report and protocol	Product subject to Inspection
Post-Market status	・Adverse event Report	MAH

3-day On-site Inspection Schedule (Example)

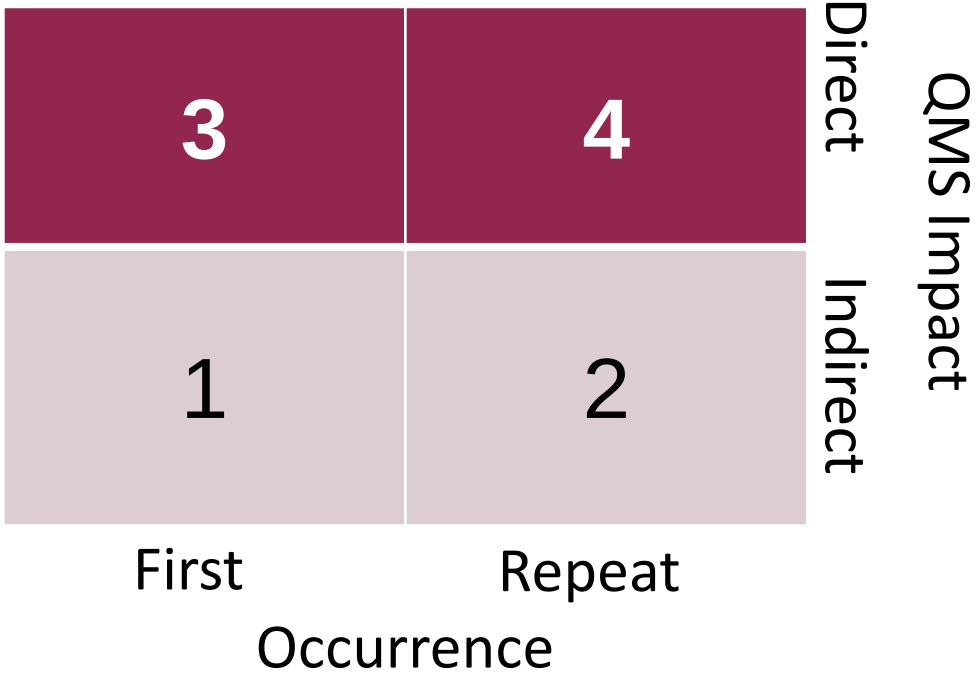
Date	Time	Item
Day 1	9:00-12:00	1.Opening Meeting (1)Introduction of Inspection (2)Overview of Company and Products 2. Management QMS organization, Quality Manual, Quality Policy and Objectives, Management Review, Internal Audit, Training 3. Documentation and Records
	13:00-17:00	4. Factory tour
Day 2	9:00-12:00	5. Design and Development (including Risk Management) 6. Purchasing Control
	13:00-17:00	7. Product and Process controls
Day 3	9:00-12:00	8. Medical Device File 9. Customer Related Processes
	13:00-17:00	10. Corrective and Preventive Actions 11. Team Meeting of Inspectors 12. Confirmation on Findings and Closing Meeting

