QMS (Quality Management System) for Medical Device in Japan

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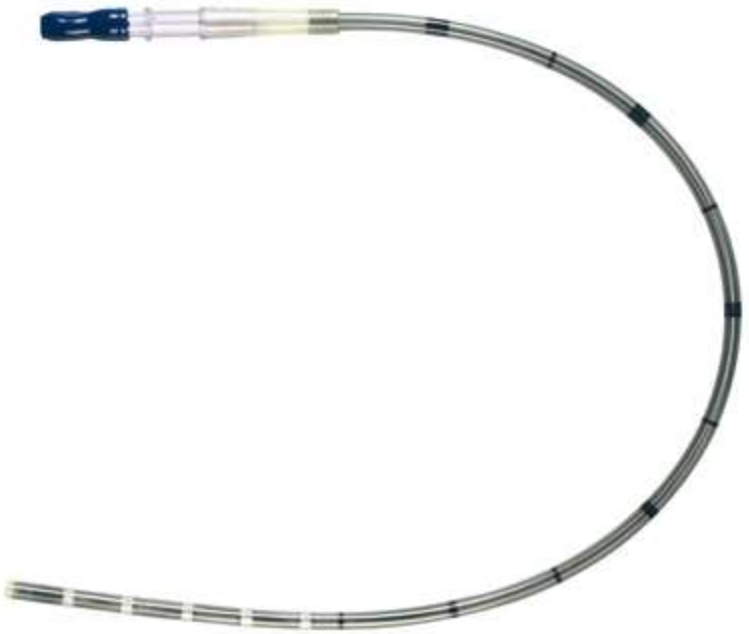
First of all,

Recent Incident

During flushing blood the tip of Cannula took off. This incident resulted in the manufacturing process of cutting tip of the Cannula.
As CAPA, Corrective Action and Proactive Action, reviewed are the setting process of cutting machine, the measurement, and those training.



Root causes of incidents

1. Defective products and mal durability

In order to prevent the incidents with high risk, establishing QMS (Quality Management System) in the facilities is important !!

QMS requirements are harmonized with ISO13485 and not so big difference from QSR.
And some local Japanese requirements are added to QMS.

How to register, how to apply for inspection are not the same.
So today's topics are ・・・・・

7. Circumstances of using medical devices

Main Topics

1. Entering Japan Market
2. QMS regulation
3. QMS inspection flow
4. MDSAP update

1. Entering Japan Market

License, Registration, Approval

Marketing license

– All the Japan organization should have this license in order to enter Japan market in Medical devices and In-vitro Diagnostics.

Manufacturing site registration

– Requirements for conducting specified manufacturing processes.
In the case of medical devices, the design, main assembling, sterilization and domestic (Japan) distribution site shall be registered.

Marketing approval

– Requirement for marketing any new medical devices and IVDs in Japan, and partial changes of authorized product.

Marketing Authorization

Marketing Authorization Holder : MAH

A Japanese organization who obtains the marketing approval. MAH should manage all the registered manufacturers to comply with Japan QMS and to release the products those specification should meet approved ones in Japan.

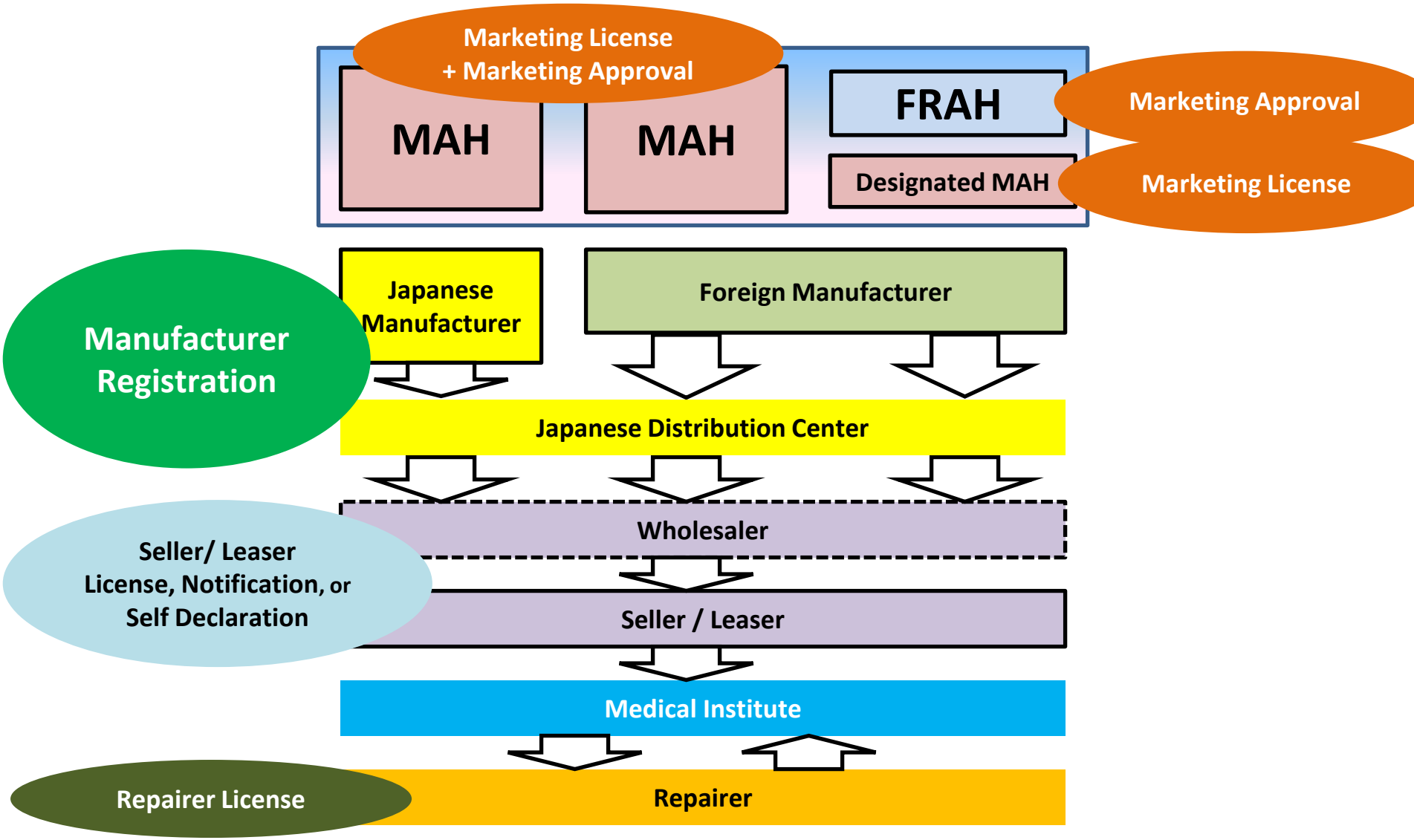
Foreign restrictive authorization holder : FRAH

