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Effective Use of Foreign Clinical Data in Approvals for Medical Devices in Japan

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Abstract

Initial clinical development of medical devices occurs mainly in the USA and EU, with many medical devices registered in Japan afterwards. As the clinical performance of medical devices is less sensitive to ethnicity than the efficacy and safety of a drug, the performance of such devices can often be evaluated using foreign clinical data. The factors affecting the requirement for Japanese clinical data was investigated in the Japanese approvals of 103 high-risk devices, occurring between April 2005 and March 2015. The requirement for Japanese clinical data was associated with no approval in the USA and EU and the absence of foreign clinical data in the submission (p<0.001). Our results suggest that Japanese clinical data are not an essential requirement when foreign clinical data are included in the Japanese data package for approval, although, for 50% of devices with approval in the USA or EU, Japanese clinical data were still required for the Japanese approval. Reasons for this included the possibility that the performance of the device was sensitive to ethnicity associated with the medical environment, and that the device had been updated from the original one.

Keywords: regulatory science, medical devices, medical device development

1. Introduction

The development of medical devices faces different regulatory frame works in the United States of America (USA), the European Union (EU), and Japan. For the protection of public health, the regulation of a medical device usually requires it to be classified according to the risk it poses to consumers [1]. Therefore, each regulatory agency determines the approval process and the data package required according to the risk classification of the particular device. For example, medical devices in the USA are categorized into three classes (Class I, II, and III). Although Class I (low risk) devices are exempt from premarket notification, Class II (moderate risk) devices are required to be accompanied by clinical data, as necessary for the premarket notification (510k) review process, and Class III (high risk) devices require clinical data for the premarket approval (PMA) review process by the Food and Drug Administration (FDA) [2, 3, 4]. In the EU, medical devices are categorized into four classes (Class I, IIa, IIb, and III), and clinical data are essential for Class III devices [2, 3, 4]. In Japan, the category consists of four classes (Class I, II, III, and IV). Class I (low risk) devices are exempt from the review for approval. Class II and parts of Class III devices are approved without clinical data. Class IV and high risk devices of Class III are submitted to Japanese authorities Ministry of Health, Labour and Welfare (MHLW)/Pharmaceuticals and Medical Devices Agency (PMDA) [4, 5]. New devices and some improvements to devices in Class III and IV require clinical data (Figure 1). Therefore, when applying for medical device approval in the three regions, the manufacturing company has to prepare different data sets for the different categories of classes of the three regional regulatory bodies.

Most medical devices have been clinically developed in the USA and EU and then introduced to Japan following global strategies. Therefore, many medical devices were registered by the Japanese regulatory agency after approval was obtained in other countries. The time lag between the Japanese approval and the previous USA/EU approval (device lag) consists of two types: development lag and assessment lag.

Development lag describes the delay of submission to the review authority which reflects the delay of development start in Japan. Assessment lag is the difference in review time between Japan and other countries. With respect to assessment lag, the device manufacturing industries and MHLW/ PMDA set up an action program 7 years ago, with the intention of re-

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Classification of medical devices	Japan	United States	European Union
Class I	Clinical data are not required.	Clinical data are not required.	Clinical data are not required.
Class II	Clinical data are not required.	Clinical data are required as necessary for the premarket notification (510(k)).	Clinical data are not required.
Class III	New devices and some improvements to devices require clinical data.	Clinical data are required for the premarket approval (PMA).	Clinical data are essential.
Class IV	New devices and some improvements to devices require clinical data.	Not applicable.	Not applicable.

Figure 1: Classification of the devise and regulatory requirements across three regions.

ducing and/or removing such delays [6]. As a result, the assessment time has been shortened from 16 to 9.5 months [7], and the assessment lag of around 0.5 years has been removed [8].

In contrast to the situation with drugs, the performance of medical devices is insensitive to ethnicity, and in many cases the extrapolation of foreign clinical data to a new region has been acceptable for regulatory review. However, a development lag for medical devices still remains in Japan. One reason for this may be that Japan has a smaller market size than the USA and EU. Efficient device development requires the initial focus to be on a larger market; the data package is therefore first prepared for the USA/EU registration. As discussed above, there are differences in the device categories and regulatory requirements across the three regions. Even though complete data packages may exist for the USA/EU, different or additional data packages may be required for Japanese registration. Moreover, if additional data from a clinical study are required, there will be a substantial time lag associated with completion of the clinical study, and additional regional development costs will be incurred.

The purpose of this study was therefore to investigate any correlation between the requirement for a Japanese clinical study, and the timing of approval in the USA/EU. In Japan, a clinical study is an essential requirement for new devices (Class III or IV), even if no clinical study was carried out for registration in the USA/EU.

2. Materials and Methods

2.1. Data Sources

All information used in this study was extracted from review reports for new devices in Class III or Class IV; these were published on the website of Japan's PMDA [9]. For this study, the approval status in the USA or EU at the time the device was submitted for approval in Japan was investigated and categorized as either "No approval in the USA and EU" or "Approval in the USA or EU". The status "Approval in the USA or EU" was also given if the device was under review in the USA or EU.

For the approval status, the information on approval date in the USA or EU was obtained from the PMDA [9] and FDA websites [10]. A medical device with more than one brand name (i.e., with each brand name sold via a different channel) was counted as a single device.

Medical devices approved using safety and/or efficacy evidence that referred only to previous reports, and devices approved without any clinical information, were excluded from this study.

