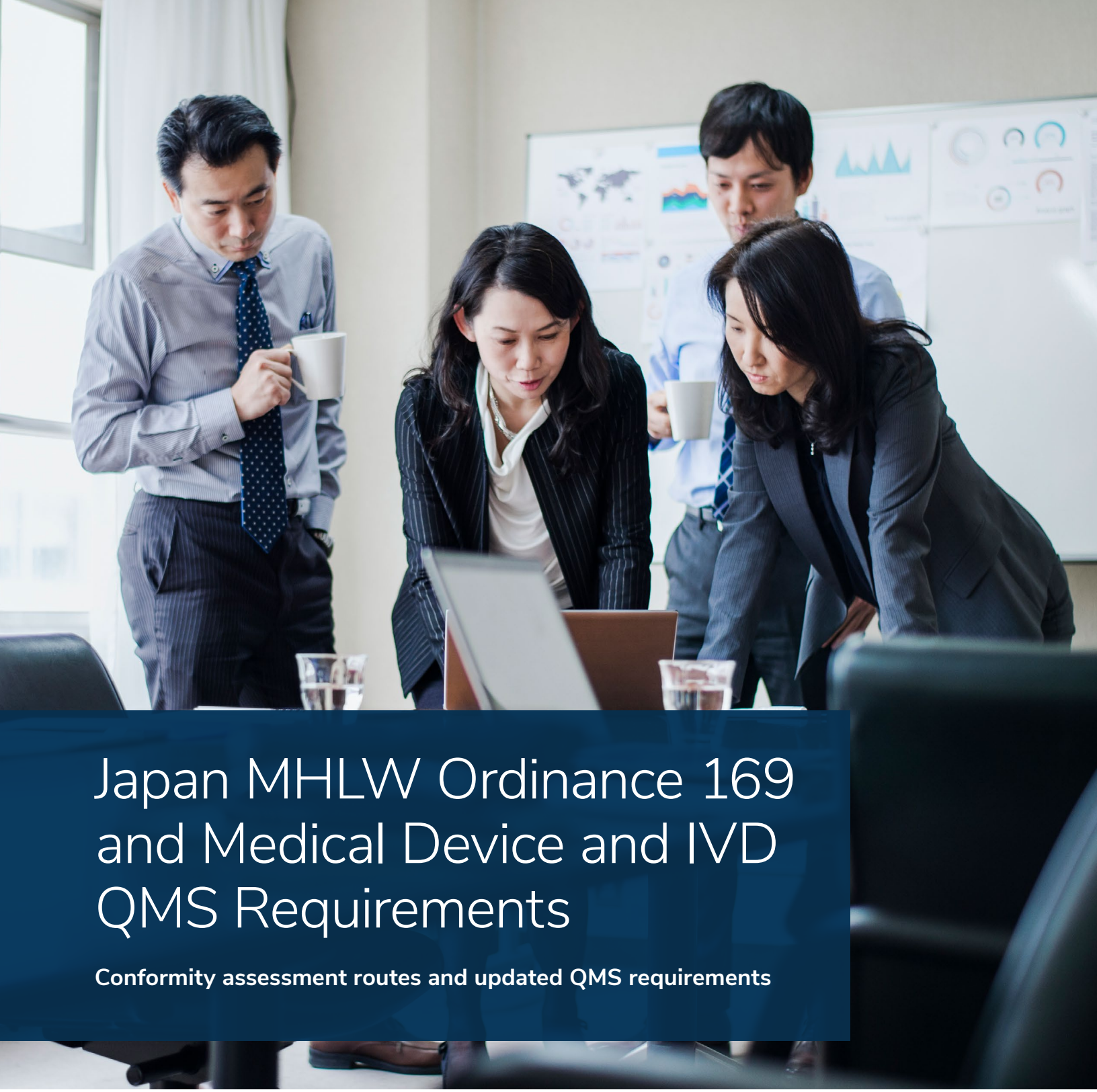

Japan MHLW Ordinance 169 and Medical Device and IVD QMS Requirements

Conformity assessment routes and updated QMS requirements

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October 2024

Japan QMS Regulation

The Ministry of Health, Labour and Welfare (MHLW) regulates medical devices and in vitro diagnostics (IVDs) under the Pharmaceuticals and Medical Devices Act (PMD Act). Quality management system (QMS) requirements for medical devices and IVDs under the PMD Act are prescribed by the MHLW Ministry Ordinance No. 169 (MO#169). The MHLW initially established MO#169 in 2004 by referring to ISO 13485:2003 from a global harmonization perspective and then amended it for harmonization with ISO 13485:2016 in 2021.

