QMS (Quality Management System) for Medical Device in Japan

1st Korea – Japan Symposium

23 June, 2016

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Office of Manufacturing/Quality and Compliance

Division of Medical Devices

Main Topics

1. QMS regulation
   - 1.1. Type of QMS inspection
   - 1.2. Authority of QMS inspection
   - 1.3. Scope of QMS inspection (mfg. site and products)
   - 1.4. Criteria of QMS inspection
2. QMS inspection flow
3. Nonconformity

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2. QMS inspection flow
3. Nonconformity

1.1 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..

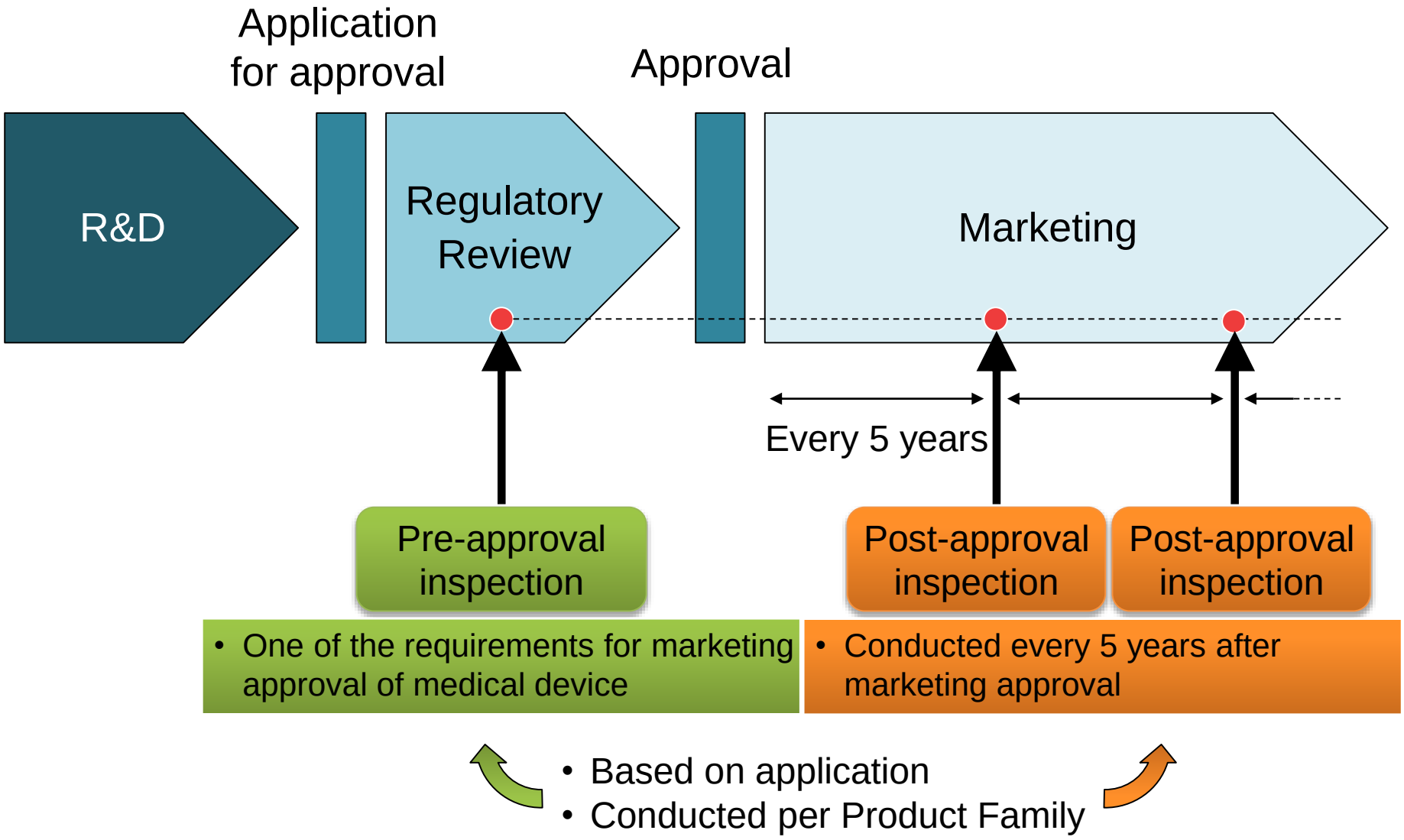
3. Periodic post-approval inspection

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..

1.1 QMS Inspection (Pre-, Post-)



1.1 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..

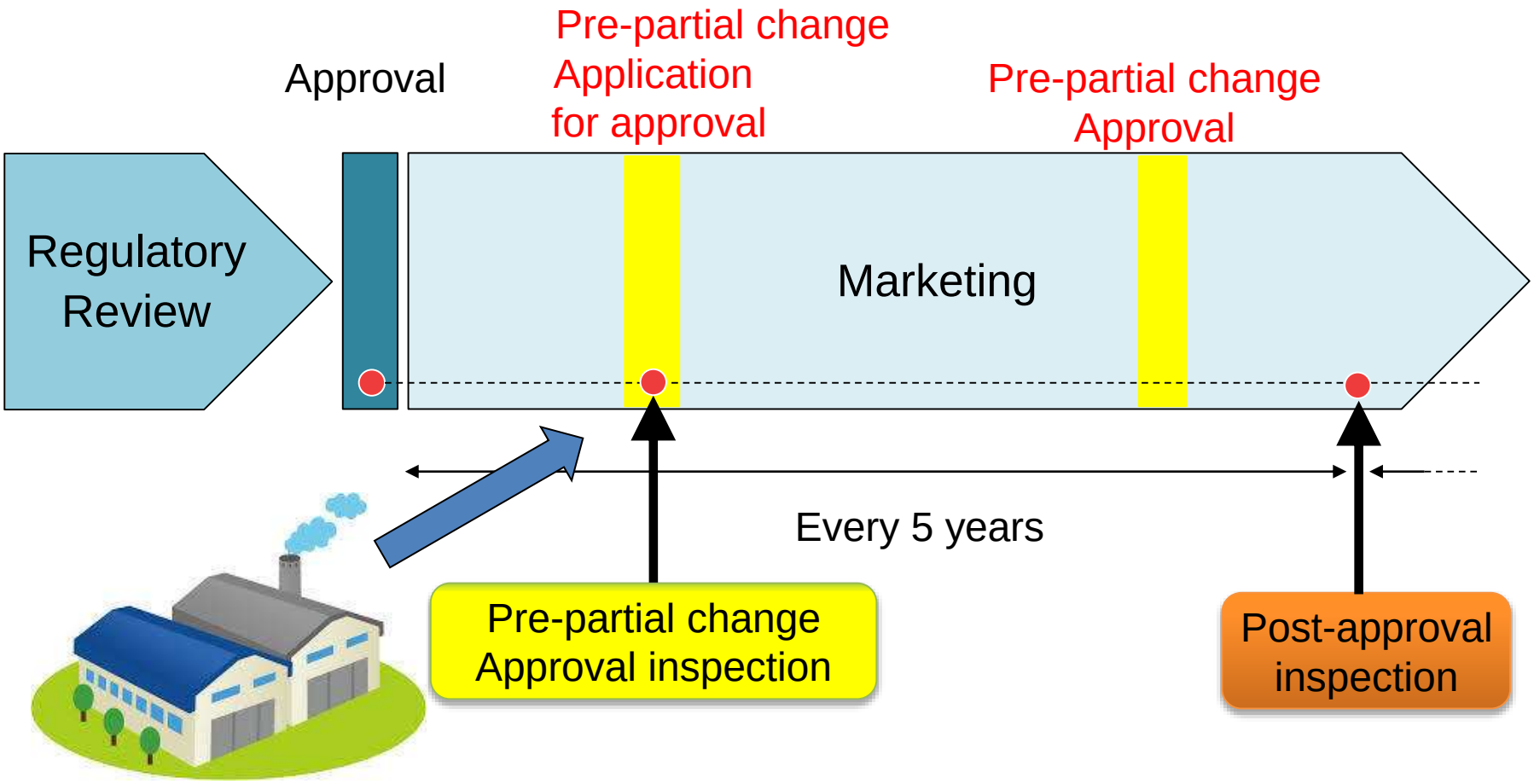
3. Periodic post-approval inspection

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..

1.1 QMS Inspection (Partial change)



ex) Main assembling site
Change

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

1.2 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

1.3 Scope of QMS inspection

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

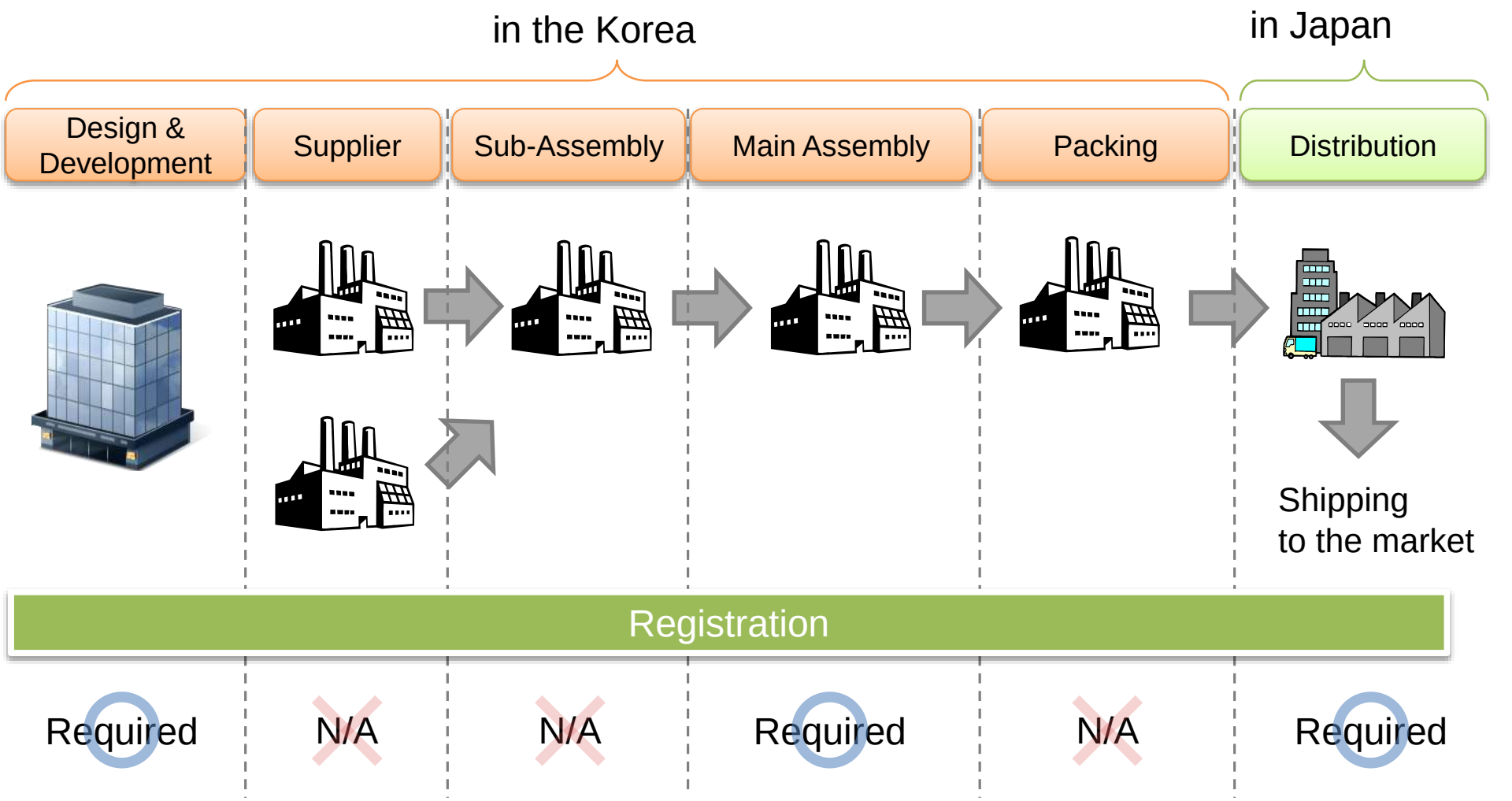
Other sites

1.3 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.