2.2. Data Analyses

Fisher's exact test was used to examine factors affecting the requirement for Japanese clinical data in the approval of high-risk devices in Japan. The variables were the approval status in the USA or EU (no approval or approval), whether foreign clinical data were used, the classification of the device (Class IV or not), and the status of orphan/priority review/expedited review devices.

Statistical analyses were conducted using SAS Enterprise Guide 5.1 (SAS Institute Inc., Cary, NC).

3. Results

One hundred and three high-risk devices were approved in Japan between April 2005 and March 2015 (Supplemental Figure A.1). Regarding the origin of clinical data, 45 devices (44%) were approved using only foreign clinical data, 22 devices (21%) were approved using both foreign and Japanese clinical data, and 36 devices (35%) were approved using only Japanese clinical data. Japanese clinical data were used for 56% (21% plus 35%) of devices. As the performance of a medical device is insensitive to ethnicity, it was assumed that foreign clinical data were used without additional Japanese clinical data when medical devices had been registered following approval in

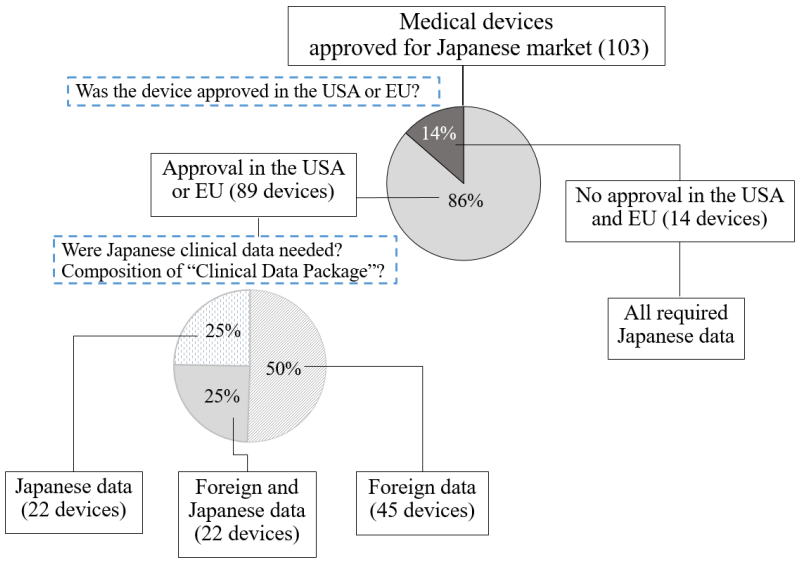

Figure 2: Relationships between foreign approval status and the submission of a clinical data package for Japanese approval.

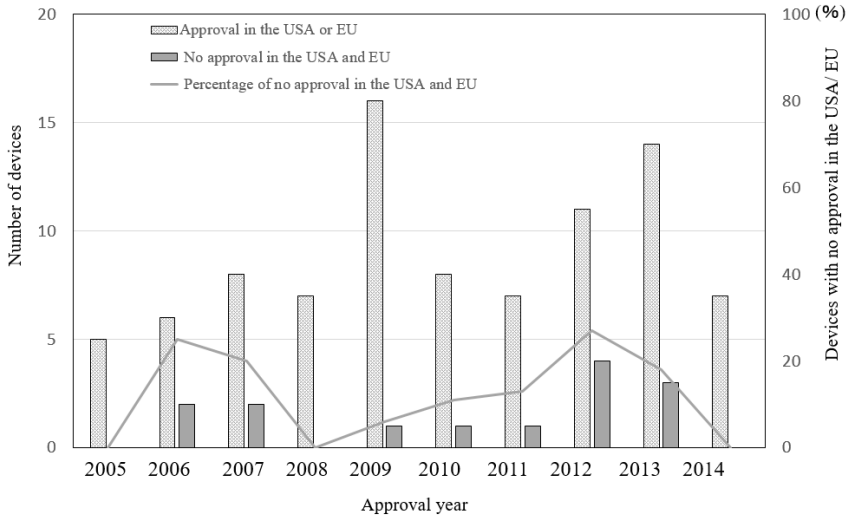

Figure 3: Approval trends for new high-risk medical devices in Japan.

other countries. However, the results showed this assumption to be incorrect.

We then investigated the status of approval in the USA and EU, to examine whether this status affected the requirement for Japanese clinical data in the Japanese approval. The number of cases with or without prior approval were 89 (86%) and 14 (14%), respectively. These results revealed that 86% of devices were registered after approval in the USA or EU, suggesting the possibility that foreign clinical data were used for the Japanese submission. However, 50% of devices with approval in the USA or EU were submitted for approval in Japan with Japanese clinical data (Figure 2). It is supposed that the foreign clinical data were considered insufficient to indicate efficacy and safety in Japanese patients. For 25% (22 devices) of devices with approval in the USA or EU, Japanese clinical data were used without the foreign clinical data (Figure 2). However, all those devices with no approval in the USA and EU (14 devices) required Japanese clinical data (Figure 2).

We also investigated the trend in the number of approvals by year. Although the number of approvals changed each year, the percentage with no prior approval in the USA or EU was between 0% and 20% (Figure 3) and had no specific trend. Therefore, it was concluded that analyses by year were not necessary.