Grading of Nonconformities



Reference: GHTF/SG3/M19:2012

Figure 1: Grading flow



Direct QMS Impact

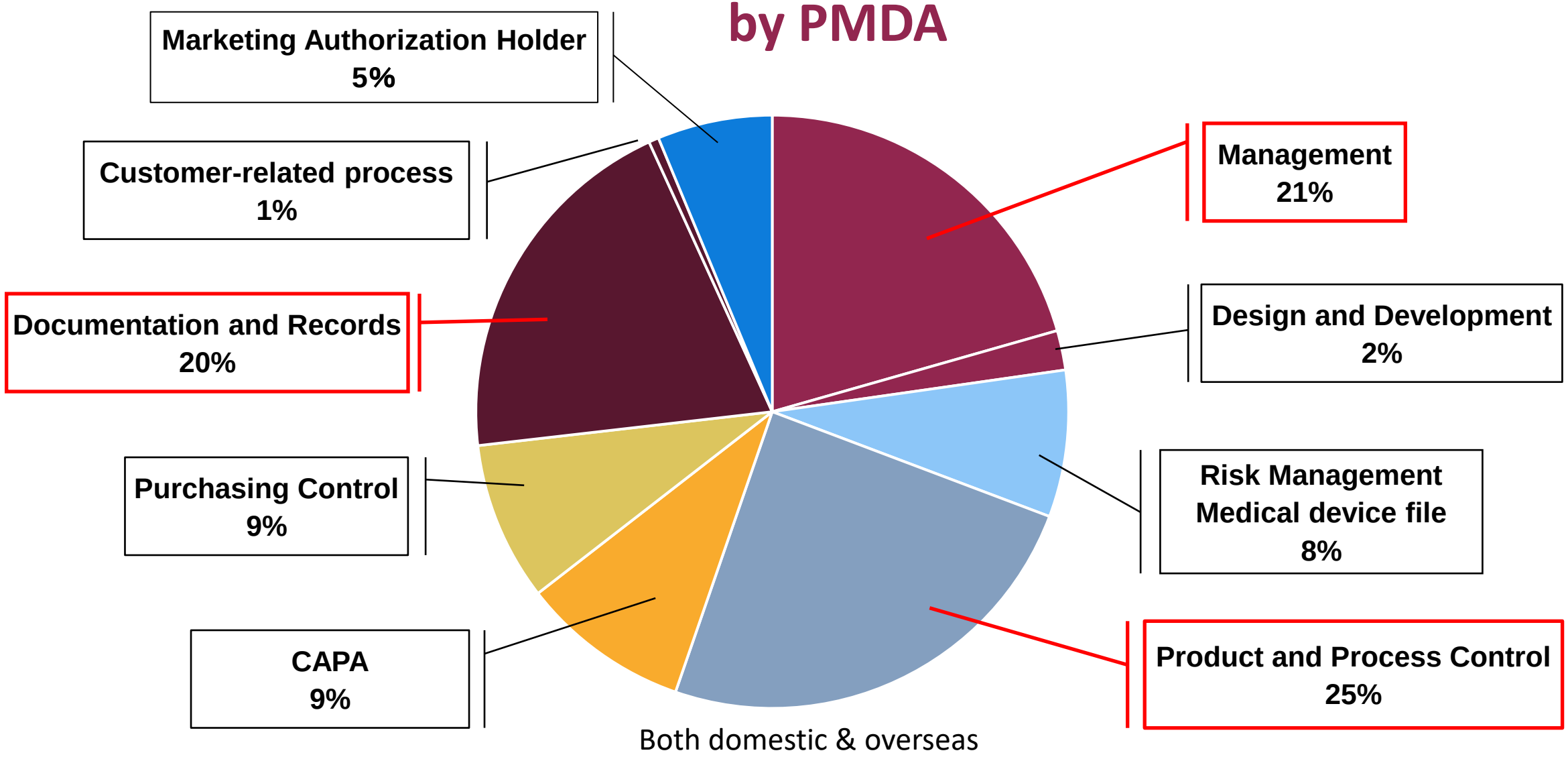
QMS Ordinance: Article 25 to 64, 69, 72, 75, 76, 81, 81-2-2, 81-2-3, 81-2-6 and 84

Indirect QMS Impact

QMS Ordinance: Article 5 to 24, 66 to 68, 70 to 71, 72-2, 73 to 74, 77 to 80, 81-2, 81-2-4, 81-2-5