1.3 Example of mfg. site registration



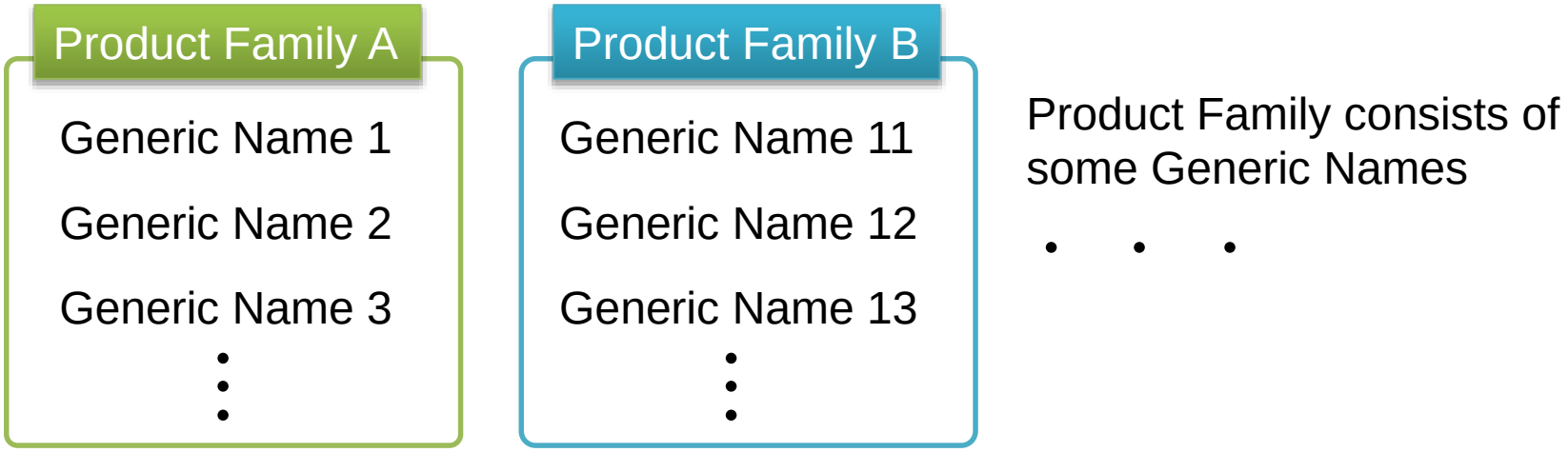
1.3 Scope of Registration and Inspection

	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

1.3 Product Family

QMS inspection is conducted per **“Product Family”**

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



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

1.3 Product Family

Medical Devices and In-Vitro Diagnostics（Class Ⅱ～Ⅳ）

[exception]

Product (High risk Product)

[exception]

Generic name (Not applicable to Product Family)

Product Family of Class Ⅳ

ex) Stent, Stent graft, Active catheter, Cardiac pacemaker and defibrillator, Ventricular assist device

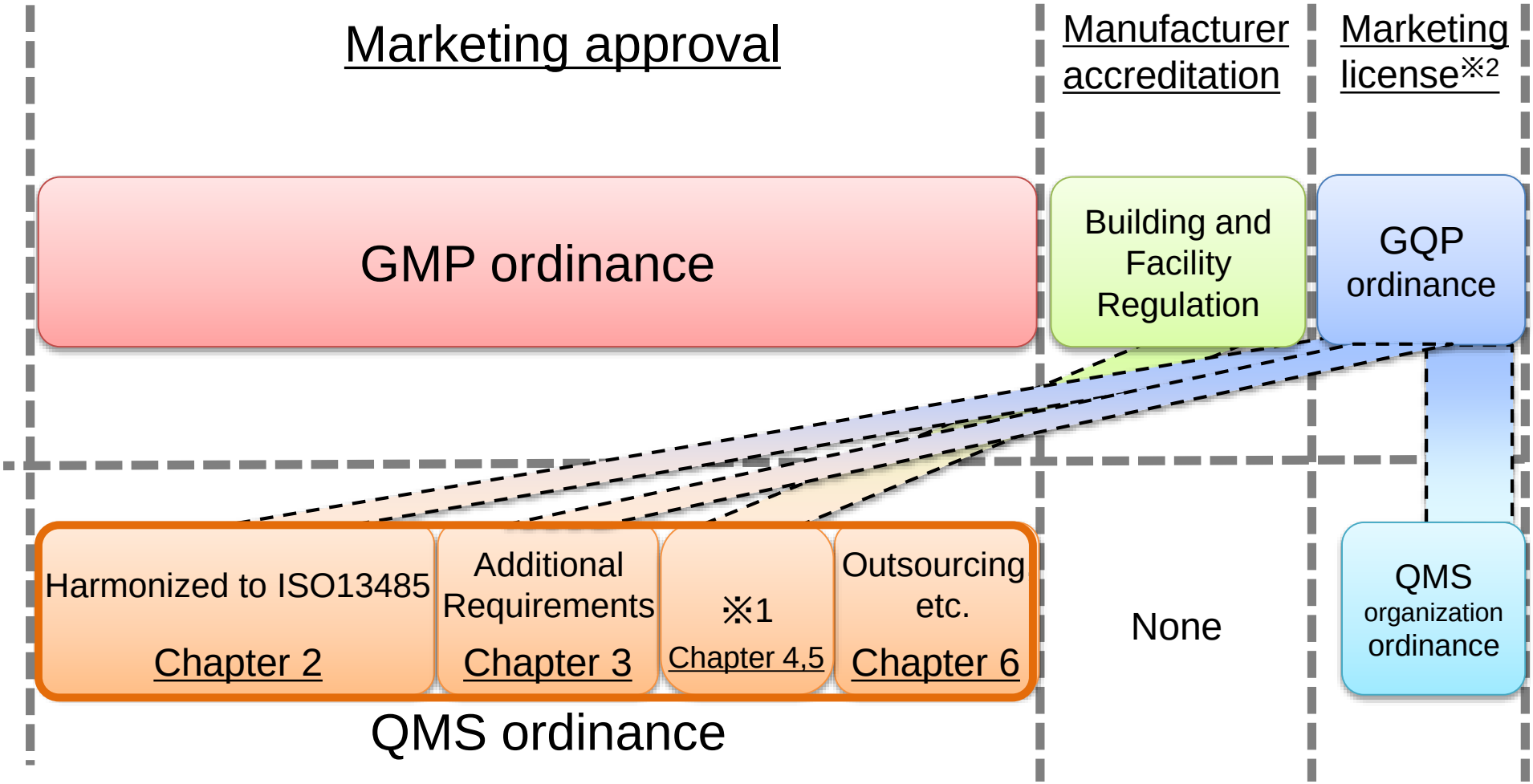
(Japanese original definition)

Product Family of Class Ⅱ/Ⅲ

ex) Non-active instruments, Non-active cardiovascular implants, Non-active dental equipment and instruments, Devices for stimulation or inhibition, Imaging devices utilizing ionizing radiation

(according to NBOG BPG 2009-3)

1.4 Comparison between GMP and QMS



※1 Chapter 4 and 5 states requirements of building and facility for manufacturer of biological medical devices and radioactive IVDs.

※2 A requirement for marketing any medical devices and IVDs in Japan. Thus, all the MAHs shall have this license.

Example

1.4 Criteria of QMS Ordinance

Chapter	Title	Article
1	General Provisions	1~3
2	Medical Devices Manufacturing Harmonized to ISO13485:2003	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

Main Topics

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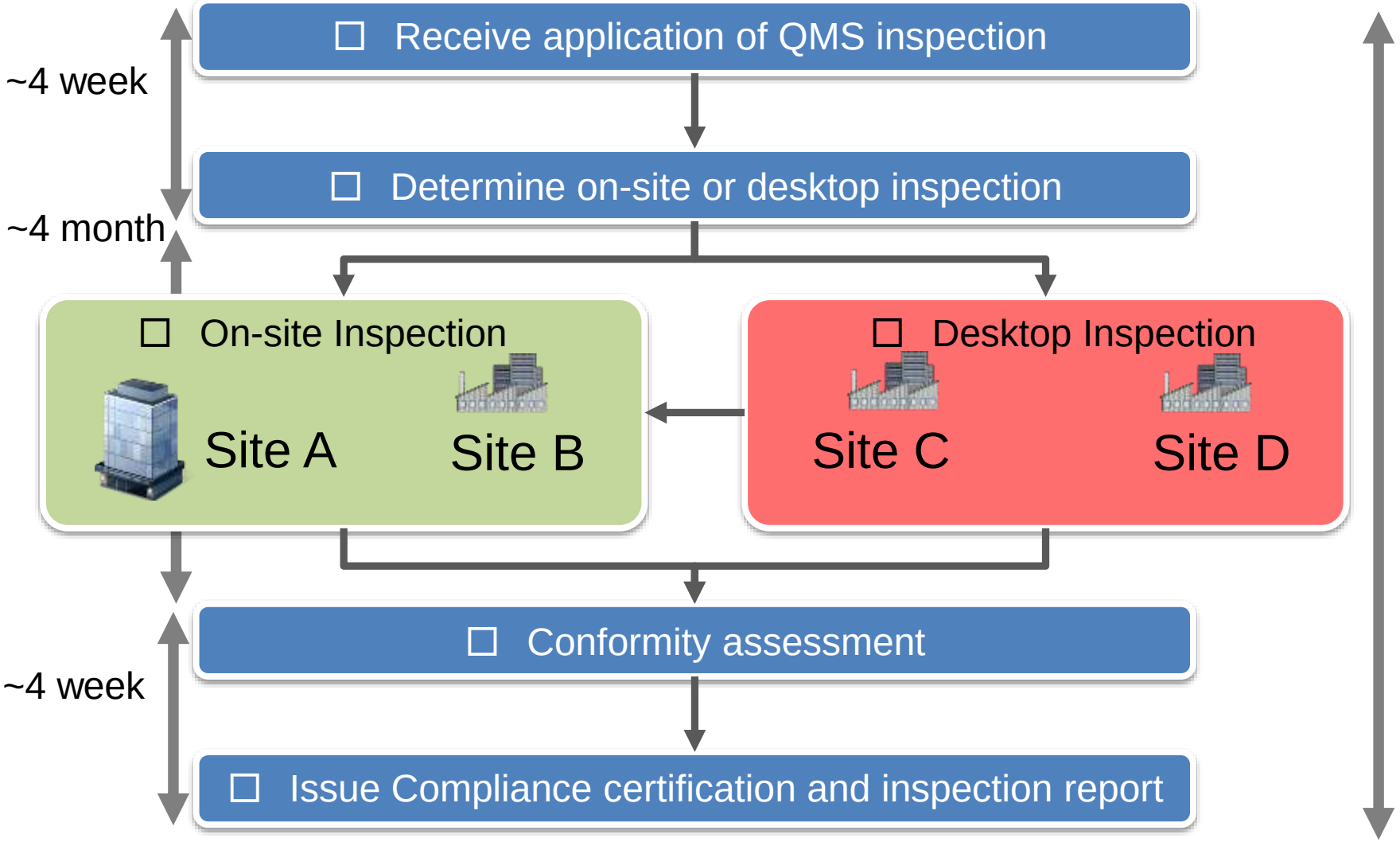
3. Nonconformity

