



## Medical Device Registration Processes of Japan: A Comparative Study with U. S. A. and Europe

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### ABSTRACT

Medical Device is an instrument or material used to support human health and there are number of medical devices present all over the world and varying rules and regulations prevails for marketing of medical devices in different countries. Medical device needs to be approved for marketing by the regulatory body of the respective country so as to sell that device in the market. The registration and approval of marketing authorization of medical device by competent regulatory authority is a lengthy and multistep process. The relevant regulatory authority issues a marketing authorization after examining the data provided by the manufacturer. The manufacturer must go through many processes and satisfy various regulatory standards depending on the country in order to market medical device. In Japan, a Federal law governing the sale of drugs and medical devices is regulated by Pharmaceutical and Medical Devices Act (PMD Act), which was enacted in 1960. Applications for marketing of drugs and medical devices in Japan are examined by the Pharmaceutical and Medical Device Agency, which collaborates with the MHLW (Ministry of Health and Labour Welfare). Grant of authorization for marketing of medical devices in Japan generally takes 6 months to 36 months depending upon class of medical device.

**Keywords:** Medical devices, Drugs, Marketing authorization, Pharmaceutical and Medical Devices Act, Ministry of Health and Labour Welfare.

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### INTRODUCTION

Pharmaceuticals and Medical Devices Agency is Self-regulating Organizational foundation responsible for ensuring quality, safety, efficacy of pharmaceuticals and medical devices in Japan. The global demand for medical devices is anticipated to be driven by the spontaneous appearance of serious illnesses like the ongoing coronavirus epidemic. Since the advent of COVID-19 in numerous countries, demand for hospital supplies, in-vitro diagnostic tools, and respiratory care equipment has greatly increased. This need is anticipated to persist in order to combat the pandemic and further reduce the chance that such illnesses would originate and spread. For instance, in 2021, the first three months of 2020 saw sales of COVID-19 test kits valued at \$2.2 billion. As a result, the global demand for medical equipment will be driven by the occurrence of such serious infections during the predicted period. Medical devices are defined as approved medical products with clearly defined structure, method of use, effect and performance to be used with objective of either “diagnosing, treating or preventing disease” or “impacting the structure or function of the human body.

Pharmaceuticals and Medical Devices Agency, Japan is an economic powerhouse as its medical device market is one of the biggest in world. According to global data report (a leading data and analytics company) the Japanese medical device market is set to reach to 74.7 Billion Dollars in 2025, growing at a compound annual growth (CAGR) of 4.6%<sup>1</sup>. Japanese medical device market is one of the world's biggest market after United States and Europe, Japanese Government consistently take Initiatives and makes policies to promote medical devices and healthcare projects, gives opportunities to Japanese and foreign manufactures. According to FY 2022 budget declared by Japanese Government, it shows that Japanese Government continuously promotes healthcare industry as an area of growth<sup>2</sup>.

Medical devices, in Japan, are classified into the following four categories based on their intended use and safety risk<sup>2</sup>.

**Medical Device Classification:** Medical devices, in Japan, are classified into the following four categories based on their intended use and safety risk<sup>3</sup>.

#### 1. General medical devices (Class I)

General medical devices (Class I) are those other than specially controlled medical devices and controlled medical devices that are deemed by MHLW to pose an almost insignificant risk to human life and health in the event of malfunction or side effects.



## ❖ Requirements:

- No QMS audit is required.
- Applicant must have a 3rd grade Marketing Authorization Holder (MAH) license.
- The manufacturing facility must have a license for medical device manufacture.

**2. Controlled medical devices/designated controlled medical devices (Class II)**

Controlled medical devices/designated controlled medical devices (Class II) are those other than specially controlled medical devices that are deemed by MHLW to require management in relation to the relatively low potential risk they pose to human life and health in the event of malfunction or side effects.

Medical devices categorized as Class II are further regulated as follows:

- Medical devices, which have not applicable certificate standards, are categorized as controlled medical device, and need approval reviewed by PMDA.
- Medical devices, which have and meet applicable certification standards, are categorized as designated controlled medical devices, and need certification reviewed by and Registered Certification Body (RCB).

## ❖ Common requirements for class II medical devices.

- The applicant must have a 2nd grade MAH license.
- The manufacturer must have a license for a medical device manufacture.
- Manufacturer must comply with the quality management system (QMS) requirements set by MHLW ordinance 169.

**3. Specially controlled medical devices (Class III and Class IV)**

Specially controlled medical devices (Class III & IV) are those deemed by MHLW to require appropriate management in relation to the relatively high or potentially fatal risk they pose to human life and health in the event of malfunction or side effects. Such devices are categorized as Class III or Class IV.