Of the total 103 device approvals, the numbers of priority review devices, expedited review devices, and orphan devices, were 18 (17%), 1 (1%), and 8 (8%), respectively (Supplemental Figure A.1). As priority review or orphan applications were made for devices used for serious diseases[11, 12, 13, 14], it

Variable	Japanese data (+)	Japanese data (-)	p value
Approval in the USA or EU			
Yes	44	45	
No	14	0	$p<0.001$
Foreign data			
Yes	22	45	
No	36	0	$p<0.001$
Orphan/priority review/expedited review			
Yes	12	15	
No	46	30	$p=0.1783$
Class IV			
Yes	31	27	
No	27	18	$p=0.5521$

p value: Fisher's exact test.

Figure 4: Factors affecting the requirement for Japanese clinical data in Japanese approvals.

was supposed that there were difficulties with conducting a clinical trial in Japan. However, five devices (19%) had no approval in the USA and EU. Of the 22 devices (81%) with approval in the USA or EU, 15 (68%) were submitted with foreign data, six (27%) required foreign and Japanese data, and one (5%) was submitted with only Japanese data. Thus, Japanese data were used for 32% of these priority review or orphan devices.

Fisher's exact test was used to identify factors affecting the requirement for Japanese clinical data for approvals in Japan (Figure 4), and demonstrated that a requirement for Japanese clinical data was associated with no approval in the USA and EU, and the absence of foreign clinical data ($p < 0.001$). No significant associations were found for Class IV designations ($p = 0.552$) and the status of orphan/priority review/expedited review devices ($p = 0.178$).

In cases with approval in the USA or EU, for which a data set sufficient for the USA or EU registration was available, additional Japanese data were submitted alongside the foreign clinical data in 25% (22 devices) of cases, while only Japanese clinical data were used for another 25% (22 devices) of cases (Figure 2). We therefore examined the reviews to investigate why Japanese clinical studies were required (Supplemental Figure A.1).

First, if the approval category were 510k in the USA, or CE mark in EU, the submitted package would not include clinical data. Therefore, for 22 devices submitted with only Japanese clinical data (Supplemental Figure A.1, no.23-44), the approval category were investigated (Supplemental Figure A.1).

As a result, the approval categories were PMA and CE mark (5 devices), PMA only (1), 510k and CE mark (10), CE mark only (6).

In the USA, when a device performance is similar to a previously approved device, the device is approved without the clinical data in 510k process [2, 3, 4]. Therefore, the device which has been improved and approved repeatedly in 510k process, has no clinical data. Similarly, for CE mark in EU, since clinical data are not mandatory for devices of Class III [2, 3, 4], no clinical data often exist for the devices. In these cases, Japanese clinical data are required for Japanese first submission (Figure 5).

For PMA process in the USA, clinical data are essentially required [2, 3, 4]. However, there are some exceptions. In our investigation, two devices (no.40,41) of six devices with PMA were approved without clinical data in the USA, which required Japanese clinical data.

Although even in PMA process, three devices (no.24, 28, 33) had foreign clinical data, Japanese clinical data were required. Since those indications were for eye diseases, it was supposed that there were ethnicity-associated differences in morphology, such as color, between foreigner and Japanese. As other cases required Japanese clinical data with foreign clinical data, the foreign clinical data were provided as former device (no.32) (Figure 5).

For 12 devices with approval in the USA or EU that required both foreign and Japanese clinical data (Supplemental Figure A.1, no.1-12), the review reports detailed that the Japanese clinical data were used to confirm the suitability of the healthcare environment. For example, for an implantable left ventricular assist device (LVAD, three devices), which is a life support system, Japanese clinical data were necessary to confirm the regional suitability of the operative technique, postoperative care in the hospital, and home care by the patients themselves. Japanese clinical data were also needed for transcatheter heart valves (two devices), to confirm the suitability of the operative technique for implantation of the transcatheter aortic valve, and for three drug-eluting stent devices, to confirm the safety, tolerability, and pharmacokinetics of the drug, safety of antiplatelet therapy for preventing stent thrombosis, and extrapolation of

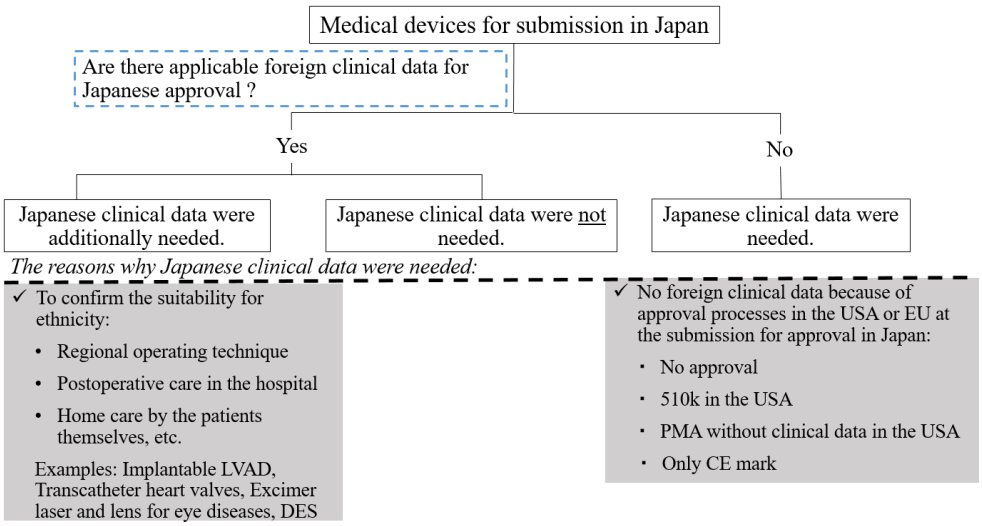

Figure 5: Relationships between foreign clinical data and requirements of Japanese clinical data.

foreign clinical data (Supplemental Figure A.1). For the four other devices, Japanese clinical data were submitted to confirm the suitability of the operating technique and healthcare environment.