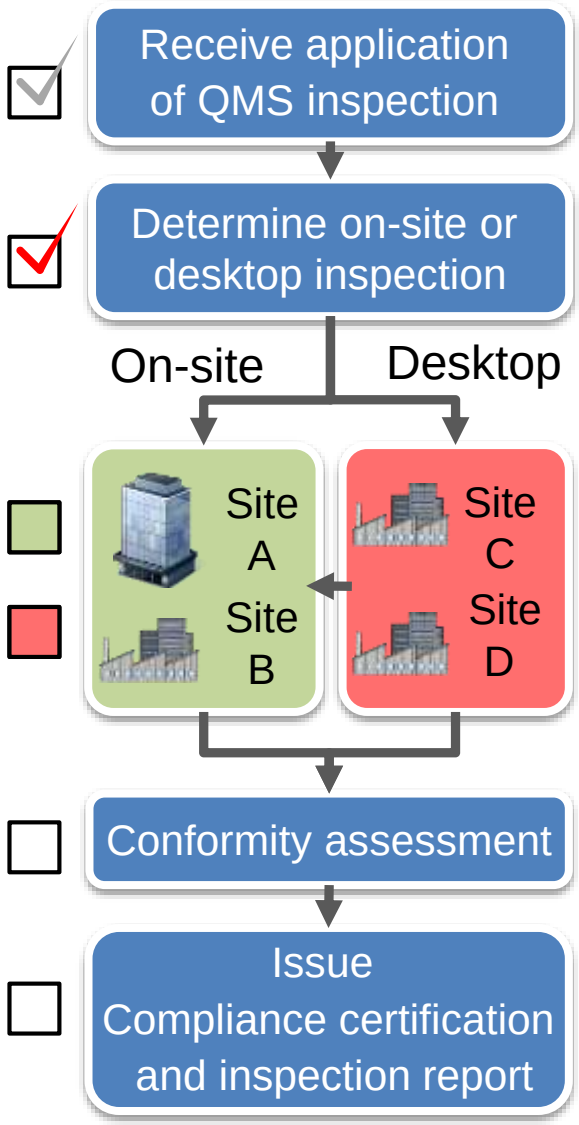
QMS inspection flow

Example

Periodic post-approval inspection



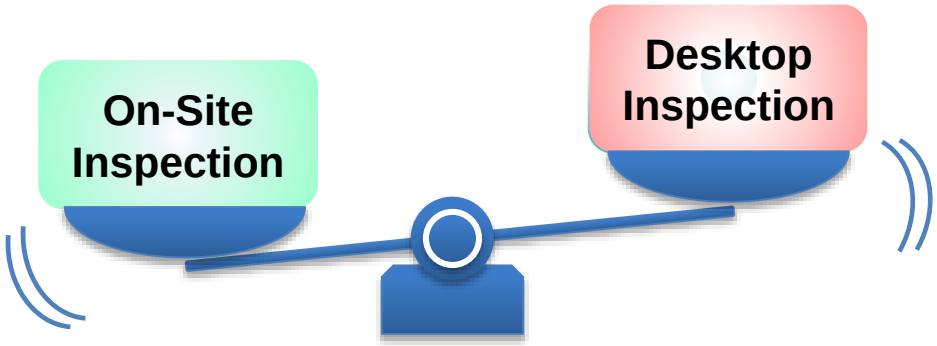
Determine on-site or desktop inspection



Determination step

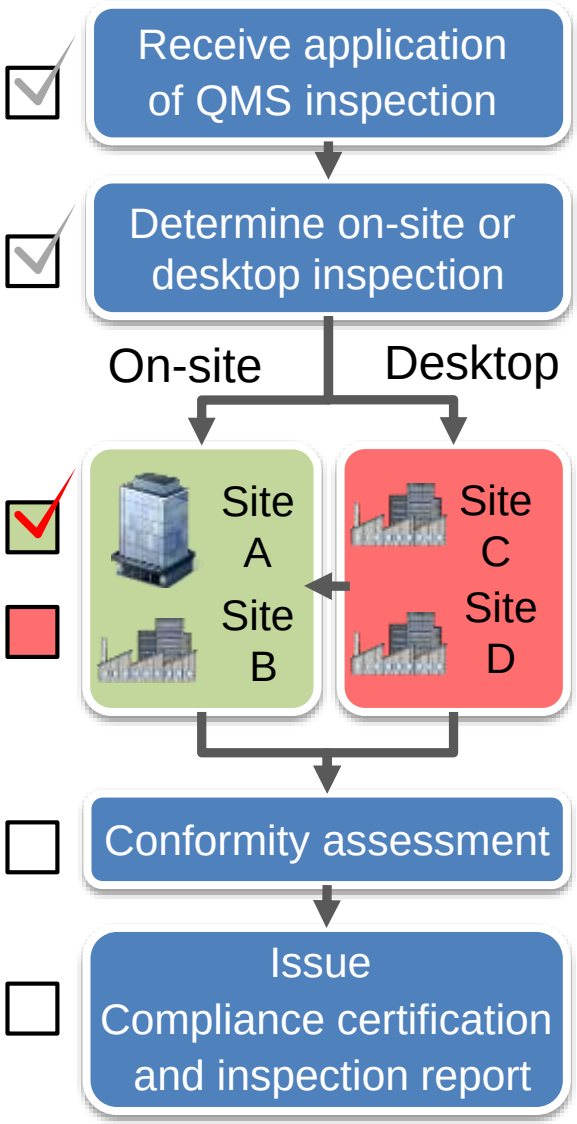
Input Information :

- 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.

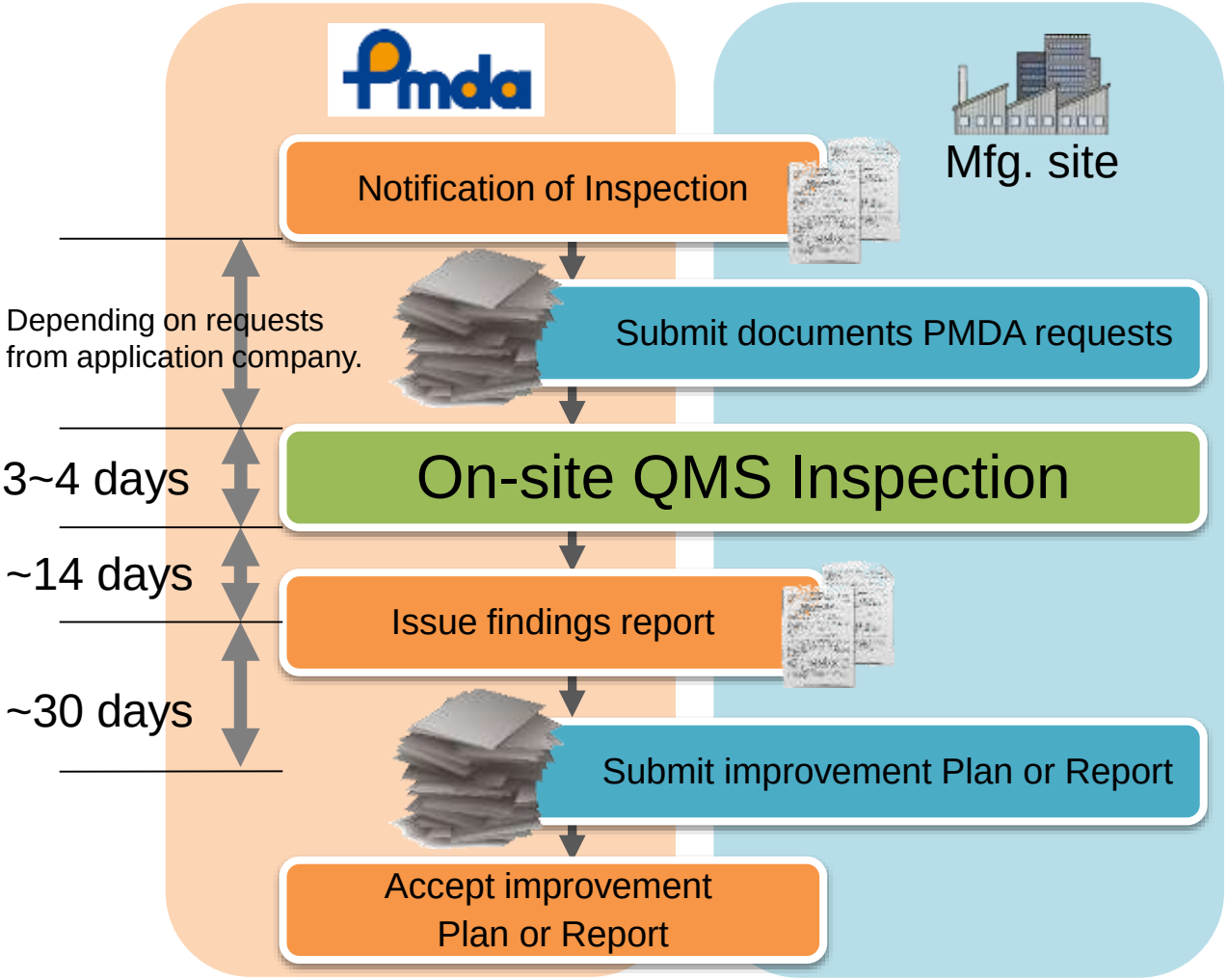


On-site inspection

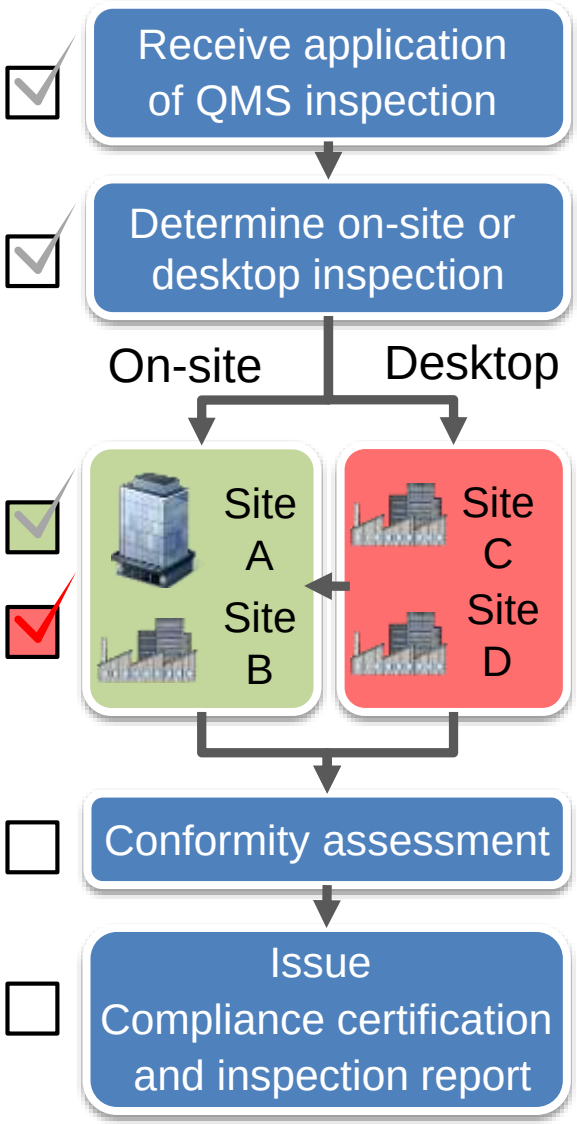
Example



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.

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

QMS inspection flow

Example

Periodic post-approval inspection

~4 week

☐ Receive application of QMS inspection

☐ Determine on-site or desktop inspection

~4 month

☐ On-site Inspection

MAH

Mfg. site A
(Assembly)

☐ Desktop Inspection

Mfg. site B
(Design)

Mfg. site C
(Distribution)

☐ Conformity assessment

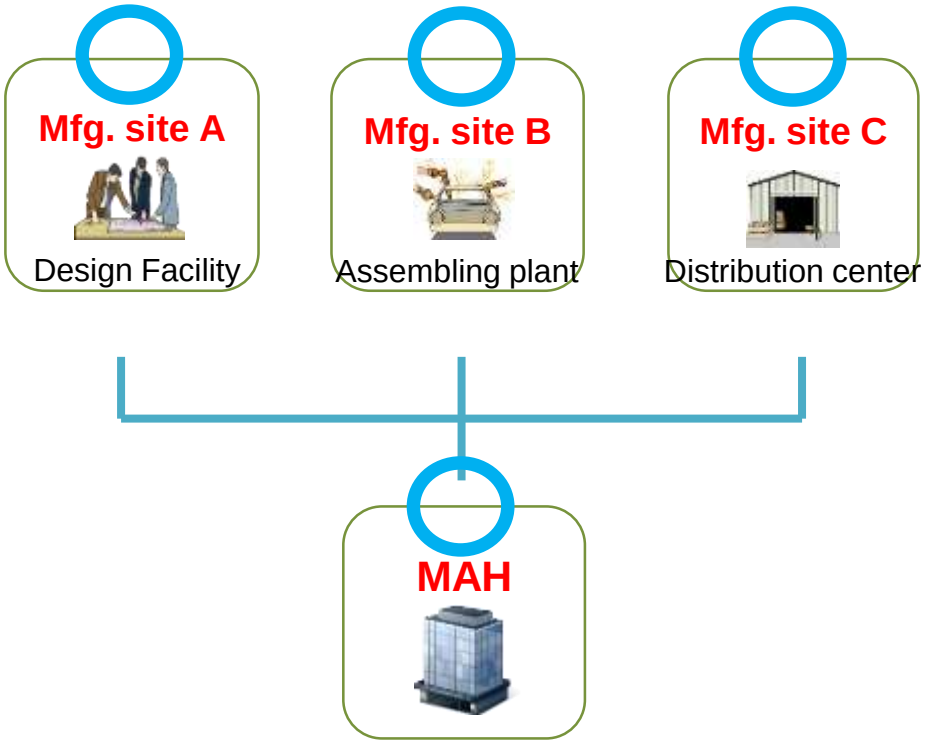
~4 week

☐ Issue QMS certification and QMS inspection report

~6 months

Final assessment

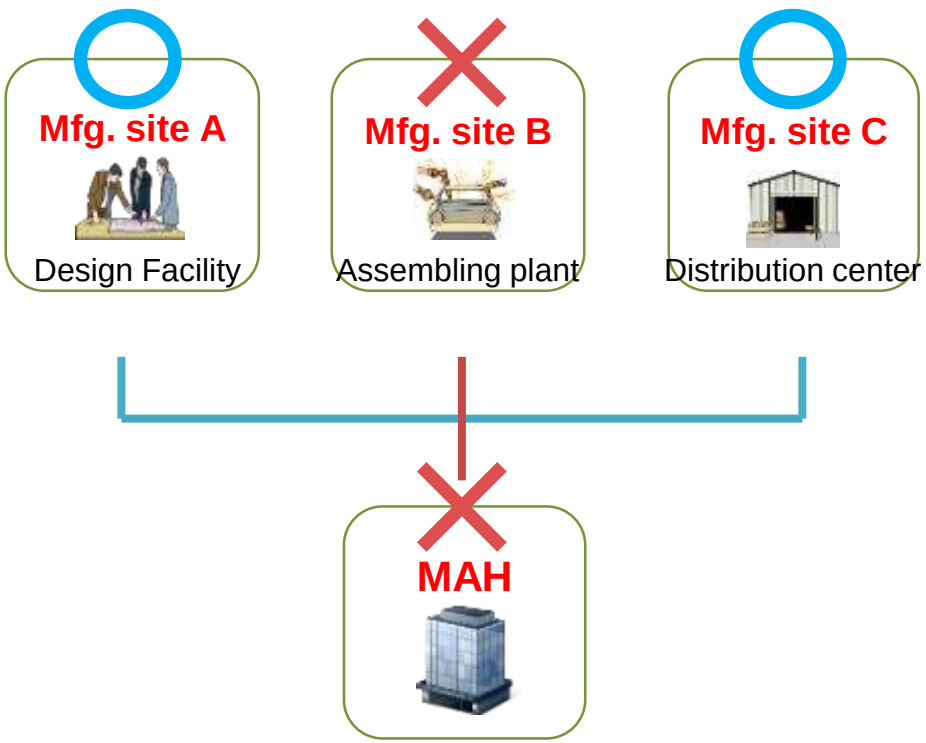
If all sites are conformity…



Conformity for application

conformity
nonconformity

If mfg. site B is nonconformity…



※ MAH is nonconformity, too.
(Reference: QMS ordinance article 65)

