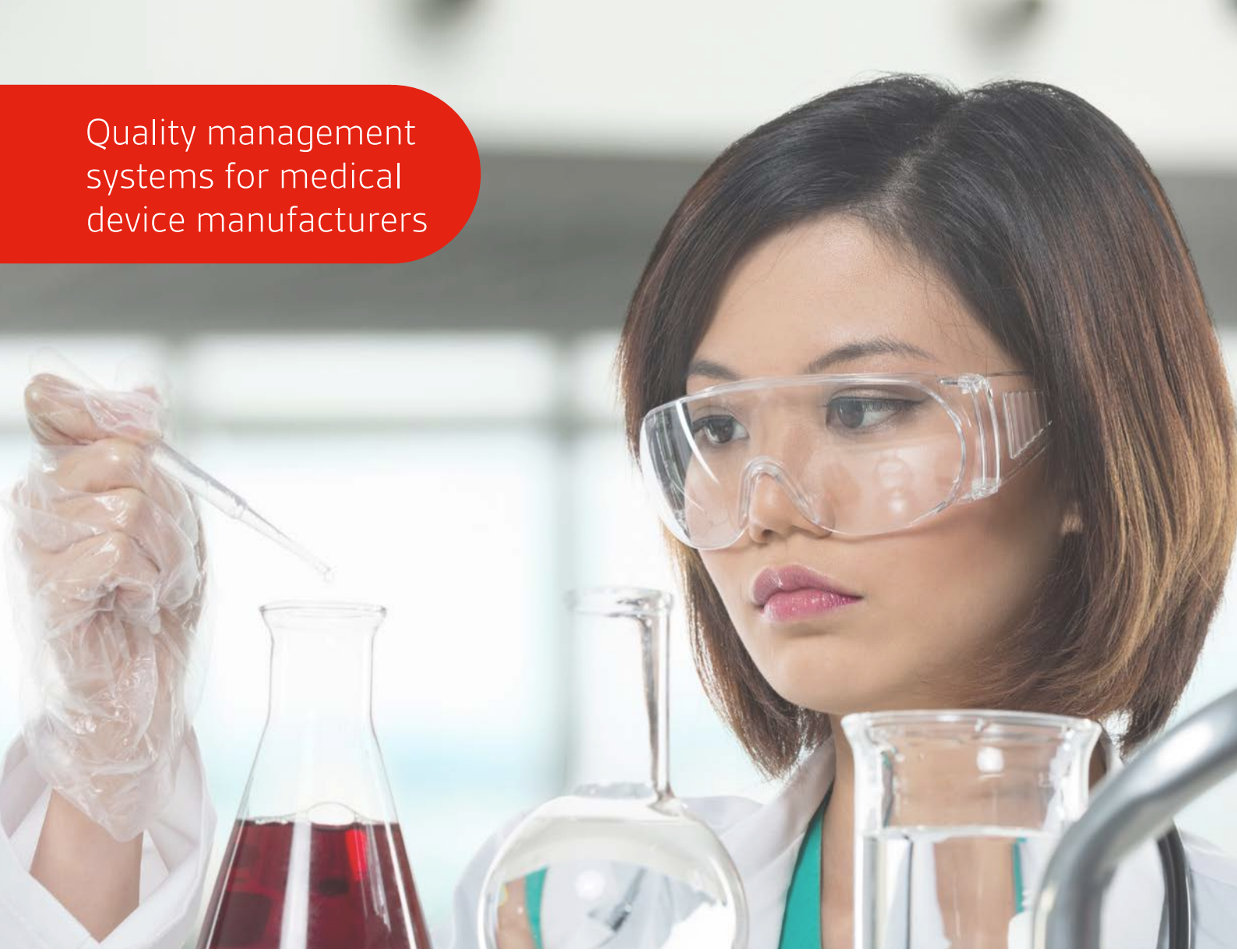
Quality management systems for medical device manufacturers



Japan Pharmaceutical Affairs Law

Practical Guide to Understanding the Quality Management System and GMP Requirements

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Introduction

Meeting Quality Management System requirements and other regulations for the manufacture and sale of Medical Devices around the world can be complex and confusing. Japan's Pharmaceutical Affairs Law (PAL) aims to harmonize requirements and reduce some of the conflicting demands by incorporating the guidance documents on the Global Harmonization Task Force (GHTF). This includes quality management system requirements based on ISO 13485:2003.