Figure 2: Grading matrix

Nonconformity of inspection by PMDA



Both domestic & overseas

Period of data collection: 2016.10 – 2020.11

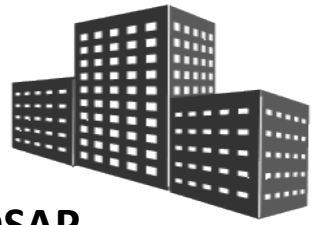
Utilization of MDSAP reports

Overview of MDSAP

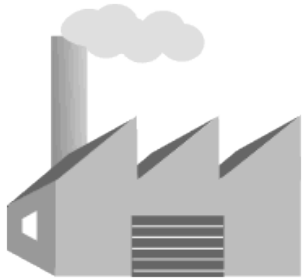
MDSAP Participating Countries

Assessment and Recognition

QMS Audit



MDSAP
Auditing Organization



Manufacturer

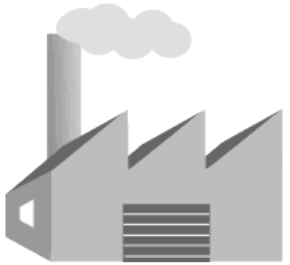
Utilization to QMS inspection

QMS application
with MDSAP Report

QMS Inspection
using MDSAP Report

MDSAP Report

MAH



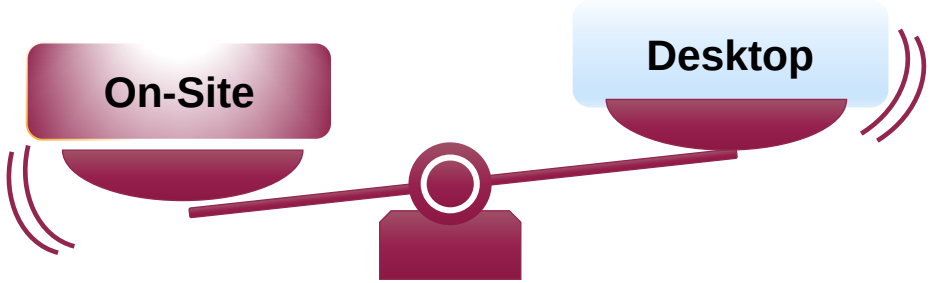
Manufacturer

Decision of On-site / Desktop inspection

Input Information

- Submitted documents
- Reported adverse events
- Reported recalls
- Complexity of manufacturing processes
- Risks associated with the use of products
- Results and nonconformities of the previous inspections
- Audit results by other regulatory authorities/organization
- **MDSAP reports inspection(Pilot phase in Japan)** etc.

Risk-based Assessment



Acceptance of MDSAP Audit Outcomes (Example)

