ISO 13485 and Japanese QMS Ordinance

2nd Korea-Japan Joint Symposium on Medical Product

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Vice-chairman of ISO/TC210 Japanese National Committee

Agenda

1. ISO/TC210

   a) ISO/TC210 Structure and Activities

   b) ISO/TC210 Japanese National Committee

2. History of QMS standards

3. Structure of Present Japanese QMS Ordinance

4. Major difference between ISO 13485:2016 and Japanese QMS ordinance

5. ISO 13485:2016 certification in Japanese regulation

6. Future of Japanese QMS Ordinance

ISO/TC210

ISO/TC 210
    "Quality management and corresponding general
    aspects for medical devices"

- Established in 1994

- Member
    – P member   38 countries

                    (including KOREA and JAPAN)

    – O member   17 countries
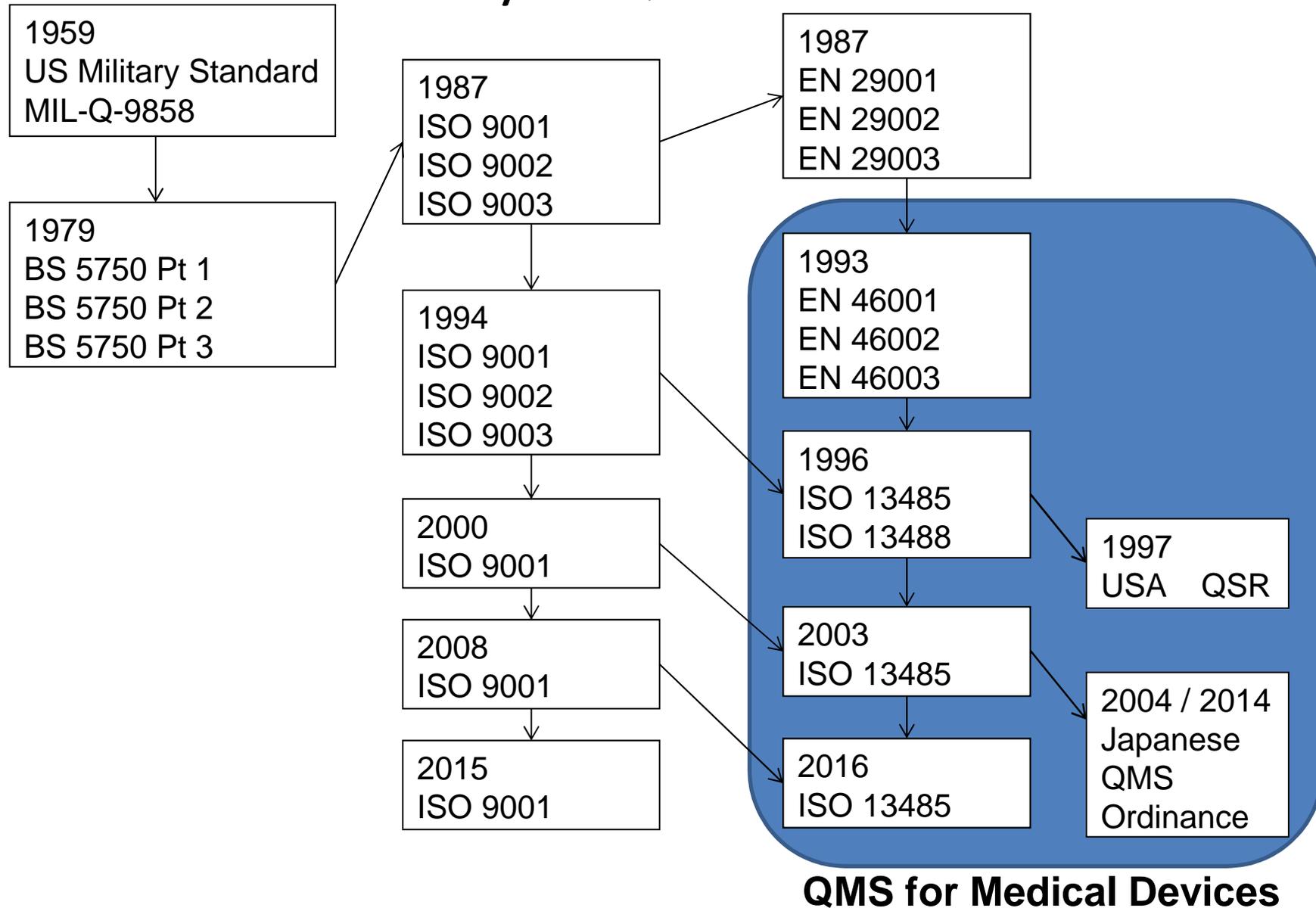
WGs of ISO/TC210

- **WG 01**
  "Application of quality systems to medical devices"   ISO 13485
- WG 02
  "General aspects stemming from the application of quality principles to medical devices"
- WG 03
  "Symbols and nomenclature for medical devices"
- WG 06
  "Application of post market surveillance systems to medical devices"

- JWG 01
  "Joint ISO/TC 210-IEC/SC 62A WG ; Application of risk management to medical devices"
- JWG 02
  "Joint ISO/TC 210-IEC/SC 62A WG ; Medical device software"
- JWG 03
  "Joint ISO/TC 210-IEC/SC 62A WG ; Medical device usability"

- JWG 04
  "Joint ISO/TC 210-IEC/SC 62D; Small bore connectors"
- WG 05
  "Connectors for reservoir delivery systems"

History of QMS Standards

1959
US Military Standard
MIL-Q-9858

1979
BS 5750 Pt 1
BS 5750 Pt 2
BS 5750 Pt 3

1987
ISO 9001
ISO 9002
ISO 9003

1994
ISO 9001
ISO 9002
ISO 9003

2000
ISO 9001

2008
ISO 9001

2015
ISO 9001

1987
EN 29001
EN 29002
EN 29003

1993
EN 46001
EN 46002
EN 46003

1996
ISO 13485
ISO 13488

2003
ISO 13485

2016
ISO 13485

1997
USA   QSR

2004 / 2014
Japanese
QMS
Ordinance

QMS for Medical Devices

TC210 Japanese National Committee

- Same Committee/WG Structure as TC210
  - TC210 Japanese National Committee
    - TC210/WG1 Japanese National Sub-Committee
    - TC210/WG2 Japanese National Sub-Committee
    - ·····························

- Chairman   Dr. Tei (Prof of Tokyo Univ.)
- Secretary   JFMDA
- Members   Academia
         Government(MHLW, PMDA)
         Industry (JFMDA)

Japanese QMS ordinance

- Present Japanese QMS ordinance is based on ISO 13485:2003 and have additional requirements.

- Design Control applies to class 2, 3, and 4

- QMS ordinance is also applied to class1 device but no pre-market inspection.

- QMS ordinance is applied both MAH and manufacturing site.

Structure of Japanese QMS Ordinance

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

Chapter 2 of Japanese QMS ordinance

	QMS Ordinance (Chapter 2)	ISO 13485:2003
Section 1	General Requirements (Article 4)	1. Scope
Section 2	Quality Management System (Article 5 to Article 9)	4. Quality management system
Section 3	Management responsibility (Article 10 to Article 20)	5. Management Responsibility
Section 4	Resource Management (Article 21 to Article 25)	6. Resource management
Section 5	Product Realization (Article 26 to Article 53)	7. Product realization
Section 6	Measurement, Analysis and Improvement (Article 54 to Article 64)	8. Measurement, analysis and improvement

ISO 13485:2016

- Purpose of the change
  - To reflect changes in regulatory requirements and expectations, current practices employed by medical device providers (e.g., manufacturers, distributors, and service providers) to ensure safe and effective medical devices that meet customer requirements.
  - To reflect changes to the ISO 9001:2008 standard on which this Standard is based.

Structure of New revision of ISO 13485

- New Revision of ISO 13485 is not followed Annex SL of ISO Directive because of this is not match Regulatory Purpose.

- Basic structure is identical to ISO 13485:2003.

- Correlation Matrix of ISO 9001:2015 and ISO 13485:2016 are described in Annex B.

- No. of Sub clause changed for MDSAP grading issue. (7.5.1 – 7.5.11)

Contents of ISO 13485:2016

Foreword

Introduction

1. **Scope**
2. **Normative references**
3. **Terms and definitions**
4. **Quality management system**
5. **Management Responsibility**
6. **Resource management**
7. **Product realization**
8. **Measurement, analysis and improvement**

Annex A (informative) Comparison of content between ISO 13485:2003 and ISO 13485:2016

Annex B (informative) Correspondence between ISO 13485:2016 and ISO 9001:2015

Bibliography

Major difference
between ISO 13485:2016 and QMS ordinance

4.1 General requirements

4.1.2 (QMS Processes)

<Risk based thinking>

- The organization shall:

a) determine the processes needed for the quality management system and the application of these processes throughout the organization **taking into account the roles undertaken by the organization;**

b) **apply a risk based approach to the control of the appropriate processes needed for the quality management system;**

c) determine the sequence and interaction of these processes.

Major difference
between ISO 13485:2016 and QMS ordinance

4.1 General requirements

    4.1.6

    New Requirement (Expanded)

    (Validation of the application of QMS software)

- **The organization shall document procedures for the validation of the application of computer software used in the quality management system. Such software applications shall be validated prior to initial use and, as appropriate, after changes to such software or its application.**
- **The specific approach and activities associated with software validation and revalidation shall be proportionate to the risk associated with the use of the software.**
- **Records of such activities shall be maintained (see 4.2.5).**

Major difference
between ISO 13485:2016 and QMS ordinance

4.2.3 Medical Device File

 New requirement

 = "SEIHIN HYOJUNSYO" in Japanese QMS ordinance

(concept is already in 2003 version /New sub-clause)

- For each medical device type or medical device family, the organization shall establish and maintain one or more files either containing or referencing documents generated to demonstrate conformity to the requirement of this International Standard and compliance with applicable regulatory requirements.

- The content of the file(s) shall include, but is not limited to:

a)   general description of the medical device, intended use/purpose, and labelling, including any instructions for use;

b)   specifications for product;

c)   specifications or procedures for manufacturing, packaging, storage, handling and distribution;

d)   procedures for measuring and monitoring;

e)   as appropriate, requirements for installation;

f)   as appropriate, procedures for servicing.

Major difference
between ISO 13485:2016 and QMS ordinance

7.3 Design and development

    7.3.1 General

    7.3.2 Design and development planning

    7.3.3 Design and development inputs

    7.3.4 Design and development outputs4

    7.3.5 Design and development review

    7.3.6 Design and development verification

    7.3.7 Design and development validation

    7.3.8 Design and development transfer **(New Sub-clause)**

    7.3.9 Control of design and development changes

    7.3.10 Design and development files **(New Sub-clause)**

Major difference
between ISO 13485:2016 and QMS ordinance

7.5.8 Identification

Added requirement for unique device identification(UDI).

- The organization shall document procedures for product identification and identify product by suitable means throughout product realization.
- The organization shall identify product status with respect to monitoring and measurement requirements throughout product realization. Identification of product status shall be maintained throughout production, storage, installation and servicing of product to ensure that only product that has passed the required inspections and tests or released under an authorized concession is dispatched, used or installed.
- **If required by applicable regulatory requirements, the organization shall document a system to assign unique device identification to the medical device.**
- The organization shall document procedures to ensure that medical devices returned to the organization are identified and distinguished from conforming product.

Major difference
between ISO 13485:2016 and QMS ordinance

8 Measurement, analysis and improvement

    8.1 General.

    8.2 Monitoring and measurement

        8.2.1 Feedback

        8.2.2 Complaint handling　　　　　　　　**(New Sub-clause)**

        8.2.3 Reporting to regulatory authorities　　**(New Sub-clause)**

        8.2.4 Internal audit

        8.2.5 Monitoring and measurement of processes

        8.2.6 Monitoring and measurement of product

    8.3 Control of nonconforming product **(re-arranged)**

        8.3.1 General

        8.3.2 Actions in response to nonconforming product detected before delivery

        8.3.3 Actions in response to nonconforming product detected after delivery

        8.3.4 Rework

    8.4 Analysis of data

    8.5 Improvement
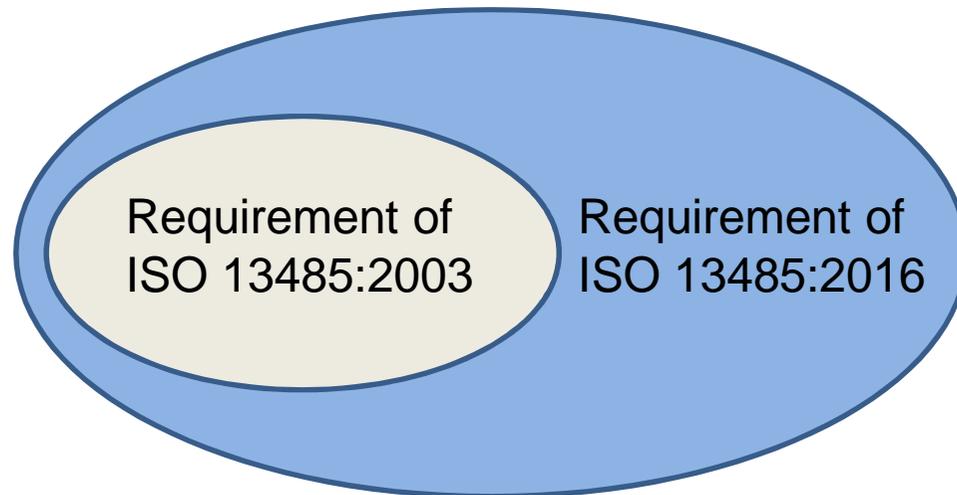
        8.5.1 General

        8.5.2 Corrective action

        8.5.3 Preventive action

ISO 13485:2016 certification
in Present Japanese Regulation

- Compliance to ISO 13485:2016 is considered to comply to the Chapter 2 of Japanese QMS Ordinance.