Nonconformity for application

QMS inspection flow

Example

Periodic post-approval inspection

~4 week

☐ Receive application of QMS inspection

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Mfg. site C
(Distribution)

☐ Conformity assessment

~4 week

☐ Issue QMS certification and QMS inspection report

~6 months

QMS Compliance Certification

Example

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

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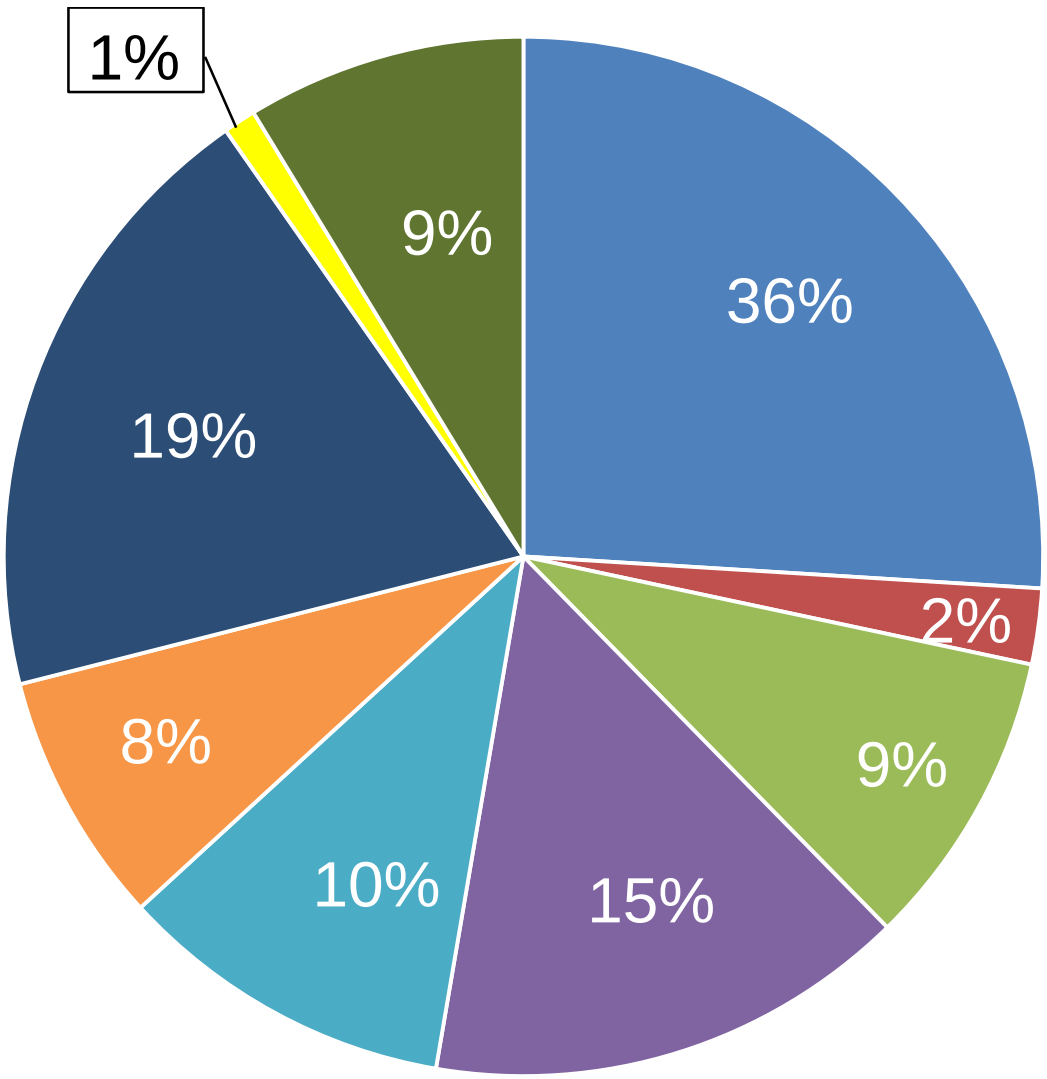
Nonconformity - Overview

25/11/2014 ～ 19/05/2016



Sub-System

- Management Control
- Design and Development
- Product Documentation
- Manufacturing
- CAPA
- Purchasing Control
- Documents and Records Control
- Customer-related process
- Marketing Authorization Holder(MAH)

Nonconformity

Example

- No Biological indicator(BI) requirements such as temperature, humidity and cultivation condition.
- No documentation process challenge devices(PCD). No rationale for sterility assurance level(SAL) requirements.
- No PV or verification for mfg. process without any rationale.

  Ex) Color CL: curing, washing, hydration, sealing, etc.
- No qualification for the stability of monomer neither mixed monomer nor polymerization initiator.

  Ex) storage condition and shelf life.
- No traceability forward raw material.

  Ex) Color CL: monomer mixed color, saline solution, etc.
- No record for the reason why no CAPA.(ISO13485:2003 8.5.1)

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

ご清聴ありがとうございました。

Thank you for your attention!

Overview of Korea MFDS Approval Processes for Medical Devices

June 23 2016

Seonghee Lee

MFDS/NIFDS

식품의약품안전처

식품의약품안전처

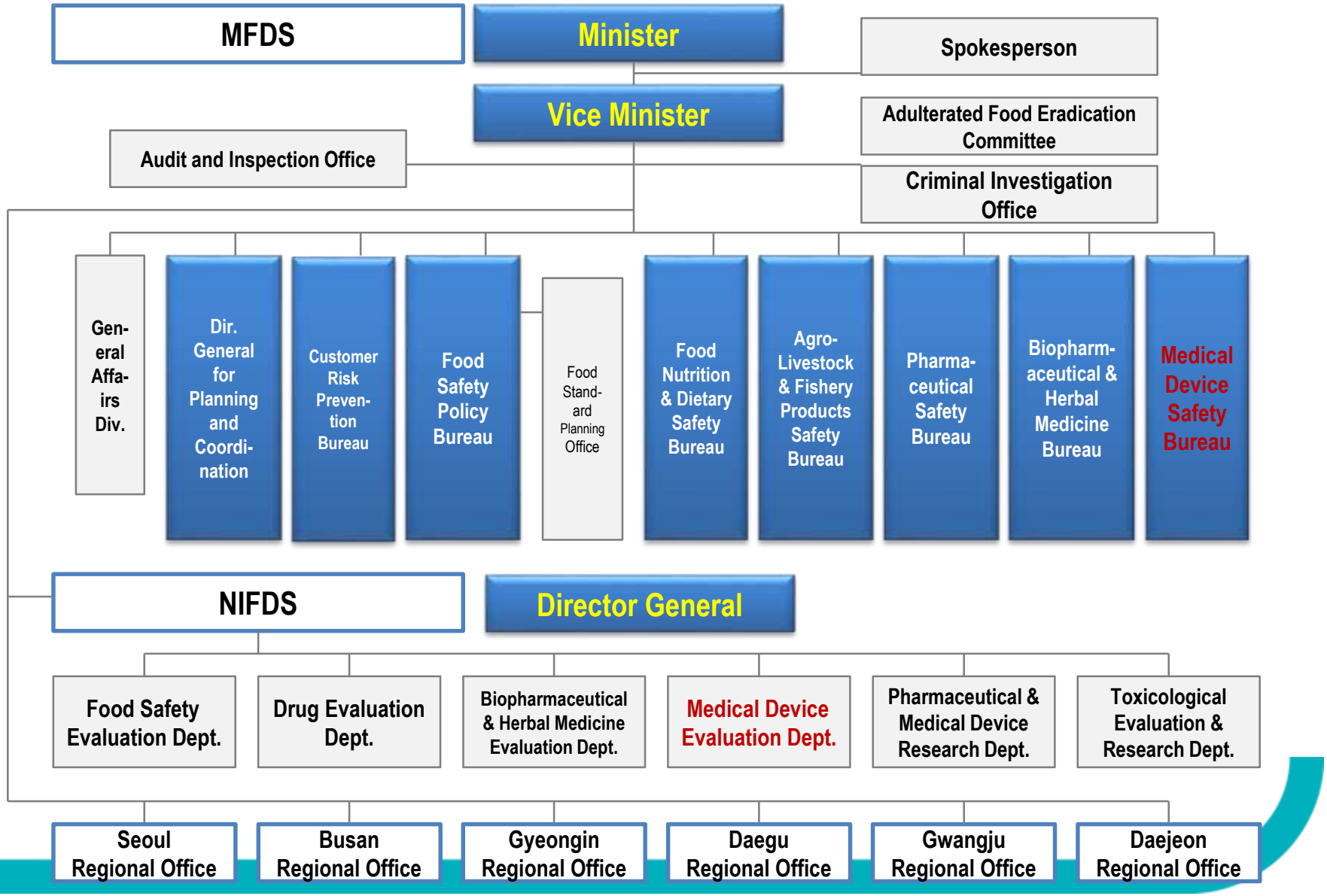
Content

1. Organization of MFDS/NIFDS
2. Medical Device Regulations
3. Medical Device Approval Processes

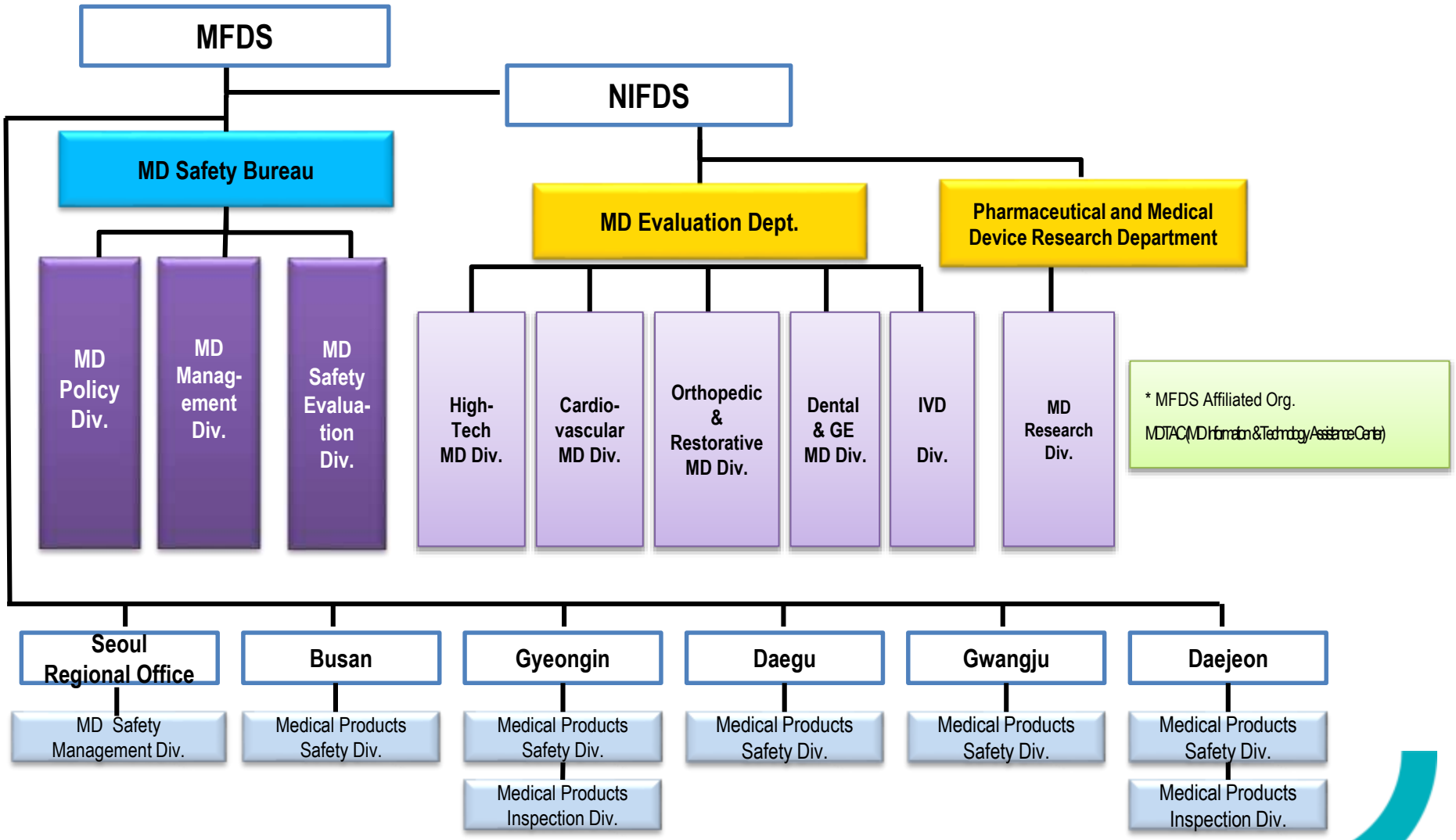
식품의약품안전처

1. Organization of MFDS/NIFDS

MFDS/NIFDS


MFDS
Minister
Spokesperson
Vice Minister
Adulterated Food Eradication Committee
Audit and Inspection Office
Criminal Investigation Office
Gen-eral Affa-irs Div.
Dir. General for Planning and Coordi-nation
Customer Risk Preven-tion Bureau
Food Safety Policy Bureau
Food Stand-ard Planning Office
Food Nutrition & Dietary Safety Bureau
Agro-Livestock & Fishery Products Safety Bureau
Pharma-ceutical Safety Bureau
Biopharm-aceutical & Herbal Medicine Bureau
Medical Device Safety Bureau
NIFDS
Director General
Food Safety Evaluation Dept.
Drug Evaluation Dept.
Biopharmaceutical & Herbal Medicine Evaluation Dept.
Medical Device Evaluation Dept.
Pharmaceutical & Medical Device Research Dept.
Toxicological Evaluation & Research Dept.
Seoul Regional Office
Busan Regional Office
Gyeongin Regional Office
Daegu Regional Office
Gwangju Regional Office
Daejeon Regional Office

MD related organization



MD Safety Bureau(MFDS)

Medical Device Safety Bureau

Medical device Policy division	Develop and Establish MD Policies MD Regulations, Standards, etc..
Medical Device Management Division	Management of Post market Surveillances Inspections, Recalls, Advertisements, etc..
Medical device Safety evaluation division	Management of Adverse event and Safety information Re-examination, Re-evaluation, GMP, etc..