A foreign organization who obtains the marketing approval. FRAH should designate MAH in Japan responsible for the product in Japan market.

Designated MAH

A Japanese organization designated by FRAH to conduct manufacturing and quality control duties in Japan. Designated MAH should take necessary measures for the prevention of occurrence of hazards to the public health and hygiene in Japan caused by the product.

Supply Chain in Japan



2. QMS regulation

Type of QMS Inspection

1. Pre-approval inspection

Requisition of the marketing approval.
Conducted prior to obtain the approval.

2. Pre-partial change approval inspection

Conducted prior to obtain the partial change approval.
ex) main assembling site change etc..

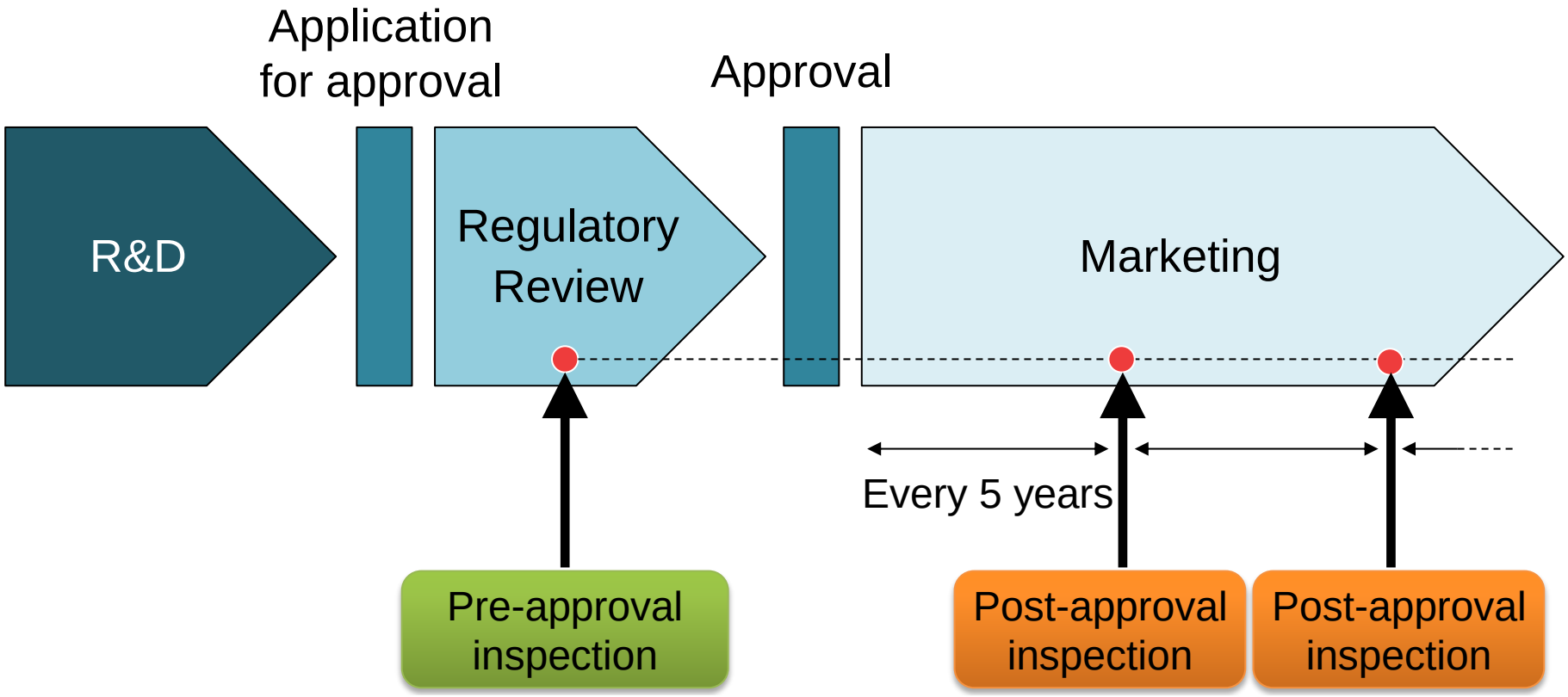
3. Periodic post-approval inspection

Requisition of maintaining existing marketing approval.
Conducted every 5 years after obtaining the marketing approval.

4. Additional inspection

Conducted where appropriate.
ex) specialized inspection for biological products, micro machine and medical devices utilizing nano-materials etc..

QMS Inspection (Pre-, Post-)



Type of QMS Inspection

1. Pre-approval inspection

Required before the marketing approval.