(Administrative Circular 2016/July)

Requirement of ISO 13485:2003

Requirement of ISO 13485:2016

事　務　連　絡
平成 28 年 7 月 29 日

各都道府県衛生主管部（局）薬務主管課　御中

厚生労働省医薬・生活衛生局監視指導・麻薬対策課

QMS調査における ISO 13485 の改訂の取扱いについて

「医療機器及び体外診断用医薬品の製造管理及び品質管理の基準に関する省令」（平成 16 年厚生労働省令第 169 号。以下「QMS省令」という。）第2章とISO13485:2003 の各要求事項との整合については、「薬事法等の一部を改正する法律の施行に伴う医療機器及び体外診断用医薬品の製造管理及び品質管理の基準に関する省令の改正について」（平成 26 年 8 月 27 日付け薬食監麻発 0827 第4号厚生労働省医薬食品局監視指導・麻薬対策課長通知）及び「QMS調査要領の制定について」（平成 26 年 10 月 24 日付け薬食監麻発 1024 第 10 号厚生労働省医薬食品局監視指導・麻薬対策課長通知）により取扱い等が示されているところです。
　今般、平成 28 年 3 月 1 日付けで IS013485:2016 が発効し、IS013485:2003 からの移行期間は発効日から 3 年間とされたことから、QMS省令第 2 章の規定と IS013485:2016 の各条項の関係について、下記のとおり取り扱うこととしますので、貴管内の関係業者、関係団体等に対し、その旨周知いただきますよう御配慮願います。
　なお、本事務連絡の写しを各地方厚生局、独立行政法人医薬品医療機器総合機構、一般社団法人日本医療機器産業連合会、一般社団法人日本臨床検査薬協会、一般社団法人米国医療機器・IVD 工業会、欧州ビジネス協会医療機器委員会、欧州ビジネス協会臨床検査機器・試薬（体外診断）委員会及び医薬品医療機器等法登録認証機関協議会宛て送付することとしています。

記

ISO13485:2016 は、IS013485:2003 で規定されていたプロセスアプローチに基づく品質管理監督システムによる管理及びそれを構成する基本的な要素が変更されたものではないことを踏まえ、IS013485:2016 に基づき適切に製造管理及び品質管理が行われている場合は、当面の間、QMS省令第 2 章に適合しているとみなすものとする。

Future of Japanese QMS ordinance

- JIS Q 13485:201X(=ISO 13485:2016) will be issued soon.
- Health Labor Science Research Study Group for Medical Device QMS (Chair: Dr Sakurai/PMDA)
  - Research gaps between ISO 13485:2016 and Japanese QMS ordinance.
  - Recommend to introduce ISO 13485:2016 to Japanese QMS ordinance to MHLW.
- It is expected that Japanese QMS ordinance will harmonize with ISO 13485:2016 / Global QMS standard soon.

Guidance for ISO 13485:2016

- WG1 drafted the ISO 13485 handbook for ISO 13485:2016 guidance.
- The draft version of this Handbook circulated for CIB and passed CIB (positive 28, negative 1)
- Handbook Writing Team is working resolve the comment for draft version now.

- This handbook draft will issue for final 1 month ballot soon and final version will be published in June 2017.

- ISO/TC210/WG1 Japanese National sub-committee will translate this handbook to Japanese and issue it soon after the final version is published.

Questions ?

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Quality Management System(QMS) for Medical Devices in Korea

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- AHWP WG member

Korea
Ministry of Food and
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Quality Management System (QMS)

Table of Contents

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I. Status of Korea Medical Device Industry

Rank	Country	2013 Market scale(Mn)
1	USA	127,159
2	Japan	28,208
3	Germany	25,554
4	China	16,075
⋮		
11	Korea	5,083

Rank	Country	2014 Market scale(Mn)
1	USA	133,593
2	Japan	28,100
3	Germany	26,256
4	China	17,207
⋮		
10	Korea	5,441

Rank	Country	2015 Market scale(Mn)
1	USA	140,143
2	Japan	26,012
3	Germany	22,667
4	China	17,773
⋮		
9	Korea	5,503

ranking it 9th in global market

※ Ref : Espicom. The World Medical Markets Fact Book 5, Forecasts to 2018
    Unit: US Million Dollars

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I. Status of Korea Medical Device Industry

About 5,800 medical device manufacturers & importers in 2016

Number of medical device business entities

	2010	2011	2012	2013	2014	2015	2016.6
Manufacturer	2,168	2,245	2,550	2,711	2,993	3,272	3,406
Importer	1,626	1,662	1,898	2,027	2,239	2,365	2,459
Total	3,794	3,907	4,448	4,738	5,232	5,637	5,865

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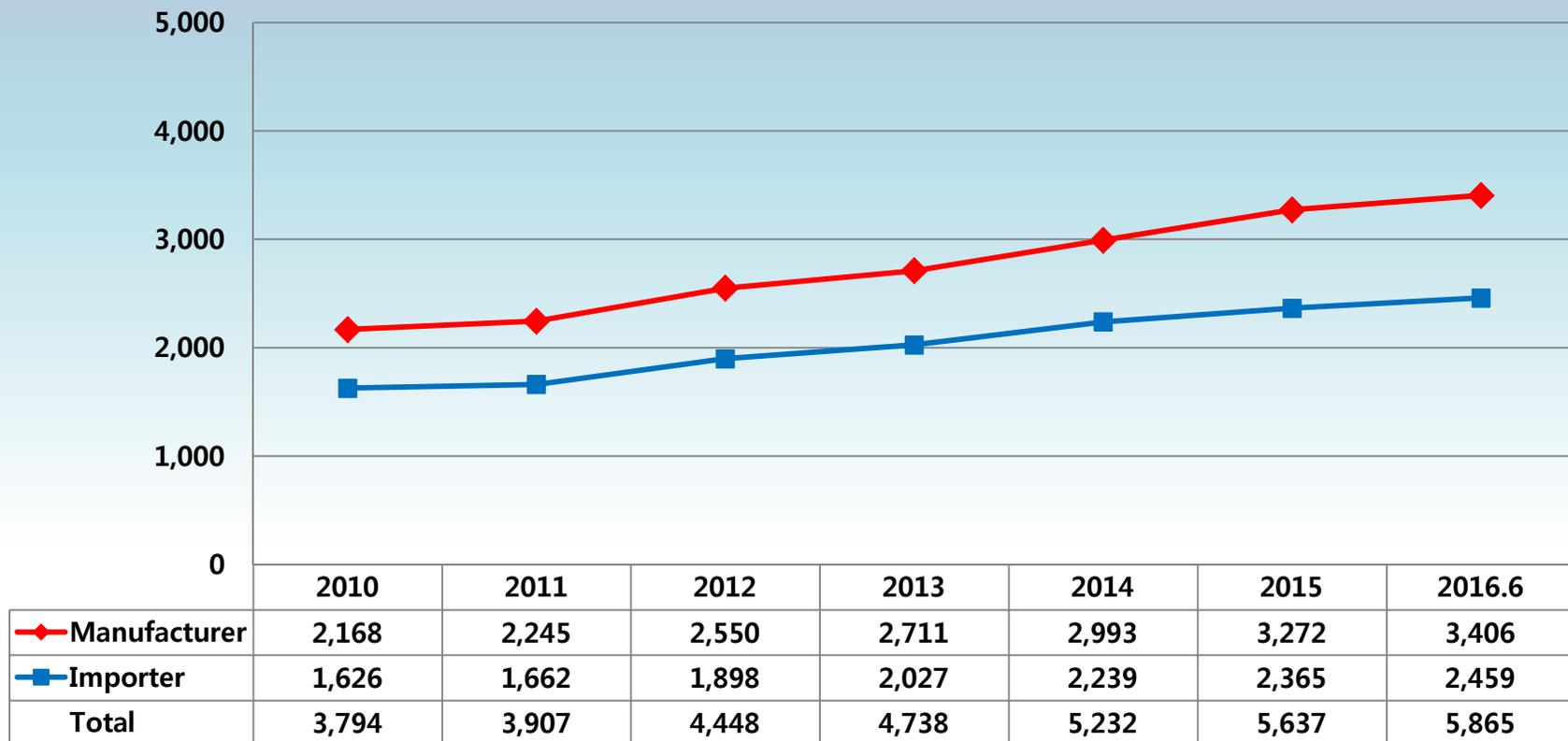
I. Status of Korea Medical Device Industry

Statistic Result on KQMS Audit

Legend: Manufaturer, Importer, Total

- 2007: 2,979
- 2008: 1,202
- 2009: 1,530
- 2010: 2,770
- 2011: 1,908
- 2012: 1,885
- 2013: 2,372
- 2014: 1,762
- 2015: 2,403

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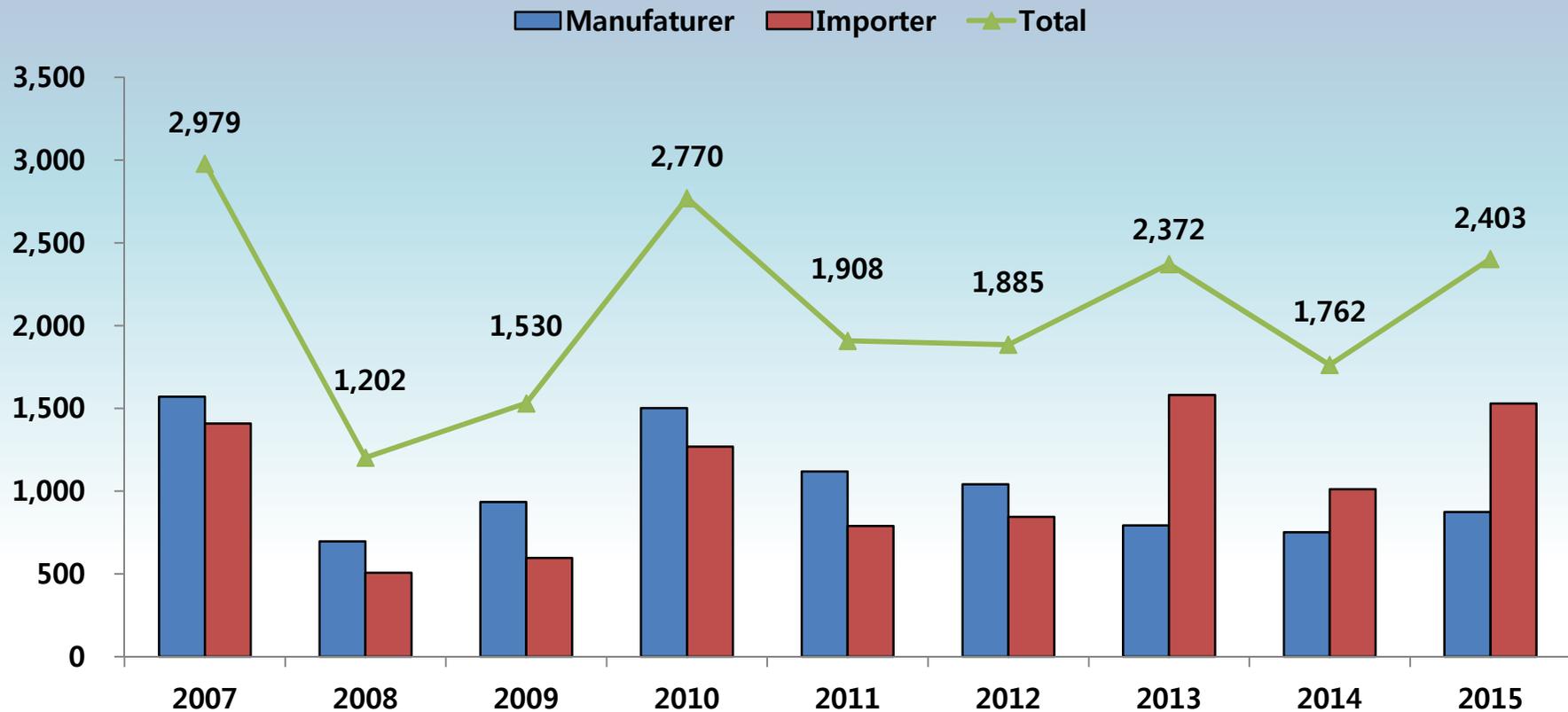
II. Organization and Regulations for medical device QMS
- Changed responsibility of MFDS & KFDA -

| Clinical Trials | → | Approval, Manufacturing | → | Distribution | → | Patient (Consumer) |

NOW | **MFDS** | **Make regulations and policies as a control tower of medical device safety management**

2013 - ⬆ **Combination of policy and enforcement**

Before

(MoH) | **To establish policies and draft laws regarding medical device safety management**