This guide will help you to identify the key PAL issues in order to prepare yourself for:

- Understanding
- Implementation
- QMS/GMP certification

This guide has also been written with the understanding that your organization may currently be registered to ISO 13485:2003, or in the process of registration.

What about ISO 13485?

Manufacturers may be confused about whether their registration to ISO 13485:2003 meets with the quality management system requirements of PAL. The requirements are based on ISO 13485:2003; however, the actual quality management systems requirements are stipulated in Ministry of Health, Labor and Welfare (MHLW) Ministerial Ordinance 169, 2004 (as of September 5, 2005).

Both the medical device manufacturer and their Market Authorization Holder (MAH) have the responsibility for product certification under PAL. A manufacturer's registration to ISO 13485:2003 provides confidence to the MAH; however, under the PAL a separate QMS/GMP certificate is required for each product or family of products.

BSI's experience

BSI has over 70,000 registered clients in 150 countries, making us the largest, most experienced registrar and notified body. This places BSI in an unrivalled position of knowledge about companies' needs, irrespective of size and industry sector.

The expanse of BSI's services allows you to purchase the standards, train your staff and gain registration - all from one committed business partner.

Here are some more reasons to choose BSI:

- Internationally experienced assessment staff who undergo the most thorough training and qualification process of any other registrar and notified body to ensure that when they visit your company they understand the needs and specific requirements of your industry
- Our registration service is accredited by an independent accreditation service, ensuring integrity of the registration decision
- Use of the highly regarded and powerful BSI Registered Logo
- Strong links with other standards and registration bodies and technical consultancies

Important information about compliance with **Japan PAL** requirements

1. Japan 's Ministry of Health, Labor and Welfare (MHLW) have published in English three key Ministerial Ordinances which detail compliance requirements for manufacturers of medical devices and the MAH:

- MHLW Ministerial Ordinance No. 169 – Standards for Manufacturing Control and Quality Control for Medical Devices and In-Vitro Diagnostic Reagents
- MHLW Ministerial Ordinance No. 2 – Regulations for Buildings and Facilities of Pharmacies, etc.
- MHLW Ministerial Ordinance No. 136 – Standards for Quality Assurance for Drugs, Quasi-drugs, Cosmetics and Medical Devices.

2. The QMS for medical devices specifies the "manufacturing control and quality control" required for all class IV, III and II medical devices and certain class I medical devices as specified by MHLW.

3. MHLW has registered BSI Japan as a Certification Body to conduct QMS audits for Designated Control Medical devices (eligible Class II devices). BSI will conduct these audits in accordance with the requirements of Ministerial Ordinance No. 169.

4. The contents of MHLW Ministerial Ordinance No. 169:

- Chapter 1 General provisions in terms of purpose definitions and scope of applications or the ordinance;
- Chapter 2 "Manufacturing control and quality control requirements to be applied in manufacturing sites of medical device manufacturers;
- Chapter 3 "Manufacturing control and quality control" requirements to be applied in the manufacturing sites of Japanese importers of medical devices.
- Chapter 4 "Manufacturing control and quality control" requirements to be applied in the manufacturing sites of medical devices containing materials of biological origin and;
- Chapter 5 "Manufacturing control and quality control" requirements to be applied in the manufacturing sites of In-Vitro Diagnostic Reagent manufacturers.

5. The statement "Provisions to be applied Mutatis Mutandis" is used throughout many Japanese ordinances and must be well understood. For example, the statement is used in Chapter 5 of the Ministerial Ordinance No. 169. Chapter 5 contains only Article 80, which describes the QMS requirements for manufacturers of In-Vitro Diagnostic Reagents.

However, Article 80 contains a statement that the provisions of "Chapter 2 and Chapter 3 shall be applied mutatis mutandis" meaning that all requirements of Article 3 to Article 72 are applicable to manufacturers of IVD Reagents with specific modifications indicated in Article 80.

6. MHLW Ministerial ordinance No. 2, Regulations for Building and Facilities, must be met by the medical devices manufacturers in order to obtain accreditation by MHLW as a Foreign manufacturer. Compliance with the requirements is determined by PMDA and not by any of the Registered Certification Bodies.