2. Pre-partial change approval inspection

Required before the partial change approval.
ex) main assembling site change etc..

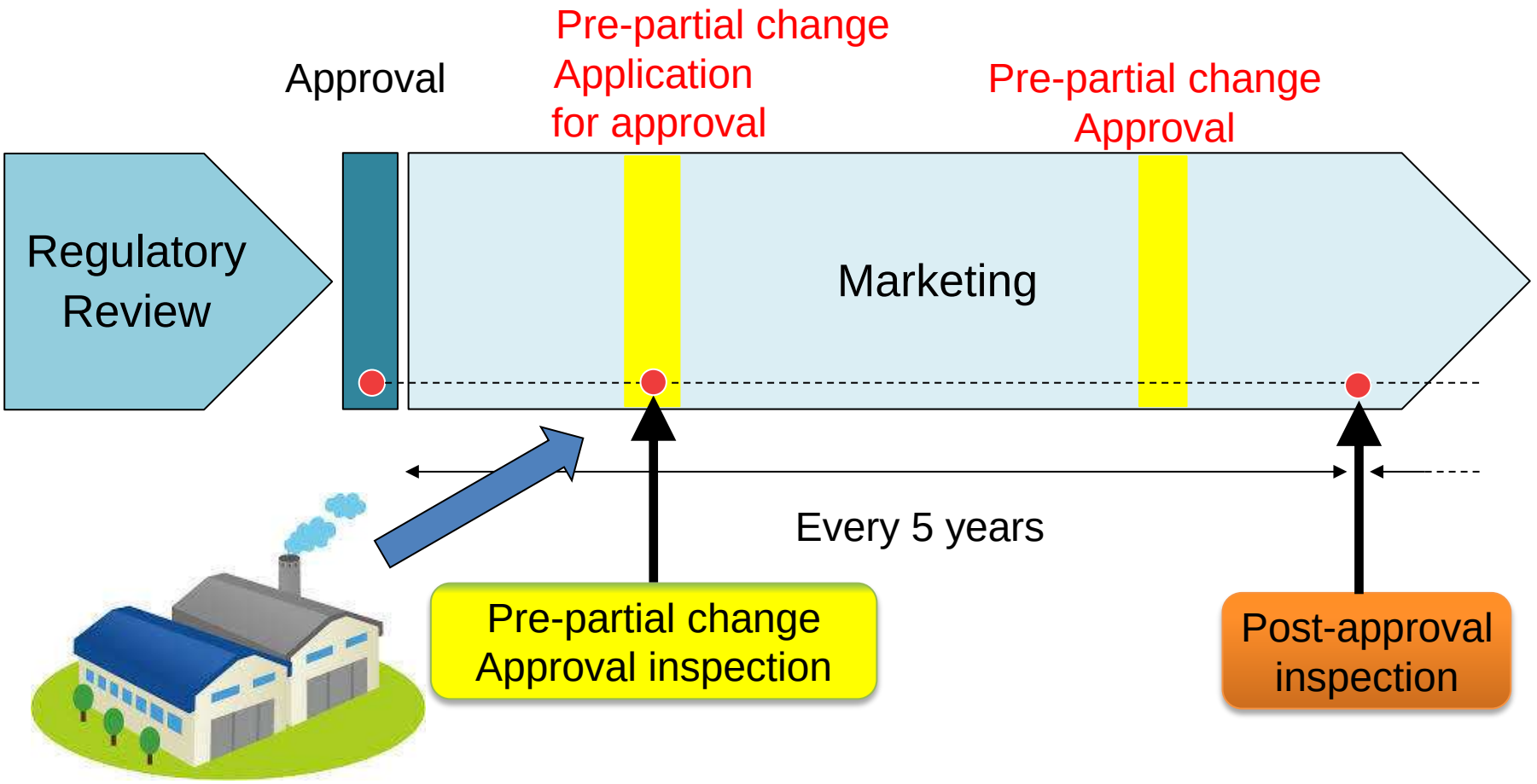
3. Periodic post-approval inspection

Required for maintaining marketing approval every 5 years since the initial marketing approval.

4. Additional inspection

Required for the notified cases.
 ex) specialized inspection for biological products, micro machine and medical devices utilizing nano-materials etc..

QMS Inspection (Partial change)



ex) Main assembling site
Change

- Based on application
- Inspection scope : MAH and the change-related sites.

Authority of QMS inspection

Product		Inspection Authority (Based on application)
Medical Devices	• Class IV • New medical devices • Cell / Tissue-based medical devices	PMDA
	• Class III and Class II (without CS*)	PMDA
	• Class III and Class II (with CS*)	Registered certification body
IVDs	• New IVDs • Radioactive IVDs	PMDA
	• Products without CS*	PMDA
	• Products with CS*	Registered certification body

*CS : Certification Standards

QMS inspection and scope

QMS inspection

1. Pre-approval inspection

2. Pre-partial change approval inspection

3. Periodic post-approval inspection

4. Additional inspection

Scope

Marketing Authorization Holder (MAH)