+

(KFDA) | **GCP** | **QMS** | **GSP** | **Post-market surveillance**

Only responsible for legal enforcement and management related to medical devices
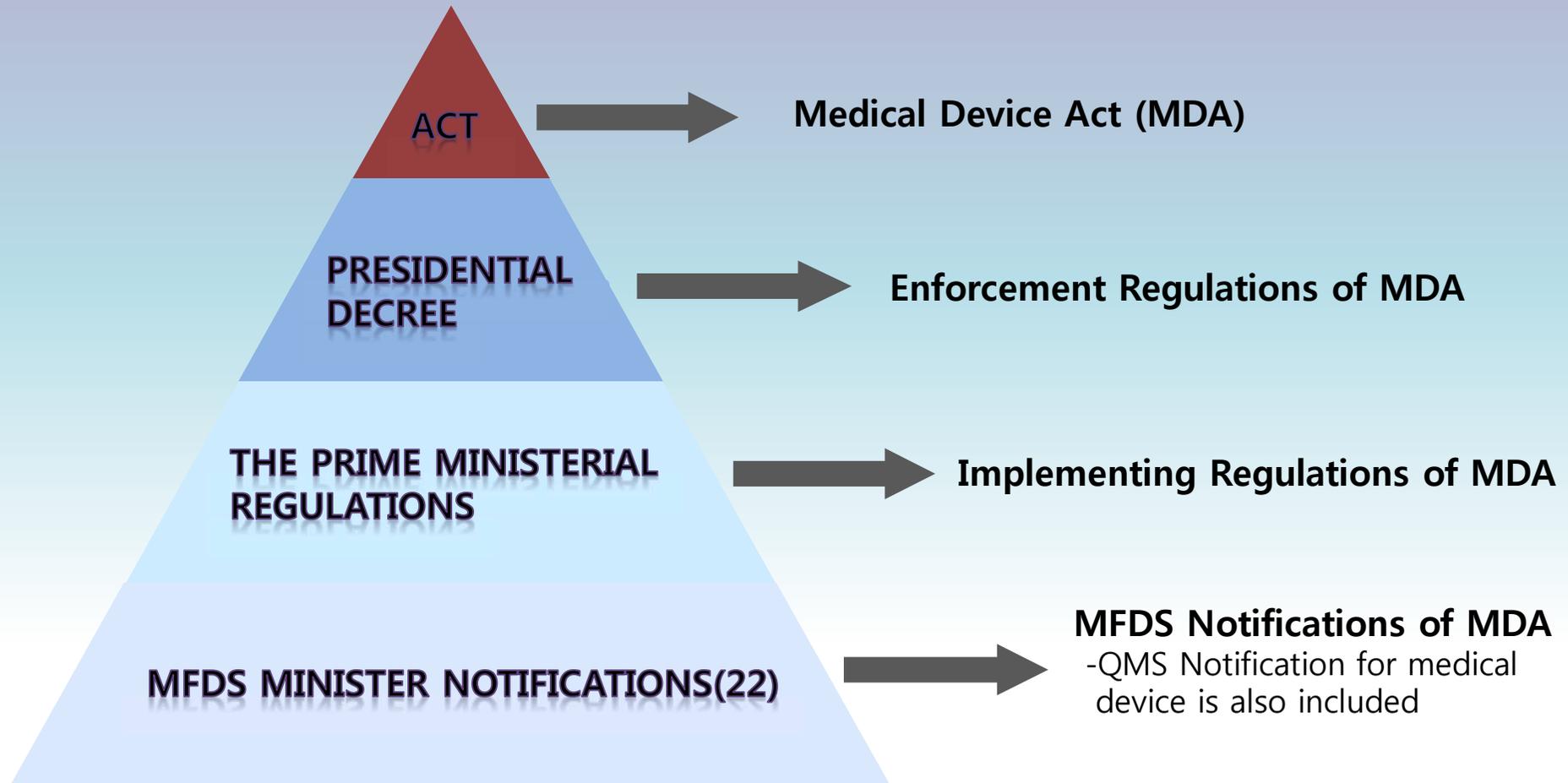
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II. Organization and Regulations for medical device QMS
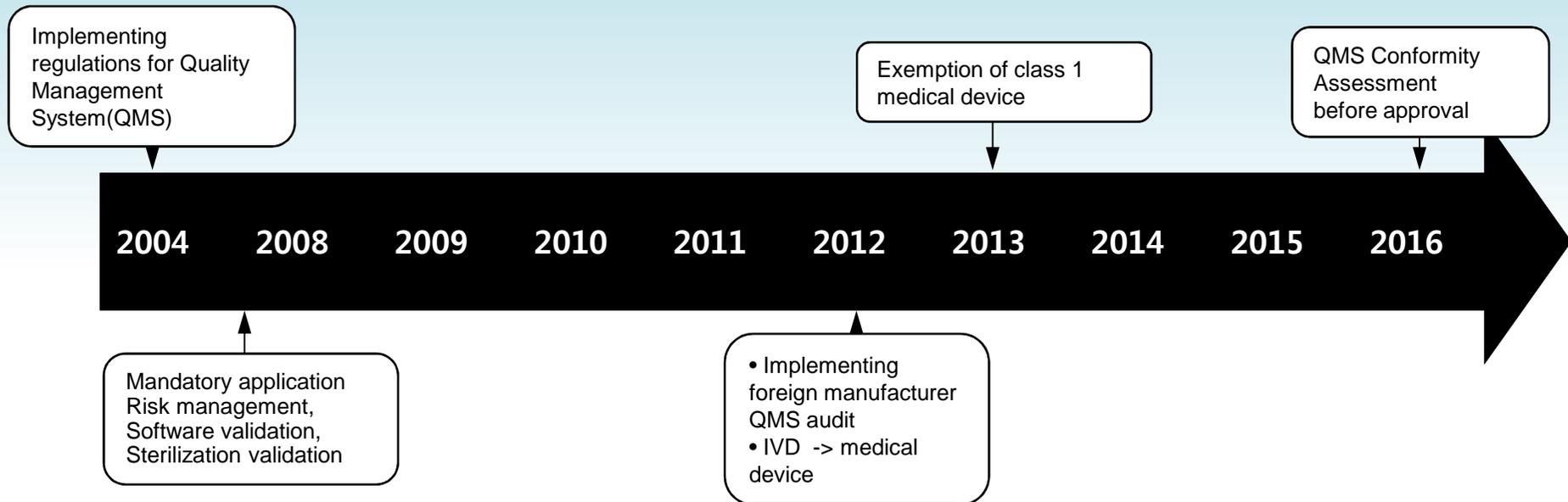## - Organizational Chart for QMS Control of MD in Korea MFDS -

Medical device Safety Evaluation Division (QMS Control tower_MFDS, 2)

Third-party Organization (40)

- Korea Testing Laboratory(KTL, 9)
- Korea Testing & Research Institute(KTR, 13)
- Korea Testing Certification(KTC, 11)
- Korea Conformity Laboratory(KCL, 7)

Cooperation Group(MFDS, 40)

- Six Regional Branch Offices(15) (Medical Product Safety Division)
- NIFDS (25) (National Institute of Food & Drug Safety Evaluation)

- High-tech medical devices division
- Cardiovascular devices division
- Orthopedic & Restorative devices division
- Dental & Gastroenterology devices division
- In vitro diagnostic device division

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II. Organization and Regulations for medical device QMS

– Medical Device Regulations at Four Hierarchical Orders –

ACT ➡ **Medical Device Act (MDA)**

PRESIDENTIAL DECREE ➡ **Enforcement Regulations of MDA**

THE PRIME MINISTERIAL REGULATIONS ➡ **Implementing Regulations of MDA**

MFDS MINISTER NOTIFICATIONS(22) ➡ **MFDS Notifications of MDA**
-QMS Notification for medical device is also included

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III. History and Regulation of Korea QMS

① **'04.05.30** : First Introduced the MD QMS regulation

② **'07.05.31** : QMS audits including S/W validation and risk management were set to be mandatory

③ **'12.04.08** : QMS audits have been conducted on oversea manufacturing companies

④ **'13.09.16** : Class 1 medical device were exempted from QMS audits

⑤ **'16.01.28** : QMS conformity assessment before medical deivce approval

Implementing regulations for Quality Management System(QMS)

Exemption of class 1 medical device

QMS Conformity Assessment before approval

| 2004 | 2008 | 2009 | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 | 2016 |

Mandatory application Risk management, Software validation, Sterilization validation

• Implementing foreign manufacturer QMS audit
• IVD -> medical device

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III. History and Regulation of Korea QMS
- Korea QMS regulation in details -

○ **Applied standard :** The standard for Korea QMS conformity assurance audit, equivalent to **ISO 13485 : 2003.**

○ **Target :**
① A person who is going to manufacture or import medical devices (including overseas manufacturer company) => Initial audits
② Periodic audits every 3 years on manufactures where initial audits were conducted

○ **Audit types :**
① Initial audit : An initial audit to approve QMS conformity assurance
② Periodic audit : After the initial audit, at least one audit will be conducted in 3 years
③ Audit of approval changes : Audits to be conducted again if manufacturers notify changes of manufacturing sites.
④ Supplementary audit : Audits to be conducted if a product is added from a different product group.

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III. History and Regulation of Korea QMS
- Korea QMS regulation in details -

○ **Audit method :** Conducting on-site audits and document review for each

   product groups of manufacturing company

   ※ Product group : Products whose raw materials, manufacturing process and quality
                      management system are similar to those of which have been classified
                      into 26 group

○ **Certification period : 3 years** (QMS conformity certification should be renewed)

○ **Miscellaneous information :**

   ① Low-risk class 1 medical devices **excluded**

   ② 6 regional offices and 4 medical device quality evaluation institutions are
      jointly conducting on-site audit and document review

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III. History and Regulation of Korea QMS

<The list of 26 product groups for Korea QMS conformity assurance>

Medical Device → classified → 2,200 Product items → Re-categorized → 26 Product groups

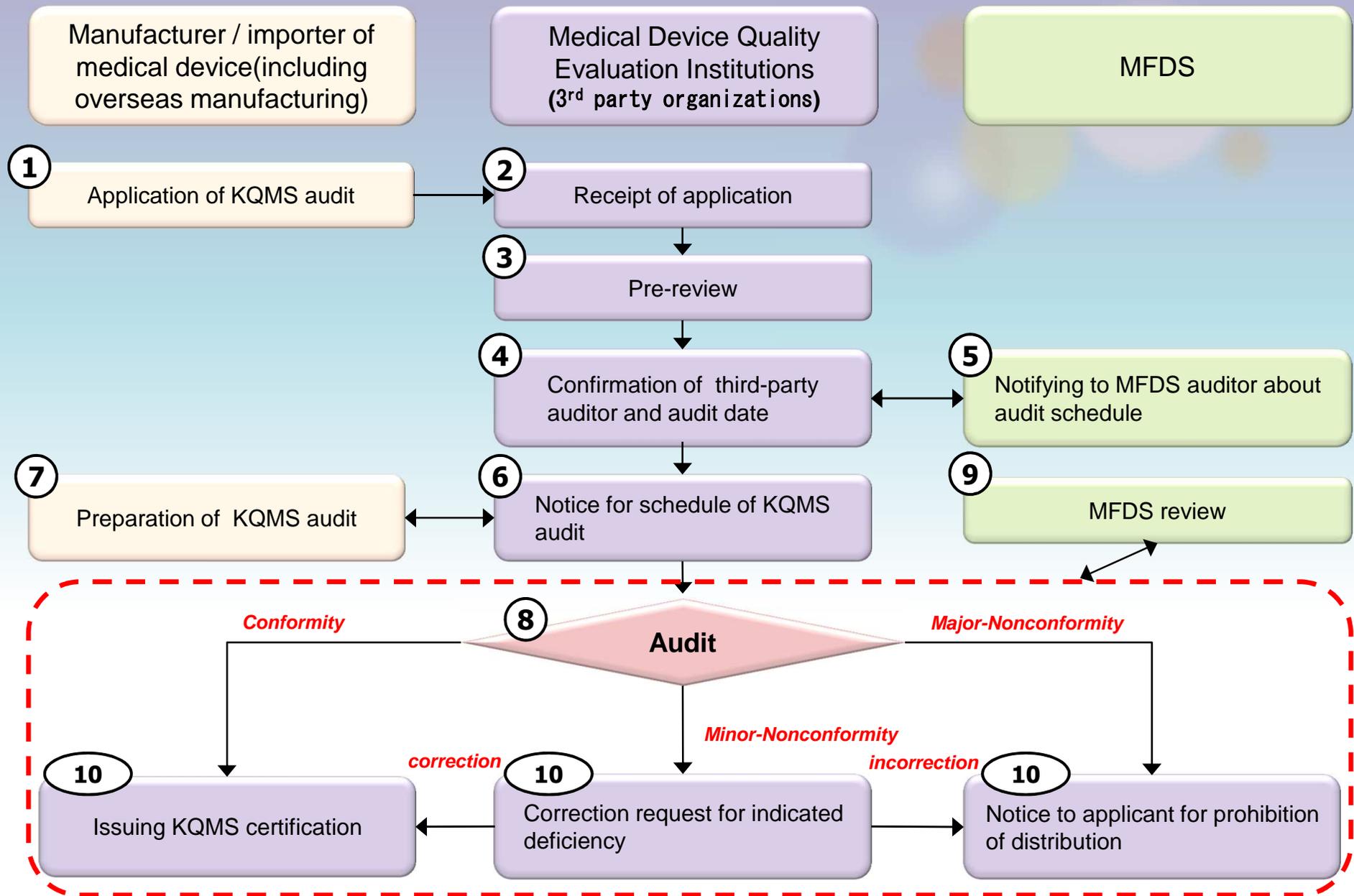| No.	Product Groups of Medical Devices	No.	Product Groups of Medical Devices
1	General Equipment for Treatment	14	Syringes and Needles
2	Surgical Devices	15	Instruments for Dental Treatment
3	Medical Chambers	16	Sight Corrective Ophthalmic Lens
4	Life-support System	17	Hearing Aid
5	Artificial Internal Organ	18	Medicinal Substance-Producing Equipment
6	Diagnostic Devices	19	Implantable Medical Supplies
7	Medical Stimulating Instruments	20	Human Tissue and Organ Substitute
8	Surgical Instruments	21	In Vitro Medical Supplies
9	Patient Transport	22	Contraceptive Device
10	Physiological Measuring Instruments	23	Dental Alloy
11	In Vitro Diagnostics	24	Materials for Dental Treatment
12	Speculums for Medical Use	25	Analyzing Products for In Vitro Diagnosis
13	Instruments for Medical Treatment	26	U-Healthcare Medical Device

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III. History and Regulation of Korea QMS

<The main body for QMS conformity audit in Korea>

	Classification	Initial Audit	Supplementary audit	Audit of approval change	Periodic Audit
Manufacturer or Importer of M.D	Class II	3rd party organizations			
	Class III	MFDS + 3rd party organizations			
	Class IV				

∗ Class I medical devices are not required to have a QMS conformity assessment.