Regional Offices

Practice of Post market Surveillance Programs, GMP Inspections, etc..

MDTAC (MD Information & Technology Assistance Center)

MD Notification(class I) and Certification(class II)

MD Evaluation Department(NIFDS)

Medical Device Evaluation Department

High-tech medical Devices division	Approve and review technical documents on robotic system, Laser apparatus, electric stimulator, U-healthcare device, etc.
Cardiovascular Devices division	Approve and review technical documents on cardiovascular devices, X-ray system, respiratory apparatus, anesthesia apparatus, etc.
Orthopedic & Restorative devices division	Approve and review technical documents on orthopedic implants, rehabilitation devices, suture, etc.
Dental & Gastroenterology devices division	Approve and review technical documents on dental system, endoscope, urology devices, infusion instruments, etc.
In vitro diagnostic device division	Approve and review technical documents on hematological testing apparatus, reagents for hematology, clinical immunochemistry, etc.

Pharmaceutical and Medical Device Research Department

Medical Device Research Division	Develop test method and standards, research on evaluation technology of safety and performance , etc.

식품의약품안전처

2. Medical Device Regulations

MD Regulations

The Medical Device Act Framework

- The Medical Device Act : Definition of Medical Device, etc.
- The Enforcement Decree : Medical Device Committee, Delegation of Authorities
- The Enforcement Regulations : Document and format of technical regulations
- MFDS Notice: Classification, Approval process, standard for GMP, etc.

  (specified and published by the MFDS)

MD Act

Medical Device Act [Chapter1~8, Article1~56]

- CHAPTER 1. **General Provision** (Purpose, Definition, Classification and Designation)
- CHAPTER 2. **Medical Devices Committee**
- CHAPTER 3. **MD Manufacturing, Importing, etc.** (Manufacturer, Importer, Repairer, etc.)
- CHAPTER 4. **Treatment of MD, etc** (Prohibition, Standards, Labeling and Advertisement, etc.)
- CHAPTER 5. **Management of MD**(Medical Devices Subject to Tracking, etc.)
- CHAPTER 6. **Supervision of MD**(Report, Inspection, Order for Destroy, etc., etc.)
- CHAPTER 7. **Supplementary Provisions** (Delegation or Entrustment of Authorities, etc.)
- CHAPTER 8. **Penalty** (Penalty, Administrative Default Fine, etc.)

MD Enforcement Decree & Regulations

Enforcement Decree of the Medical Device Act Article1~14

- Article 1. Purpose
- Article 2. ~ 10. Constitution of Medical Device Committee
- Article 11. ~ 14. Fine, Penalty, etc..

Enforcement Regulations of the Medical Device Act Article1~66

- Stipulation of the matters delegated by the 「Medical Device Act」and the Enforcement Decree of the Act, and any necessary matters concerning the enforcement.
- Classification, GMP, GCP, GSP, Administrative measure, etc..

3rd Parties for MD

MD Notifi. & Certifi. Issuance	MDTAC(1) (Medical Device Information & Technology Assistance Center, MFDS affiliated org.)
MD Technical File Review	3rd Parties : KTL(Korea Testing Lab), KTC(Korea Testing Certification), KTR(Korea Testing & Research Institute), KCL(Korea Conformity Laboratories), TUV Sud Korea, SGS Korea, MDTAC (7 institutions)
MD Testing Lab.	KTL, KTC, KTR, ..(14 institutions)
MD GMP Inspection	KTL, KTC, KTR, KCL(4 institutions)

MD Premarket Approval

MDITAC

CLASS I

Notification

Application for Product Notification

* GMP requirements

CLASS II

Certification

GMP conformity assessment (30days)
* Regional Branches & 3rd Parties

Technical file Review (25 days)
*Third-Parties

Certification Issue (5 days)

NIFDS

CLASS II, III, IV

Approval

GMP conformity assessment (30days)
* Regional Branches & 3rd Parties

Technical file Review (55, 70 days)

Approval Issue (10 days)

식품의약품안전처

3. Medical Device Approval Processes

Notification, Certification and Approval based on MD classification

Notification — Class I MD Not include a.

Certification — Class II MD commissioned in 3rd Parties

Approval

a. Non-Substantially Equivalent Class I & II MD in market

b. Class II MD not commissioned in 3rd Parties (IDE, IVD, U-healthcare, Not classified, Combination Products, Soft & Hard Contact lenses)

c. Class III, IV MD

Technical documents and files

Technical documents

Documents related to quality of medical devices, such as, functions, safety. etc.

- Including information on raw materials, structure, purpose of use, instruction for use, principles of functions, precautions for use, test standards, etc.

Data on raw materials, Characteristics, purpose of use, operation method, mechanism, precautions, test specification, etc

Technical files

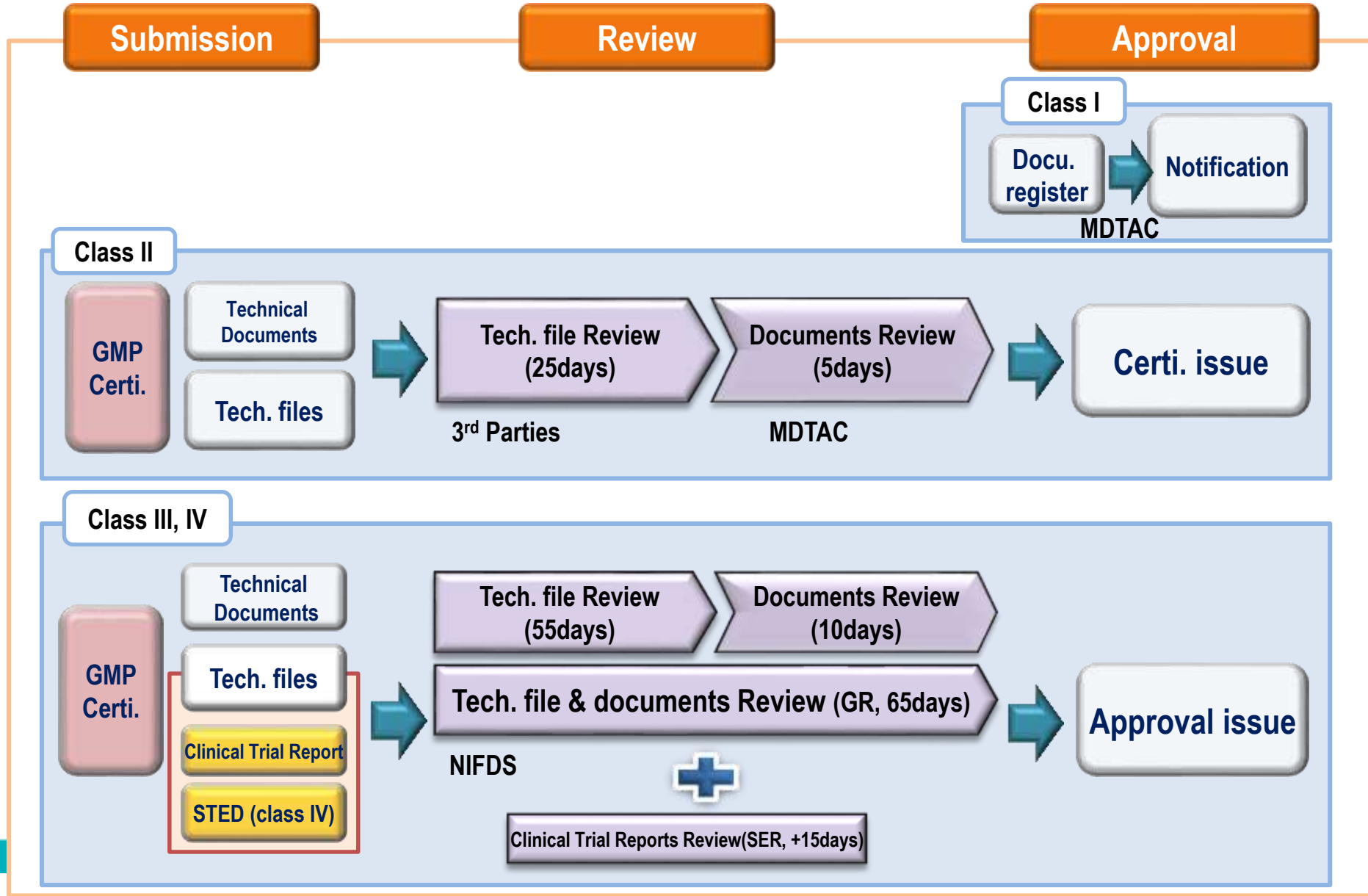
Technical file is consist of application form and supportive documents and is divided into two different types of technical file reviews: (1)'General Review'(GR); and (2) 'Safety and Effectiveness Review' (SER)

Types of Technical files

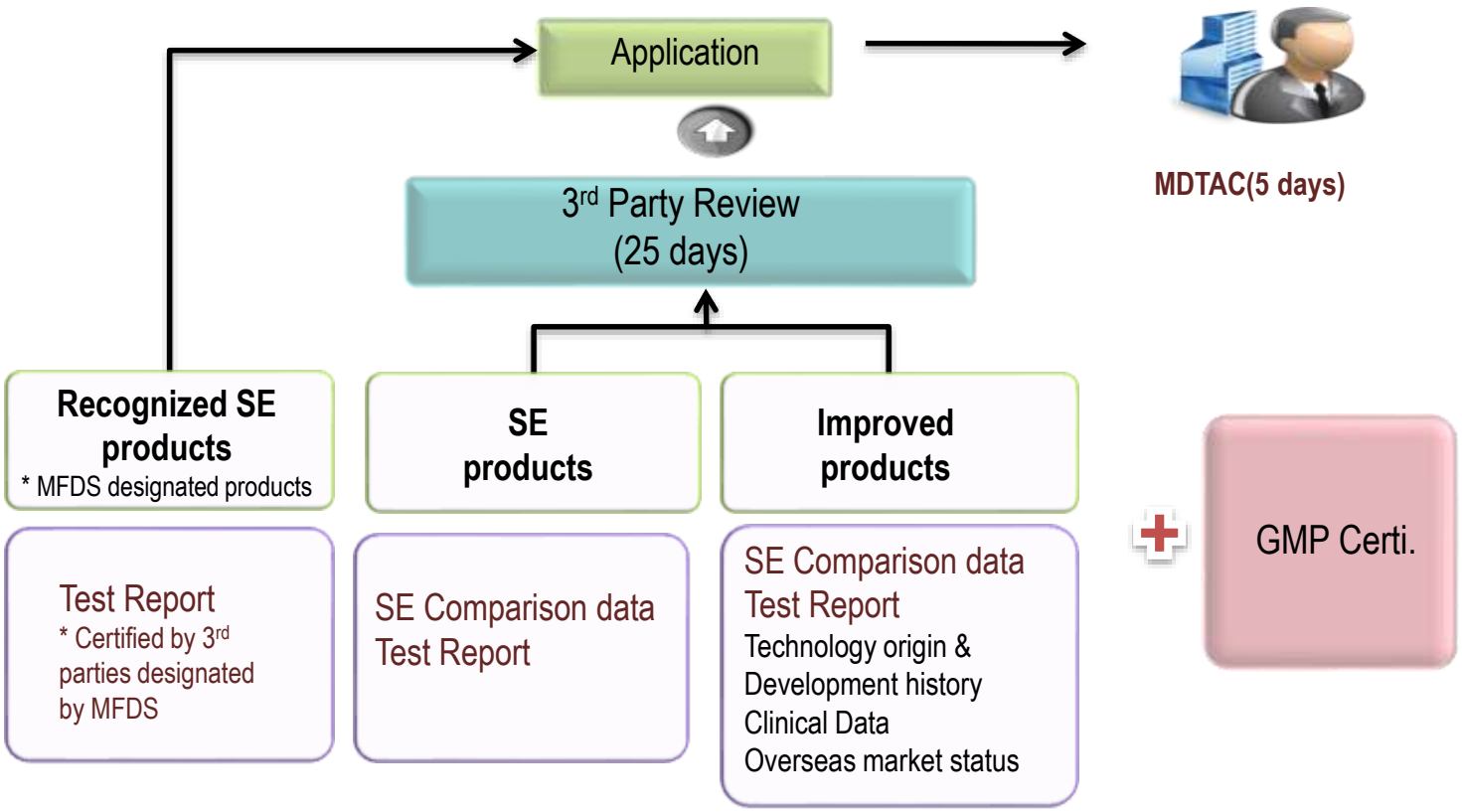
- **General Review (GR)**
  - ➢ Devices substantially equivalent to previously approved products
  - ➢ Does not require clinical trial reports