Class III and IV medical devices require submission of applications for approval, which are reviewed by PMDA (the Pharmaceuticals and Medical Devices Agency). As Class III and Class IV cover a variety of medical devices, there are several application categories as shown in the table below. The requirements, review term and cost depend on the application categories.

## ❖ Devices of Class III are further regulated as follows:

- Medical devices without certification standards that are classed as specially controlled medical devices need PMDA approval.

- Medical devices with certification standards that are classed as specially controlled medical devices need review by an RCB (registered certification body – a third-party organization).

For Class III medical devices without certification standards:

- An application for approval must be submitted to PMDA.

For Class III medical devices with certification standards:

- Certification by an RCB is necessary.
- The applicant must have a MAH license.
- The manufacturing facility must advance registration for manufacture.
- Manufacturing facilities must comply with the quality management system (QMS) requirements set by MHLW ordinance.

❖ **The following requirements apply to all Class IV medical devices**

- An application for approval must be submitted to the Pharmaceuticals and Medical Devices Agency (PMDA – the approvals review body).
- The applicant must have a Marketing Authorization Holder (MAH) license.
- The manufacturing facility must advance registration for manufacture.
- Manufacturing facilities must comply with the quality management system (QMS) requirements set by MHLW ordinance.

The description for classification of all the four classes for medical devices is given in **Figure 1**.

**Government Initiatives**

Japanese Government consistently takes Initiatives and makes policies to promote medical devices and healthcare projects, gives opportunities to Japanese and foreign manufactures. According to FY 2022 budget declared by Japanese Government it shows that Japanese Government continuously promotes healthcare industry as an area of growth. Recently, during covid-19 pandemics the Government demonstrates the innovative life supporting (healthcare) products. After this covid-19 incidence Japanese Government has paid more importance to pharmaceutical, medical device / healthcare products such as wearable device for better health management. Every year, Japanese Government / Ministries declare budget, and the budget declaration for healthcare field is based on Japanese Government Healthcare Policies and aim. The budget is then executed as a subsidy to the Japan Agency for Medical Research and Development (AMED). The Japanese Government declares approximately US\$ 100 million for AMED's medical devices and healthcare projects in FY 2022. This budget will go toward research



and development for medical devices and healthcare contributing to the innovation of diagnosis and

treatments, as well as the improvement of quality of life utilizing artificial intelligence (AI).