While the vital portion of MO#169:2021 aligns with ISO 13485:2016, there are distinct differences in the requirements and conformity assessment approach between the two standards. Understanding these differences is key to navigating the regulatory landscape, and this white paper aims to provide a comprehensive overview of these variations. In addition to outlining the requirements of MO#169 as well as the variations between Japanese QMS regulations and ISO 13485, this white paper also provides recommended approaches for entities subject to QMS audits by Japanese regulators.

Manufacturers outside Japan have gradually become familiar with the requirements of MO#169 by obtaining the Medical Device Single Audit Program (MDSAP) Certification. However, manufacturers planning to introduce medical devices into Japan will still need to overcome that challenge.

In addition to outlining the requirements of MO#169 and the variations between MO#169 and ISO 1348, this white paper includes an approach for those entities subject to a conformity assessment (QMS audit) between the two standards.

QMS requirements under the PMD Act

The following regulations stipulate QMS requirements under the PMD Act:

- MHLW Ministry Ordinance No. 94 (MO#94 - Requirements for Organizational structure of QMS implementation)
- MHLW Ministry Ordinance No. 169 (MO#169 - Requirements for QMS)

MO#94 specifies requirements for corporate organizational structure and staffing of Marketing Authorization Holders (MAHs). Specifically, it requires MAHs to establish and maintain their organizational structure to implement QMS, assign a management representative, and deploy a General MAH Director in their corporate organizational structure. MO#94 is a set of requirements specific to MAHs and is not applied to manufacturers outside Japan.

MO#169 stipulates the detailed QMS requirements. MO#169 is organized into six chapters as follows (See Table 1):

Table 1: MO#169 organization

Chapter	Requirements
Chapter 1	**General Provisions** (Article 1 to Article 3) Chapter 1 defines the intent of the MO#169, the terms used after Chapter 2, and the application scope.
Chapter 2	**Basic Requirements Regarding Manufacturing Control and Quality Control of Medical Devices, etc.** **Section 1** General Requirements (Article 4) **Section 2** Quality Management System (Article 5 to Article 9) **Section 3** Management Responsibility (Article 10 to Article 20) **Section 4** Resource Management (Article 21 to Article 25-2) **Section 5** Product Realization (Article 26 to Article 53) **Section 6** Measurement, Analysis, and Improvement (Article 54 to Article 64) Chapter 2 is organized into six sections. Since Sections 2 to 6 (Articles 5 to 64) align with Articles 4 to 8 of ISO 13485:2016, their requirements are almost identical, while some minor differences exist.
Chapter 3	**Additional Requirements Regarding Manufacturing Control and Quality Control of Medical Devices, etc.** (Article 65 to Article 72-3) Chapter 3 defines supplemental requirements for Chapter 2. Particularly, it defines the requirements for 1) the deployment, roles and responsibilities of the General MAH Director, Quality Management Supervisor, the Safety Management Supervisor in MAH organizational structure, 2) reporting from manufacturers to MAH, the relationship with the MHLW Ministry Ordinance No.135 (Good Vigilance Practice, MO#135), the roles and responsibilities of the Designated MAH), also commonly called DMAH.
Chapter 4	**Manufacturing Control and Quality Control of Biological Medical Devices, etc.** (Article 73 to Article 79) Chapter 4 defines supplemental requirements specific to biological medical devices. Particularly, it stipulates requirements for the manufacturing facility's structure and equipment, manufacturing process, quality control, and training. This chapter does not apply to devices other than biological medical devices.
Chapter 5	**Manufacturing Control and Quality Control of Radioactive In-Vitro Diagnostics** (Article 80 to Article 81) Chapter 5 defines supplemental requirements specific to radioactive IVDs. Particularly, it stipulates requirements for the manufacturing facility's structure, equipment, and manufacturing processes. This chapter does not apply to IVDs other than radioactive in-vitro diagnostics.
Chapter 5-2	**Manufacturing Control and Quality Control of Remanufactured Single-Use Devices** (Article 81-2 to Article 81-2-6) The MHLW added Chapter 5-2 with the amendment in 2021. Chapter 5-2 defines supplemental requirements specific to remanufactured single-use devices. Particularly, it stipulates requirements for the manufacturing facility's structure and equipment, manufacturing processes, quality control, and traceability. This chapter does not apply to medical devices other than remanufactured single-use devices.
Chapter 6	**Application mutatis mutandis to Manufacturers, etc. of Medical Devices, etc.** (Article 82 to Article 84) While Chapter 1 stipulates that MAHs are responsible for implementing QMS based on MO#169, Chapter 6 stipulates that Chapters 2 to 5-2 also apply mutatis mutandis to manufacturers involved in the manufacturing of medical devices placed on the Japanese market, including contract manufacturers, and Japanese manufacturers of medical devices exclusively for export.