In the review reports numbered 13-19 in Supplemental Figure A.1, no reasons were given as to why the Japanese clinical studies were conducted, and we therefore considered the reasons according to our own judgement. For an implantable LVAD (no.16), a transcatheter heart valve (no.19), and a brain artery stent (no.17), we supposed that the Japanese clinical data were used to confirm the suitability of the high-risk operative technique. With the use of beads for arterial embolization (no.14), the target disease in the foreign study was uterine fibroid where those for approval in Japan were hypervascular tumors including uterine fibroid. For capsule endoscopy (no.13), only Japanese clinical data were used when the data package was submitted, although European clinical data were added during the review process. For an implantable stimulator to control urination and defecation (no.15), foreign data concerning the use of the previous model of this device were insufficient for Japanese approval. Thus, it is suggested that Japanese clinical data were used in those cases where foreign clinical data were insufficient to confirm the suitability of the device for Japanese patients. For a radiopharmaceutical synthesis device for diagnosis of Alzheimer's disease (no.18), it was assumed that the evaluation of a device for manufacturing of the radiopharmaceuticals in a hospital required the same application as a drug, because the drug approval is not required for the drug prepared in the hospital but for the medical device in Japan. The same diagnostic endpoint was used in Japan as that used for drug in the USA. Then, clinical data of Phase I, II and III clinical studies were additionally required to evaluate ethnicity-associated differences [15].

Since the development periods for a drug-eluting stent (no.20) and vascular stents (no.21 and 22) were the same in the USA and Japan, the clinical trials were conducted globally.

Thus, most of the requirements for Japanese clinical data were due to the differences in regional medical environments between Japan and the original approving region.

4. Discussion

Although the majority of medical devices have been registered with the Japanese regulatory agency following approvals in the USA or EU, Japanese clinical data were still required in part of the cases. The purpose of this study was therefore to clarify the factors affecting the requirement for Japanese clinical data for approvals of high-risk devices in Japan.

Our results suggest that Japanese clinical data were not an essential requirement for submission when foreign clinical data were included in the Japanese data package for approval. As the clinical performance of a medical device is less sensitive to ethnicity than the efficacy and safety of drugs, the performance of a device can be evaluated using foreign clinical data, without additional Japanese clinical data.

However, this idea that medical devices are insensitive to ethnicity did not apply in all cases. Japanese clinical data were required for the Japanese approval for 50% of devices with prior approval in the USA or EU (Figure 2).

This study indicated two reasons why Japanese clinical data were a necessary addition to foreign clinical data. One was that the performance of the device was sensitive to ethnicity, which includes regional differences in the medical environment. For example, for an implantable LVAD, the new implantation techniques, treatment after the operation, and home care requirements were new medical management practices in Japan. For a transcatheter heart valve, the transcatheter aortic valve implantation was a new operating technique in Japan. For a drug-eluting stent, the safety and similarity of the pharmacokinetics of the eluting drug and the duration and safety of the antiplatelet therapy for prevention of stent thrombosis were confirmed using the Japanese clinical data. Therefore, Japanese clinical data

were necessary to confirm the suitability of the regional operating technique, postoperative care in the hospital, and home care by the patients themselves (Figure 5).

The other major reason why Japanese clinical data were necessary was that a device had undergone improvements from the original device that had been approved in a foreign region. A medical device usually undergoes repeated improvements over its lifecycle. For most of these improvements, clinical data were not required for approval in the USA [16, 17]. Therefore, no clinical data were available for the improved medical devices, although the devices were available for clinical use in foreign regions. In this situation, new clinical data were required for the Japanese approval.

When a global medical device is being developed, its development normally starts in the region with the largest market size. As the Japanese market size is smaller than that of the USA and EU, development for the Japanese market may lag behind.

In contrast to the situation with drugs, as the performance of a medical device is insensitive to ethnicity, extrapolation of foreign clinical data to a new region is frequently allowed. However, it is suggested that, if a simultaneous multi-region submission is not made, the device may undergo improvement, and new clinical data may be required for the new region with a smaller market, such as in Asian countries. New clinical data may also be required to confirm the suitability of a device for regional operating techniques and medical environments.

5. Conclusion

In conclusion, our findings suggest that Japanese clinical data were not an essential requirement for the Japanese data package for approval when foreign clinical data were included. However, there were some exceptions: one was the situation where the performance of a device was sensitive to the ethnicity associated with the medical environment. Another case was where devices had undergone repeated improvements from the original device approved in the foreign region.

It is suggested that, if simultaneous submission is missed, a device may undergo repeated improvements, and then new clinical data are required for approvals in new regions.

6. Declaration of Conflicting Interest

The authors declare no conficts of interest.

7. Disclaimer

The views expressed in this article are those of the authors and do not necessarily reflect the official views of the Pharmaceuticals and Medical Devices Agency.