### Medical Device Classification

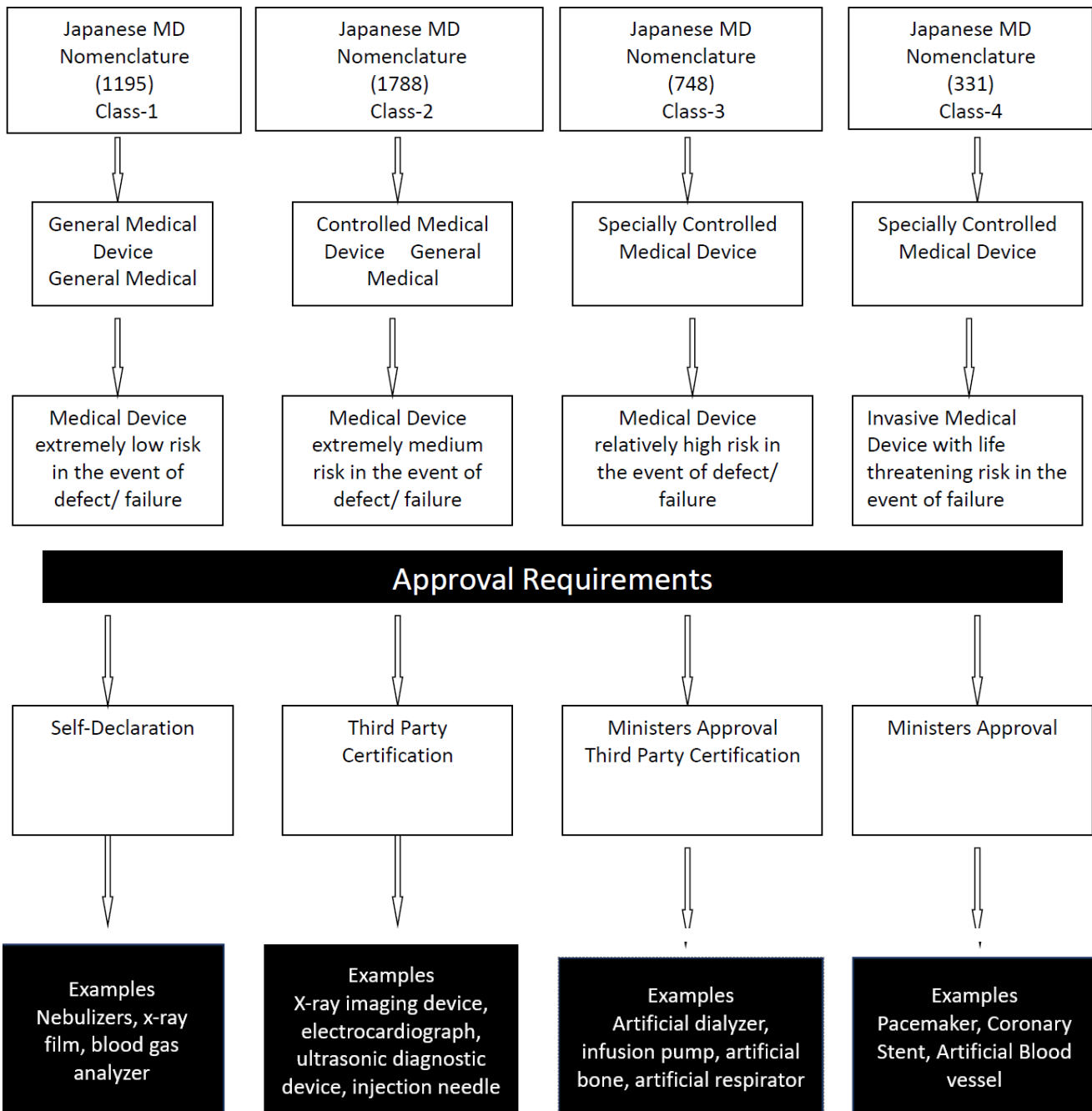


Figure 1: Classification of Medical Device in Japan<sup>4</sup>

There are three important things while inspecting the policies related to medical devices:

1. Research and development
2. Regulatory Aspects of efficacy and safety
3. Reimbursement pricing

Japan began focusing these three points in January 2017 and, after continuous discussions, the cabinet approved the Regulatory Reform Implementation Plan in June

2021. This plan includes various policies to solve most of the issues to be tackled in the future.

Use of AI in Healthcare identified six priority areas to be developed for AI utilization in healthcare

1. Diagnostic imaging support
2. Diagnostic and therapeutic support (including testing, disease management, and disease prevention)

3. Surgical support
4. Nursing care and dementia
5. Genomic medicine
6. Drug development Amendment of Pharmaceuticals and Medical Devices Act (PMD Act) to Establish Post-Approval Change Management Protocol for Medical Devices (PACMP).

By Amendment of the PMD Act, the Post-Approval Change Management Protocol for Medical Devices (PACMP) was developed as an approval review system for medical devices including AI-based medical devices. In Japan, the PACMP is also commonly known as IDATEN (Improvement Design within Approval for Timely Evaluation and Notice).

### Clinical Trials for Medical Device

As medical gadgets get more complicated, clinical trials for new ones are popping up more frequently. Clinical data proving the usefulness and safety of devices are required due to the increased complexity. Now, American businesses are attempting to enter Japan's expanding medical equipment sector. The creation of clinical trial strategies would be impacted by the recently updated Japanese Pharmaceutical Affairs Law (PAL), according to clinical and regulatory affairs managers, to stay up with advancements in science and the global medical device industry, the Japanese government is upgrading its regulatory framework for medical devices. The Ministry of Health, Labor, and Welfare (MHLW) started the first stage of its extensive modernization effort in April 2004. It created a single Pharmaceuticals and Medical Devices Agency by combining the Organization for Pharmaceutical Safety and Research (OPSR), the Japan Association for the Advancement of Medical Equipment (JAAME), and the Pharmaceuticals and Medical Devices Evaluation Center (PMDEC). Previously, Japan's device and pharmaceutical regulatory system was supported by three organizations: PMDEC, JAAME, and OPSR, next stage was began in April 2005, consist of third party evaluation programme for low-risk medical devices. In this stage, PMDA started using the new Summary of Technical Documentation (STED) application format that the Global Harmonization Task Force had created initially (GHTF). In 1992, MHLW released a document that served as regulatory advice for good clinical practice (GCP). This advice has now been replaced by specific rules in the new Pharmaceutical Affairs Law that deal with clinical trials for medical devices, a written informed consent is now required by the GCP; in the past, verbal consent was frequently obtained. The new informed-consent document is built upon the ethical precepts outlined in the Declaration of Helsinki. Japanese Government made stringent clinical trial regulations according to need and to improve both patient protection and the quality of clinical investigation<sup>5,6</sup>.