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III. Medical Device QMS audit process

| Manufacturer / importer of medical device(including overseas manufacturing) | Medical Device Quality Evaluation Institutions (3rd party organizations) | MFDS |

1 Application of KQMS audit → **2** Receipt of application

3 Pre-review

4 Confirmation of third-party auditor and audit date ↔ **5** Notifying to MFDS auditor about audit schedule

7 Preparation of KQMS audit ↔ **6** Notice for schedule of KQMS audit

9 MFDS review

8 *Conformity* — **Audit** — *Major-Nonconformity*

Minor-Nonconformity

correction — *incorrection*

10 Issuing KQMS certification ← **10** Correction request for indicated deficiency → **10** Notice to applicant for prohibition of distribution

List of Published Guidelines for QMS

MFDS Guidelines describes specific requirements for QMS audits.

No.	The Title of Guidelines
1	Guidelines for **Software Validation** of Medical Devices
2	Guidelines for **Sterilization Validation** of Medical Devices
3	Guidelines for **Risk Management** of Medical Devices
4	HandbooK for QMS audit of Medical Devices
5	Guidelines for Installation Medical Devices
6	Guidelines for Packaging Process Validation of Medical Devices
7	Guidelines for Design Control of Medical Devices
8	Guidelines for Washing Process Validation of Medical Devices
9	Guidelines for Cleanliness Control of Medical Devices
10	Guidelines for Corrective action and Preventive action of Medical Devices
11	Guidelines for Raw Material Purchasing and Outsourcing Process Quality Control of Medical Devices
	etc.
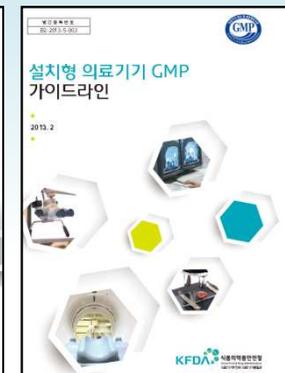
IV. Future Plan

❍ MFDS promotes to apply new ISO 13485, which was revised in March, 2016 to Korea QMS for medical devices.

❍ To promote harmonization and communication with global partners

- MFDS is going to publish an English version of "Standard of Medical Device Manufacturing and Quality Management(MFDS QMS Notification)" in early 2017

  ※ Requirement for QMS audits and audit methods & process will be described in this Standard.

❍ To harmonize and improve professionalism in QMS audit

- "Class 2 medical device" is going to be fully outsourced to third parties for QMS audit

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Thank you.

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Japanese QMS system/ Overview of MDSAP

Office of Manufacturing/Quality and Compliance Division of Medical Devices

Pharmaceuticals and Medical Devices Agency

Junichi Ohishi, Ph.D.

Organization Chart (As of April 1, 2017)

Manufacturing/Quality and Compliance

- Division of Medical Devices (QMS)
- Division of Pharmaceuticals (GMP)
- Division of Registered Certification Body Supervision
- Division of Administration

2
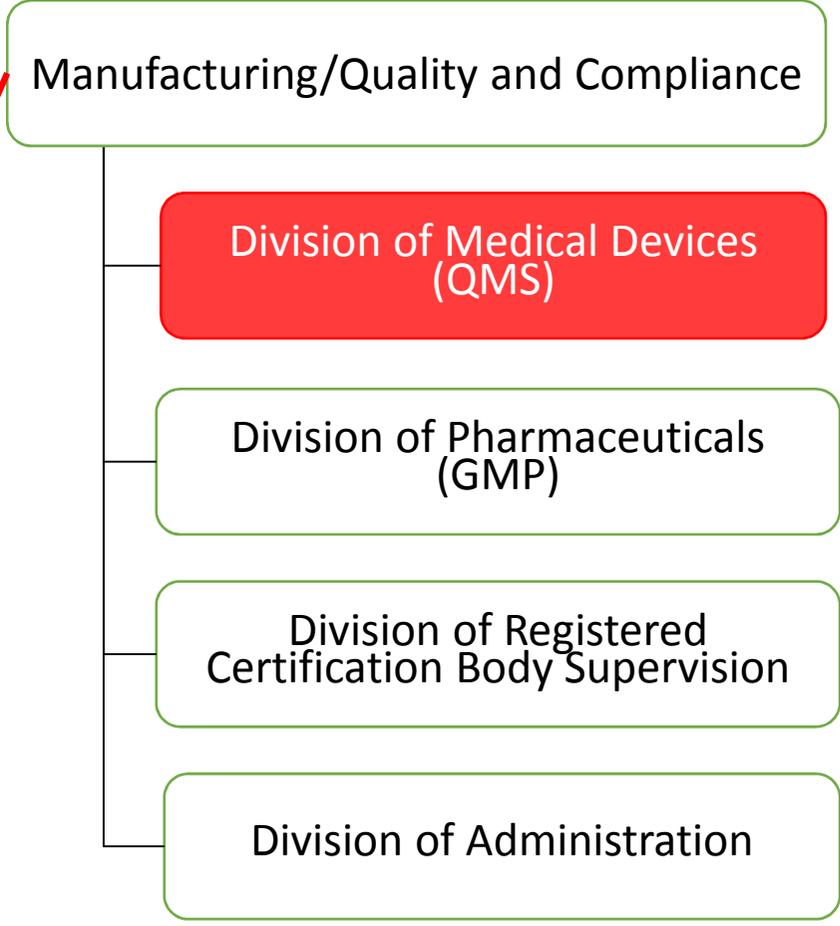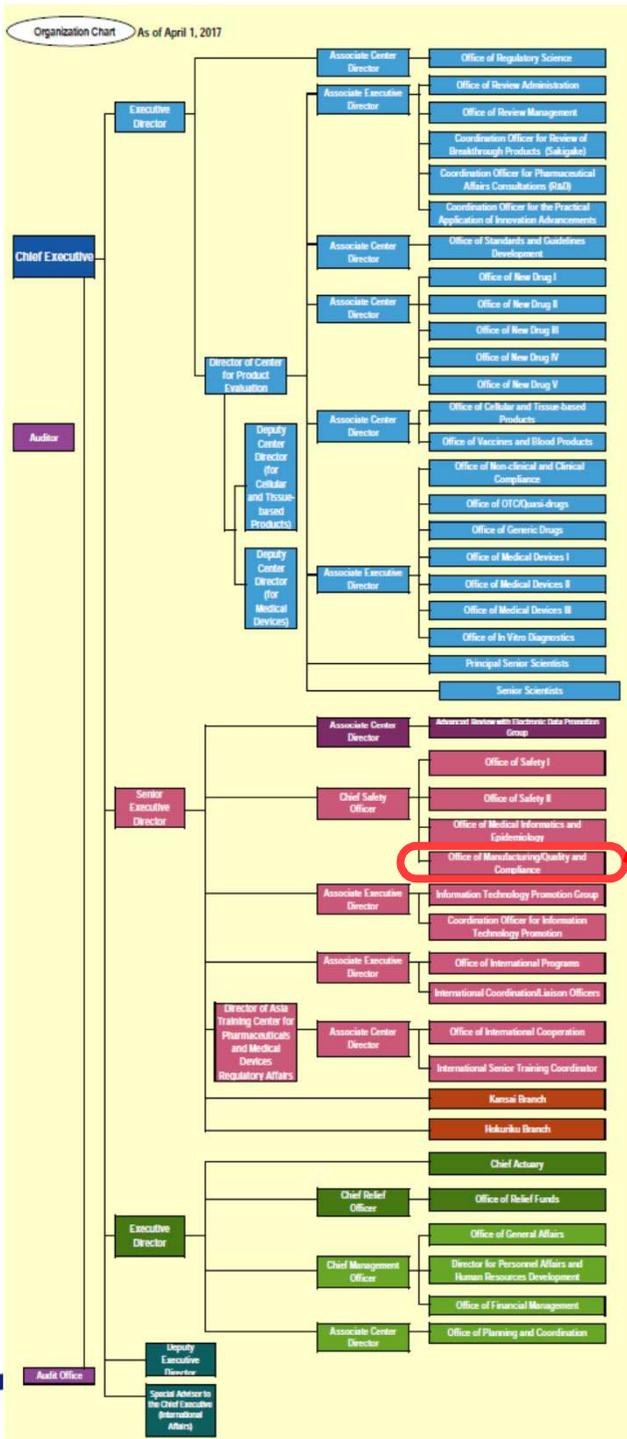
1. QMS Inspection

Outline of QMS Inspection

MAH and Manufacturing Sites

Marketing Authorization Holder (MAH)

QMS Application

Inspection (On-site or Desktop)

PMDA

Report

MHLW

Minister
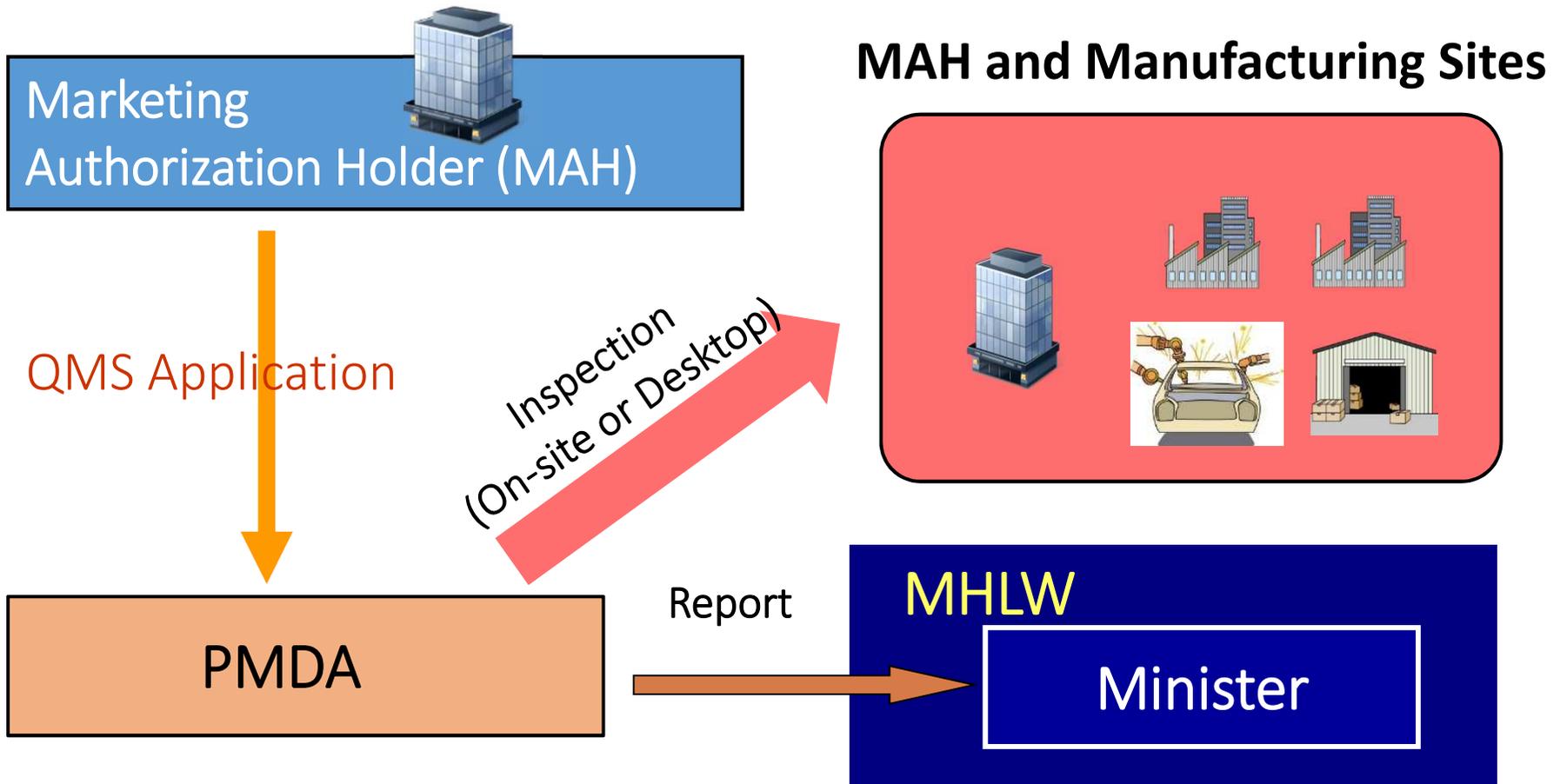
Types of QMS Inspection

1. Pre-Marketing Approval Inspection

Required before the marketing approval.

2. Pre-partial Change Approval Inspection

Required before the partial change approval.

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) biological products, micro machine and medical devices utilizing nano-materials etc.