8. Article Information

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10. Supplemental Materials

	Date of approval[a]	Date of submission[a]	Brand name of medical device[b]	Use of medical device	Categorized class[c]	Previous USA approval[d]	Previous EU approval[e]	Orphan, priority, or expedited review?[f]	Foreign clinical data[g]	Japanese clinical data[h]	Reasons for using Japanese clinical data (as written in the review reports)[i]
1	Nov. 18, 2009	27 Feb. 2004	HeartMate XVE LVAS	Implantable ventricular assist device for severe heart failure	IV	Y (PMA)	Y	Orphan	Y	Y	To evaluate the safety and efficacy in the hospital and patient's house.
2	Dec. 8, 2010	17 Sep. 2009	DuraHeart	Implantable ventricular assist device for severe heart failure	IV	N	Y	Orphan	Y	Y	To confirm the suitability of the implantation technique, treatment after the operation, and home care in Japan.
3	Nov. 29, 2012	5 Jul. 2011	HeartMate II	Implantable ventricular assist device for severe heart failure	IV	Y (PMA)	Y	-	Y	Y	To evaluate the safety and efficacy in the Japanese medical and life environment.
4	Jun. 21, 2013	23 Mar. 2012	Sapien XT	Transcatheter heart valve for severe aortic stenosis	IV	Y (PMA)	Y	-	Y	Y	To confirm the suitability for the Japanese medical environment, especially the operative technique.
5	Mar. 25, 2015	2 Apr. 2014	CoreValve	Transcatheter heart valve for severe aortic stenosis	IV	Y (PMA)	Y	-	Y	Y	To confirm the extrapolation of American clinical data and the suitability for the Japanese medical environment, such as operative technique and adverse events.
6	Mar. 30, 2007	22 Dec. 2005	TAXUS express 2 stent	Coronary artery stent for ischemic heart disease	IV	Y (PMA)	Y	-	Y	Y	To confirm the safety with antiplatelet therapy in the Japanese medical environment.
7	Mar. 24, 2009	9 May. 2007	Endeavor coronary stent system	Coronary artery stent for ischemic heart disease	IV	Y (PMA)	Y	-	Y	Y	To confirm the extrapolation of foreign clinical data.
8	Mar. 9, 2011	25 Dec. 2009	Nobori	Coronary artery stent for ischemic heart disease	IV	N	Y	-	Y	Y	To evaluate the safety and pharmacokinetics of the eluting drug.
9	Sep. 28, 2007	28 Jun. 2006	Precise stent system	Carotid artery stent for stenosis	IV	Y (PMA)	Y	Priority review	Y	Y	To confirm the suitability for the Japanese medical environment.
10	Jan. 8, 2010	12 Mar. 2009	Codman Enterprise VRD	Transarterial chemoembolization for cerebral arterial aneurysm	IV	Y (HDE)	Y	Orphan	Y	Y	To confirm the suitability of the operative technique in the Japanese medical environment.
11	Aug. 31, 2011	17 Dec. 2010	Cryoseal disposable kit	Blood component separator kit for autotransfusion	III	Y (PMA)	Y	-	Y	Y	To confirm the safety and efficacy of actual use in the Japanese medical environment.

Figure A.1: Clinical data packages for high-risk medical devices approved in Japan (continues on following pages).

12	Aug. 31, 2011	17 Dec. 2010	Cryoseal CS-1	Blood component separator for autotransfusion	II	Y (PMA)	Y	-	Y	Y	To confirm the safety and efficacy of actual use in the Japanese medical environment.
13	Apr. 23, 2007	15 Apr. 2004	Given diagnostic imaging system	Capsule endoscopy for disease of small intestine	II	Y (510k)	Y	-	Y	Y	-
14	Jun. 21, 2013	29 Feb. 2012	Embosphere	Transarterial chemoembolization for hypervascular tumors	IV	Y (510k)	Y	-	Y	Y	-
15	Sep. 20, 2013	30 Aug. 2012	InterStim II sacral neurostimulator	Implantable stimulator for controlling urination or defecation	IV	Y (PMA)	Y	-	Y	Y	-
16	Nov. 22, 2013	29 Jan. 2010	Jarvik2000	Implantable ventricular assist device for severe heart failure	IV	N	Y	Orphan	Y	Y	-
17	Nov. 22, 2013	14 Sep. 2012	Wingspan stent	Cerebral artery stent for stenosis	IV	Y (HDE)	Y	Priority review	Y	Y	-
18	Jul. 3, 2014	14 May. 2013	NEPTIS plug-01	Radiopharmaceutical synthesis device for diagnosis of Alzheimer disease	III	Y (Drug)	Y	-	Y	Y	-
19	Mar. 24, 2015	28 Mar. 2014	Sapien XT	Transcatheter heart valve for severe aortic stenosis	IV	Y (PMA)	Y	-	Y	Y	-
20	Sep. 6, 2012	18 Aug. 2011	Promus element plus stent system	Coronary artery stent for ischemic heart disease	IV	Y (PMA)	Y	-	GCTI	Y	Concern with ethnic differences.
21	Jan. 24, 2012	14 Jan. 2011	Zilver Flexs SFA vascular stent	Blood vessel stent for femoral artery stenosis	III	N	Y	-	GCTI	GCTI	Concern with lifestyle differences, such as the Japanese sitting style and frequency of walking.
22	Jan. 24, 2012	30 Jul. 2010	Zilver PTX	Drug-eluting femoral artery stent for femoral artery stenosis	IV	Y (PMA)	Y	-	GCTI	GCTI	-
23	Dec. 8, 2005	30 Jan. 2004	Cool-tip RF system	Electric cauterizer for liver tumor	III	Y (510k)	Y	Expedited review	N	Y	-
24	Oct. 25, 2006	27 Oct. 2003	Excimer laserEC-5000	Excimer laser operation device for ophthalmology for myopia	III	Y (PMA)	Y	-	ref[a]	Y	-