- **Safety and Effectiveness Review (SER)**
  - ➢ Significant concerns for safety and effectiveness compared to previously approved products(New technology, design, performance, purpose for use, etc..)
  - ➢ Clinical trial reports are essential

Notification, Certification and Approval processes

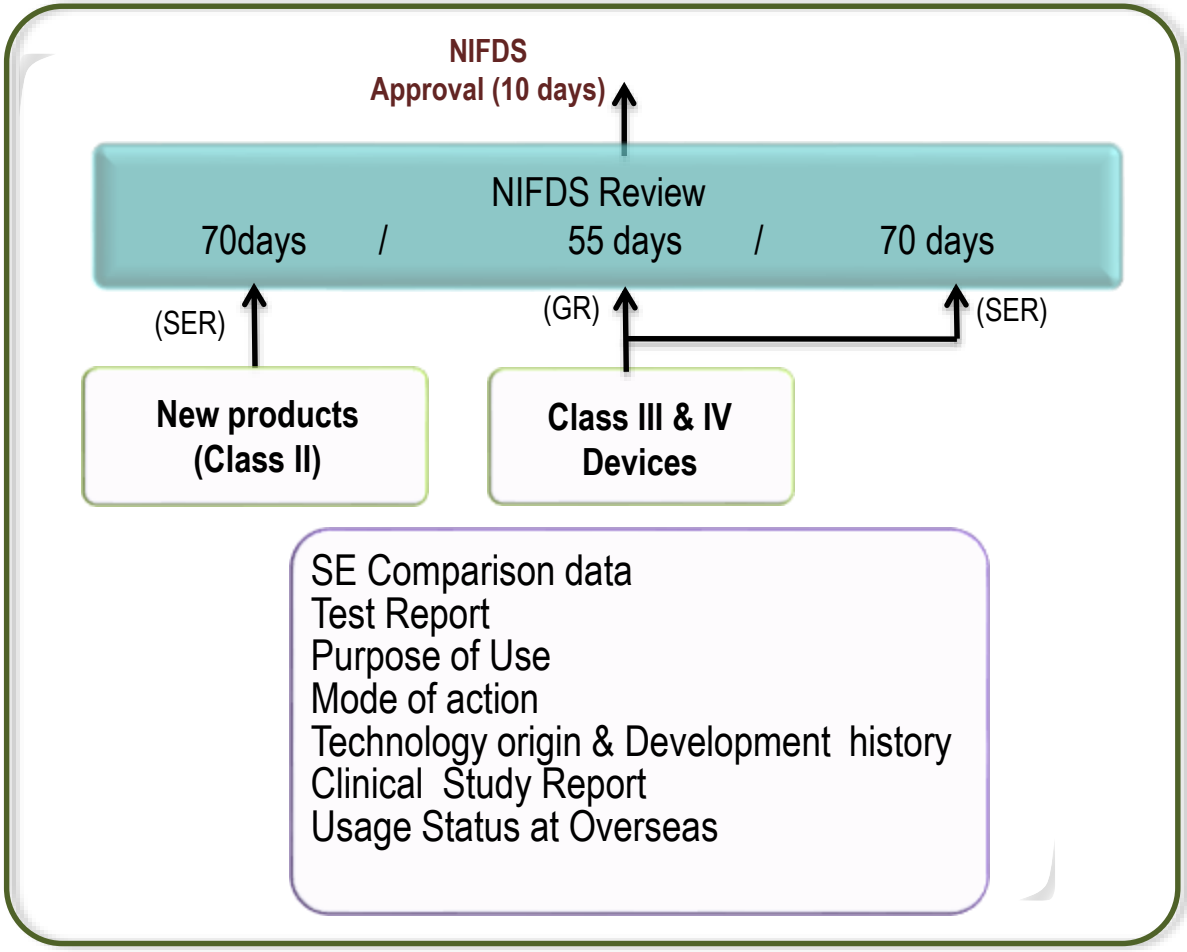


Certification processes for Class II MD



SE products : Devices that is equivalent in the purpose of use, working mechanism, raw materials(limited to medical supplies), performance, test specifications and instructions for use with the already approved medical device.
Improved products : Devices that is equivalent in the purpose of use, working mechanism, raw materials(Limited to medical supplies) with the already approved medical device, but not equivalent in performance, test specifications, instructions for use etc.

Approval processes for Class II(New), III, IV MD

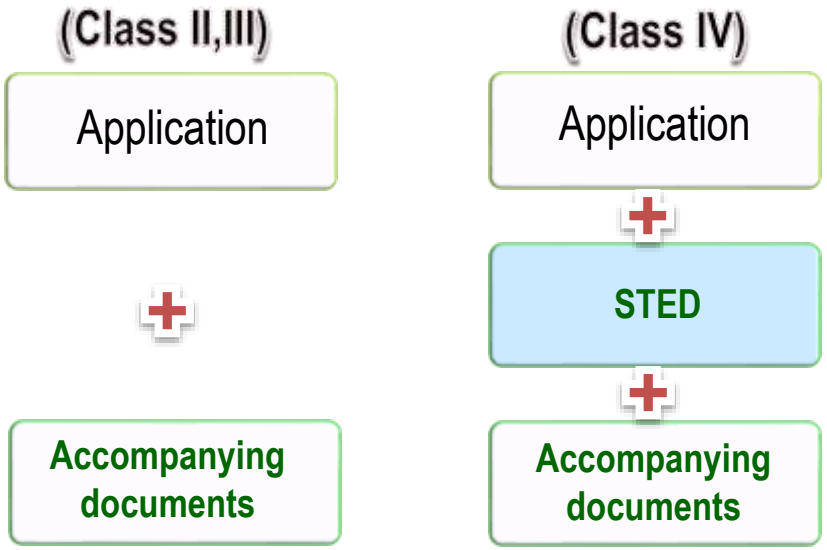


New products : MD that is not equivalent in the purpose of use, working mechanism or raw materials (Limited to medical supplies) etc. with the already approved medical device.

Tech. files for Class IV MD(STED)

STED are required for Class IV

- enforced as of 2014.Jan.1
- optional for other Classes



❖ STED : Summary Technical Documentation for demonstrating conformity to the safety and performance of medical devices
: proposed by GHTF(IMDRF) including design verification, risk analysis & manufacturing process regarding safety and performance

식품의약품안전처

Thank you for your attention!

Biological evaluation framework for medical devices; International view

Keisuke Sakaguchi

Terumo Corporation

Japan Federation of Medical Devices Associations (JFMDA)

ISO/TC194 activities

- the Latest developments regarding the biological evaluation framework for medical devices -

INTRODUCTION

- The biological safety evaluation for medical devices on the basis of ISO 10993 standards.
- The latest ISO/TC194 activities setting forth the session theme.

- ISO 10993: International standard for biological evaluation of medical devices
- ISO/TC194: ISO technical committee 194. Standardization of the approach to biological and clinical evaluation of medical and dental materials and devices together with standardization of biological test methods applicable to those materials and devices as well as good clinical practice principles to clinical investigations in humans of those devices.

ISO 10993

What is preclinical study for medical devices?

Medical Devices

Biological risks of clinical use

Toxicity of leachables and particular matters

- Plasticizers, antioxidants and etc. from plastics
- Highly toxic ion from metals
- Particular matters (ex. artificial replacement joint)

Adverse effects by contacting the materials

- Blood -> Hemolysis, thrombosis
- Tissues -> Inflammation, allergy

《Non-clinical study》

extract

(direct exposure)