### Clinical Trial Notification

The Pharmaceutical Affairs Law amendment now requires that clinical investigation sponsors submit a clinical trial notification (CTN) 30 days before starting a trial for a new device. The amendment also requires mandatory reports to MHLW of adverse events that occur during a clinical trial. It also includes patient confidentiality protection provisions. The Clinical Trial Notification contains a device description, preclinical data, clinical trial protocol, and an analysis plan, much like a U.S. Investigational Device Exemption application.

### Clinical Trials Network

In 2003, the Japanese Medical Association (JMA) initiated a clinical trial promotion program called the Network for Multi-Center Clinical Trials (NMCCT). The project is being subsidized by the Japanese MHLW. NMCCT has created a network of national hospitals, hospitals with residency training programs, and other clinical research-oriented facilities. The network's goal is to facilitate large clinical trials that generate high-quality clinical data. Until 2006, MHLW will create oversight and administrative offices to help coordinate, organize, and evaluate distinct clinical trial networks for 10 specific disease entities defined by NMCC. MHLW also set up a grant program to establish clinical trial management offices in 45 national hospitals. The goal of this program is to improve clinical trial management in Japan.

### Medical Device Single Audits (MDSAP)

The Medical Device Single Audits (MDSAP) aims to enable MDSAP auditing organizations to conduct a single audit of a medical device manufacturer that will satisfy the pertinent requirements of the participating medical device regulatory authorities. Since June 2015, the Japanese Pharmaceuticals and Medical Devices Agency (PMDA) and the Ministry of Health, Labour, and Welfare have been taking part in the initiative. International partners that are participating in the MDSAP include: Therapeutic Goods Administration of Australia, Health Canada and U.S. Food and Drug Administration etc.<sup>7</sup>.

### Acceptance of MDSAP Audit Reports

MDSAP audit reports may be used as a way to demonstrate conformance to Japanese medical device Quality Management System requirements. PMDA has been accepting MDSAP audit reports since 2016.

### Quality Management System (QMS)

PMDA conducts on-site and document-based inspections of manufacturing sites located in Japan or overseas. It is to ascertain whether their manufacturing facilities and manufacturing and quality controls comply with standards such as the Quality Management System (QMS) and whether manufacturing sites have a system for manufacturing products of adequate quality<sup>8</sup>.



## Japan Medical Device Nomenclature (JMDN) codes

The Ministry of Health, Labor, and Welfare (MHLW) maintains a database of generic device descriptions associated with Japan Medical Device Nomenclature (JMDN) codes. This JMDN system is similar to the Global Medical Device Nomenclature (GMDN) system or the US FDA nomenclature system. If the Ministry of Health, Labor, and Welfare (MHLW) database does not contain the device code, then the product needs to undergo a new registration pathway based on the device class.

## Registration procedures for medical devices sold in Japan

The Japanese regulatory process can be lengthy and expensive. Regulations and documents are published almost exclusively in Japanese and the PMDA Act imposes stringent requirements and clinical standards for foreign manufacturers. An experienced regulatory partner with a presence in Japan is essential. As such, large corporations with the resources to push through the regulatory process already have a strong hold on the Japanese market. Foreign manufacturers can also expect hefty competition from domestic manufacturers as Japan is home to leading consumer technology companies that also design medical devices. The greatest competition is in the diagnostic imaging, therapeutic and surgical equipment, home therapeutics, dialyzers, and endoscopes. The registration pathway for your device is determined by its class and associated Japan Medical Device Nomenclature (JMDN). To market medical devices in Japan, your Marketing Authorization Holder (MAH) must register your device through one of the following procedures<sup>8,9</sup>.

**For medical devices, there are three different types of registration procedures:**

### 1. Pre-market submission (Todokede)

To register General Medical Devices (Class I), has to file a pre-market submission to the PMDA. This is a notification, and no review/assessment by the PMDA will be conducted.

Some of the requirements for the approval of Class I device includes: The device category, name (generic/proprietary), intended use of the device, device shape and structure etc.

The MAH needs to file a notification for approval, and since these devices are of low risk, they may not require the assessment by the PMDA. The sponsor shall apply for the Quality Management System (QMS) that complies with the PMDA Act with the Ministry of Health, Labour and Welfare (MHLW). The sponsor needs to register the manufacturing facilities too. Applications are submitted to the PMDA and are considered accepted upon submission. It takes one week to issue a PMS (Pre-market submission) number. There is no PMDA fee to process the application.

### 2. Pre-market certification (Ninsho)

Class II (and a limited number of Class III) devices which have an associated certification standard (JIS), are subject to pre-market certification. Many, but not all, Japan

Industrial Standards are based on existing ISO/IEC standards. MAH will file the application with a Registered Certification Body (RCB). The process is similar to the European CE marking process where reviews are outsourced to a third party similar to a Notified Body.

