

The Japanese Pharmaceutical Affairs Law – Application to Medical Devices and In-Vitro Diagnostic Reagents.

Practice-oriented summary of the most important aspects and requirements contained in Japanese PAL and related ordinances.

Scope of PAL

- Drugs (pharmaceuticals and in-vitro diagnostic reagents)
- Quasi-drugs (sanitary and toiletry products)
- Cosmetics
- Medical devices

Structure of Japanese legislation

1. Law (e.g. PAL)
2. Governmental Ordinances
3. Ministerial Ordinances (SHOUREI)
4. MHLW Notice (KOKUJI)
5. Announcements

Important MHLW Ordinances related to medical devices and IVD reagents

- Ord. No. 169/2004 – QMS/GMP
- Ord. No. 135/2004 – GVP
Good Vigilance Practice
- Ord. No. 136/2004 – GQP
Good Quality Control Practice
- Ord. No. 180/2004
Standards of buildings and facilities

Important MHLW Notices related to medical devices and IVD reagents

- MHLW Notice No. 122/2005 – Essential Requirements for Medical Devices
- MHLW Notice No. 126/2005 – Essential Requirements for IVD Reagents
- MHLW Notice No. 112/2005 – Certification Assessment Criteria for Medical Devices
- MHLW Notice No. 121/2005 – Certification Assessment Criteria for IVD Reagents
- MHLW Notice No. 85 – GMP Applicable Medical Devices
- MHLW Notice No. 84 – Design Control Required Medical Devices
- MHLW Notice No. 78 – Specially Designated Control Required Medical Devices
- MHLW Notice No. 77 – Installation Control Required Medical Device

Classification of medical devices (MD) and responsible organizations

Class	Description	Product assessment	GMP Audit (Jap. Mfct.)	GMP Audit (Foreign Mfct.)
IV	Specially controlled MD	PMDA (approval)	PMDA	PMDA
III			Prefect. Govt.	
II	Controlled MD	RCB (certification)	RCB	RCB
	Designated Controlled MD			
I	General MD			

The correct classification of every medical device is published in the JMDN list.

Basis of product assessment

The conformity assessment criteria are essential requirements and listed JIS standards for each product category if the RCB performs product certification.

If the PMDA performs approval of a device, it is based on scientific judgment.

Basis of QMS (GMP) audit

Basis of the GMP audit for medical devices is MHLW Ordinance No. 169/2004.

The Japanese GMP for Medical Devices is structured according to ISO 13485:2003; however, it is not fully identical.

Main differences between J-GMP and ISO 13485 concern:

- Control of document (J-GMP Art. 8/ISO 13485 clause 4.2.3)
- Control of records (J-GMP Art. 9/ISO 13485 clause 4.2.4)

- Competence, awareness and training (J-GMP Art. 23/ISO 13485 clause 6.2.2)
- Infrastructure (J-GMP Art. 24/ISO 13485 clause 6.3)
- Work environment (J-GMP Art. 25/ISO 13485 clause 6.4)
- Design and development (J-GMP Art. 30, 31/ISO 13485 clause 7.3)
- Particular requirements for sterile medical devices (J-GMP Art. 44/ISO 13485 clause 7.5.1.3)
- Installation - activities (J-GMP Art. 42-1, 42-2/ISO 13485 clause 7.5.1.2.2.)
- Traceability for specified products (J-GMP Art. 4/ISO 13485 clause 7.5.3.2.2.)
- Improvement – general (J-GMP Art. 61/ISO 13485 clause 8.5.1)

It is important that all manufacturing facilities which manufacture medical devices or IVD reagents applied for approval or certificate, must comply with MHLW Ordinance No. 169/2004 and receive GMP Audit as outlined in the classification table.

Role of MAH (Marketing Authorization Holder)

The MAH has a very central function in the Japanese PAL. The MAH is responsible for the GVP (Good Vigilance Practice) and the GQP (Good Quality Control Practice). The MAH has to be based in Japan. Therefore every foreign manufacturer has to appoint an MAH. The MAH can either take the responsibility for the applications himself and becomes the owner of the product specific certificates and approvals or, in case the manufacturer wants to keep those rights, the MAH has to confirm for every application that he will act as designated MAH for this product. All applications have to be submitted in Japanese.

The MAH will also need to register the manufacturing facilities at PMDA.

Documentation needed for assessment by RCB (information marked with * must be provided in Japanese)

To certify a medical device, the following documents must be submitted to the RCB:

- Application form*
- Summary of the device (form)*
- Draft package insert/label/instructions for use*
- Color photograph of the device
- Essential requirement checklist
- Manufacturing flow chart/information about sterilization method/QC method
- Raw material/experience from previous usage
- Explanation of additional functions
- Recall/advice history in foreign markets
- Specification of device

- Documents referred to in essential requirement checklist, e.g.
 - certificate or report for test according to JIS T 0601-1
 - risk analysis summary according to JIS T 14971
 - stability data
- Comparison with existing devices
- Declaration of conformity*

To certify an in-vitro diagnostic reagent the following documents must be submitted to the RCB:

- Application form*
- Summary of the IVD reagents (form)*
- Draft package insert*
- Color photograph of the device
- Essential requirement checklist
- Manufacturing flow chart/QC method
- Specification of IVD reagents
- Performance information (performance / correlation data)
- Documents referred to in essential requirement checklist, e.g.
 - risk analysis summary according to JIS T 14971
 - stability data
- Declaration of conformity*

In both cases the following must be submitted for preparation of the GMP audit:

- Application form*
- Quality management system information for involved facilities (e.g. certificates, existing GMP audit reports).

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Reasons to choose TÜV SÜD Japan Ltd. as RCB (RCB number "AA")

- TÜV SÜD Japan Ltd. is accredited as RCB for all designated controlled medical devices and in-vitro diagnostic reagents.
- As a member of the TÜV SÜD Group, TÜV SÜD Japan Ltd. can use the worldwide auditor network of the TÜV SÜD Product Service for GMP audits.
- GMP audits, MDD audits and ISO 13485 audits can be combined easily.
- TÜV SÜD Japan Ltd. is well known for offering certification services to the medical device industry in Japan and has been offering these services for more than 10 years.
- TÜV SÜD Japan's auditors and assessors are well trained and know not only the Japanese regulations, but also the European, Canadian and American regulations.
- TÜV SÜD Japan Ltd. has offices in Tokyo and Osaka, and is therefore present in the two most attractive regions of Japan: Kanto and Kansai.
- TÜV SÜD Japan Ltd. plays an active role in the ARCB – Association of Registered Certification Bodies – to support clarification of upcoming implementation problems of the new PAL at an early stage.
- TÜV SÜD Japan Ltd. can also offer product safety and EMC testing services for active medical devices in Japan via TÜV SÜD Ohtama Ltd.

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