The relationship between the sub-systems required by MO#169 and each article is as follows (See Table 2):

Table 2: Sub-system based on MO#169

Requirement by sub-system	
Sub-system	**Requirements of Japan QMS Regulation**
Quality management	**Article 5:** General Requirements for Quality Management System **Article 5-2:** Establishment of Quality Management System **Article 5-3:** Implementation of Quality Management System **Article 5-4:** Management of Quality Management System **Article 5-5:** Outsource **Article 5-6:** Application of Computer Software **Article 7:** Quality Manual **Article 10:** Management Commitment **Article 12:** Quality Policy **Article 13:** Quality Objectives **Article 14:** Quality Management System Planning **Article 15:** Responsibility and Authority **Article 16:** Responsible Engineering Manager **Article 17:** Internal Communication **Article 18:** Management Review **Article 19:** Review Input **Article 20:** Review Output **Article 21:** Provision of Resources **Article 22:** Personnel **Article 23:** Competence, Awareness and Training **Article 56:** Internal Audit **Article 77, 81-2-4:** Training
Design control	**Article 30:** Design and Development Planning **Article 31:** Design and Development Inputs **Article 32:** Design and Development Outputs **Article 33:** Design and Development Review **Article 34:** Design and Development Verification **Article 35:** Design and Development Validation **Article 35-2:** Design and Development Transfer **Article 36:** Control of Design and Development Changes **Article 36-2:** Design History File
Product documentation	**Article 6 Section 2 and 3:** Documentation of Quality Management System **Article 7-2:** Medical Device File **Article 26:** Planning of Product Realization **Article 74:** Documents Related to Manufacturing Control and Quality Control
Manufacturing	**Article 24:** Infrastructure **Article 25:** Work Environment **Article 25-2:** Contamination Control **Article 40:** Control of Production and Service Provision **Article 41:** Cleanliness of Products and Contamination Control **Article 42:** Installation Activities **Article 43:** Servicing Activities **Article 44:** Manufacturing Control of Sterile Medical Devices **Article 45:** Validation of Processes for Production and Service Provision **Article 46:** Validation of Sterilization Process **Article 47:** Identification **Article 48:** Traceability **Article 49:** Traceability of Implantable Devices

Manufacturing Continued	**Article 51:** Customer Property **Article 52:** Preservation of Products **Article 53:** Control of Monitoring and Measuring Devices **Article 58:** Monitoring and Measurement of Products **Article 60:** Control of Nonconforming Products **Article 60-2:** Actions in Response to Nonconforming Product Detected before Delivery **Article 60-3:** Actions in Response to Nonconforming Product Detected after Delivery **Article 60-4:** Rework **Article 73:** Infrastructure of Manufacturing Sites of Marketing Approval Holder, etc. of Specified Biological Medical Devices, etc. **Article 75:** Process Control **Article 76:** Testing **Article 80:** Infrastructure of Registered Manufacturing Sites of Radioactive In-Vitro Diagnostics **Article 81:** Compliance with Regulations for Manufacturing Control and Quality Control of Radiopharmaceuticals
CAPA	**Article 54:** Measurement, Analysis and Improvement **Article 55:** Feedback **Article 55-2:** Complaint Handling **Article 55-3:** Reporting to MHLW **Article 57:** Monitoring and Measurement of Processes **Article 61:** Analysis of Data **Article 62:** Improvement **Article 63:** Corrective Actions **Article 64:** Preventive Actions
Purchasing	**Article 37:** Purchasing Process **Article 38:** Purchasing Information **Article 39:** Verification of Purchased Products **Article 84:** Control by MAH
Control of documents and records	**Article 6 Section 1:** Documentation of Quality Management System **Article 8:** Control of Documents **Article 9:** Control of Records **Article 59:** Monitoring and Measurement of Implantable Devices **Article 67:** Retention Period of Quality Management System Documents **Article 68:** Retention Period of Records **Article 78:** Control of Documents and Records **Article 79:** Exceptions in Retention of Records (Biological Medical Devices) **Article 81-2-5:** Control of Documents and Records (Remanufactured Single-Use Devices)
Customer	**Article 11:** Customer Focus **Article 27:** Determination of Requirement Related to the Products **Article 28:** Review of Requirements Related to Products **Article 29:** Customer Communication
MAH related	**Article 66:** Additional Requirements Regarding Quality Management System **Article 69:** Reporting Adverse Events, etc. **Article 70:** Relationship with Good Vigilance Practice (GVP, MO#135) **Article 71:** Duties of General MAH Director of Medical Devices, etc. **Article 72:** Quality Management Supervisor **Article 72-2:** Other Items to be Complied **Article 72-3:** Duties of Designated Marketing Authorization Holders for Foreign Manufactured Medical Devices