7. MHLW Ministerial Ordinance No. 136 describes the Good Quality Practices (GQP) applicable to all Market Authorization Holders (MAH). Medical device manufacturers should familiarize themselves with these requirements as part of establishing and maintaining good relationships with their MAH.

English translation of these Ministerial Ordinances are available for download at medicaldevices.bsigroup.com/content/jpal

A section by section breakdown of **Ministerial Ordinance No. 169**

The following is a review of the main differences in each section of the QMS requirements of Japan's PAL, as compared with ISO 13485:2003. This should also give a company that has never been registered to a management system a clear understanding for meeting Japan's regulatory requirements. The table below shows topics with each section of the ordinance that deviate from ISO 13485:2003 or contain specific reference to PAL requirements along with details of the deviations.

Note: *This information is published for guidance only and should not be used as the basis for GMP implementation. Please refer to the exact text of the ordinance before implementing Japan PAL requirements.*

ISO 13485:2003	Japan PAL requirements
Section 1: General rules	
This section sets the scene and "scope" of what the ordinance has been written to achieve as required by the pharmaceutical affairs law	
Permissible exclusions	• The provisions of "design and development", are applicable to those specially designated medical devices specified by Paragraph 1 of Article 77-5 of the PAL and those designated by MHLW. • The manufacturer may not apply any of the requirements of Section 5, "Product Realization", which are not applicable due to the nature of the medical device.
Section 2: Quality Management System	
This section covers some of the basic approach, structure and key elements that need to be included within a qms compliant system.	
Outsourcing	• Manufacturers are responsible for controlling outsourced activities and processes, but excludes any outsource processes where Japan PAL requires either a license or an accreditation by MHLW as a foreign manufacturer (i.e., contract sterilization facilities, contract design and development firms, etc.)
Documentation	• Manufacturers shall establish a file called Seihin Hyojun Sho, for each type or model of the medical device. This file is the documentation defining the product specifications, quality management systems requirements, the complete manufacturing process including, if applicable, installation and servicing requirements for the medical device.
Control of documents & records	Obsolete QMS documents and all QMS records shall be retained at least • 5 years for documents concerned with training; • a minimum of 15 years for "specially designated maintenance management required medical devices" as defined in paragraph 8 of Article 2 or a minimum of 5 years for other devices.

ISO 13485:2003	Japan PAL requirements

Section 3: Management responsibility

This section outlines the role which management must play in an effective QMS system

Responsible engineering managers	• Equivalent to the Management Representative as required by ISO 13485:2003 • Specific qualifications for this position are detailed in the PAL (e.g. paragraph 1 of Article 68-2 for biological-origin products)

Section 4: Resource management

This section addresses the basic resource requirements and controls for an effective QMS system.

Staff	• Each manufacturer shall establish a documented procedure for identifying training needs of those employees performing work affecting product quality
Infrastructure	• Specific requirements for the control of dust, humidity, insects and rodents • Specific workroom requirements for products in a form of liquid, solid, gel or powder • Entrances leading directly to the outside are only allowed as emergency exits • Controls specified for the supply of water to production operations

Section 5: Product realization

This section is the real heart of the ordinance, outlining all the elements, controls and approaches required to ensure medical devices are manufactured and delivered effectively.

Purchasing Information	• Detailed requirements for the approval of purchased products, including requirements for approval of shipment of purchased products and procedures at supplier's facilities. • The quality management system specifications of suppliers shall be specified within the purchasing information
Installation Activities	• The manufacturer shall provide to the Market Authorization Holder the documented requirements for all "installation control required medical devices", as defined in Paragraph 1 of Article 93.
Manufacturing control of sterile medical devices	• Five additional requirements are stipulated, in addition to the general infrastructure requirements of Section 4.

Section 6: Measurement, analysis and improvement

Here the requirements for ensuring consistency, correction and traceability are set out.

Experiences from Post-Production Phase	• The review of the experiences gained during the post-production phase must be a part of the document procedure for the feedback system.

Tips for implementation

Recommended Actions for Manufacturers

The following steps will help any manufacturer prepare for Japan PAL quality management system requirements no matter what their current QMS situation is.