Pre-Marketing Approval Inspection Periodic Post-approval Inspection

Application for
Marketing Approval

Marketing
Approval

Research & Development

Regulatory Review

Marketing

Pre-approval Inspection

Post-approval Inspection

Post-approval Inspection

5 years

5 years

5 years
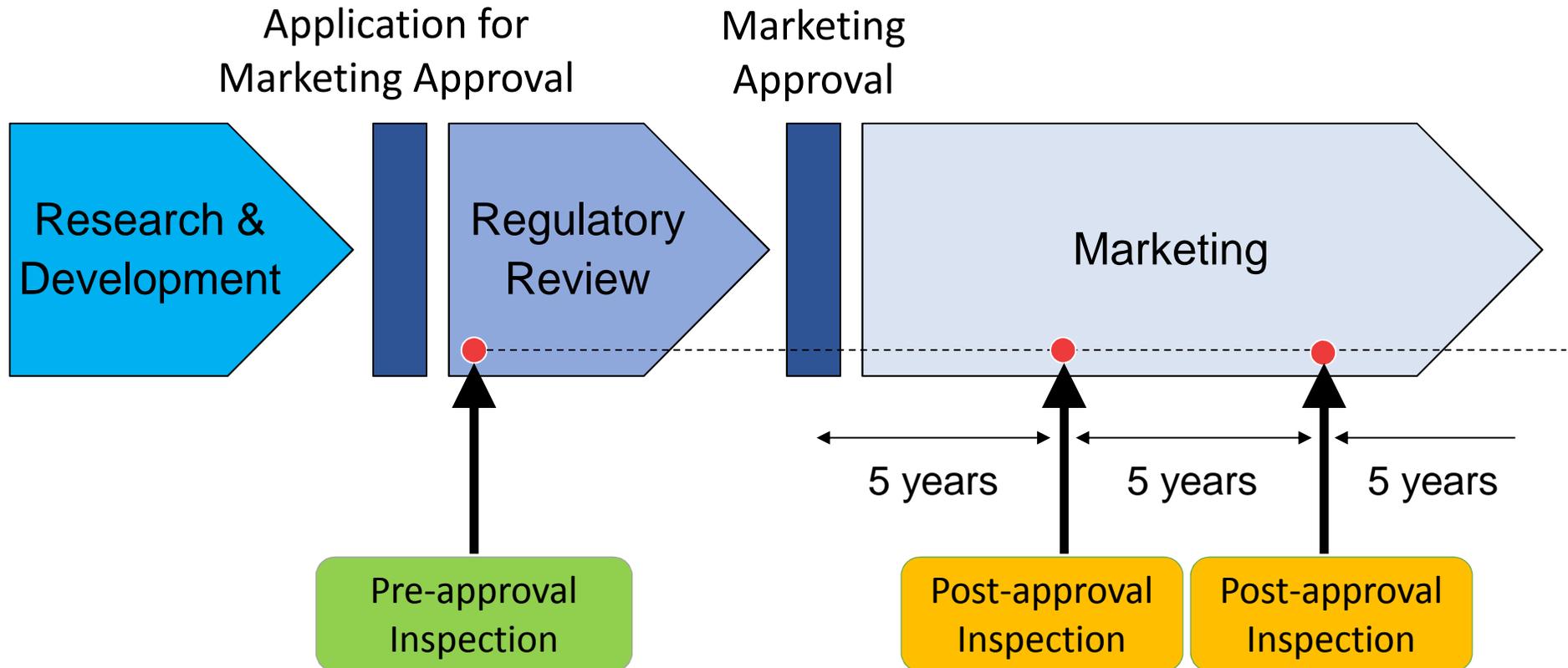
- Inspection scope : MAH and all the manufacturing sites.

- If the product is applicable to notified cases, the additional inspection is simultaneously conducted.

Pre-partial Change Approval Inspection

Marketing
Approval

Pre-partial change
Application

Pre-partial change
Approval

Marketing

Every 5 years

Pre-partial Change
Approval Inspection

Post-approval
Inspection

ex) Main assembling site
Change

- Inspection scope : MAH and the change-related sites.
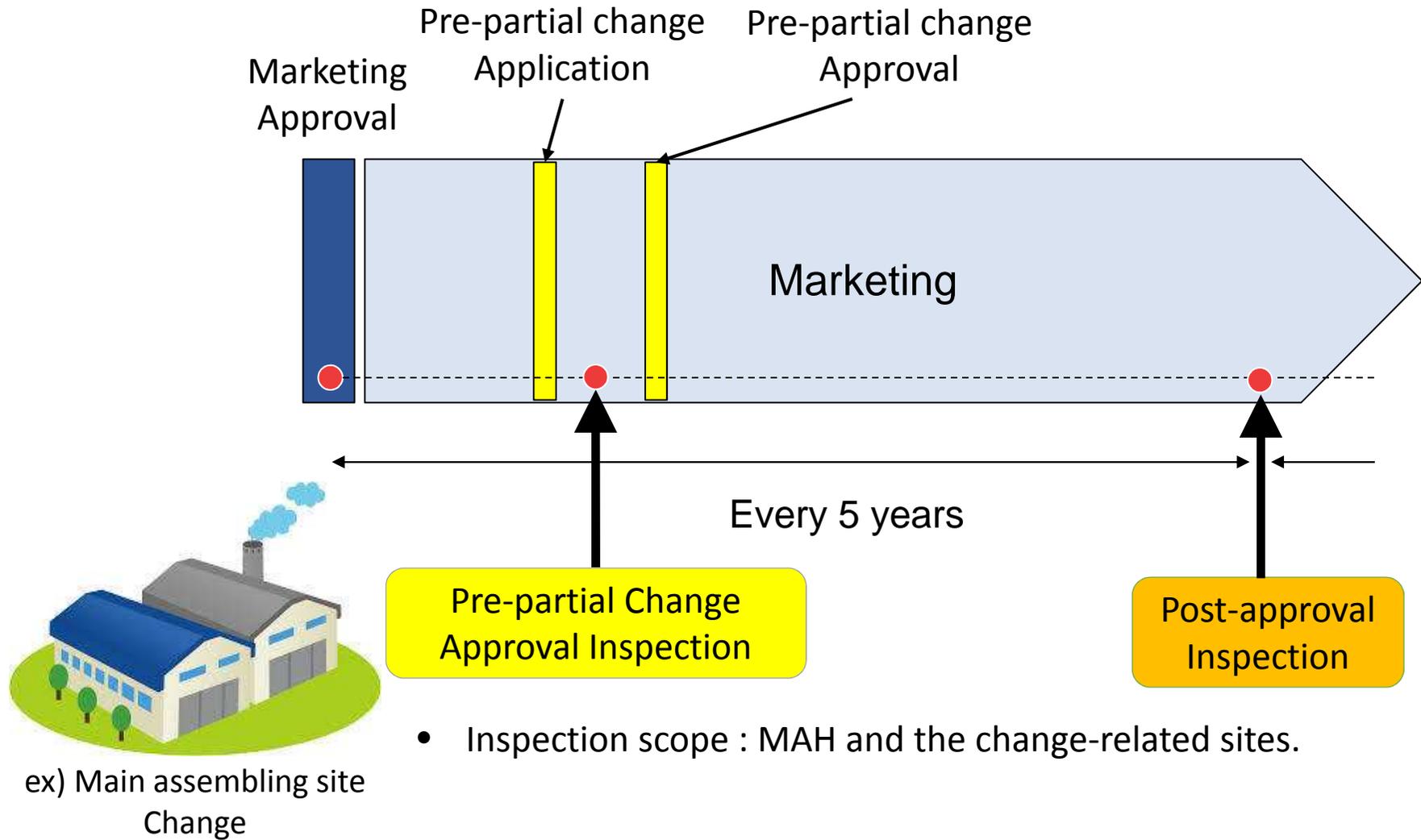
QMS Inspection Authority

Product		Inspection Authority
Medical Devices	• Class IV	PMDA
	• Class III and Class II <u>without CS</u>*	PMDA
	• Class III and Class II <u>with CS</u>*	Registered certification body
IVDs	• Products <u>without CS</u>*	PMDA
	• Products <u>with CS</u>*	Registered certification body

*CS : Certification Standards

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Manufacturing Site Registration

Manufacturing Site	Definition
Design Facility	(1) maintains records of design and development, and (2) the responsible person should work here.
Main Assembly Plant	(1) is mainly responsible for QMS or product realization, and (2) implement assembling (filling) processes.
Sterilizer	(1) implement sterilization process.
Domestic (Japan) Distribution Center	(1) store and release the products into Japanese market.
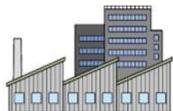
Example of Mfg. Site Registration
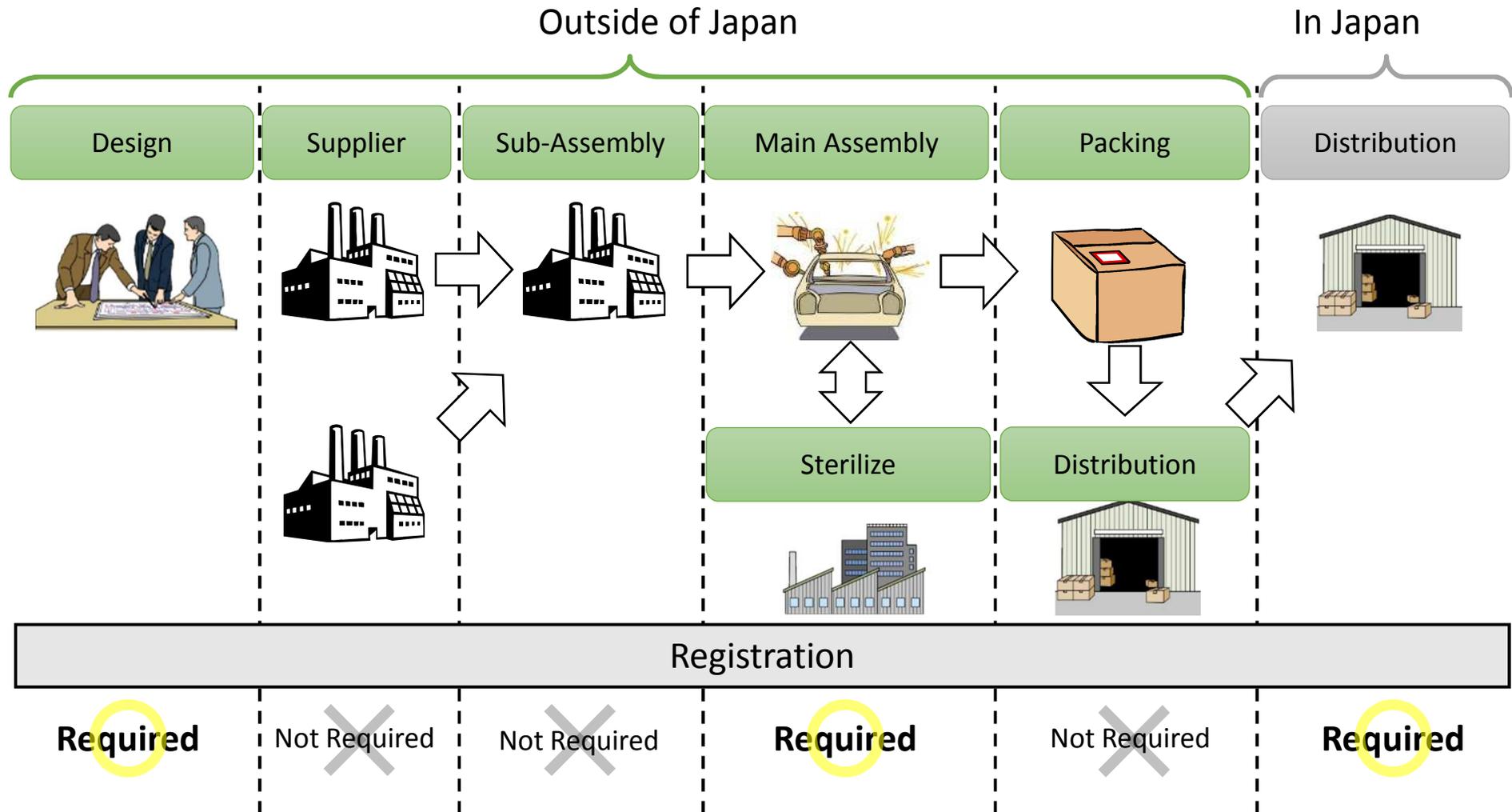
Scope of QMS Inspection

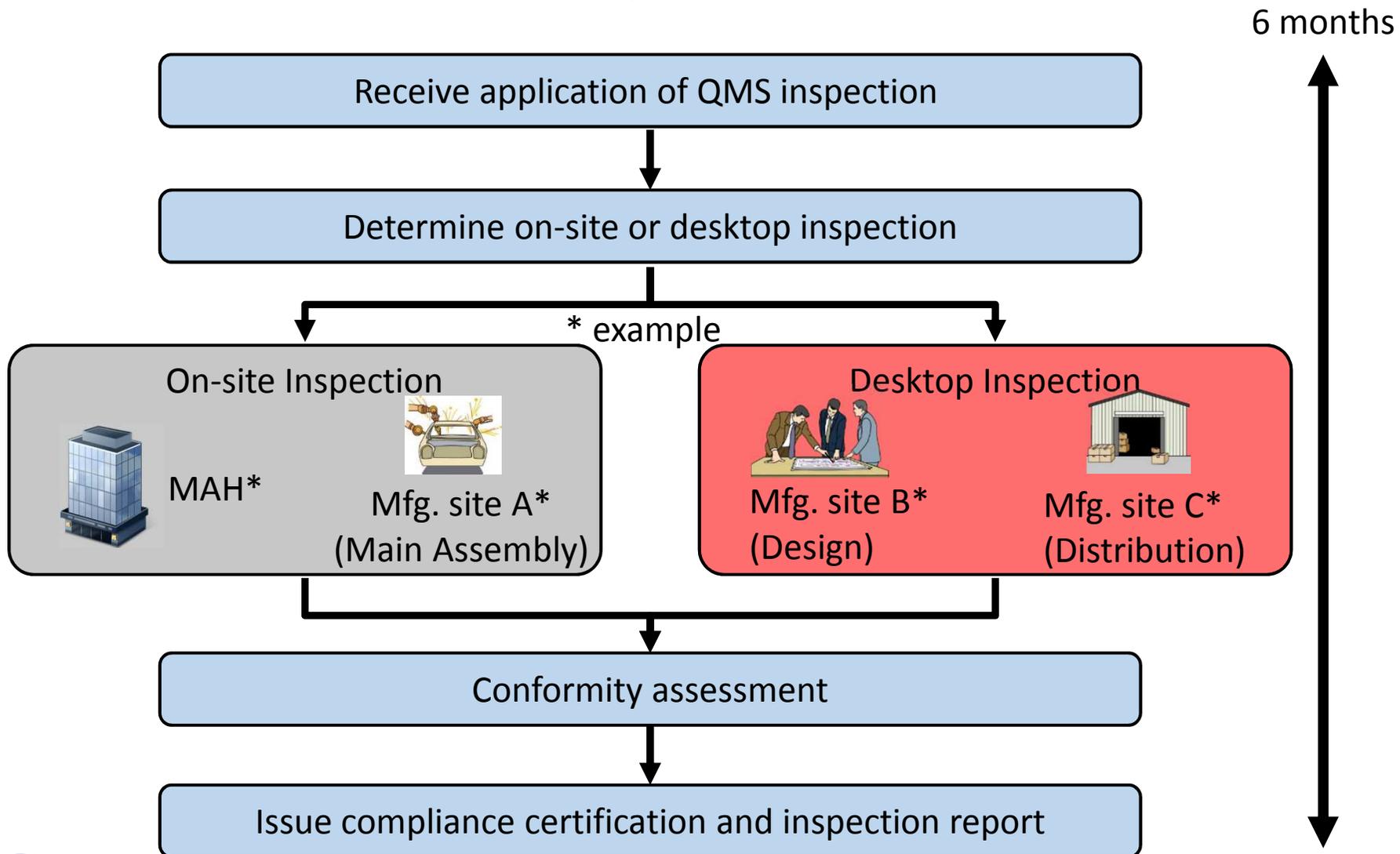|		QMS Inspection
	MAH	**Required**
	Design Facility	**Required**
	Main Assembly Plant	**Required**
	Sterilizer	**Required** only for sterile medical device
	Domestic (Japan) Distribution Center	**Required**
	Other sites	Depends PMDA determines based on risk assessment