Design Facility

Main Assembling Plant

Sterilizer

Domestic (Japan) Distribution Center

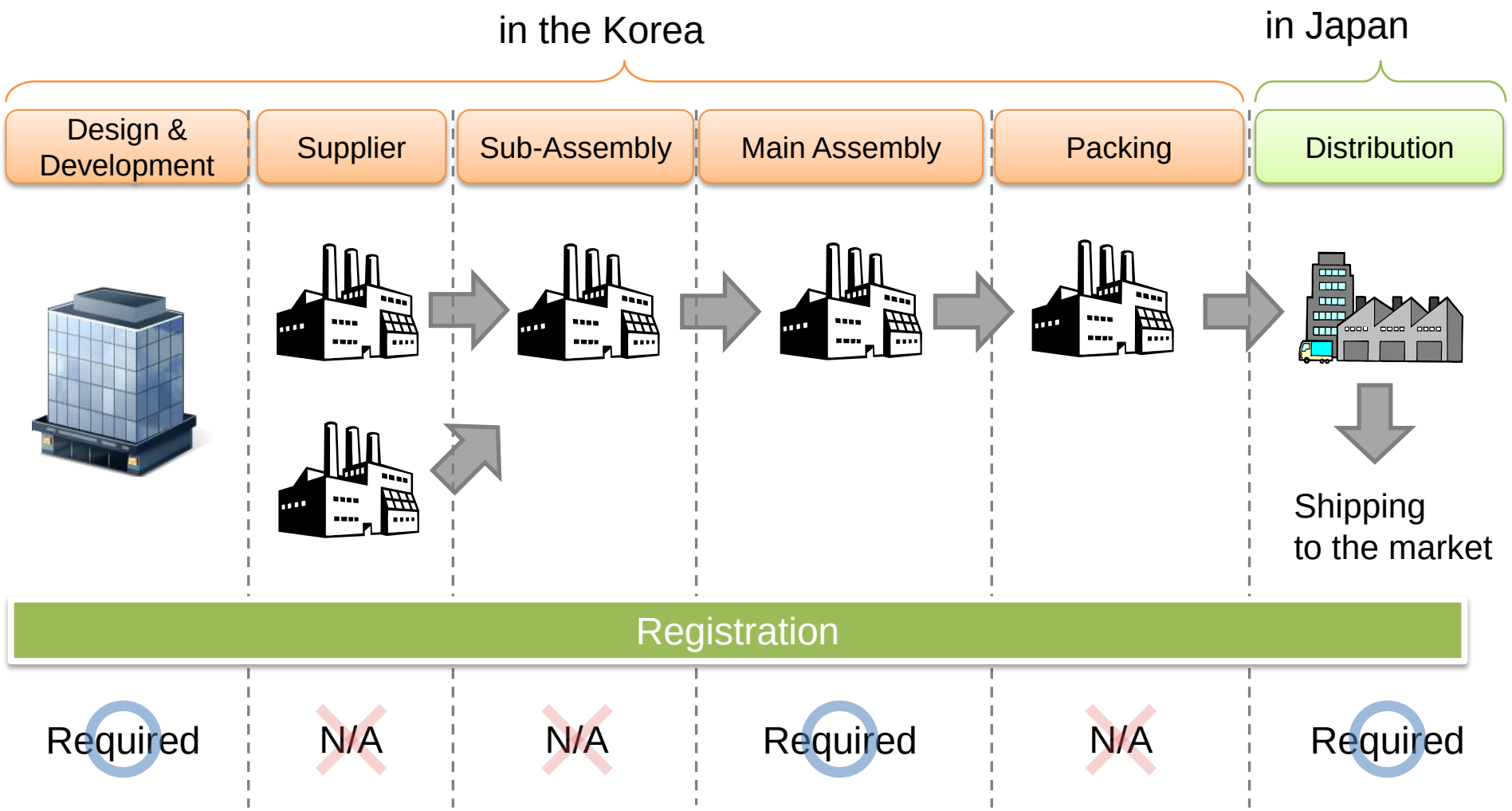
Other sites

Manufacturing site Registration

Sites listed below needs to be registered for the products.

	Site	Definition
	Design Facility	(1) maintain records of design and development (2) the responsible person should work here
	Main Assembling Plant	(1) substantially responsible for QMS or product realization of the product (2) operate assembling(filling) processes.
	Sterilizer	(1) operate sterilization process
	Domestic (Japan) Distribution Center	(1) store products until final release of shipment to Japanese market.

Example of mfg. site registration



Registration of Manufacturer

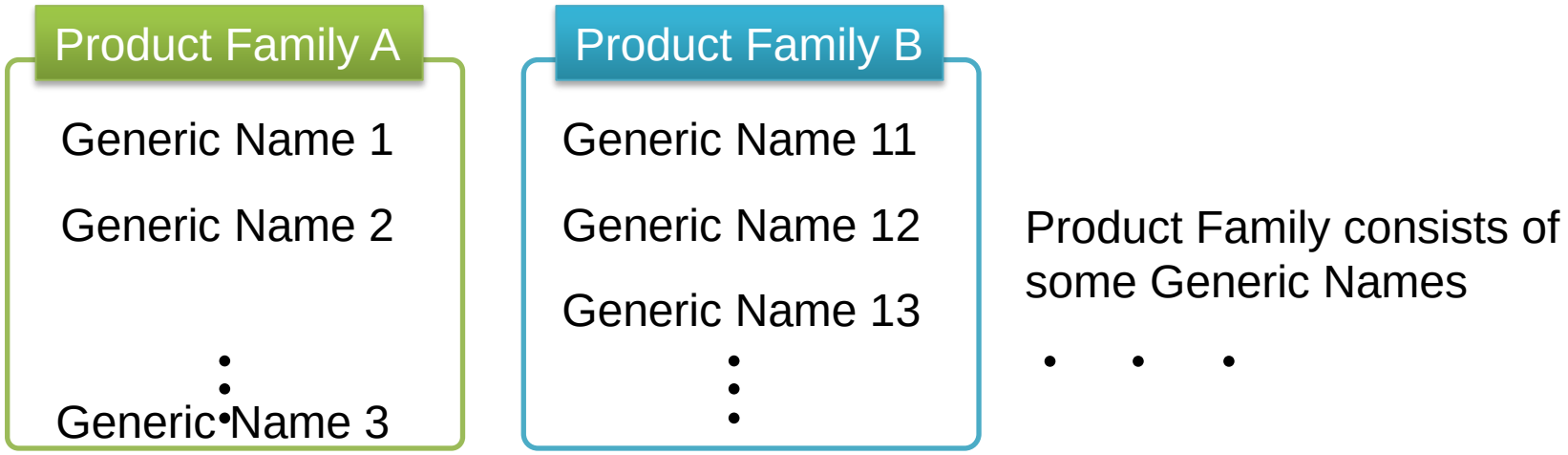
Licensing system	Registration (Domestic, Foreign)
Authority to provide license	Prefecture (Domestic) MHLW (Foreign)
Requirements for licensing	Reasons for disqualification (Health, Crime, Revocation)