25	Oct. 25, 2006	31 Oct. 2003	Menicon lifely	Contact lens for myopia	III	N	Y	-	ref[b]	Y	-
26	Sep. 28, 2007	31 Jan. 2006	OCT imaging guide wire	Optical coherence tomography (OCT) imaging catheter for coronary angiography	IV	N	Y	-	N	Y	-
27	Sep. 28, 2007	31 Jan. 2006	OCT imaging system	OCT imaging system for coronary angiography	II	N	Y	-	N	Y	-
28	Jan. 21, 2008	25 Feb. 2005	O2 optics	Contact lens for myopia	III	Y (PMA)	N	-	ref[b]	Y	-
29	Sep. 2, 2008	18 Mar. 2005	Adacolumn	Adsorptive type apheresis column for Crohn's disease	III	N	Y	Orphan	N	Y	-
30	Nov. 2, 2009	28 Mar. 2008	V.A.C. ATS system	Wound therapy system to promote healing through negative pressure	III	Y (510k)	Y	-	N	Y	-
31	Jan. 8, 2010	30 Mar. 2009	CryoHit	Cryotherapy unit for renal tumor	III	Y (510k)	Y	-	N	Y	-
32	Jan. 15, 2010	12 Feb. 2008	Deflux	Injections for vesicoureteral reflux	III	Y (PMA)	Y	-	ref[b]	Y	-
33	Feb. 2, 2010	29 Mar. 2005	ICL	Posterior chamber lens for myopia	III	Y (PMA)	Y	-	ref[b]	Y	-
34	Feb. 5, 2010	25 Apr. 2008	KYPHON BKP HV-R	Bone cement for compression fracture of spine	III	Y (510k)	Y	-	ref[b]	Y	-
35	Feb. 5, 2010	25 Apr. 2008	KYPHON BKP system	Access tools with inflatable bone tamps for vertebral body for compression fracture of spine	II	Y (510k)	Y	-	ref[b]	Y	-
36	Jun. 14, 2010	29 May. 2008	ElVeS Laser	Diode laser for varicose vein	III	Y (510k)	Y	-	N	Y	-
37	Mar. 9, 2011	17 Sep. 2009	Cochlear baha system	Bone anchored hearing aid	III	Y (510k)	Y	-	N	Y	-

38	Sep. 28, 2012	28 Jun. 2011	Amplatzer vascular plug	Plug for peripheral embolization	IV	Y (510k)	Y	-	N	Y	-
39	Jan. 28, 2013	20 Jan. 2012	EWS	Endobronchial spigot for pneumothorax	III	N	Y	-	N	Y	-
40	Mar. 22, 2013	27 Dec. 2011	Navistar RMT	Ablation catheter for ventricular tachycardia	IV	Y (PMA)	Y	-	N	Y	-
41	Mar. 22, 2013	27 Dec. 2011	Navistar RMT thermocool	Ablation catheter for ventricular tachycardia	IV	Y (PMA)	Y	-	N	Y	-
42	Mar. 22, 2013	27 Dec. 2011	Niobe magnetic navigation system	Cardiac mapping system workstation for ventricular tachycardia	II	Y (510k)	Y	-	N	Y	-
43	Jun. 21, 2013	29 Jun. 2012	Hepasphere	Occlusion of blood vessels for embolization for hypervascular tumors	IV	Y (510k)	Y	-	N	Y	-
44	Jul. 23, 2013	14 Jun. 2012	SeQuent Please drug-eluting balloon catheter	Coronary balloon catheter for coronary stent restenosis	IV	N	Y	-	N	Y	-
45	Jul. 6, 2005	15 Aug. 2001	Easytrak CS, Easytrak CS lead	Implantable cardioverter defibrillator, pacemaker lead for heart failure	IV	Y (PMA)	Y	-	Y	N	-
46	Jul. 6, 2005	15 Aug. 2001	Easytrak lead, Easytrak JL	Implantable cardioverter defibrillator, pacemaker lead for heart failure	IV	Y (PMA)	Y	-	Y	N	-
47	Jul. 6, 2005	15 Aug. 2001	Contak CT, Contak CD GDT	Cardiac resynchronization therapy defibrillator (CRT-D) for heart failure	IV	Y (PMA)	Y	-	Y	N	-
48	Jul. 6, 2005	15 Aug. 2001	Contak CRTD, Contak CD GDT	Cardiac resynchronization therapy defibrillator (CRT-D) for heart failure	IV	Y (PMA)	Y	-	Y	N	-
49	May. 11, 2006	7 Jan. 1999	Heart laser	Carbon dioxide laser and laser coagulator for angina	III	Y (PMA)	N	-	Y	N	-
50	Jul. 11, 2006	13 Jun. 2003	Cook Zenith AAA	Endovascular graft for abdominal aortic aneurysm	IV	Y (PMA)	N	-	Y	N	-