Gaps MO#169 vs. ISO 13485

While MO#169 contains requirements that apply only to MAHs, the requirements that apply to manufacturers outside Japan are equivalent to ISO 13485:2016. Nevertheless, since there are some differences between the two, manufacturers outside Japan must address the differences below (see Table 3) and upgrade their QMS to conform with MO#169. The main differences that manufacturers outside Japan need to address are:

Table 3: Gaps between MO#169 and ISO 13485

Article	Requirement gaps
Article 7-2	**Medical device file** For each medical device type or family, MAH and manufacturers must create and maintain a Medical Device File containing information about their devices as required by Article 7-2. "Medical Device File" required by MO#169 differs from "Technical documentation" required by the Medical Device Regulation (MDR, EU 2017/745) and the In Vitro Diagnostic Medical Device Regulation (IVDR, EU 2017/746). Rather, it is similar to "Device Master Record" required by 21 CFR part 820.181(US).
Article 55-3	**Reporting to MHLW (Adverse Events and Recall)** Manufacturers must stipulate the deadline for reporting to MHLW in their SOP for adverse events (AE) reporting. Article 68-10 and Article 68-11 of the PMD Act stipulate the obligations regarding AEs and recall, respectively. Also, Article 228-20 of the enforcement regulation of the PMD Act stipulates the deadlines for reporting AEs (15 days or 30 days, depending on AE severity). For imported medical devices placed on the Japanese market, AEs and recalls reported to authorities outside Japan must also be reported to the MHLW within the deadline.
Article 67 and 68	**Retention Period of Quality Management System Documents and Records** Unlike Articles 4.2.4 and 4.2.5 of ISO 13485, Articles 67 and 68 clearly define the retention periods for QMS Documents and Records. Retention periods vary depending on medical device classifications. Manufacturers must stipulate the retention period in their SOP for document control. • QMS Documents and Records relevant to "Specially designated maintenance control required medical devices" : 15 years after product delivery or shelf life + one year • QMS Documents and Records other than "Specially designated maintenance control required medical devices" : five years after product delivery or shelf life + one year • Training records: five years "Specially designated maintenance control required medical devices" refers to a category different from device risk classes. The MHWL specifies devices groups assuming periodic inspection, maintenance and calibration after marketing to maintain their quality, effectiveness and safety as "Specially designated maintenance control required medical devices." Primarily, reusable devices, such as measurement, examination and diagnostic devices, are specified.
Article 69	**Reporting Adverse Events, etc.** Manufacturers report AEs to the MHLW via MAHs. Therefore, manufacturers must stipulate in their reporting SOP that manufacturers shall report to MAHs when they become aware of AEs stipulated in Article 228-20 of the enforcement regulation of the PMD Act. In addition, manufacturers must specify a deadline for reporting to MAHs so that MAHs can report to the MHLW within the deadline stipulated in Article 228-20 of the enforcement regulation of the PMD Act. Manufacturers must ensure that manufacturing facilities/establishments involved in manufacturing, including contract manufacturers, include in their reporting SOPs a stipulation that if they become aware of AEs defined in Article 228-20 of the enforcement regulation of the PMD Act, those facilities must report the AEs to the manufacturers.

Article 72-3	**Duties of Designated Marketing Authorization Holders for Foreign Manufactured Medical Devices** Note: This requirement only applies when manufacturers outside Japan register their devices as legal manufacturers themselves. When manufacturers outside Japan register their devices as legal manufacturers themselves, they must designate an MAH as local representatives and delegate local QMS duties to the Designated MAH (DMAH). Specifically, the manufacturers must delegate the local QMS duties stipulated in Article 72-3 of MO#169 to the DMAH. The manufacturers must conclude a DMAH contract agreement with DMAHs, and in that agreement, it must stipulate to delegate the local QMS duties to the DMAH.

In addition to the above gaps, manufacturers are encouraged to add the PMD Act and MO#169 to the QM scope.

Compliance with MO#169 is investigated in a QMS conformity investigation (audit) conducted in parallel with the product registration review. Therefore, manufacturers must establish compliance with MO#169 before product registration.

QMS conformity assessment (QMS audit) approach

Product registration and QMS audit

Unlike ISO 13485 registration and audits, initial MO#169 QMS audits for manufacturers are conducted in parallel with the product registration reviews. An applicant of product registration will file both the product registration and QMS conformity assessment applications simultaneously.

- In Japan, there are three product registration routes, i.e., Pre-Market Approval (PMA), Pre-Market Certification (PMC), and Pre-Market Notification (PMN), based on the product's classification, equivalence to similar devices, and compliance with standards (See Table 4).
- Among the three product registration routes, the PMA and PMC routes have a QMS audit conducted in parallel with product registration; the PMN route is a self-declared product registration route, and a QMS audit is omitted.
- The PMDA conducts the product registration review and QMS audit in the PMA route while a RCB conducts those in the PMC route.