Scope of Registration and Inspection

	Registration	QMS Inspection
 MAH Marketing Authorization Holder	N/A The license of marketing is required	○ Required
 Design Facility	○ Required	○ Required
 Main Assembling Plant	○ Required	○ Required
 Sterilizer	○ Required only for sterile medical device	○ Required only for sterile medical device
 Domestic (Japan) Distribution Center	○ Required	○ Required
 Other sites	× N/A	△ Depends PMDA determines based on risk assessment

Product Family

- Generic names of Medical Devices and IVDs are grouped into **“Product Families”** depending on factors such as characteristics, usage method, risk etc. QMS inspection is conducted per **“Product Families”**



- The relationship between product family and generic name is announced by notification

QMS Ordinance

Chapter	Title	Article
1	General Provisions	1~3
2	Medical Devices Manufacturing Harmonized to ISO13485:2003=>2016	4~64
3	Additional Requirements.	65~72-3
4	Biological-origin Medical Device, etc. Manufacturers (Domestic, Foreign) Additional requirements according to the characteristics of the products	73~79
5	In-Vitro Diagnostic Radioactive Reagents Manufacturers(Domestic, Foreign) Additional requirements according to the characteristics of the products	80~81
6	Provisions Applied *Mutatis Mutandis* of Medical Device, etc. Manufacturing Sites, etc.	82~84

3. QMS inspection flow

Outline of QMS Inspection

Example

Inspection Unit

QMS Application

Product family

Marketing Authorization Holder

On-site Inspection

Inspection Report

Manufacturing Site (Design Facility)

Desktop Inspection

Manufacturing Site (Assembling Plant)

On-site Inspection

Inspection Report

Manufacturing Site (Contract Sterilizer)

Desktop Inspection

Manufacturing Site (Domestic Distribution Center)