51	Jan. 23, 2007	27 Aug. 1998	Carisolv	Chemo-mechanical system for caries removal	III	Y (PMA)	Y	-	Y	N	-
52	Sep. 28, 2007	28 Jun. 2006	Angioguard XP	Emboli capture guidewire system for carotid artery stenosis	IV	Y (510k)	Y	Priority review	Y	N	-
53	Mar. 12, 2008	6 Nov. 2006	Gore TAG thoracic aortic stent graft system	Endovascular stent graft for thoracic aortic aneurysm	IV	Y (PMA)	Y	Priority review	Y	N	-
54	Mar. 25, 2008	26 Dec. 2001	Dornier epos ultra	Shockwave therapy machine for plantar fascia inflammation	III	Y (PMA)	Y	-	Y	N	-
55	Jul. 1, 2008	28 Feb. 2007	Excimer laser for defibrillator lead	Cardiac lead remover system	IV	Y (PMA)	Y	Priority review	Y	N	-
56	Sep. 26, 2008	30 Mar. 2005	ONYX liquid embolic system LD	Embolic system for cerebral arteriovenous malformation	IV	Y (PMA)	Y	Priority review	Y	N	-
57	Dec. 22, 2008	28 May. 2008	VEPTR system	Vertical expandable prosthetic titanium ribs for thorax failure syndrome	III	Y (HDE)	Y	Priority review	Y	N	-
58	Dec. 22, 2008	25 May. 2007	Excimer laser EC-5000	Ophthalmic laser system for myopia	III	Y (PMA)	Y	-	Y	N	-
59	Dec. 26, 2008	31 Aug. 2006	PDA closure set	Occlusion of blood vessels for embolization for patent ductus arteriosus	IV	Y (PMA)	Y	-	Y	N	-
60	Sep. 1, 2009	23 Oct. 2007	Ex-Ablate 2000 (additional indication)	Magnetic resonance-guided focused-Ultrasound incisionless surgery system for tumor	III	Y (PMA)	Y	-	Y	N	-
61	Nov. 18, 2009	22 Dec. 2008	da Vinci surgical system	Robotic surgery system	III	Y (510k)	Y	-	Y	N	-
62	Nov. 18, 2009	22 Dec. 2008	EndoWrist instrument	Robotic surgery instrument	II	Y (510k)	Y	-	Y	N	-

63	Nov. 18, 2009	22 Dec. 2008	EndoWrist bipolar instruments	Robotic surgery instruments	II	Y (510k)	Y	-	Y	N	-
64	Nov. 18, 2009	22 Dec. 2008	EndoWrist monopolar instruments	Robotic surgery instruments	II	Y (510k)	Y	-	Y	N	-
65	Jan. 8, 2010	29 May. 2008	PROMUS drug-eluting stent	Coronary artery stent for ischemic heart disease	IV	Y (PMA)	Y	-	Y	N	-
66	Jan. 8, 2010	29 May. 2008	XINENCE V drug-eluting stent	Coronary artery stent for ischemic heart disease	IV	Y (PMA)	Y	-	Y	N	-
67	Jan. 8, 2010	11 Nov. 2008	VNS Therapy system	Vagus nerve stimulation system for epilepsy	IV	Y (PMA)	Y	Priority review	Y	N	-
68	Apr. 30, 2010	27 Jan. 2009	Merci retriever	Revascularization device for cerebral infarction Recanalization catheters	IV	Y (510k)	Y	Priority review	Y	N	-
69	Apr. 30, 2010	19 Dec. 2008	Crosser system	using mechanical vibration for chronic total occlusion of artery	IV	Y (510k)	Y	-	Y	N	-
70	Jun. 14, 2010	30 Jan. 2009	X-STOP PEEK Implant	Interspinous process decompression system for lumbar spinal canal stenosis	III	Y (PMA)	Y	-	Y	N	-
71	Jun. 14, 2010	30 Sep. 2008	Bard agento I.C.	Tracheal suction tube for intubation	III	Y (510k)	N	-	Y	N	-
72	Jun. 9, 2011	15 Feb. 2010	Penumbra system	Revascularization device for cerebral infarction	IV	Y (510k)	Y	-	Y	N	-
73	Mar. 29, 2012	8 Oct. 2010	Medtronic Advisa MRI	Pacemaker for bradycardia	IV	N	Y	-	Y	N	-
74	Mar. 29, 2012	8 Oct. 2010	CapSure FIX MRI lead	Pacemaker lead for bradycardia	IV	Y (PMA)	Y	-	Y	N	-
75	Jun. 25, 2012	3 Dec. 2007	Thermogard system	Temperature management system for fever by sever cerebral disorder	IV	Y (510k)	Y	-	Y	N	-
76	Jul. 27, 2012	25 Mar. 2010	MOMA ultra	Proximal cerebral protection catheter system for internal artery carotid	IV	Y (510k)	Y	-	Y	N	-