Table 4: Product registration route

Registration route	Review body	QMS audit
Pre-Market Approval (PMA)	Pharmaceuticals and Medical Device Agency (PMDA) Registered Certification Body (RCB)*	X
Pre-Market Certification (PMC)	Registered Certification Body (RCB)*	X
Pre-Market Notification (PMN)	Pharmaceuticals and Medical Device Agency (PMDA)	–

*PMC route is similar to the 510(k) Third-Party Review Program in the U.S. MHLW delegates the review of PMC to third-party Registered Certification Body(ies).

Conformity assessment (audit) scope

Manufacturers must identify the manufacturing facilities involved in the following manufacturing activities (See Table 5) in the submissions for product registrations. Every manufacturing facility identified in the submissions must complete the Manufacturing Establishment Registration in advance.

Table 5: Manufacturing activities requiring Manufacturing Establishment Registration

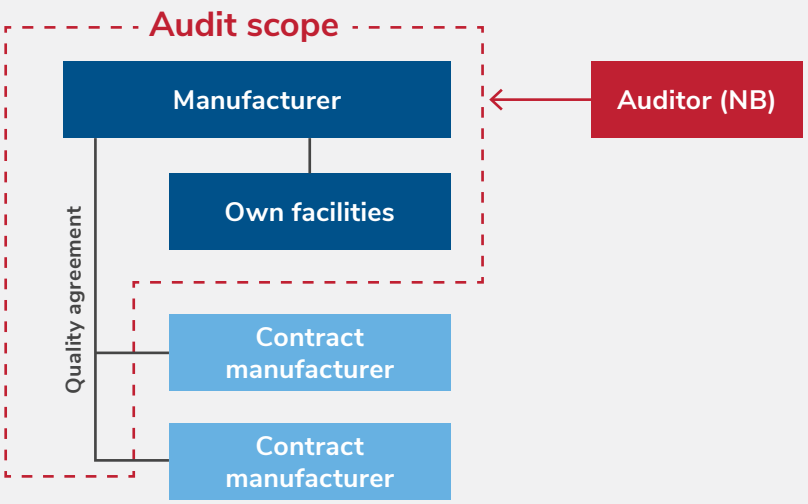
Medical devices				
Manufacturing activities	**Medical device other than on the right**	**Class I Medical device**	**SaMD**	**SaMD with recording medium**
Design and development	X	–	X	X
Key manufacturing process	X	X	–	–
Sterilization	X	X	–	–
Warehouse of final product in Japan	X	X	–	X

IVD			
Manufacturing activities	**IVD other than on the right**	**Radioactive IVD**	**Class I IVD**
Design and development	X	X	–
Key manufacturing process	X	X*	X
Warehouse of final product in Japan	X	X	X

* All the processes from filling process

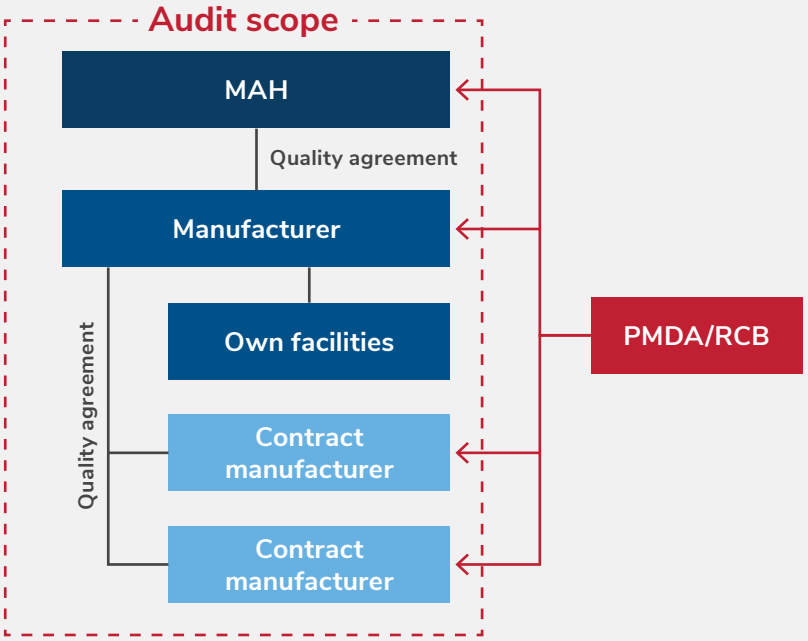
A QMS audit by the PMDA or an RCB targets the MAH and every manufacturing facility identified in the PMA/PMC submission. Most notably, unlike an ISO 13485 audit for a manufacturer, the PMDA/RCB conducts the audit individually for each manufacturing facility identified in the PMA/PMC submission.