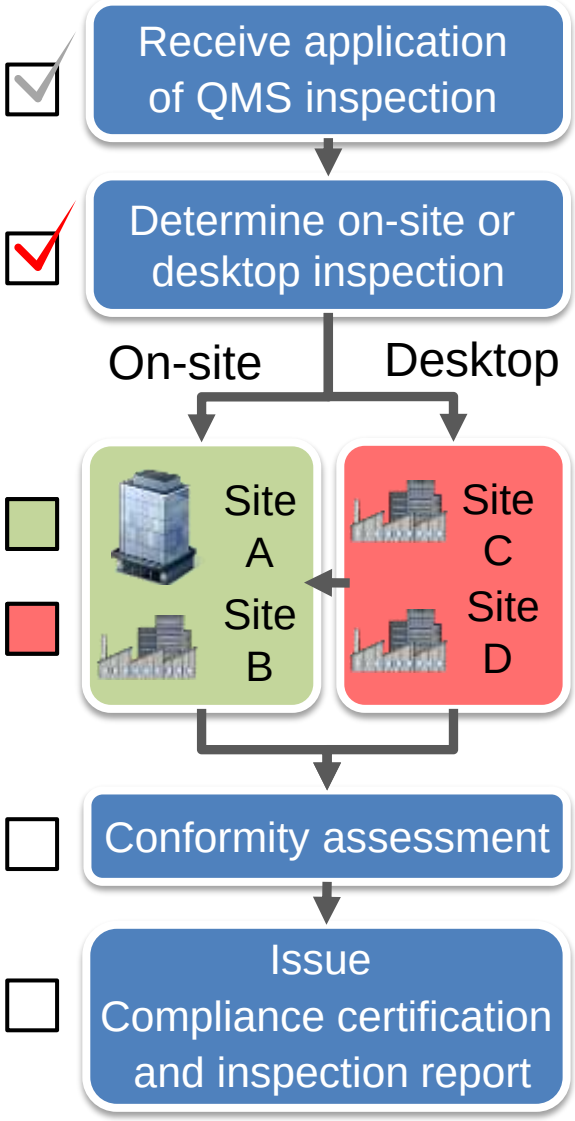
Desktop Inspection

Conformity of Application

QMS Compliance Certification

Summary Report

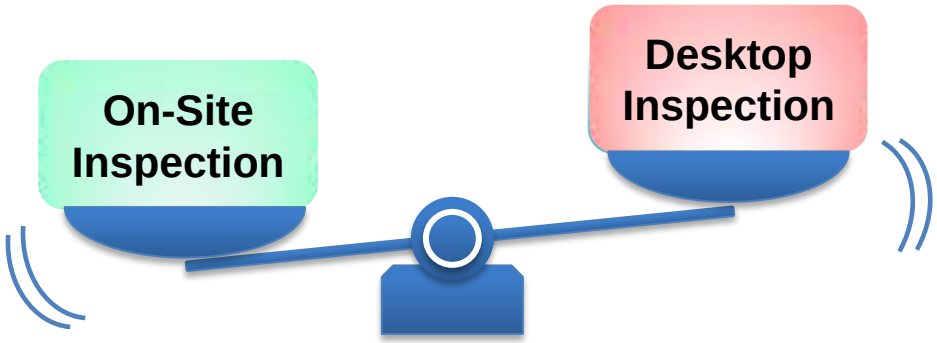
Determine on-site or desktop inspection



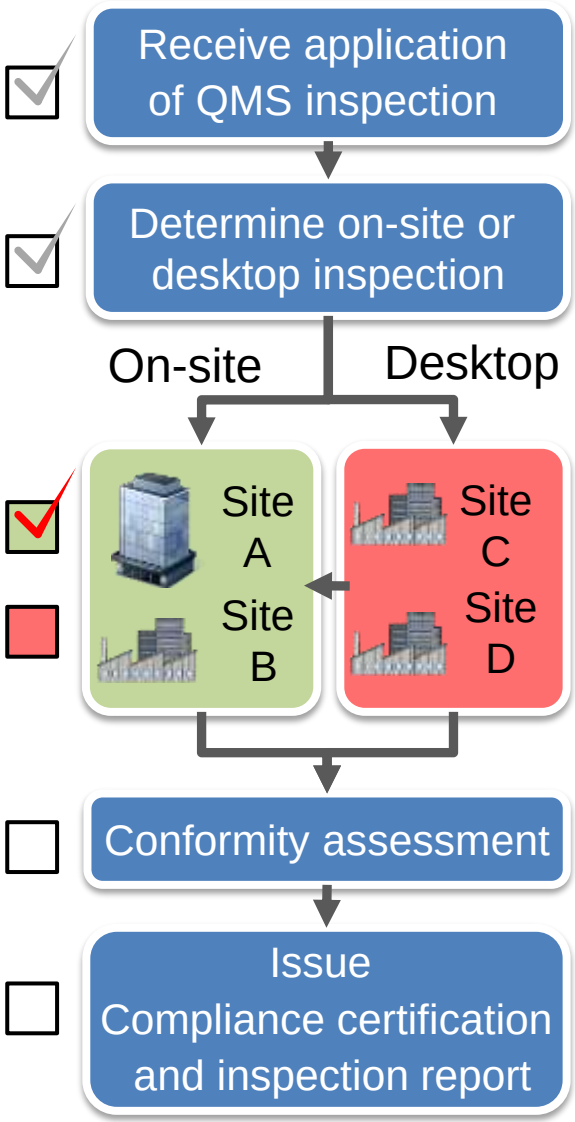
Determination step

Input Information :

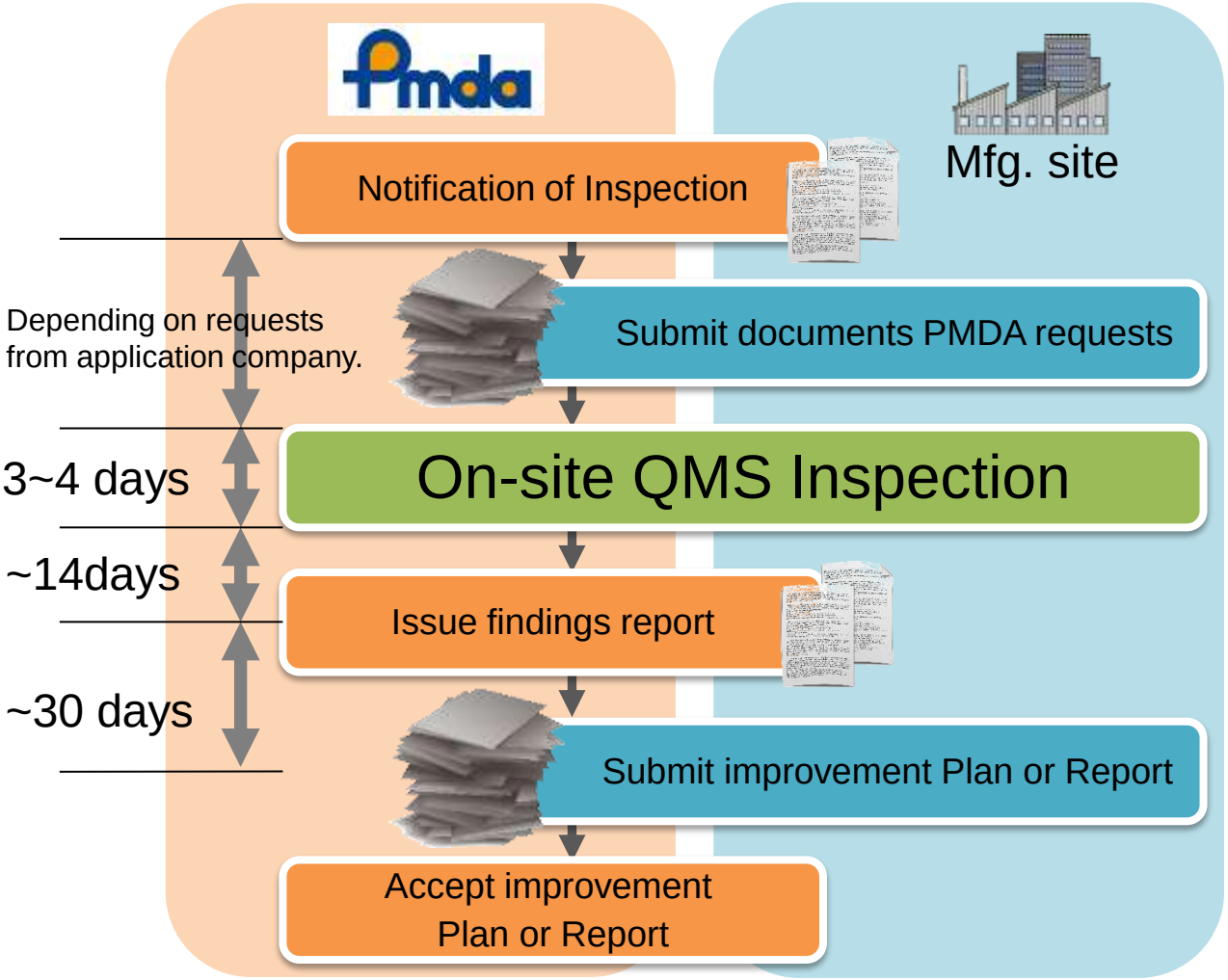
- Submitted documents
- Reported adverse events and recalls
- Records of previous QMS inspections
- Complexity of manufacturing processes
- Risk associated with the use of products
- Previous nonconformities and recalls
- Results of the previous on-site inspections
- Certificate of ISO13485 etc.