QMS Application
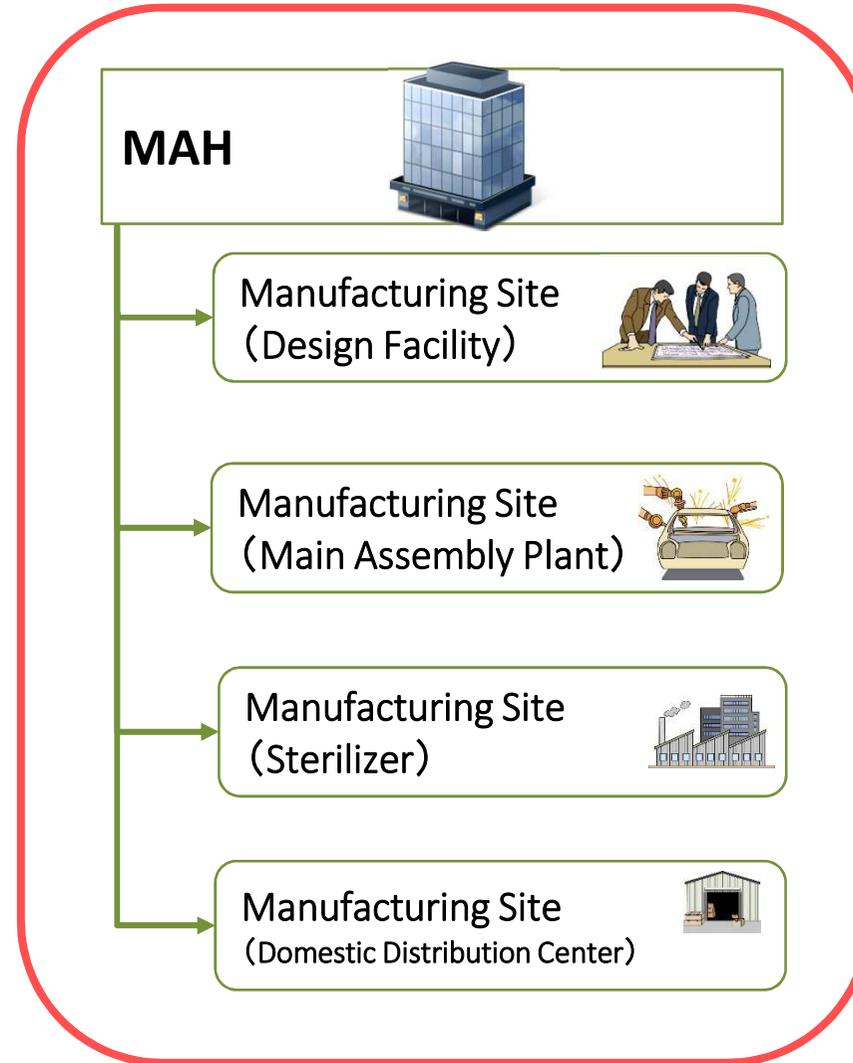
Product Families

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 Family".

Stent	**Catheter**	**Non-active instruments**
Coronary stent	Cardiovascular catheter	Single-use surgical knife
Carotid stent	Pulmonary artery catheter	Esophageal tube
Drug-eluting stents for femoral artery	Cerebrospinal catheter	Filter for pulmonary functional testing
⋮	⋮	⋮

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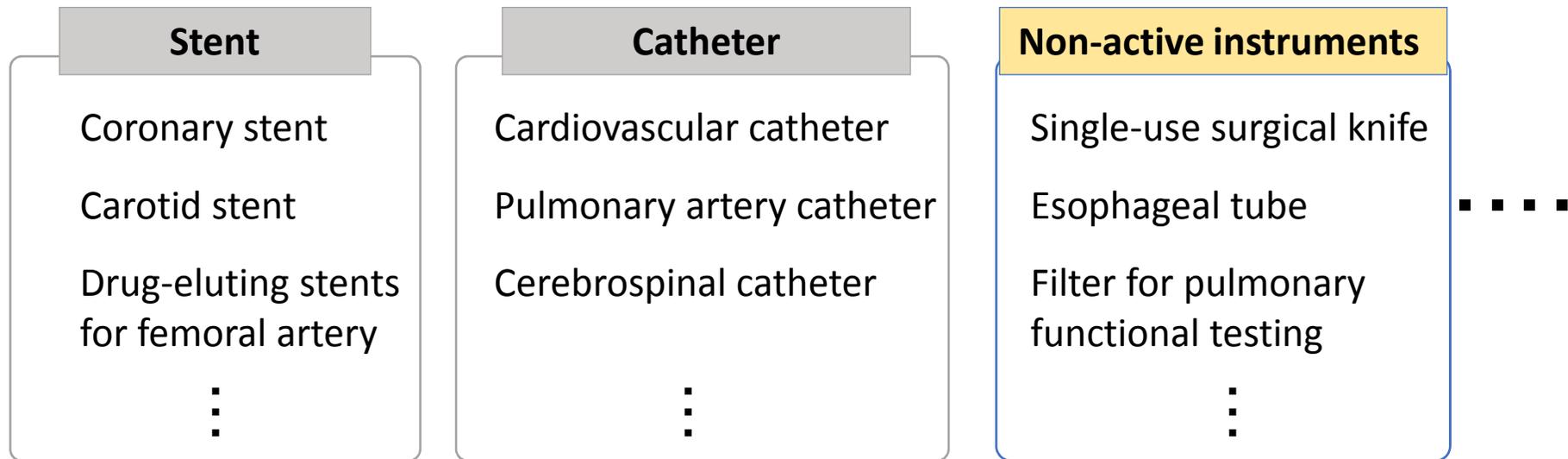
The relationship between product family and generic name is announced by notification.

QMS Inspection Flow

6 months

Receive application of QMS inspection

↓

Determine on-site or desktop inspection

* example

On-site Inspection

MAH*

Mfg. site A*
(Main Assembly)

Desktop Inspection

Mfg. site B*
(Design)

Mfg. site C*
(Distribution)

Conformity assessment

↓

Issue compliance certification and inspection report

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Documents of QMS Inspection

No.	Documents	Scope
1-1-3	ISO13485 Certification, registered certification body's Inspection report, etc	Mfg. sites
1-1-4	Manufacturing process flow	Product
1-1-5	Mutual relations of QMS between MAH and mfg. sites.	Mfg. sites
1-2-1	Outline of mfg. site (Number of employees, address, products, etc)	Mfg. sites
1-2-2	Product list for application	Product family

Example of MAH On-site Inspection Schedule

Date	Time	Item

Day 1	9:30-12:00	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 etc.

	13:00-17:30	3. **Marketing Authorization Holder (MAH)** 4. **Documentation and Records** 5. **Product Documentation (including Risk Management)**
Day 2	9:30-12:00	6. **Design and Development** 7. **Product and Process controls**
	13:00-17:30	8. **Purchasing Control** 9. **Customer Related Processes** 10. **Corrective and Preventive Actions (CAPA)** 11. Team Meeting of Inspectors 12. Confirmation on Findings and Closing Meeting

Example of Documents for Desktop Inspection

No	Documents	Outline of Documents	Subject
2-1-1	Layout of all mfg. site building	・Bird's eye-view photograph or location map of mfg. site	Mfg. sites
2-1-2	Floor plan	・Clean room grade ・Differential pressure ・List or layout of representative manufacturing and test equipment	Mfg. sites
2-2-1	Organization chart	・Responsible persons and departments under QMS	Mfg. sites
2-2-2	Quality management system	・Quality Manual	Mfg. sites
2-2-3	List of documents identified with QMS	・Including name, number, and retention period of QMS documents	Mfg. sites
2-3-1	Seihin Hyojun Sho	・The document of Seihin Hyojun Sho is all the related documents to the product under QMS.	Product
2-3-3	Validation states of mfg. process	・List showing plan about the mfg. process validation.	Product

Timeline after QMS Inspection

Nonconformity is graded from 1 to 6.
(Reference：GHTF/SG3/N19:2012)

Rank 1 to 3

Inspection

Nonconformity Report

about 30 days

within 14 days

Improvement Report (or Plan*)

Compliance Cert. & Audit Report

*in case of Rank 1

Confirmation of the effectiveness

Next Inspection

Rank 4 to 6

Inspection

Nonconformity Report

Within 15 days

within 14 days

Improvement Report

Compliance Cert. & Audit Report

Confirmation of the effectiveness

Next Inspection

QMS Compliance Certification

<＜基準適合証番号＞>

基準適合証

申請者の住所

申請者の氏名

調査を行った品目	一般的名称	
	販売名	
	承認番号	
区分		

製造所		名称	所在地	登録番号	製造工程

　医薬品医療機器等法第23条の2の6第1項の規定により、上記の　　　　　　　　　　　に係る同項各号に規定する　　　　　　　　　　　　が、同法第23条の2の5第2項第4号に規定する基準に適合していることを証明する。

　　　　　年　　　月　　　日

　　　　　　　　　　　　　　　　　　　　　　　独立行政法人医薬品医療機器総合機構理事長　　印

有効期間　　　年　　月　　日から

　　　　　　　年　　月　　日まで

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QMS Compliance Certification

<Certification No.>

QMS Compliance Certification

<MAH name>
<MAH address>

Generic Name	
Product Name	
Marketing Approval Number	
Product Family	
Registered Manufacturing Site (Name, Address, Registered No., Manufacturing Process)	

We certify that the manufacturing control and quality control of the above product conforms to the QMS ordinance.

<Issue Date>

Chief Executive,
Pharmaceuticals and Medical Devices Agency

<Term of validity>

Typical Nonconformity

N = 995 nonconformities
(204 domestic sites)

INTERNAL AUDIT: 9.0%
CONTROL OF DOCUMENTS: 7.1%
PLANNING OF PRODUCT REALIZATION: 6.8%
DOCUMENTATION OF QMS: 6.1%
COMPETENCE, AWARENESS AND TRANING: 5.2%
PURCHASING PROCESS: 4.6%
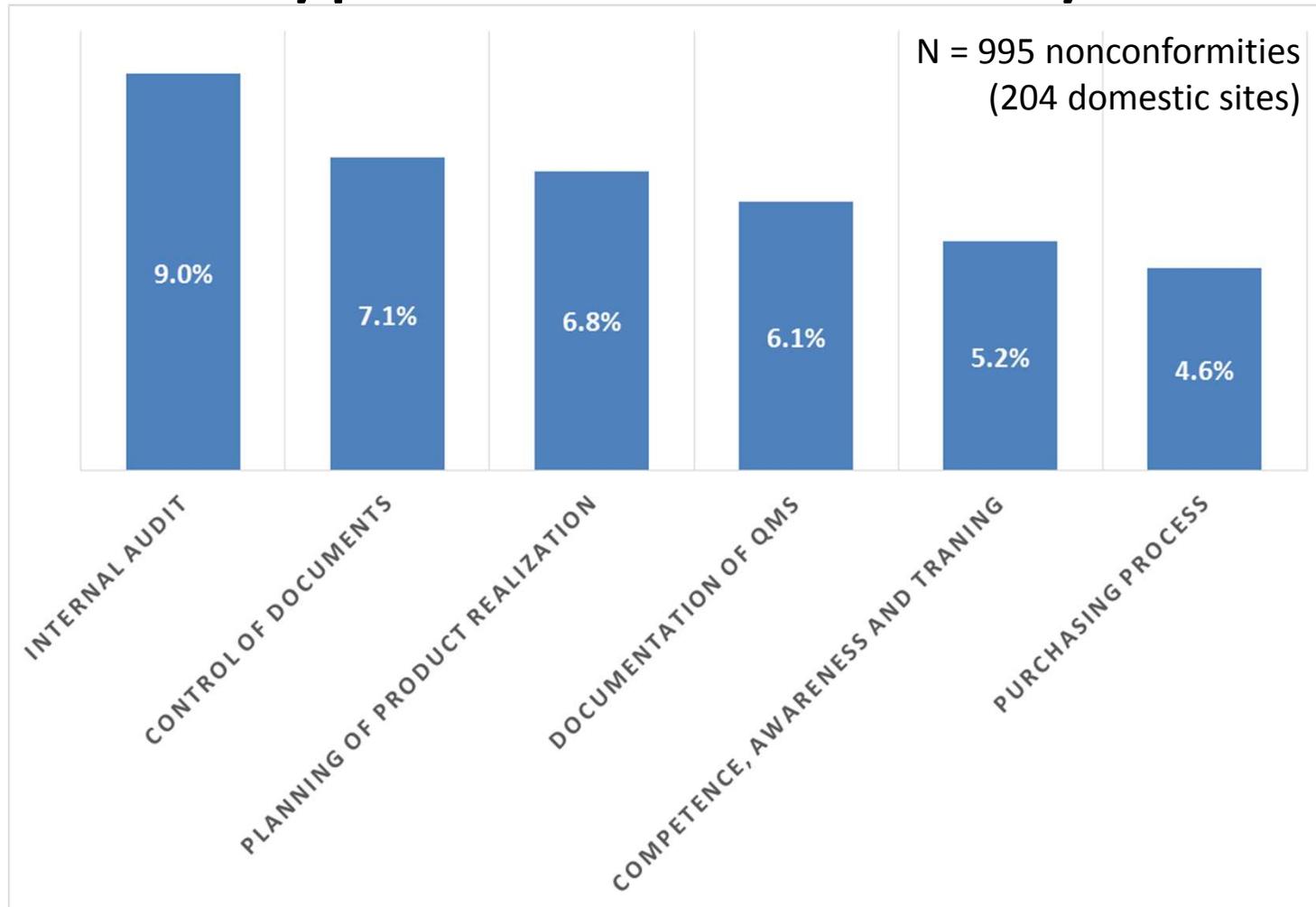
From Nov 1st 2015 to Mar 31st 2016
Researched by Health Labor Sciences Research, Japan

Example of Nonconformity

Japanese QMS Ordinance, Article 65 and 84
(Verification of QMS of Registered Manufacturing Site)

Marketing authorization holder should perform the verification that the manufacturer performs the manufacturing control and quality control <u>based on the Japanese QMS ordinance</u>.
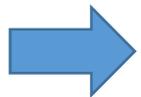
Failure to implement the verification.