administration

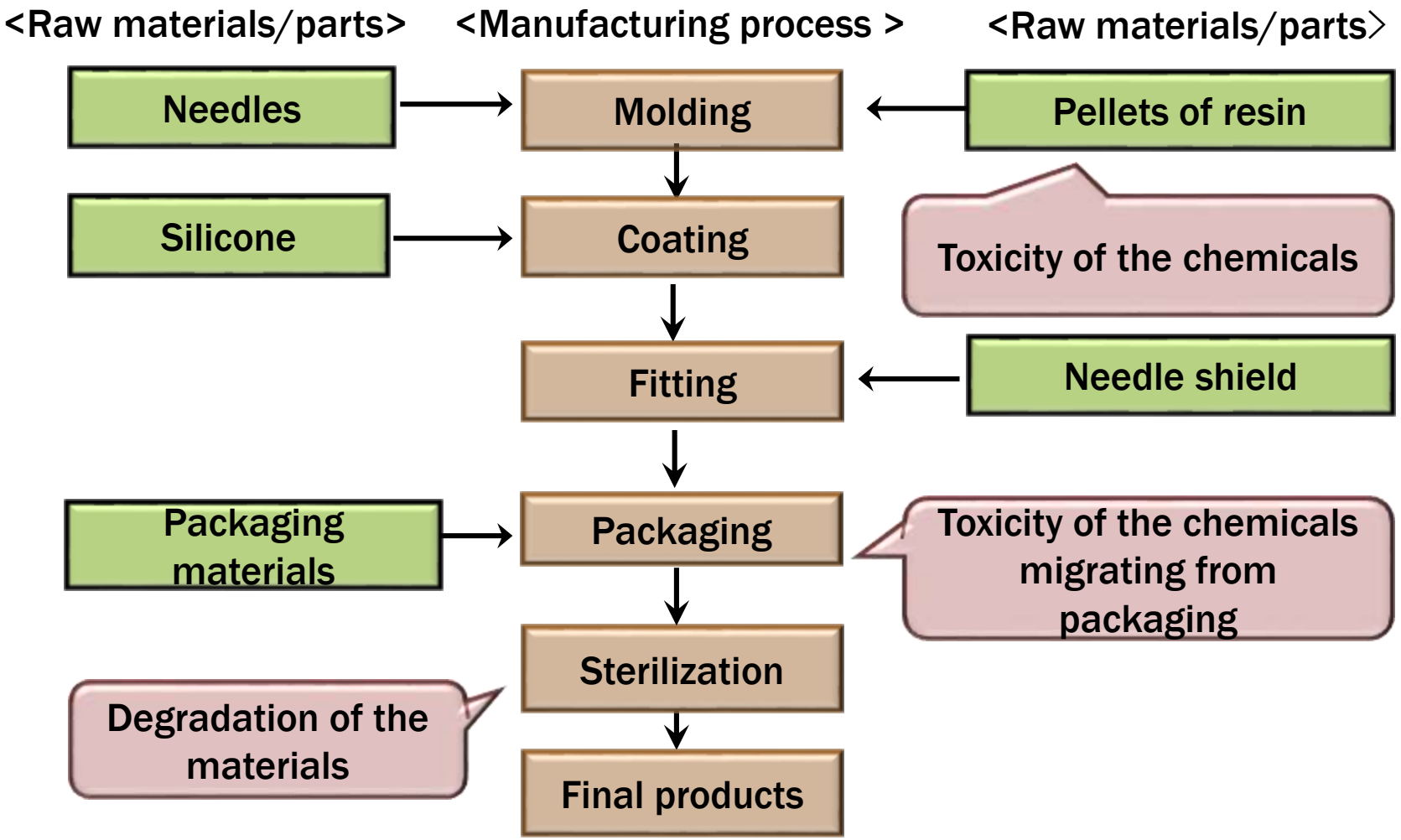
Toxicity tests examine

Biological Safety tests（ISO 10993）

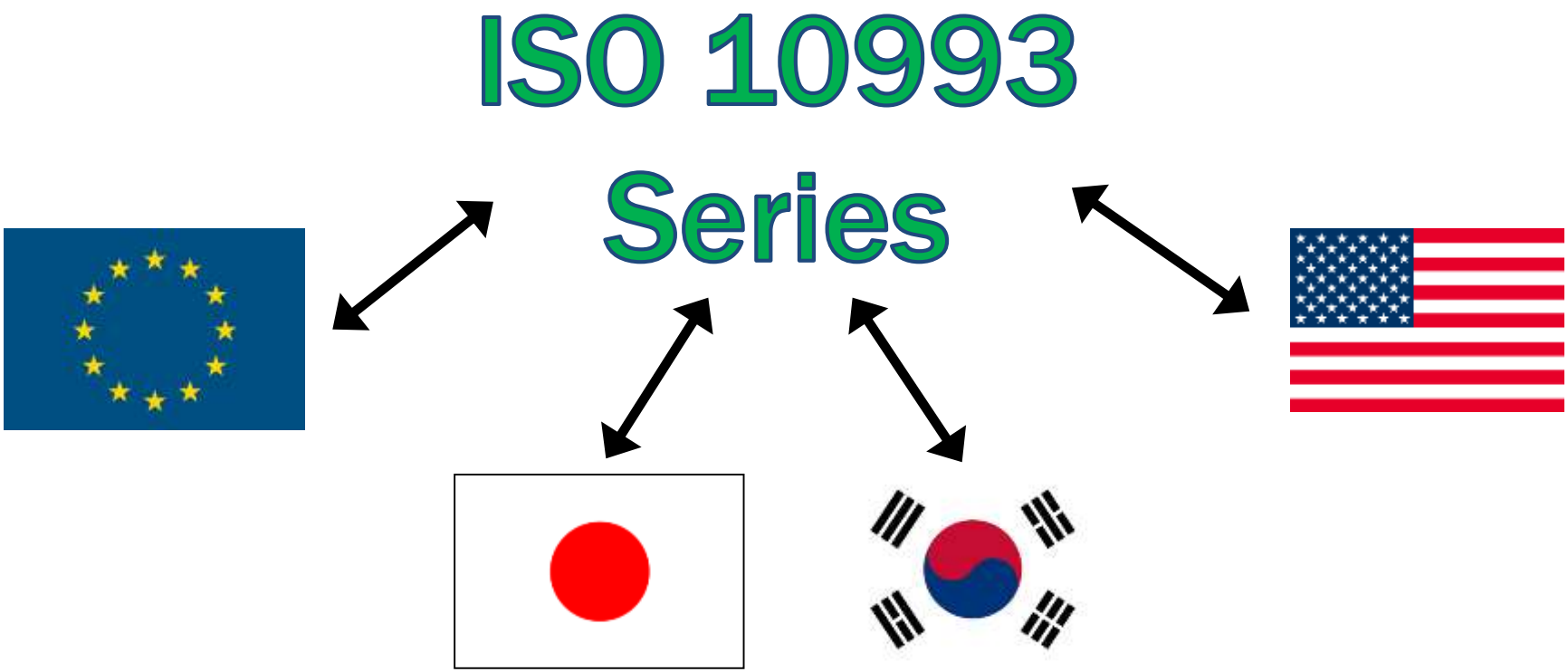
Evaluation of the potential for toxic effects

Influencing factors affecting biological safety

For protection of humans from potential biological risks arising from the clinical use of medical devices



ISO 10993: INTERNATIONAL STANDARDS FOR MEDICAL DEVICE SAFETY EVALUATION



Medical device regulations of each country are harmonized by using ISO 10993 series.

Summary of requirements of ISO 10993-1

1. Identification of component materials
（If required, analysis of extractables from polar/non-polar solvent）

2. Verify the equivalency of commercially available devices（If the equivalency is permitted, you can skip No. 3; biological safety tests）

3. Conduct of biological safety tests

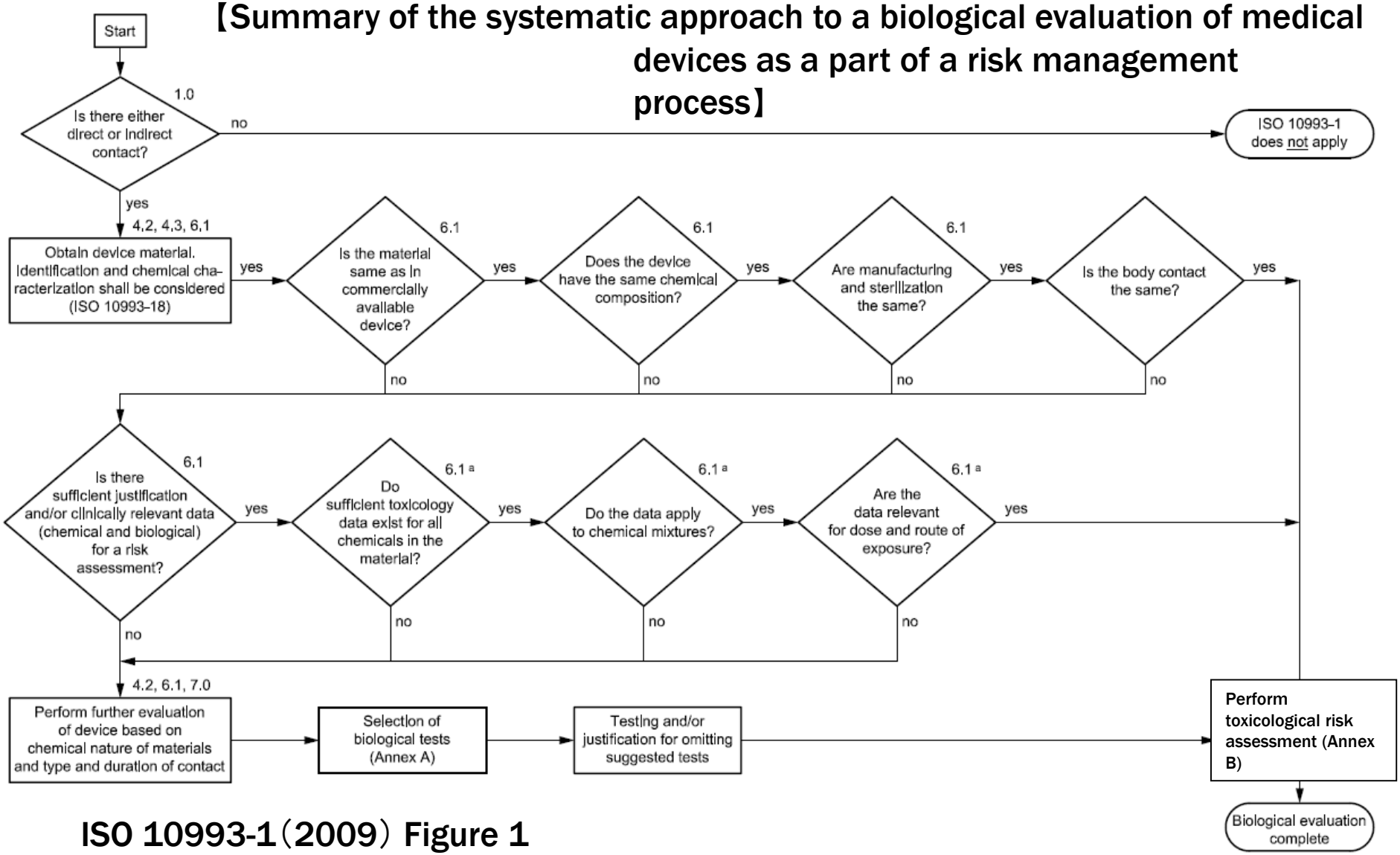
4. Assessment of toxicological risk

← Test results, NOAEL data, tolerable daily intake

5. Documentation: ISO 10993 overall biological safety assessment report

ISO 10993-1　EVALUATION FLOWCHART

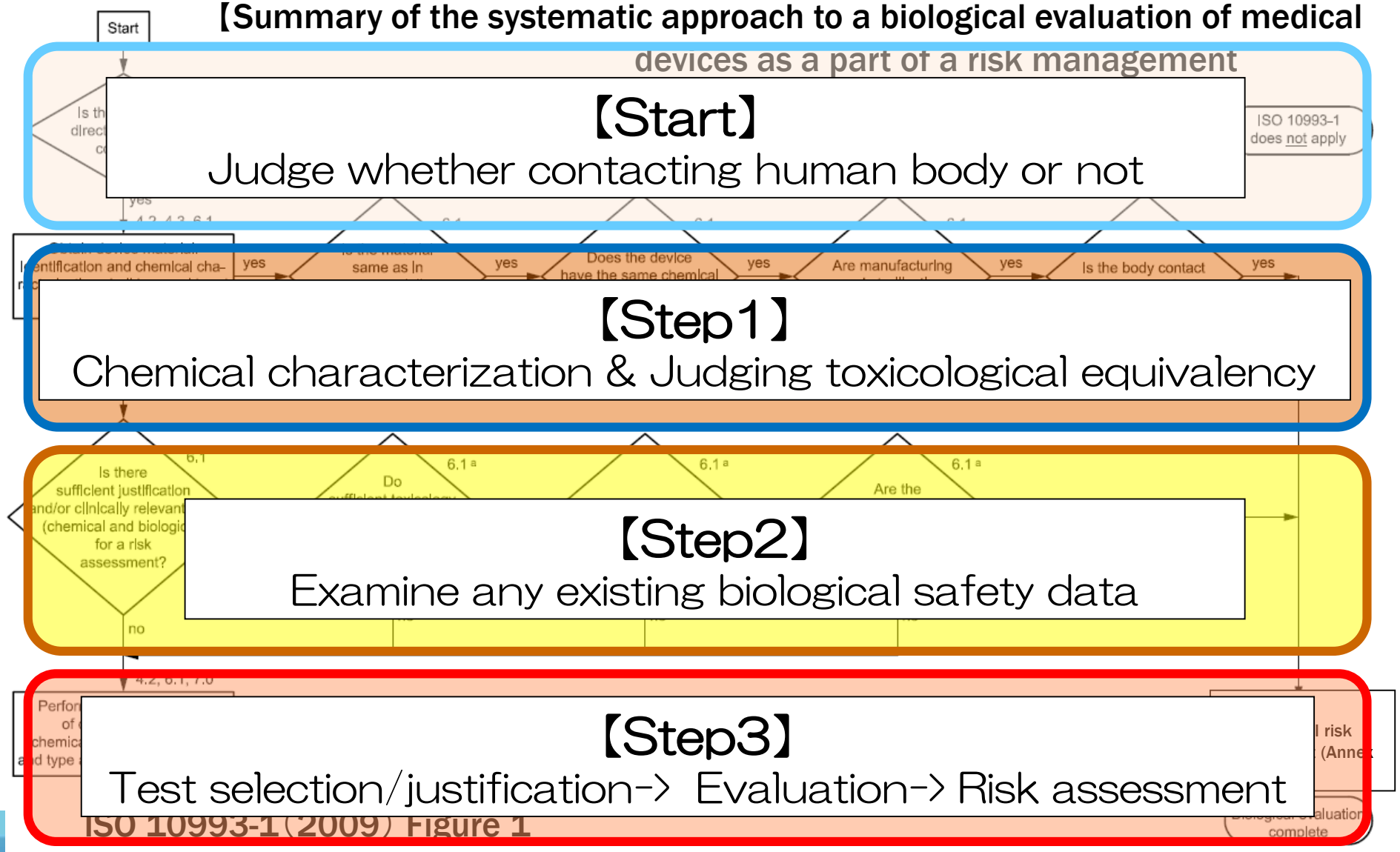
【Summary of the systematic approach to a biological evaluation of medical devices as a part of a risk management process】



ISO 10993-1（2009）Figure 1

ISO 10993-1　EVALUATION FLOWCHART

【Summary of the systematic approach to a biological evaluation of medical devices as a part of a risk management



【Start】
Judge whether contacting human body or not

【Step1】
Chemical characterization & Judging toxicological equivalency

【Step2】
Examine any existing biological safety data

【Step3】
Test selection/justification-> Evaluation-> Risk assessment

THE LATEST ACTIVITIES OF ISO/TC194

Progressing situation of revision work of ISO/TC194 in 2015-16

Current standards /working group	Title	Present Status*				
ISO 10993-1 (2009,10) /WG1	Systematic approach to evaluation	NWIP	WD	CD	DIS	FDIS
ISO 10993-5 (2009) /WG5	Cytotoxicity	NWIP	WD	CD	DIS	FDIS
ISO 10993-11 (2006) /WG7	Systemic toxicity	NWIP	WD	CD	DIS	FDIS
ISO 10993-4 (2002,6) /WG9	Effects on blood	NWIP	WD	CD	DIS	FDIS
ISO 10993-6 (2007) /WG10	Implantation	NWIP	WD	CD	DIS	FDIS

* NWIP: New Work Item Proposal, WD: Working Draft, CD: Committee Draft, DIS: Draft International Standard, FDIS: Final Draft International Standard

《UNDER DEVELOPMENT》 N38: ISO/WD 10993-1

SYSTEMATIC APPROACH TO EVALUATION

The main points of change from ISO 10993-1: 2009

- Adding the “Physico-chemical information” endpoints required for all categories of medical devices.
- The testing of “Physico-chemical information” and “Cytotoxicity” shall be conducted unless justified.
- Adding the “Chronic toxicity,” “Carcinogenicity,” “Reproductive / developmental toxicity,” and “Biodegradation” endpoints.
- Adding “Indirect, Packaging” to medical device categorization.