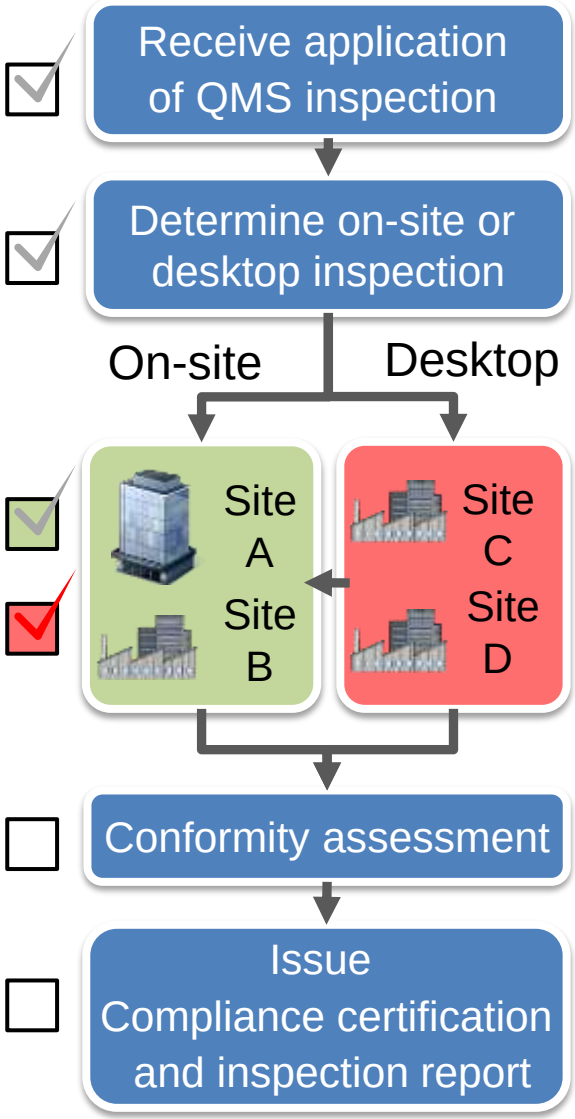
On-site inspection



On-site inspection flow



Desktop inspection



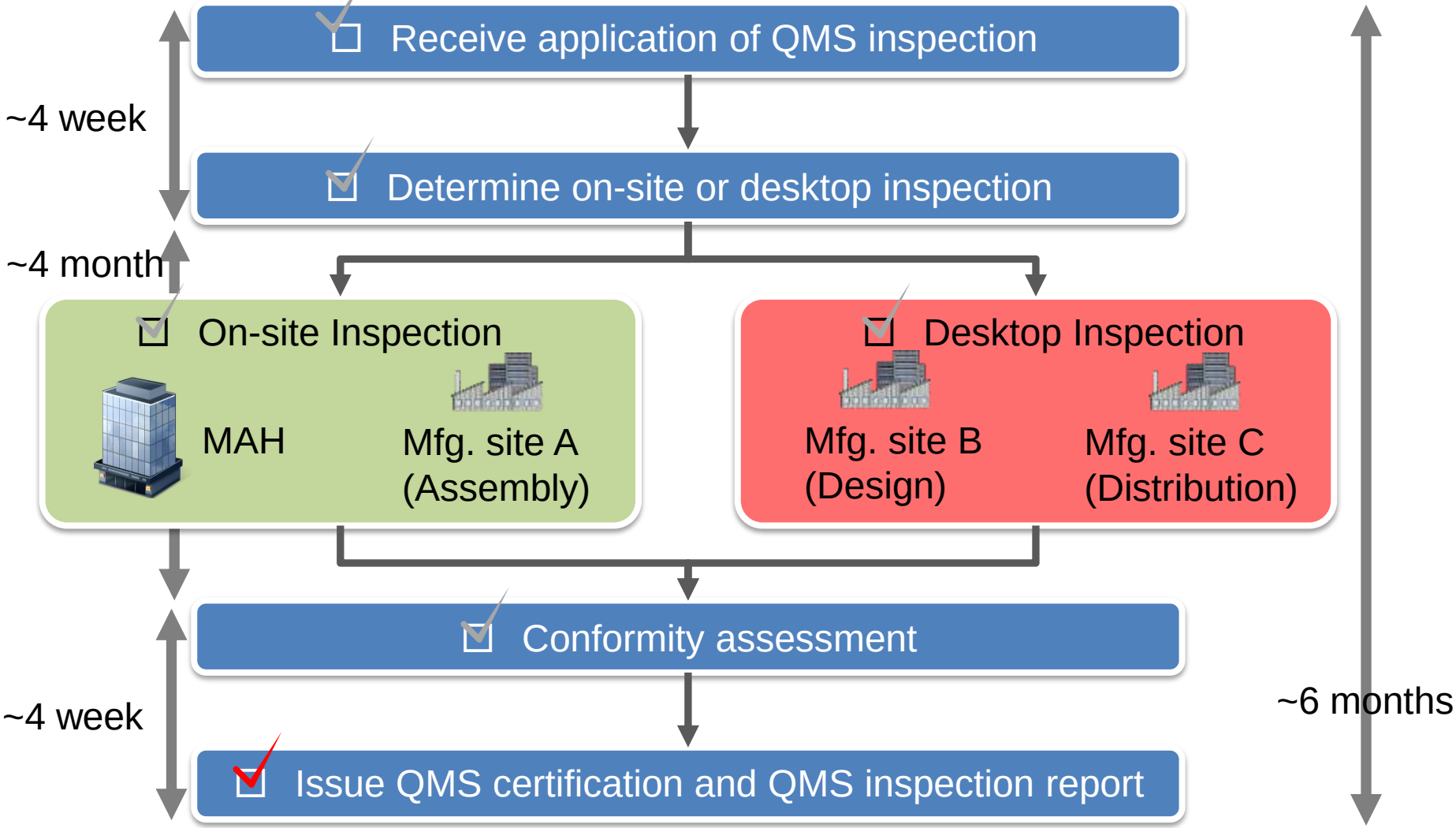
Required documents for Desktop inspection