The necessary documents to register Class II devices includes: Details of intended use, the proprietary name of the device, device shape, device structure, direction for use, method of manufacturing, storage conditions, shelf life, etc.

The MAH needs to initiate the application with a notarized body. In a few cases, some Class II devices may require review by both i.e. the PMDA and MHLW. The foreign manufacturers may require an extra step for approval because, with device approval, the foreign manufacturer needs to obtain the FMA (Foreign Manufacturer Accreditation). This class of medical devices requires maintaining the QMS. Since the approval timeline depends on the completeness of the application. Review of the medical device and quality systems conformity assessments are outsourced by the PMDA to Registered Certification Bodies (RCB). There are 14 RCBs, 7 of which are international companies that also offer Notified Body/Registrar services. The average time to process a PMC (Pre-market Certification) application is 3 months, with an average cost of US\$30,000.

### 3. Pre-market approval (Shonin)

Class II and III devices without a specific certification standard are subject to the pre-market approval process. This also applies to all Class IV devices. In this case your MAH will file a pre-market approval application with the PMDA and ultimately obtain approval from the MHLW.

The documents necessary for Class-3 & Class-4 include: medical device category, intended use, efficacy risk analysis data, clinical data, etc. also requires Summary of Technical Documentation (STED), If risk associated with the Class III and Class IV devices are the same, the application remains almost the same with a few differences. Based on the risk, in few cases, this review process is also applied to Class II controlled devices. The sponsor needs to apply to the PMDA, and the PMDA conducts a QMS conformity assessment inspection at the manufacturing site. The approval depends on factors such as completeness of the application, QMS, and risk associated with the device, the timeline for approval varies accordingly. Application processing time and PMDA/MHLW fees will vary from 6 months to 36 months and average cost is US\$20,000 to US\$120,000 depending on class, JMDN code application, and requirements for clinical evidence.

PMDA Clinical Evaluation Consultation: If clinical evidence is required as part of the registration application, it is recommended to take this formal meeting with the PMDA to determine if your data is sufficient for a successful application. The PMDA fee for the 2- hour meeting is approximately US\$10,000.