In an ISO 13485 audit, a Notified Body audits the manufacturer but does not directly audit the contract manufacturers. The Notified Body confirms the conformity of the contract manufacturer's QMS through the quality/ contract agreement concluded between the manufacturer and their QMS certification, such as ISO 13485 certificates.



On the other hand, PMDA/RCB separately audits QMS(s) of the MAH, manufacturer, and manufacturing facilities, including the contract manufacturers, and determines whether the entire QMS complies with MO#169.

Article 83 of MO#169 stipulates that Chapter 2 through Chapter 5-2 apply *mutatis mutandis* to manufacturing facilities involved in the abovementioned manufacturing activities. Therefore, the manufacturer must make its manufacturing facilities and contract manufacturers implement a QMS that complies with MO#169. Even if the manufacturer's manufacturing facilities and the contract manufacturer have ISO 13485 certificates, they must address the gaps with ISO 13485, particularly Articles 7-2, 55-3, 67, 68, and 69 of MO#169, as shown in Gaps MO#169 vs ISO 13485 above. Also, contract/quality agreements with the contract manufacturers should include their responsibility to address those gaps.



Conformity assessment (audit)

PMDA and RCB will conduct on-site or off-site (document review) QMS audits depending on the QMS status of MAH, manufacturer, and contract manufacturers being audited. PMDA and RCB usually conduct QMS audits in two phases.

First Phase

PMDA and RCB confirm the current QMS status of subjects to be audited first. Specifically, they confirm the organization, resources, ISO 13485 and/or MDSAP certification, and audit history (audit reports) of subjects to be audited to determine whether an on-site audit is necessary. It should be noted that PMDA and RCB will confirm each subject to be audited, including contract manufacturers.

From the perspective of global harmonization, PMDA and RCB principally audit manufacturers who have obtained ISO 13485 or MDSAP certificates off-site. However, for biological devices, etc., they may conduct audits on-site, regardless of ISO 13485 or MDSAP certification.

Second phase

Off-site audit: Although the materials submitted for off-site audit vary slightly between PMDA and RCB, manufacturers typically submit the following materials of each subject to be audited. Like the first phase, it should be noted that PMDA and RCB audit each subject to be audited, including contract manufacturers.

1. **Manufacturing facility information**
    a. Drawing(s) showing the arrangement of manufacturing site buildings and around the site
    b. Floor plans in the subject's facility
    c. Lists of major equipment used in the manufacturing and QC processes

2. **Information about QMS**
    d. A copy of the Quality Manual
    e. A list of all regulatory procedures, including procedures for sub-systems and SOPs
    f. Organization chart
    g. An SOP that stipulates document/record retention rules and retention periods
    h. An SOP that stipulates procedures to report adverse events that occurred outside Japan to MAH
    i. Medical device file (Device Master Record)
    j. Track record of process validation
    k. Quality agreement (between manufacturer and contract manufacturer, manufacturer and MAH)

Among the above materials, items g. through i. must have addressed the gaps between MO#169 and ISO 13485.

On-site audit: When PMDA/RCB decides to audit on-site, the manufacturer will discuss and arrange audit dates with PMDA/RCB through the MAH. The audit methodology used by PMDA and RCB is almost the same as that used for ISO 13485 QMS audits. The QMS audit guideline defines the detailed audit approach.[1] Cooperation from contract manufacturers is essential in the first and second phases. Even for off-site audits, contract manufacturers are required to disclose a large number of internal documents. Manufacturers must obtain consent to cooperate with audits by PMDA and RCB in their contract agreements with contract manufacturers.

1 https://www.mhlw.go.jp/hourei/doc/tsuchi/T240613I0030.pdf (Only Japanese version is available)

Beforehand, obtain the consent of contract manufacturers to cooperate with PMDA/RCB audits.