Verification of QMS of Registered Manufacturing Site (Article 65)
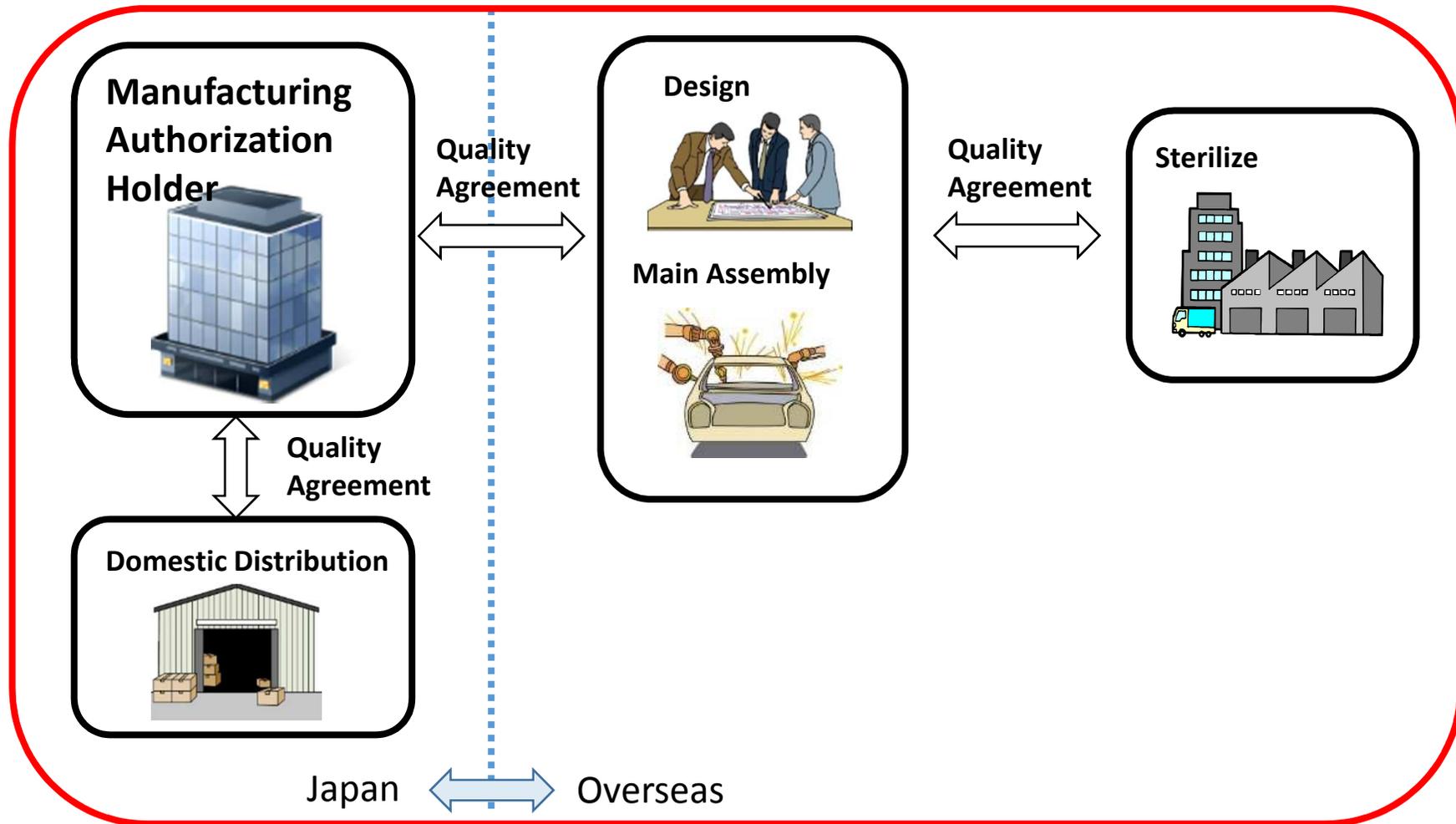
2. Participation in MDSAP

Japan's participation in Medical Device Single Audit Program (MDSAP)

- MDSAP is an international initiative to implement a program where auditing organizations can conduct a <u>single audit</u> of a manufacturer of medical devices <u>across the different regulations.</u>

- Japan announced its participation in MDSAP Pilot in June 2015. Australian TGA, Brazilian ANVISA, Health Canada, US FDA and Japanese MHLW have been running MDSAP.

Trial acceptance of MDSAP Audit Reports

- PMDA accepts MDSAP audit reports as a trial.

- The trial period :
  from June 22, 2016 to December 31, 2016
  extended to March 31, 2018

- The MDSAP Audit Report can reduce the manufacturer's burden in the inspection process, when it is appropriate.

- PMDA basically performs desktop inspection to a site to which the MDSAP audit report is submitted at the timing of QMS inspection application.

Example of Documents for Desktop Inspection using MDSAP Audit Report

No	Documents	Need or not
1-1-3	ISO13485 Certification, registered certification body's Inspection report, etc	Not
1-2-1	Outline of manufacturing site	Not
2-1-1	Layout of manufacturing site building	Not
2-1-2	Floor plan	Not
2-2-1	Organization chart	Not
2-2-2	Quality management system manual	Not
2-2-3	List of documents identified with QMS	Not
2-3-3	Validation states of mfg. process	Not
2-4-4	Quality agreement between MAH and manufacturing sites	Depends

References

- PMDA / QMS
http://www.pmda.go.jp/english/review-services/gmp-qms-gctp/0002.html
- Documents to be submitted list for QMS inspection
http://www.pmda.go.jp/files/000212615.pdf
http://www.pmda.go.jp/files/000212616.pdf

Thank you for your attention!

ISO 13485:2016
QMS Application Strategy

May 11, 2017
ILOODA Co. Ltd.

Seol Yeong-soo
responsible for quality management

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2. Application of Regulatory Requirements QMS

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6. Re-establishment of Complaints Handling Procedure

7. Summary

1. ISO 13485:2016 Key Changes

◆ Focus on internationalized "regulatory requirements"

◆ Apply "risk management" throughout the quality system

◆ A clear need for "design validation and validation activities"

◆ Improvement of the "supplier management" process

◆ Improved "feedback process"

◆ Clear requirements for "software validation"

◆ Enhanced requirements for "identification and traceability"

* Source: SGS ACADEMY

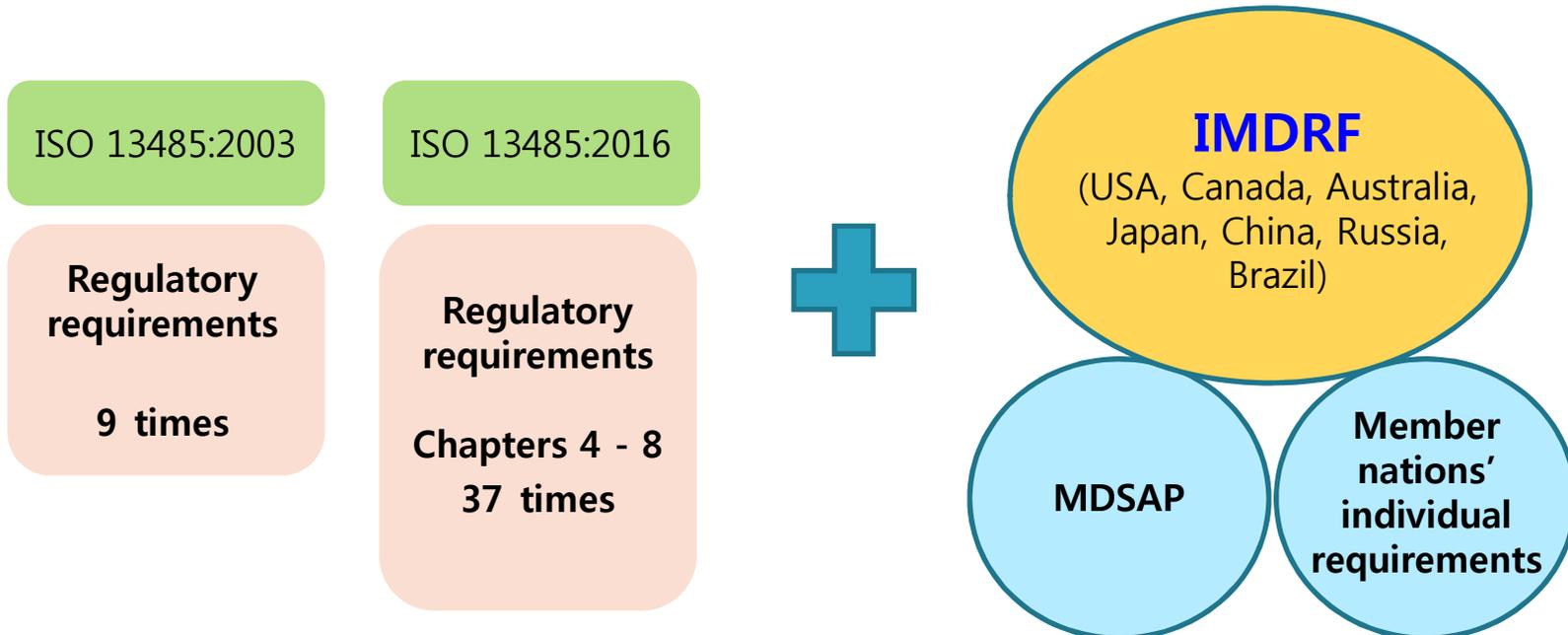| Regulatory Requirements	Risk Management
◆ Organizational emphasis on the regulatory requirements for customer safety and performance ◆ Requires assessment of the impact on the regulatory requirements in the activities of the manufacturer ◆ Communication with and reporting to the regulatory agencies on the applicable regulatory requirements ◆ Evaluation of the impact of the "applicable regulatory requirements "when changing the product design, and reporting it to the approving or regulatory body	◆ Documentation of one or more processes for risk management across the product realization activities ◆ Expansion of the quality management system as well as the product realization process (design management) - Introduction of the lifecycle concept ◆ Review of the results of the design change through risk management ◆ Documentation of the assessment of the risk management on the data in the feedback process
Design Control	**Validation**
◆ Documentation of the planning and review of the design and development throughout the design process ◆ The outputs of the design and development should be traceable in the relevant design inputs. ◆ Documentation of the resources of the design and development process, including the suitability of the participants ◆ Establishment of a design validation & validation plan, and design transfer ◆ Usability, clinical and performance evaluation for validation, application of the design history file concept	◆ Documentation of the acceptance criteria to be used in the validation, and of the statistical techniques and sample size ◆ If applicable, ensuring the compatibility of the product with other medical devices ◆ In the case of software, validate the extent of the potential risk of the process on the product. ◆ Documentation of the results of the validation, the conclusions, and the additional activities ◆ Expansion of the software process management requirements: QMS software, process management software, software for monitoring and measuring, etc.