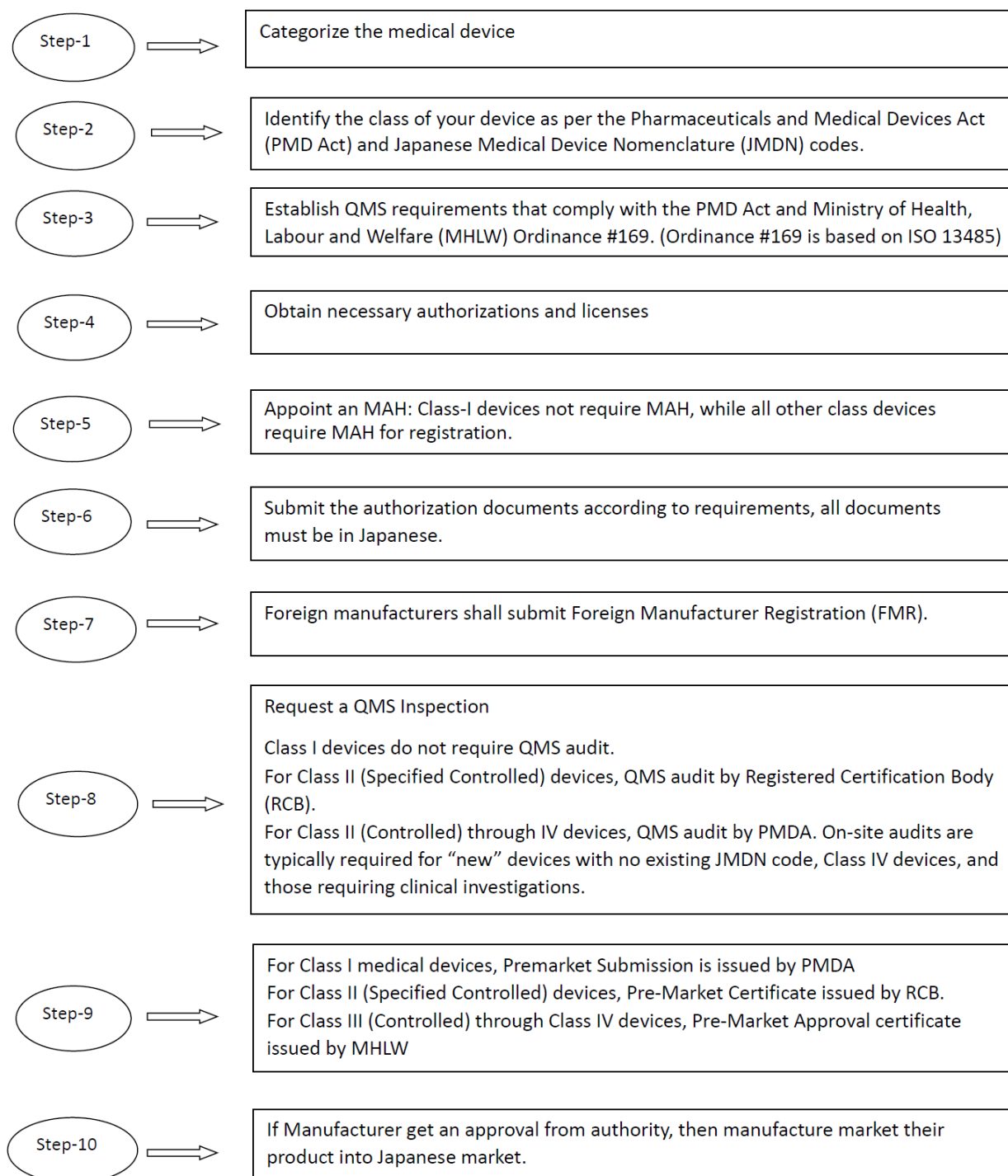


PMDA Clinical Study Consultations: It is recommended to take a formal meeting with the PMDA to confirm if your clinical study is designed such that the data will be acceptable for a medical device registration application. The PMDA fee for the 2-hour meeting is approximately US\$10,000.

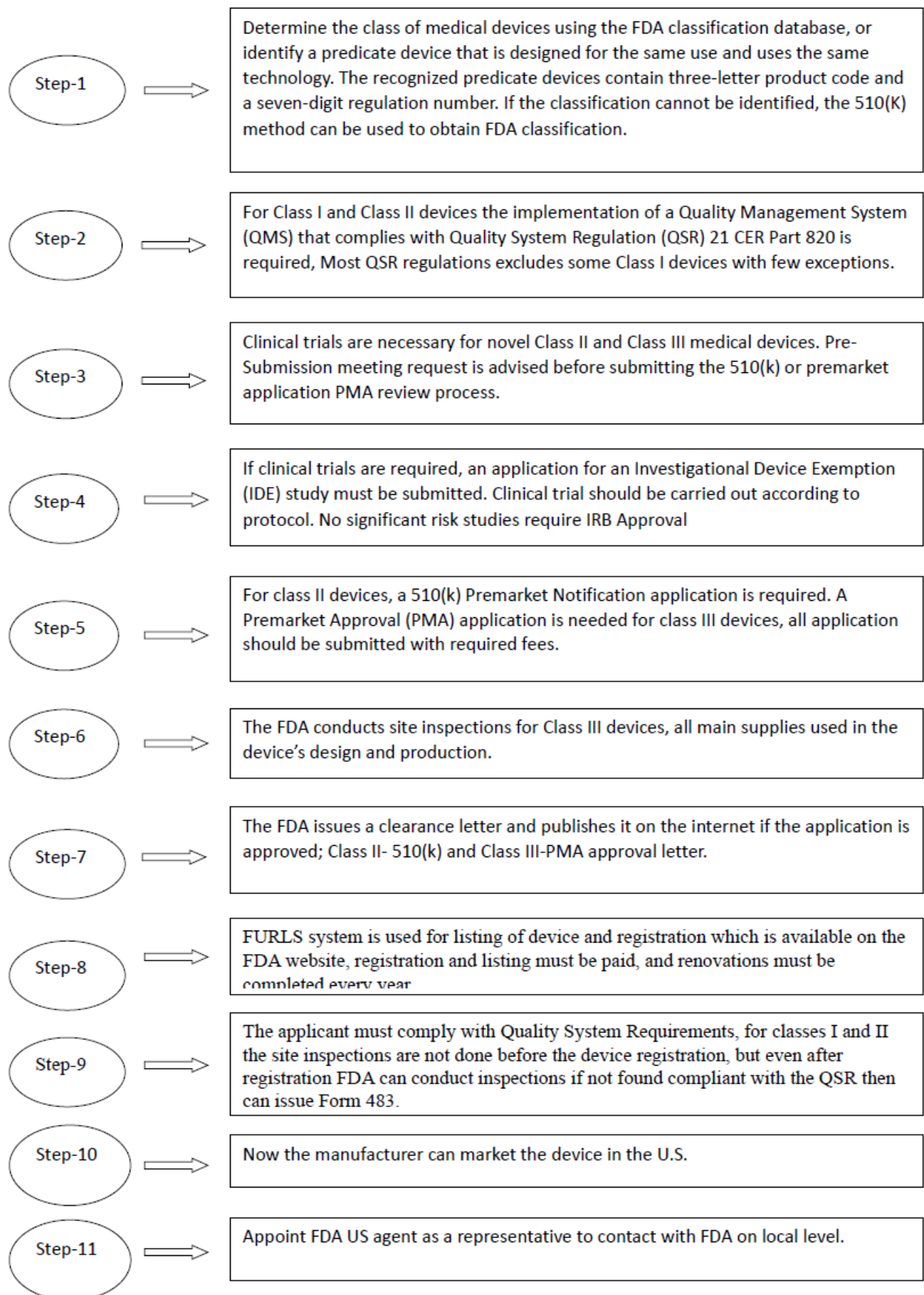
### Steps for Registration and Approval Process of Medical Device in Japan:

The process and timeline to register a medical device depends on the class to which it belongs. So, it is crucial to

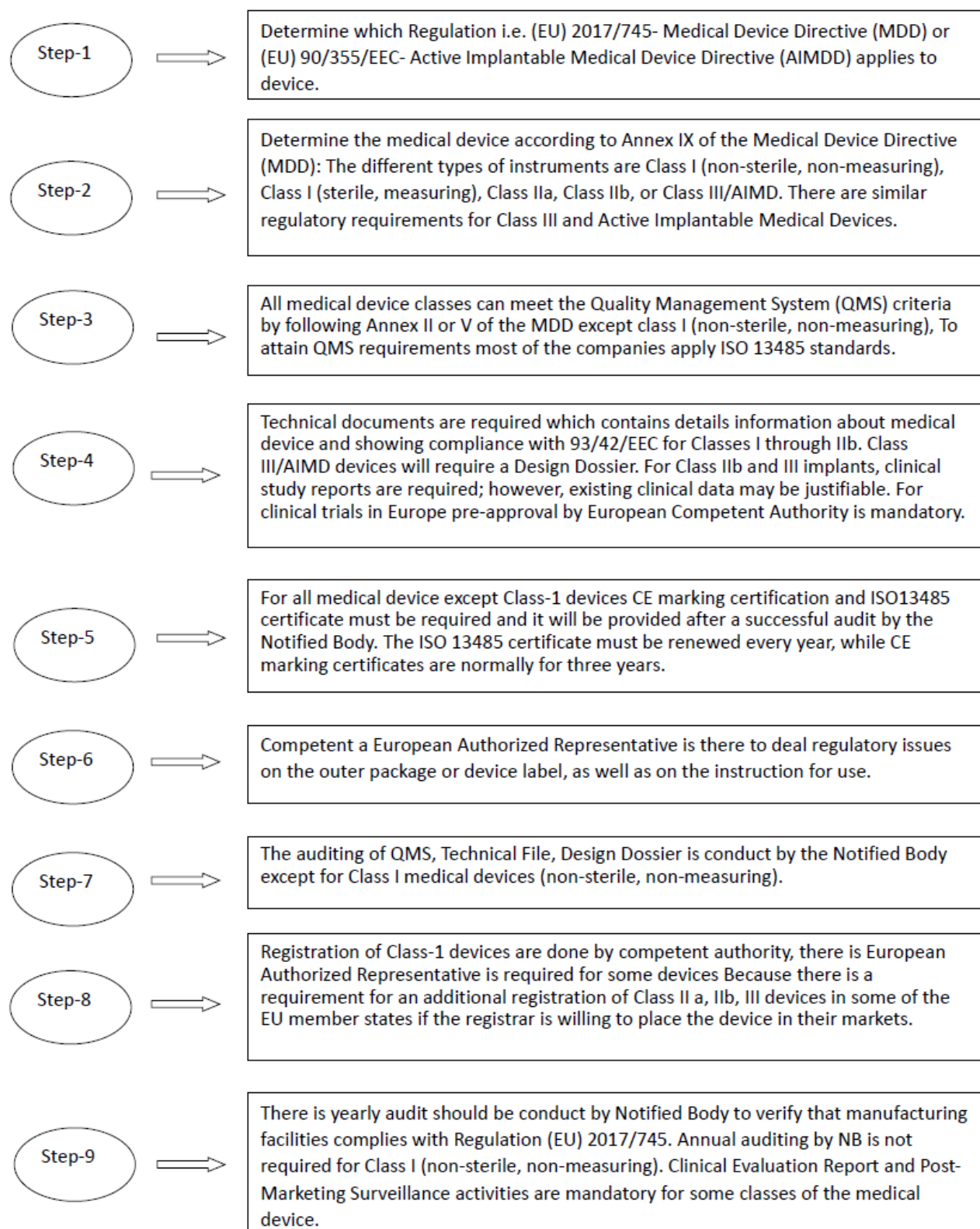
understand the class of medical devices before initiating any registration process. After the registration of medical device, the sponsor should renew the QMS certificates every five years. In order to avoid delays, the sponsor should initiate the renewal process six months before the expiration. Pre-Market certification applications may also be subject to annual surveillance audits by the authority<sup>10</sup>. **Figure 2** represents different steps for registration and approval process of medical device in Japan.