77	Sep. 28, 2012	21 Mar. 2008	Contegra pulmonary valved conduit	Conduit with valve for pulmonary artery	IV	Y (HDE)	Y	Priority review	Y	N	-
78	Sep. 28, 2012	18 Jan. 2007	Natrelle breast implant	Breast implant for breast cancer	IV	Y (PMA)	Y	-	Y	N	-
79	Apr. 12, 2013	16 Dec. 2010	DC Beads	Occlusion of blood vessels for embolization for liver cancer	IV	Y (510k)	Y	-	Y	N	-
80	Jul. 23, 2013	9 Oct. 2012	LifeVest	Wearable defibrillator for pulmonary artery and ventricular fibrillation	III	Y (PMA)	Y	Priority review	Y	N	-
81	Sep. 20, 2013	18 Jan. 2013	MED-EL electric acoustic stimulation EAS	Electric acoustic stimulation for dysacousis	III	N	Y	Priority review	Y	N	-
82	Dec. 20, 2013	22 Oct. 2012	Solitaire FR thrombectomy device	Revascularization device for cerebral ischemic infarction	IV	Y (510k)	Y	-	Y	N	-
83	Feb. 19, 2014	25 Apr. 2013	Arctic Front Advance cryoablation catheter	Cardiac ablation catheter for atrial fibrillation	IV	Y (PMA)	Y	Priority review	Y	N	-
84	Feb. 19, 2014	25 Apr. 2013	Freezor Max cryoablation catheter	Cardiac ablation catheter for atrial fibrillation	IV	Y (PMA)	Y	Priority review	Y	N	-
85	Feb. 19, 2014	25 Apr. 2013	Medtronic CryoConsole	Cryotherapy unit for atrial fibrillation	III	Y (PMA)	Y	Priority review	Y	N	-
86	Sep. 17, 2014	26 Dec. 2013	Alair	Bronchial thermoplasty catheter system for severe asthma	III	Y (PMA)	Y	Priority review	Y	N	-
87	Nov. 7, 2014	9 Nov. 2012	COOK Zenith	Endovascular stent graft for Stanford type B Aortic dissection	IV	N	Y	-	Y	N	-
88	Nov. 7, 2014	20 Dec. 2013	ExAblate 2000	Magnetic resonance-guided focused-Ultrasound incisionless surgery system for uterine fibroid	III	Y (PMA)	N	-	Y	N	-
89	Mar. 25, 2015	2 Jul. 2014	NovoTTF-100A system	Tumor treatment fields for glioblastoma multiforme	III	Y (PMA)	Y	Priority review	Y	N	-

90	Oct. 19, 2006	24 Feb. 2005	MucoUp	Submucosal injection for stomach cancer and colon cancer	III	N	N	-	N	Y	-
91	Jan. 23, 2007	22 Dec. 2004	Triplex	Vascular prostheses for aneurysm	IV	N	N	-	N	Y	-
92	Oct. 29, 2007	6 Oct. 2004	Jace	Autologous cultured epidermis for burn	IV	N	N	Priority review	N	Y	-
93	Oct. 31, 2007	31 Jul. 2000	Seamdura	Bioabsorbable artificial dural substitute	IV	N	N	-	N	Y	-
94	Apr. 28, 2009	4 Dec. 2006	Ortho-K	Orthokeratology contact lens for myopia	III	N	N	-	N	Y	-
95	Dec. 8, 2010	19 Jan. 2009	EVAHEART	Implantable ventricular assist device for severe heart failure	IV	N	N	Orphan	N	Y	-
96	Dec. 20, 2011	14 Jun. 2010	Matsudaito	Non-absorbable topical hemostatic material for central circulatory system for artificial blood vessel	IV	N	N	-	N	Y	-
97	Jun. 25, 2012	21 Sep. 2011	Adacolumn	Adsorptive type apheresis column for psoriasis	III	N	N	Orphan	N	Y	-
98	Jul. 27, 2012	24 Aug. 2009	Jacc	Autologous transplant for knee joint	IV	N	N	-	N	Y	-
99	Dec. 27, 2012	10 Aug. 2011	Kawasumi Najuta thoracic aortic stent graft system	Endovascular stent graft for thoracic aortic aneurysm	IV	N	N	-	N	Y	-
100	Mar. 22, 2013	29 Feb. 2012	Nerbridge	Nerve regeneration conduits for peripheral nerve neurotmesis	IV	N	N	-	N	Y	-
101	Jun. 21, 2013	21 May. 2012	TMU-1100	Magnetic stimulation treatment equipment for overactive bladder	II	N	N	-	N	Y	-
102	Sep. 20, 2013	28 Dec. 2012	PD laser BT	Photodynamic therapy (PDT) semiconductor laser for malignant brain tumor	III	N	N	Orphan	N	Y	-

103	Feb. 28, 2014	28 Oct. 2011	Coopdech i-cool	Temperature management system for therapeutic hypothermia	II	N	N	-	N	Y	-

[a]The dates of submission and approval in Japan were obtained from review reports [7].

[b]The name of new devices in the review reports published on Japan's Pharmaceuticals and Medical Devices Agency website [7].

[c]The class of medical device is based on their risk to patients and users. Class IV is high risk, Class III is moderate, and Class II is moderate-low.

[d]"Y" indicates "an approval", whereas "N" indicates "no approval".

"PMA" indicates the premarket approval review process by the Food and Drug Administration (FDA). "510k" indicates the premarket notification review process by the FDA.

"HDE" indicates humanitarian device exemption review process for severe patients by the FDA.

[e]"Y" indicates "CE mark certified", whereas "N" indicates "no CE mark".

[f]"—" indicates the medical device was not orphan, priority review, or expedited review.

[g]"Y" indicates that foreign clinical data were used in the data package for approval in Japan, whereas "N" indicates that foreign clinical data were not used.

[h]"Y" indicates that Japanese clinical data were used in the data package for approval in Japan, whereas "N" indicates that Japanese clinical data were not used.

[i]Reasons for using Japanese clinical data as written in the review reports [7]. "—" indicates that no description of the reasons for using Japanese clinical data was found in the review reports.

[j]"GCT" indicates a global clinical trial that was conducted in Japan as well as in multiple countries, according to a single protocol.

[k]"ref" indicates that foreign clinical data were used as reference data or for queries during the review process.