Supplier Control	Feedback Process
◆ Provision of a documented "agreement" between the organization and the supplier, including notification of any major change made. ◆ Inspection of the purchased product with regard to its risk based on the evaluation of the supplier ◆ Conduct of the purchased-product change through the product realization and the impact of the medical device ◆ Expansion of the supplier monitoring process	◆ Documentation of systematic ways of collecting feedback ◆ The data supporting feedback include the production and post-production activities. ◆ Feedback is applied as an input to the risk management, product realization, and development process. ◆ Strengthening of the requirements for the handling of segmented and specialized customer complaints ◆ Adding vigilance reports and a post-management system (PMS)
Identification & Traceability	**FDA 21 CFR Part 820 Compliant**
◆ Identification of the status of the product throughout the product realization process ◆ Documentation of UDI(unique device identification)-applied systems ◆ Specific requirements, including the traceability records of the implanted devices	◆ Application of additional requirements of FDA, such as design transfer, DMR, and DHF ◆ Clarification of the applicable provisions of the regulatory authorities' reporting procedure (MDRs) ◆ Adding the change notification procedure of the supplier

2. Application of Regulatory Requirements QMS

ISO 13485:2003

ISO 13485:2016

Regulatory requirements

9 times

Regulatory requirements

Chapters 4 - 8 37 times

+

IMDRF
(USA, Canada, Australia, Japan, China, Russia, Brazil)

MDSAP

Member nations' individual requirements

Construction of Quality Management System

3. Risk Management throughout the Product Realization

ISO 14971

**Risk identification
Risk analysis
Risk assessment
Risk control**

- Feedback process
- Design change process
- Design and development process
- Purchase process
- Supplier selection & evaluation process
- Inspection process
- Manufacturing process
- Work standard process
- HR management process
- Complaint assessment process

4. Re-establishment of the Organization's Files for Design and Development

Requirements	DMR (Device Master Record)	DHF (Design History File)
7.3.2 Design & development planning		- Customer requirements documents (marketing requirements, users, user interface, clinical requirements, product requirements) - Product concept (design strategy documents) - Project plan (plan by department) - Risk management plan - Design review (selection of sales markets, review of whole schedule, review of responsibility and authority)
7.3.3 Design & development inputs	- Laws and standards by nation - Semi-finished specifications - Parts specifications - Product specifications	- Risk analysis report - Design review (review of the content conflict, ambiguity, etc., and of the measurability)
7.3.4 Design & development outputs	- Labeling (product labels, packaging labels) - List of processes, devices, and measuring instruments - Test and inspection standards - Work standards - Product drawings (final products, semi-finished products, parts) - BOM (bill of material) - Parts list - User manual, service manual	- Design review (review of the output status and design traceability)

* Source: SGS ACADEMY

4. Re-establishment of the Organization's Files for Design and Development

Requirements	DMR (Device Master Record)	DHF (Design History File)
7.3.6 Design & development verification		- Software verification report - Hardware verification report - Product verification report (external agency) - Design review (review of the measurable requirements and outputs, and of the re-implementation due to the problems found during the review)
7.3.7 Design & development validation		- Process validation protocol and report - Documents to be submitted to the regulatory body - Software validation report - Final version of the risk management report - Product validation report - Clinical evaluation report - Usability evaluation report - Design review (review of the customer requirements and outputs, and of the fulfillment of the legal requirements)

* Source: SGS ACADEMY

5. Re-establishment of Supply Products/ Service Management

Step	Process	Objective Evidence
Plan	Description of what to be supplied with	Confirmation of the products and services, manuals, and specifications
	Confirmation of technology and process information	Specifications, parts requirements, procedures, and work instructions
	Confirmation of potential suppliers	Potential suppliers' names and contact information
	Identification of risks associated with products or services	Documentation of the identified risks
	Identification and evaluation of the type and extent of risk management	List of the identified risk results and of the potential risks to be managed
Selection of potential supplier	Survey of the supplier's business capability	Code of Conduct, business practices, goodwill, etc.
	Survey of the supplier's operational capability	Evidences of technology, infrastructure, logistics, quality, and risk management
	Selection of potential supplier	Criteria for the potential supplier documentation and selection, and grounds for the decision
Evaluation and approval of the supplier	Plan establishment for the evaluation selection criteria	Documented criteria for evaluation and selection
	Improvement of the communication with the potential supplier and of the requirements	The first documented contract
	Evaluation based on the selection criteria	Evidences that meet the criteria for the documentation and records
	Approval of the supplier	Documented decision grounds (including the list of approved suppliers)

* Source : QMS-Guidelines for management of products and services received from suppliers / GHTF Study Group 3 / GHTF/2008-12-11

5. Re-establishment of Supply Products/ Service Management

Step	Process	Objective Evidence
Final decision on management	Establishment of purchase information	Final contract, purchase order, agreement, etc.
	Approval decision and verification activities	Approval procedure, purchase/specification requirements, review/approval records
Delivery, measurement, monitoring	Product/service warehousing, measurement/ monitoring and approval activities	Warehousing records, inspection/test records, approval records
	Data analysis	Recording of the data analysis results
	Identification of problems and corrective action	Recording of the corrective-action results
	Regular re-evaluation of suppliers	Recording of the results of the evaluation of the ability to continuously comply with the requirements
Feedback and monitoring	Feedback and communication – results of whether to meet the requirements	Letters of the manufacturer and/or supplier
	Corrective and preventive process - CAPA (re-evaluation of the suppliers)	Documents and records of the corrective and prevention action process

* Source: QMS - Guidelines for the management of the products and services received from the suppliers/ GHTF Study Group 3/ GHTF/2008-12-11
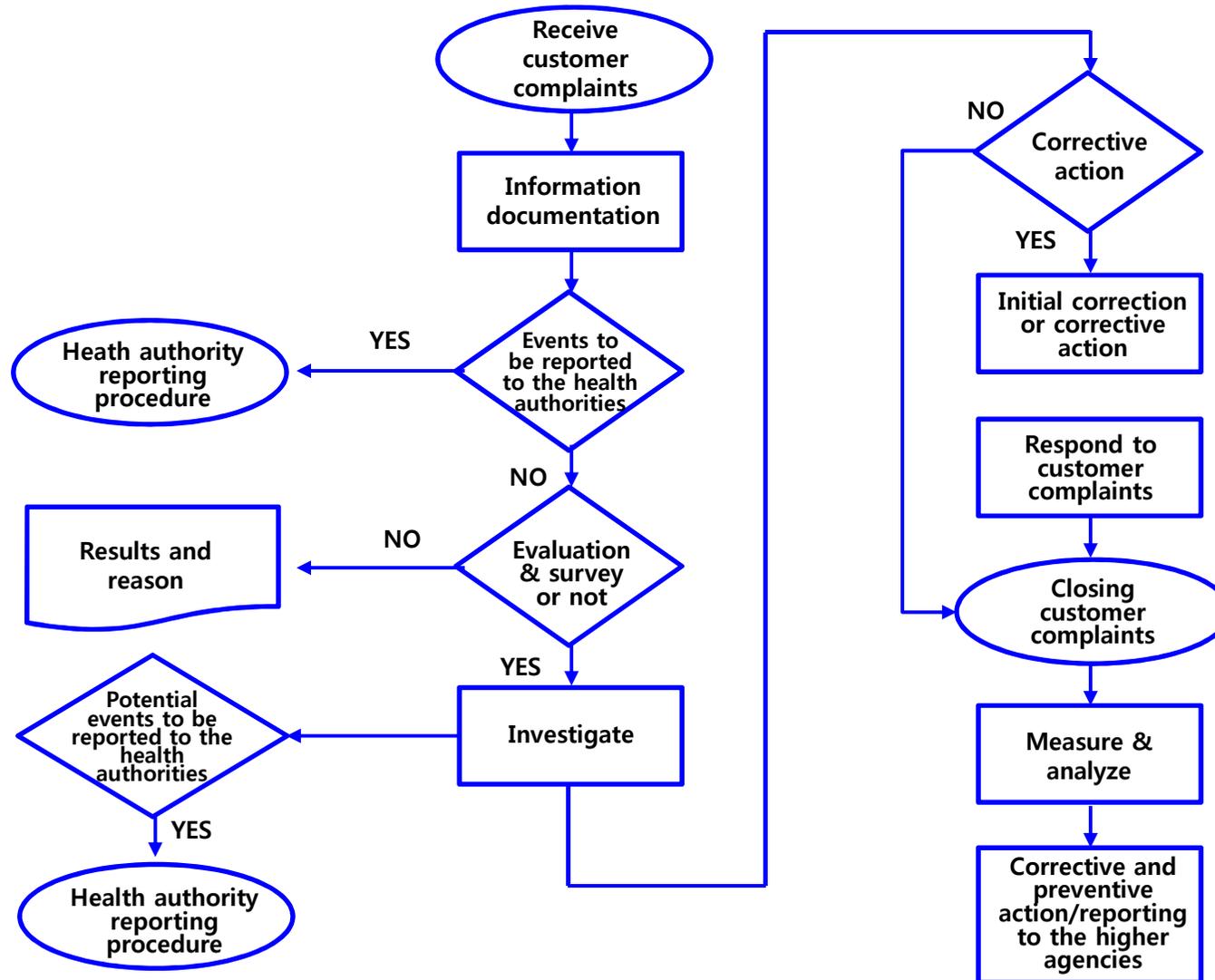
5. Re-establishment of Supply Products/ Services

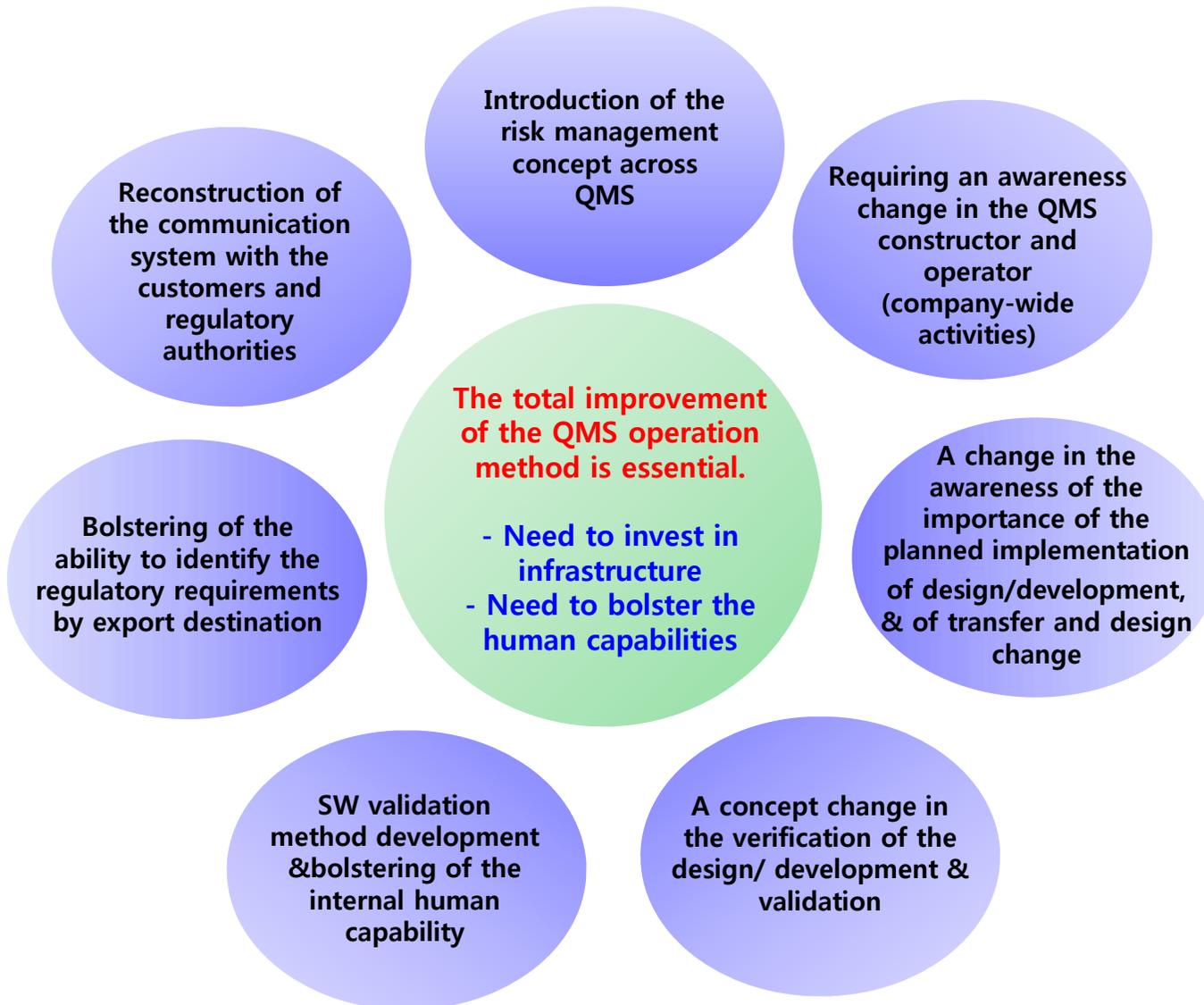| Supplier Rating	Initial Evaluation & Selection	Periodic Management Method	Inspection & Acceptance Activities
Key supplier (Risk Class A)	- ISO 13485, CE, cGMP registration review - Review of the external audit agency reports - Establishing the obligation to change the contract - Product/service risk assessment - QMS onsite audit	- Review of the annual supplier performance & conclusion of the quality contract - Review of the monthly corrective-action processing status - Review of the monthly pass/fail ratio for the received products & of the monitoring progress - Issuance of corrective-action requests against continuous quality problems	- Regular analysis of the supplier suitability & of the trend assessment report - Performance of independent testing for the verification of the suitability analysis report - Inspection of the supplied products according to the acceptance & sampling criteria - Inspection and acceptance activities performed at the supplier site
Middle-tier supplier (Risk Class B)	- QMS onsite audit - Acceptance of self-assessment questionnaire - Review of the internal audit results	- Review of the pass/fail ratio for the received products, & of the monitoring progress - Review of the quarterly corrective actions taken	- Issuance of supplier's product inspection/compliance report or compliance analysis report according to the established acceptance criteria - Inspection and acceptance activities at the supplier's site
General supplier (Risk Class C)	- Interview of the supplier manager - Assessment of the supplier's financial status	- Review of the annual pass/fail ratio for the received products, & of the monitoring progress - Review of the annual corrective actions taken	- Considering non-inspection

* Source : SGS ACADEMY

6. Re-establishment of Complaints Handling Procedure

*Source: SGS ACADEMY

7. Summary

Introduction of the risk management concept across QMS

Requiring an awareness change in the QMS constructor and operator (company-wide activities)

Reconstruction of the communication system with the customers and regulatory authorities

The total improvement of the QMS operation method is essential.

- Need to invest in infrastructure
- Need to bolster the human capabilities

A change in the awareness of the importance of the planned implementation of design/development, & of transfer and design change

Bolstering of the ability to identify the regulatory requirements by export destination

SW validation method development &bolstering of the internal human capability

A concept change in the verification of the design/ development & validation

Thank you