**Figure 2:** Steps for Registration and Approval Process of Medical Device in Japan



**Figure 3:** Medical Device Registration Process in United States of America<sup>11,12,13,15,16</sup>



**Figure 4:** Medical Device Registration Process of Europe<sup>14,15,16</sup>

**Medical Device Registration Process of U.S.A.:**

The process and timeline to register the medical device is depending on the classification of medical devices. In USA, there are two applications present for the registration of medical device i.e. 510K application which requires 90 days for approval, and PMA application which requires 180 days

for approval. Overall the approval should be given by FDA. The various steps for medical device registration process in United States of America are presented in **Figure 3**.

**Medical Device Registration Process of Europe:**

The various steps for medical device registration process in Europe are presented in Figure 4.



The process and timeline to register the medical device depends on Classification of medical device, Medical device can't be placed into European market without conforming to the strict safety requirements of EU, A device must bear CE mark, except for custom-made devices; Devices for clinical investigations, health protecting-urgent unusual circumstances; humanitarian use and In-house use.

## CONCLUSION

The primary aim of this review is to understand the medical device market, legislative changes, government initiatives, schemes, and the advancement of the medical device market in Japan, which has become a world's largest medical device market without compromising on quality, safety, and efficacy. The registration process of medical devices in Japan is lengthy and strict process and it requires complying with Japanese regulation standards. Japan has shown innovation (AI based technology) in the medical device industry and Government also consistently takes initiatives in development of medical device industry.

## REFERENCES

1. Drug Development and Delivery  
<https://drug-dev.com/japans-medical-device-market-set-to-reach-74-7-billion-in-2025/>
2. Official Website of the International Trade Administration  
<https://www.trade.gov/market-intelligence/japans-medical-device-market>
3. JHPN Japan Health Policy Now  
<https://japanhpn.org/en/section-6-4/>
4. Japan MDC-Evolutionary Solution for Medical Device  
<https://www.j-mdc.com/en/product/classification.php>
5. Official Website of Medical Device and Diagnostic Industry  
<https://www.mddionline.com/news/medical-device-clinical-trials-japan>
6. Rana A, Deshwal M and Rahi S, Comparative study of marketing authorization procedure for medical devices in USA, EU and Japan, World Journal of Pharmaceutical Sciences, 2020;9:1627-1650, DOI: 10.20959/wjpps20208-16701.
7. Official Website of Pharmaceutical and Medical Device Agency  
<https://www.pmda.go.jp/english/review-services/gmp-qms-gctp/0004.html>
8. Official Website of EMERGO  
<https://www.emergobyul.com/resources/japan-process-chart>
9. <https://www.pmda.go.jp/files/000164006.pdf>
10. Chandan BV, Venkatesh MP, Arjun M, Pasupuleti Dheeraj Krishna and Indraprasad S, Comparison of Medical Device Regulations in India, Japan and South Korea, Journal of Pharmaceutical Research International, 2021;33(53A):8-23, DOI: 10.9734/JPRI/2021/v33i53A33634NLM ID: 101631759.
11. U.S. Food and Drug Administration -Classify Your Medical Device. Department of Health and Human Services.  
<https://www.fda.gov/medical-devices/overview-device-regulation/classify-your-medical-device>
12. World Health Organization-Clinical evidence for medical devices: Regulatory processes focusing on Europe and the United States of America. Medical Devices.
13. Pisano DJ, Mantus D (2014) FDA Medical Device Regulation: FDA Regulatory Affairs (3rd edn.), CRC Press, USA.
14. European Council (2007) Council Directive of 14th June 1993 concerning medical devices. Council of the European Communities.
15. Ganesh GNK, Nishanthini B, Lakshmi T. Vidya, Medical Device Regulation in US, Europe, China and India, International Journal of Drug Regulatory Affairs. 2017;5(2):17-25. DOI: <https://doi.org/10.22270/ijdra.v5i2.198>.
16. Sawant AM, Mali DP and Bhagwat DA, Regulatory Requirements and Drug Approval Process in India, Europe and US, Pharmaceutical Regulatory Affairs. 2018;12(7), DOI: 10.4172/2167-7689.1000210.

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