1
Download the ordinances

You can only really get a true understanding of the requirements by reading the ordinances. Visit medicaldevices.bsigroup.com/content/jpal to download an English version of the Ministerial Ordinance No. 169.

2
Consider training

Consider training in Japan PAL as well as ISO 13485:2003. Many of the ISO 13485:2003 requirements are identical to the QMS requirements of the PAL, and BSI's experiences related to registration to the standard can be valuable learning for medical device manufacturers.

3
Prepare an implementation plan

Be sure to prepare a clear implementation plan. Experience has shown us that while the implementation of a quality management system should not be too hard for manufacturers, it does need to be well thought out and planned effectively

Conduct a Gap Analysis

Identify the differences between your existing registration status and the Ordinance.
This will help identify the key areas where you need to focus.

Identify Resources

Ensure you involve as many people and departments as efficiently possible.
Then allocate responsibilities and activities.

4
Implement the QMS according to the requirements of PAL

Implement the QMS as described in Ministerial Ordinance No. 169. You should expect to modify your existing ISO 13485:2003 management system to meet the specific Japanese requirements

Some key points to consider

- While efforts have been made to harmonize with GHTF requirements, these are Japan's requirements for medical device quality management systems. Don't expect that a CE certificate or CMDCAS certificate will be accepted for product registration in Japan.
- Make sure Top Management is involved – Japan looks for leadership, commitment and active involvement from the top management.
- Determine the appropriate scope and exclusions allowed by MHLW. Contact your local BSI office to obtain more information if you are unsure.
- Consider outsource processes and how they are controlled. If any of your contracted services are required to meet with license or foreign manufacturer accreditation, discuss with them how they will meet their responsibilities under the Japan PAL.

5
Communicate changes internally

Employees are the ultimate owners of the QMS. They need to fully understand the changes in order for the new quality management system to be effective.

6
Update intgernal audit procedures

Update internal audit procedures and start using audit plans which make reference to the specific Articles of Ministerial Ordinance No. 169. It may be necessary to consider auditor-training requirements.

7
Consider a pre-assessment

A pre-assessment can be a great help in ensuring you pass the registration assessment the first time.

8
Schedule registration assessment

Contact your local BSI office or BSI Japan to determine more about scheduling your QMS assessment. Remember each product certification or certification of a family of products under the Japan PAL requires a QMS certificate to be included with the application.

ISO 13485 training courses

Introduction to ISO 13485 Medical Devices

BSI's Introduction to ISO 13485 course provides an insight into the use of ISO 13485 as the basis for a Quality Management System implemented by medical device manufacturers. Time is spent reviewing the requirements of ISO 13485 and making comparisons to ISO 9001 and the FDA's Quality System Regulation. Participants will also gain an awareness of the relationship between ISO 13485 and ISO 14971, Risk Management to Medical Devices.

Course duration: 1 day

Implementing ISO 13485 Medical Devices

BSI's Implementing ISO 13485 course provides you with the knowledge and process steps to effectively implement a Quality Management System in line with the requirements for ISO 13485 certification. The course introduces the concepts needed to understand, develop, and implement a quality management system.

Course duration: 2 days

Internal Auditor ISO 13485 Medical Devices

BSI's Internal Auditor ISO 13485 course is intended for medical device quality professionals aiming to build on their current knowledge of ISO 13485 and evaluate the effectiveness of the quality management system in their organization. This intensive course teaches the principles and practices of effective quality management systems process audits in accordance with the ISO 13485 and ISO 19011. "Guidelines for Quality and/or Environmental Management Systems Auditing." The tutor guides students through the internal audit process, from planning an audit to reporting on audit results and following up on corrective actions.

Course duration: 2 days

Lead Auditor ISO 13485 Medical Devices

BSI's Lead Auditor ISO 13485 course teaches the principles and practices of effective quality management systems and process audits in accordance with ISO 13485 and ISO 19011. Tutors guide students through the entire audit process, from managing an audit programme to reporting on audit results.

Course duration: 5 days

Talk to BSI

We believe excellence should follow in everything we do, so if you would like to find out more about BSI QMS solutions, please **call or email us for an initial conversation**

Your partner in worldwide compliance: Call BSI today on +44 845 086 9000 or visit medicaldevices.bsigroup.com – to start your partnership

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