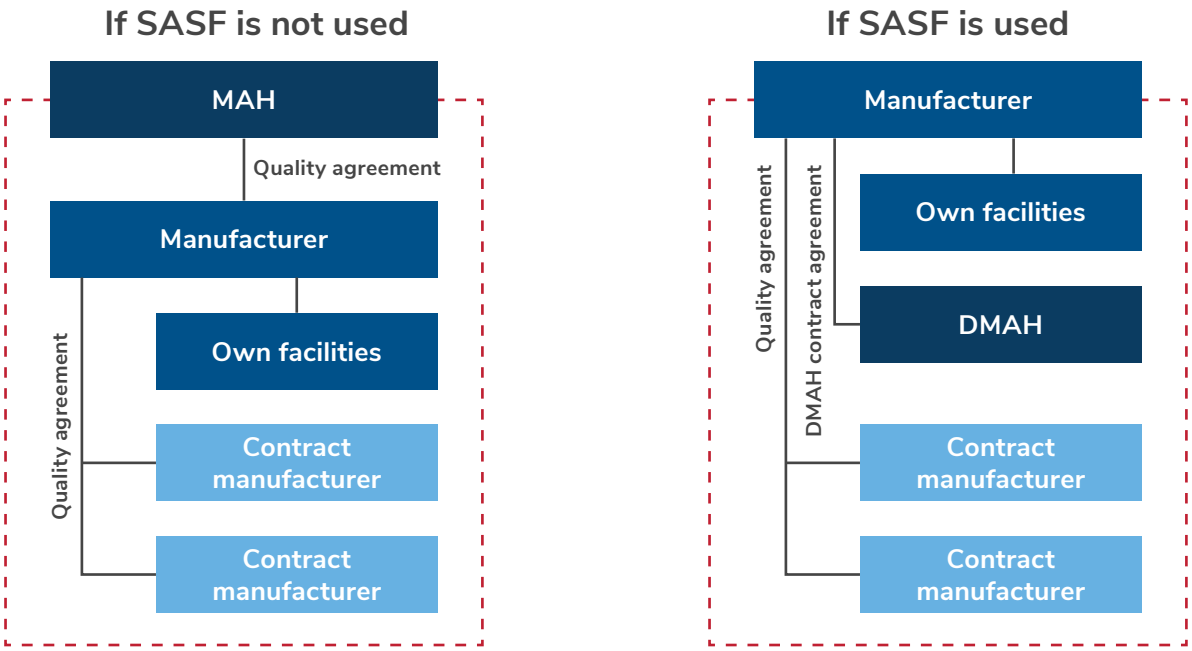
Responsibility for QMS implementation – Who is responsible?

Who is responsible for implementing the overall QMS depends on who registers the product.

First of all, you need to know the PMD Act is based on the assumption that Japanese entities with MAH license, i.e., MAHs, become legal manufacturers of medical devices. This is similar to the Brazil Registration Holder system. However, the PMD Act does not prevent foreign manufacturers from becoming legal manufacturers, and as an exception, it allows foreign manufacturers to become legal manufacturers of their own medical devices in Japan. This is the Special Approval System for Foreign (SASF) manufactured devices, which is stipulated in Article 23-2-17 and 23-2-23 of the PMD Act. In other words, if SASF is not used, MAHs will be the legal manufacturers, and only if the SASF is used will manufacturers outside Japan be the legal manufacturers. However, the SASF is available only for the PMA and PMC routes and not for the PMN route (Class I device registration). Therefore, MAHs will be always the legal manufacturers of Class I devices.

When using the SASF on PMA and PMC routes, manufacturers outside Japan must designate an MAH (Designated MAH, commonly called DMAH) for each device registration as the local representative and delegate the local QMS duties stipulated in Article 72-3 of MO#169 and the local vigilance duties stipulated by MHLW Ministry Ordinance No.135 (Good Vigilance Practice, MO#135), to the DMAH.

As with the European Medical Devices Regulation (MDR) and In Vitro Diagnostic Medical Devices Regulation (IVDR), as well as U.S. Food and Drug Administration (FDA) regulations, the legal manufacturer registering the product is responsible for implementing the QMS. Thus, while the MAH is responsible for implementing the entire QMS if the SASF is not used or the products are registered through the PMN route, the manufacturer outside Japan is responsible for implementing the entire QMS if the SASF is used.



Whether or not the SASF is used does not affect the scope of a QMS audit. In either case, the manufacturer, MAH/DMAH and the contract manufacturer will be subject to the audit separately.

Meanwhile, if the SASF is not used, since the MAH becomes the legal manufacturer, the manufacturer is considered a contract manufacturer from the MAH's point of view. Also, the manufacturer will be managed by the MAH's QMS, just like other manufacturing facilities.

QMS certificate

After all the subjects pass the audit successfully, PMDA/RCB issues a certificate of QMS conformance to the legal manufacturer, i.e., MAH or manufacturer if SASF, separately from the device registration certificate.

Device registrations do not expire. Instead, the legal manufacturer must maintain the valid certificate of QMS conformance to continue commercial distribution of the product. Certificates of QMS conformance are valid for five years and must undergo a renewal QMS audit every five years.