	Documents	Outline of Documents
Documents about subject of QMS Inspection mfg. site	Layout of all mfg. site building	・Bird's eye-view photograph or location map of mfg. site
	Floor plan	・Clean room grade ・Differential pressure ・List or layout of representative manufacturing and test equipment
	Organization chart	・Responsible persons and departments under QMS
Documents about QMS	Quality management system	・Quality Manual
	List of documents identified with QMS	・Including name, number, and retention period of QMS control documents
Documents about product subject to the Inspection	*Seihin Hyojun Sho*	・The document of *Seihin Hyojun Sho* showed all the related documents to the product under QMS.(Device master record OK) ・Reference：Aug27, 2014 PFSB/CND No.0827-2
	Validation status of mfg. process	・List showing mfg. process , mfg. site, and date about the validation.

QMS inspection flow

Example

Periodic post-approval inspection



QMS Compliance Certification

QMS Compliance Certification

Summary Report*

Marketing Authorization Holder

On-site Inspection

Inspection Report

Manufacturing Site (Design Facility)

Desktop Inspection

Manufacturing Site (Assembling Plant)

On-site Inspection

Inspection Report

Manufacturing Site (Contract Sterilizer)

Desktop Inspection

Manufacturing Site (Domestic Distribution Center)

Desktop Inspection

4. MDSAP update

Trial for MDSAP Audit Reports

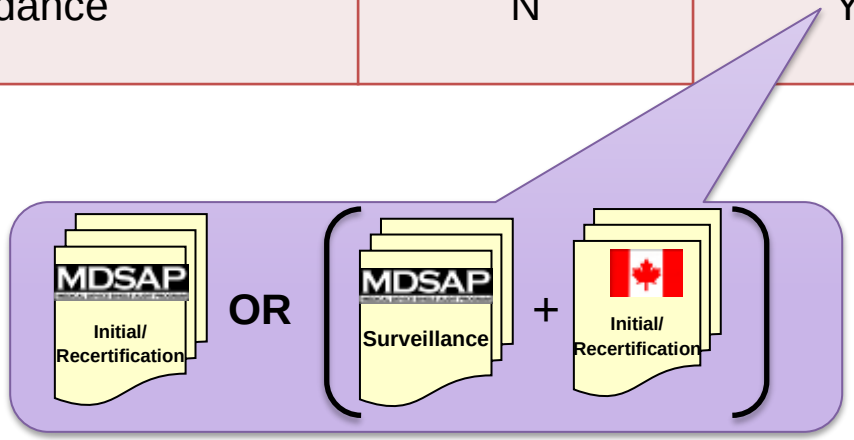
- PMDA accepts MDSAP audit reports as a trial.
  from June 22, 2016 to December 31, 2016

- The MDSAP Audit Report can reduce the manufacturer's burden in the inspection process.

- PMDA performs the trial acceptance without any additional fee.

Documents for application

No.	Documents	Normal Application	Application using MDSAP
1	ISO13485 Certification, registered certification body's Inspection report, etc	Y	N
2	Outline of the site	Y	N
3	A document requested by the guidance	N	Y



Documents for desk-top inspection

No.	Documents	Normal Application	Application using MDSAP
1	Arrangement of the facility	Y	N
2	Floor plan	Y	N
3	Organization chart	Y	N
4	Quality manual	Y	N
5	List of documents used in QMS	Y	N
6	Summary of medical device file	Y	Y
7	State of implementation of validation	Y	N
8	Any documentation which indicates the confirmation result of quality of a medical device to ensure safety of it, when the device is using biologically derived raw materials etc.	Y	Y
9	Procedure etc. for communication with Marketing Authorization Holder in relation to adverse events	Y	N
10	Agreement with Registered Manufacturing Site	Y	N

Summary for MDSAP documentation

- Basically Off-Site inspection for the facility that has the MDSAP audit report when QMS inspection application.

- Exceptions: Registered Manufacturing Site are

  a) human/animal tissues
  b) radioactive IVDs
  c) A Marketing Authorization Holder (MAH)

- On-Site inspection, when necessary.

References

PMDA / QMS (Japanese)

http://www.pmda.go.jp/review-services/gmp-qms-gctp/qms/0003.html

PMDA / QMS (English)

http://www.pmda.go.jp/english/review-services/gmp-qms-gctp/0002.html

PMDA / Notifications related to PAL Revision (Japanese)

http://www.pmda.go.jp/review-services/drug-reviews/about-reviews/devices/0040.html

MHLW (English)

http://www.mhlw.go.jp/english/index.html

Now .....

- Now we are also one of MDSAP members as Brazil and we will cooperate together in MDSAP.
- Also as we are getting more close in the harmonization in the requirements and audit competence, awareness, and training, we should eliminate multiple audits in the same facility in Japan and in Brazil.

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