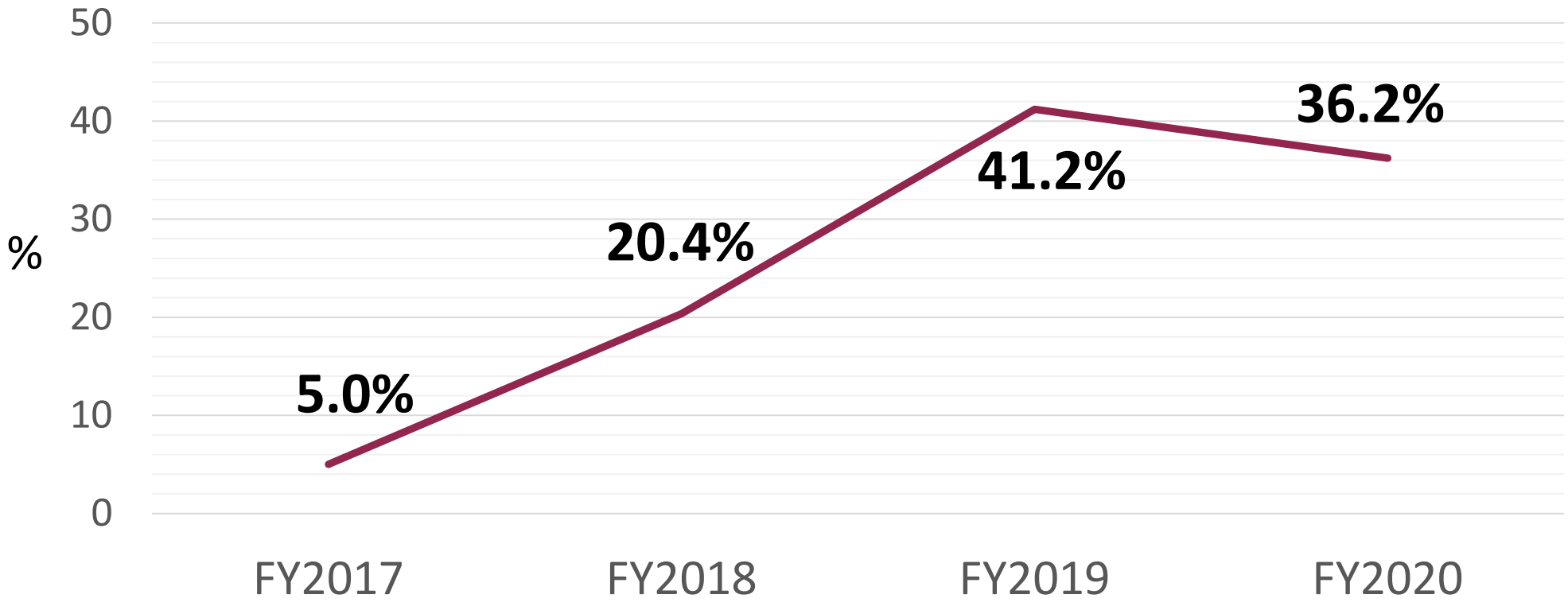
Japan

Streamline inspections

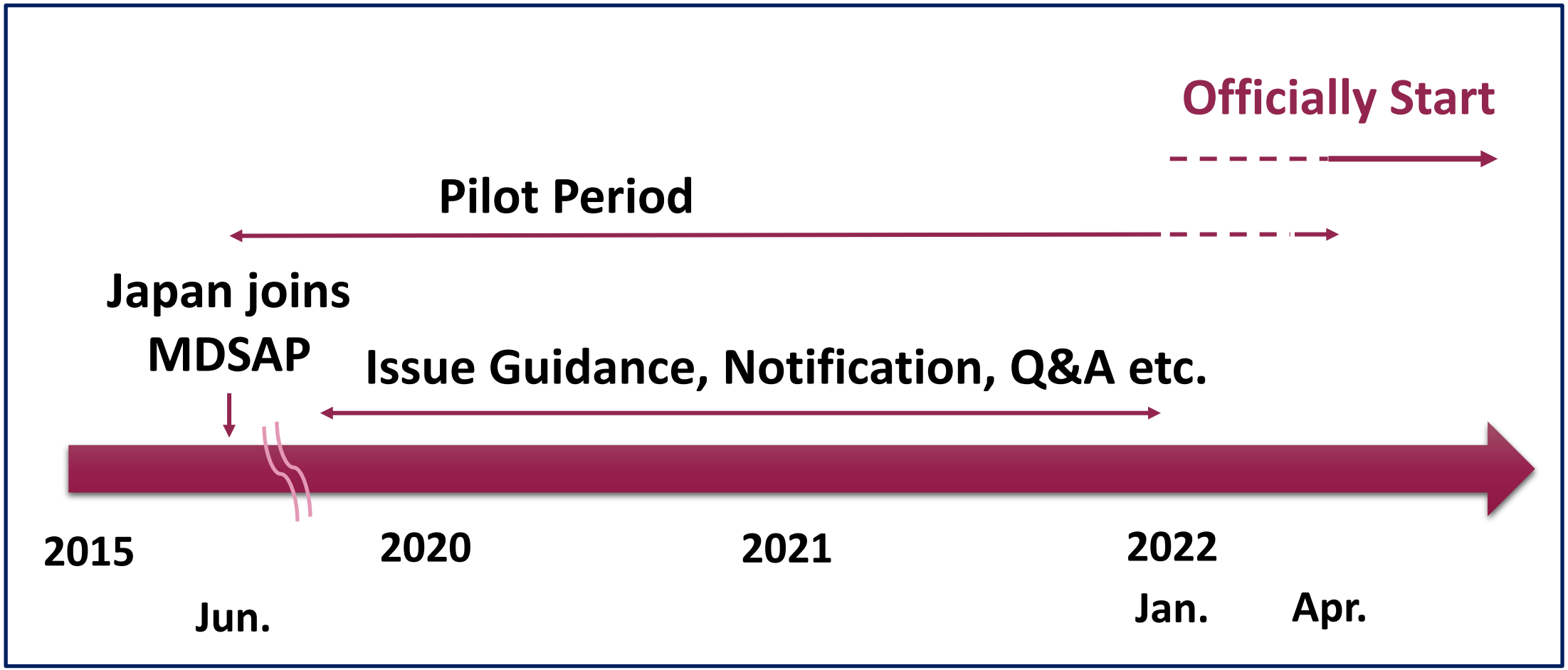
- by Switching from on-site to desktop inspections
- by Reducing the volume of documents to submit

Utilization of MDSAP Report

$$\frac{\text{No. of application for QMS inspection with MDSAP report}}{\text{Total No. of application for QMS inspection}} \times 100$$



Schedule


Officially Start
Pilot Period
Japan joins MDSAP
Issue Guidance, Notification, Q&A etc.
2015
Jun.
2020
2021
2022
Jan.
Apr.

Thank you for your attention