Medical device categorization by				Aspects of biological evaluation													
Nature of Body Contact		Contact Duration A – limited (≤24 h) B – prolonged (>24 h to 30 d) C – Long term (> 30 d)	Physico-Chemical Information	Cytotoxicity	Sensitization	Irritation or Intracutaneous Reactivity	Material Mediated Pyrogenicity	Systemic Acute Toxicity	Subacute Toxicity	Subchronic Toxicity	Chronic Toxicity	Implantation ‡	Hemocompatibility	Genotoxicity	Carcinogenicity	Reproductive/Developmental Toxicity#	Biodegradation@
Category	Contact																
Indirect	Packaging	NA	X	X													
Surface device	Intact skin	A	X	X	O	O											
		B	X	X	O	O											
		C	X	X	O	O											
	Mucosal membrane	A	X	X	O	O											
		B	X	X	O	O	O	O	O			O					
		C	X	X	O	O	O	O	O	O	O	O		O			
	Breached or compromised surface	A	X	X	O	O	O	O									
		B	X	X	O	O	O	O	O			O					
		C	X	X	O	O	O	O	O	O	O	O		O			
External communicating device	Blood path, indirect	A	X	X	O	O	O	O					O				
		B	X	X	O	O	O	O	O				O				
		C	X	X	O	O	O	O	O	O	O	O	O	O	O		
	Tissue/bone/ dentin+	A	X	X	O	O	O	O									
		B	X	X	O	O	O	O	O			O		O			
		C	X	X	O	O	O	O	O	O	O	O		O	O		
	Circulating blood	A	X	X	O	O	O	O					O	O			
		B	X	X	O	O	O	O	O			O	O	O			
		C	X	X	O	O	O	O	O	O	O	O	O	O	O		
Implant device	Tissue/bone	A	X	X	O	O	O	O									
		B	X	X	O	O	O	O	O			O		O			
		C	X	X	O	O	O	O	O	O	O	O		O	O		
	Blood	A	X	X	O	O	O	O	O	O	O	O	O	O			
		B	X	X	O	O	O	O	O			O	O	O			
		C	X	X	O	O	O	O	O	O	O	O	O	O	O		

N38: ISO/WD 10993-1 （2015）

CONCLUSION

STANDARDS DEVELOPMENT IN JAPAN

The Japanese domestic committee for ISO/TC194 has organized in MT Japan composed of the experts from the industry, government, and academia, which positively attends international conferences to support the development of ISO standards.

Advantage

- Real-time responses: Under the advancement of medical devices and the development of testing technology, we can make possible information sharing concerning the progress of documents development.
- Synchronized: The regulators and experts from the industry can work jointly and efficiently toward the same purpose.

-> Contribute to global harmonization of Japanese regulations

CONCLUSION

As advanced medical devices are developing in the world, the importance of the biological safety evaluation grows.

- ISO/TC194 develops international standards based on the latest scientific information. Use of these standards would make possible high-level biological safety evaluations.
- A globally-harmonized reviewing process of medical devices based on ISO 10993 is needed for speeding up the review time and improving animal welfare.

Recent cases
（Requirements from MFDS）

RECENT CASES（REQUIREMENTS FROM MFDS）

- Submit the material specification and MSDS of the materials which do not have direct or indirect contact with the patient's body <The materials which do not have contact with the human body need no evaluation>

- Require to conduct biological safety testing of the medical devices confirmed equivalent to an approved device <Equivalency verification is an important step of ISO 10993>

- Reject the data from the biological safety testing using mock samples (e.g., coupons) and require to conduct additional testing using the final products <Use of mock samples is acceptable if scientifically justified>

JFMDA
The Japan Federation of
Medical Devices Associations

ご清聴有難うございました

Thank you for your attention

당신의 관심을 가져 주셔서 감사합니다.

Korea Good Manufacturing Practice for Medical Device

Rachel Kim Vice Chair
International relations committee
Korea Medical Device Industry Association
June 23, 2016

Contents

- KGMP history
- KGMP certification process
- KGMP audit flow
- KGMP audit type
- Required document for KGMP audit
- Q&A

KGMP History

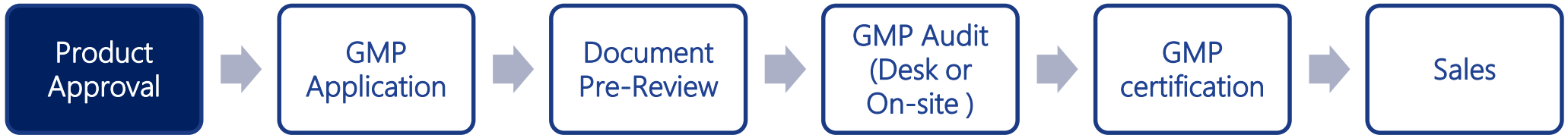
- '04 Introduction of GMP (Partial implementation)
- '07 Full GMP implementation
- '12 On-Site GMP Audit for Foreign Manufacturing Sites
- '16 GMP certification before product approval

Accumulated KGMP certified sites

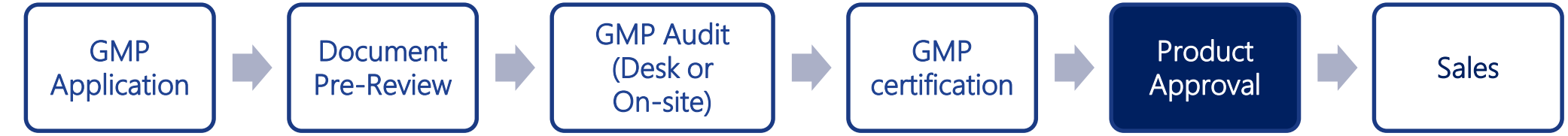
	'04	'05	'06	'07	'08	'09	'10	'11	'12	'13	'14	'15.10
Total (Accumulated)	21	281	752	2,471	2,721	3,022	3,525	3,551	3,671	3,775	3,901	4,038
Manufacture	11	157	440	1,312	1,460	1,637	1,985	1,983	2,065	2,167	2,247	2,365
Import	10	124	312	1,159	1,261	1,385	1,540	1,568	1,606	1,608	1,654	1,673

KGMP certification process

- **Old Policy** : GMP certification Prior to **Sales**

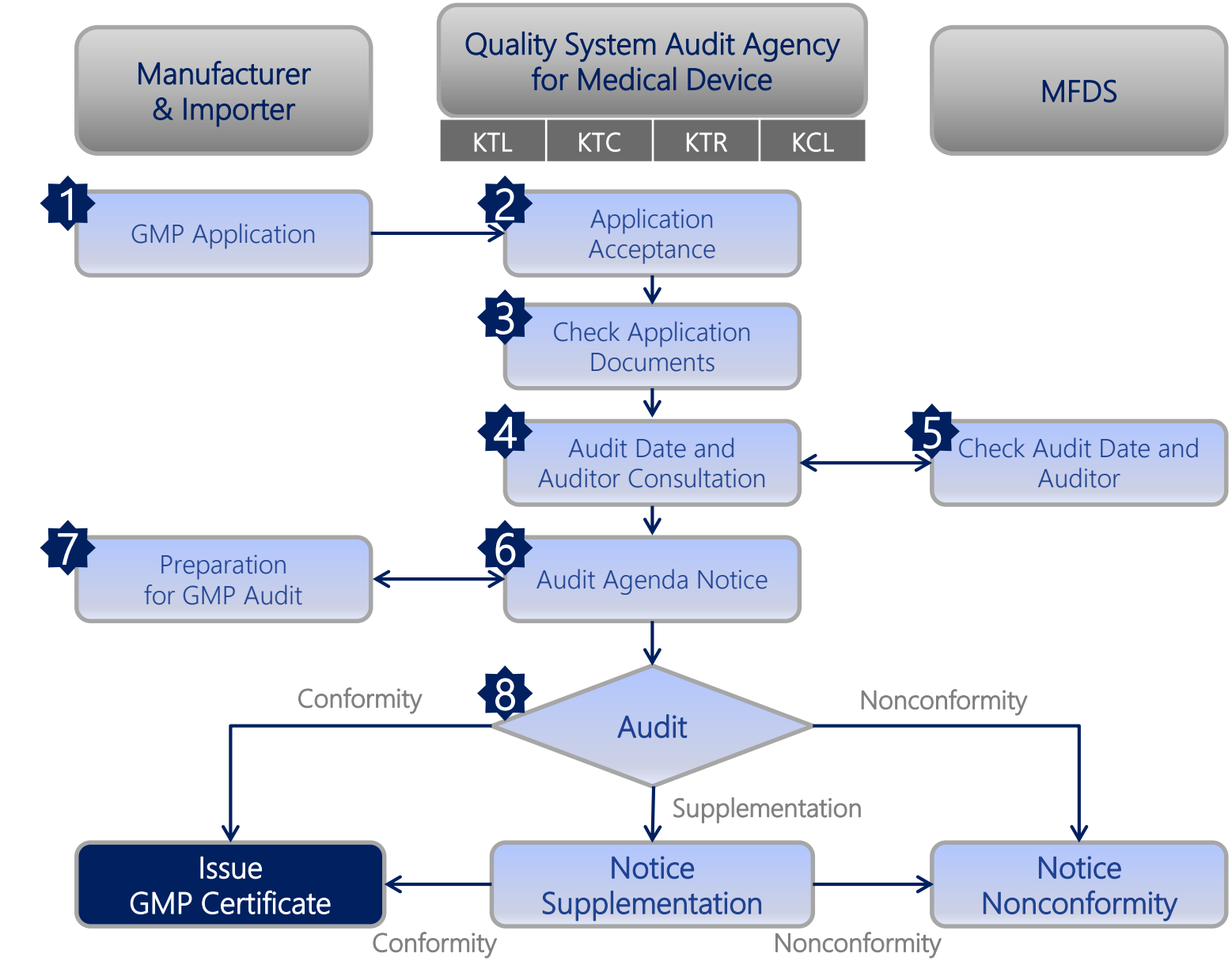


- **Current Policy** : GMP certification before product approval (implemented as of Jan. 29, 2016)



GMP Application	Document Pre-Review	GMP Audit (Desk or On-site)	GMP certification	Product Approval	Sales
• Application form • Required docs submission (e.g., business license, quality manual, DMR) • Audit type decision	• Review application form & submitted docs • Check Audit type • On site audit arrangement	• On-site Audit Document review & on site audit by Audit agency • Desk Audit Audit agency → MFDS → Audit agency	• Conformity Issue GMP Certificate • Supplementation Notify to supplement → Check in 30 days → Issue GMP Certificate • Nonconformity	• Product approval process and GMP certification process can go parallel	• Sales

KGMP Audit Flow



KGMP audit type

TYPE		DESCRIPTION	Medical Device Class		
			2	3	4
NEW SITE	INITIAL audit	**Any new manufacturer** who intends to sell medical device in Korea shall be KGMP certificated	On-Site audit	On-Site audit WITH MFDS	On-Site audit WITH MFDS
NEW CATEGORY	ADDITIONAL audit	**Any new category** of product is produced at the registered manufacturer, the manufacturer shall be KGMP re-certificated with QMS for new category of product before product approval	Desk* audit	Desk* audit	Desk* audit
SITE RELOCATIO N	CHANGE audit	**Any relocation** of registered manufacturer, the new manufacturer shall be KGMP re-certificated with QMS for new location before product approval	Desk* audit	Desk* audit	Desk* audit
RENEWAL	PERIODIC RENEWAL audit	**Any registered manufacturer shall be re-certificated by triennial audit.** This is batch renewal audit for pre-registered manufacturers at once. Submission document shall be submitted 3 months before expiry date of KGMP certificate. On-site inspection is required for 1 manufacturer.	On-Site audit	On-Site audit	On-Site audit WITH MFDS

* : on-site audit can be conducted

KGMP audit type

KGMP On-Site audit required for sites that..

1. has never been KGMP audited by MFDS
2. was selected for Triennial KGMP re-certification
3. can not provide required document for certification due to confidentiality
4. manufactures Newly developed device
5. had history of quality nonconformance or was determined as risk posing site that requires joint-audit with MFDS (in recent 3 years)

- Additional audit /Change audit
  - On-site audit can be conducted if 3,4,5
  - If applicant can not submit copy of valid QMS certificate issued by government or certified authority by government where site is located AND Audit report received from other certification authorities
- Initial audit

  Desk audit permitted if other importer holds valid KGMP certificate for the site (same expiry date)
- Periodic renewal audit

  Site will be selected based on highest import performance, highest risk class of device, that has never KGMP certified and 3,4,5

Required Documents for KGMP Audit

Physical Manufacturer

- Overview of manufacturing site (Name and Address)
- Total number of employee dedicated to manufacturing/Quality related tasks (including Organization chart)
- Medical device list manufactured
- Major supplier name, address and its work scope (including contract manufacturer)
- Copy of QMS certificate issued by government or authority designated by government where manufacturing site is located
- Manufacturer facility overview (including floor plan, facility and equipment list)
- Quality manual (including quality policy)
- Audit report or audit summary document by other certification body
- Device Master Record (including special manufacturing process e.g. sterilization, software)
- Installation or service manual (in case required for product)

Legal Manufacturer

- Overview of manufacturing site (Name and Address)
- Copy of QMS certificate issued by government or authority designated by government where manufacturing site is located
- Audit report or audit summary document by other certification body
- Quality manual (including quality policy)
- Document that shows Legal manufacturer and physical manufacturer relationship

All quality document must be approved and effective under site QMS

Thank you!

Q&A