Secondary use of a certificate of QMS conformance

Valid certificates of QMS conformance may exempt other product registrations from a QMS audit. Certificates of QMS conformance contain the following information (See Table 6):

Table 6: Information listed in certificates of QMS

Listed items	Description
Legal manufacturer's name	MAH or manufacturer outside Japan (if SASF)
DMAH's name	If SASF
Japan Medical Device Nomenclature (JMDN)	The JMDNs applicable to the product being registered (listed in PMA/PMC application) are listed. JMDN is the coding system that classifies medical devices and IVDs according to their characteristics. The JMDN code system was initially established in 2005 based upon Global Medical Device Nomenclature (GMDN) codes; since then, the two systems have operated independently and diverged to some extent.
Product name	The product name listed in PMA/PMC application is listed
Device group under MO#95	The Device groups applicable to the product being registered are listed. MHLW Ministry Ordinance No. 95 (MO#95) groups medical devices and IVDs based on the similarities of product characteristics (sterile or not, biological or not), manufacturing, and QMS activities. The device groups by MO#95 differ from the classification (Class I to IV) and JMDNs of medical devices and IVDs.
Manufacturing facilities audited	Every manufacturing facility listed in the product registration submission, i.e., manufacturing facilities audited in the QMS audit by the PMDA or RCB.

Suppose the legal manufacturer, i.e., the MAH or the manufacturer outside Japan (if SASF), is registering another product that falls into the same device group as the certificate of QMS conformance and is manufactured by a combination of listed manufacturing facilities. In that case, QMS audits for another product can be omitted. For example, certificates of QMS conformance may be used when registering a successor or improved product of an already registered product.

Takeaways

Understand the differences in the audit approach

As mentioned above, MO#169 audits differ from ISO 13485 audits in scope and methodology. Contract manufacturers must comply with MO#169 and be audited separately. Some manufacturers mistakenly believe that if they have a QMS that complies with MO#169 and have entered into a quality/contract agreement with contract manufacturers, the contract manufacturers are exempt from complying with MO#169. This is a great misunderstanding.

PMDA/RCB separately audits QMS(s) of the MAH/DMAH, manufacturer and manufacturing facilities, including the contract manufacturers, and determines whether the entire QMS complies with MO#169. If PMDA/RCB finds any non-compliant with MO#169, even in one of the subjects to be audited, PMDA/RCB determines that the entire QMS is non-compliant.

Cooperation from contract manufacturers is essential in MO#169 audits. Contract manufacturers must disclose their internal QMS documents even for off-site audits. Manufacturers must obtain consent to cooperate with audits by PMDA and RCB and comply with MO#169 in their contract agreements with contract manufacturers before submission. In particular, contract manufacturers may require revisions to the QMS and sub-system SOPs to address the gaps with ISO 13485 (Articles 7-2, 55-3, 67, 68, and 69 of MO#169). Therefore, manufacturers are advised to plan a timeline to allow contract manufacturers to complete the revisions before submission.

Manufacturing establishment registration

Before product registration and QMS conformity assessment applications, manufacturing facilities involved in the manufacturing activities shown in Table 5, including contract manufacturers, must be registered. Manufacturing sites outside Japan must apply for Foreign Manufacturing Establishment Registration (FMER) and obtain an FMER certificate. FMER is a simple facility registration and does not require audits only for the registration. The timeline for obtaining an FMER certificate is 1.5 to two months after application. The timeline should also be taken into consideration.

Maintenance

In Japan, device registrations do not expire. Instead, the manufacturer/MAH must maintain its valid certificates of QMS conformance to continue the commercial distribution of registered products. Changes in manufacturing site listed in certificates of QMS conformance are subject to a change application of the device registration and an additional QMS audit for the changed manufacturing facility. Even if the device or manufacturing facilities are kept the same, the manufacturer/MAH must renew the certificate of QMS conformance every five years.

In addition to renewing the certificate of QMS conformance, the aforementioned FMER certificates must also be renewed every five years. It is crucial to manage these two renewals effectively to ensure they are not missed, allowing you to stay in control and be proactive in your regulatory compliance.

Learn more

Emergo by UL helps medical device companies with regulatory compliance and market access in Japan and throughout Asia. Here's how we help:

- Medical device and IVD registrations
- Medical device classification
- ISO 13485 and Ordinance #169 compliance
- Pre-submission meetings with the PMDA

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About the author

Hiroshi Morishita is a senior quality and regulatory affairs consultant at Emergo. He has more than 10 years of consulting experience specializing in quality management systems (QMS) in the medical device industry. This includes QMS implementation consulting in compliance with MHLW Ordinance No. 169, 21 CFR 820 QSR, Regulation (EU) 2017/745, etc., as well as consulting on building risk management processes and software lifecycle processes. In addition, Morishita provided internal audit agency and supplier audits based on these standards and introductory seminars for start-ups in the medical device industry. In addition to medical devices, Morishita has over 12 years of experience in building QMS solutions that meet the requirements of EMS, ISMS and FSMS.

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