Overview and Way of implementation of Medical Devices Rules, 2017

By:
K.L. Sharma, Joint Secretary to the Government of India,
Ministry of Health and Family Welfare

Drugs and Cosmetics Act 1940 :

Presently, The quality, safety and efficacy of notified medical devices manufactured, imported and sold in the country are regulated under the Drugs and Cosmetics Act, 1940. Under this Central Act, medical devices are regulated as drugs as defined in Section 3 (b) (iv) that:

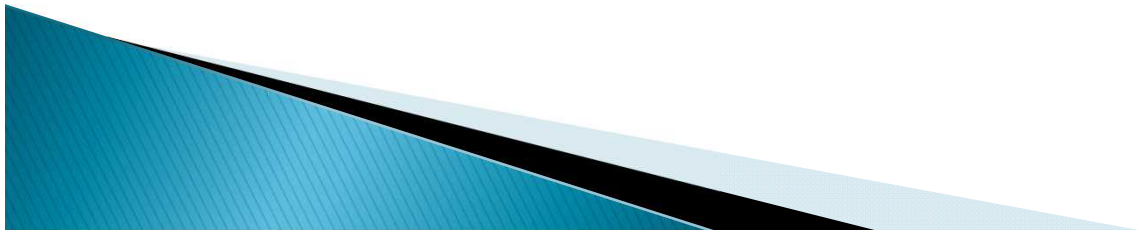
"Such devices intended for internal or external use in the diagnosis, treatment, mitigation or prevention of disease or disorder in human beings or animals, as may be specified from time to time by the Central Government by notification after consultation with the Board"

The Govt of India has notified…

S. No	Name of the device	SLA/CLAA	Date of notification
1	Disposable Hypodermic Syringes	SLA	17-03-1989
2	Disposable Hypodermic Needles	SLA	17-03-1989
3	Disposable Perfusion Sets	SLA	17-03-1989
4	In vitro Diagnostic Devices for HIV, HbsAg and HCV and blood grouping sera	SLA	27-08-2002
5	Cardiac Stents	CLAA	06-10-2005
6	Drug Eluting Stents	CLAA	06-10-2005
7	Catheters	CLAA	06-10-2005
8	Intra Ocular Lenses	CLAA	06-10-2005
9	I.V. Cannulae	CLAA	06-10-2005
10	Bone Cements	CLAA	06-10-2005
11	Heart Valves	CLAA	06-10-2005
12	Scalp Vein Set	CLAA	06-10-2005
13	Orthopedic Implants	CLAA	06-10-2005
14	Internal Prosthetic Replacements	CLAA	06-10-2005
15	Ablation Devices	*CLAA	25-01-2016

Medical Device Rules, 2017

- Medical Device Rules, 2017 under the provisions of the Drugs and Cosmetics Act, 1940 has been published, vide GSR 78(E) dated 31.01.2017 proposed to be effected from 01.01.2018.
- The said Rules shall override all the previous notifications issued under the D&C Rules,1945 related to the regulations of medical devices.
- The said rules have provisions for the regulation of devices for their import, manufacture, clinical investigation and sale.



Scope of the regulation

New Rules shall be applicable to:

(i) substances used for in vitro diagnosis and surgical dressings, surgical bandages, surgical staples, surgical sutures, ligatures, blood and blood component collection bag with or without anticoagulant covered under sub-clause (i) of section 3 of the Drugs and Cosmetics Act, 1940 (23 of 1940);

(ii) substances including mechanical contraceptives (condoms, intrauterine devices, tubal rings), disinfectants and insecticides notified under sub-clause (ii) of section 3 of the Drugs and Cosmetics Act, 1940 (23 of 1940); and

(iii) devices notified from time to time under sub-clause (iv), of clause (b) of section 3 of the Drugs and Cosmetics Act, 1940 (23 of 1940);

Proposed Medical Device rule Content

Chapter- I	Title, Application, Commencement, Definition
Chapter – II	Classification of MD, Grouping of MD, Essentials Principles
Chapter – III	Authorities, delegation of powers, Notified bodies, Medical Devices Testing Centres,
Chapter – IV	Manufacture of MD-Application, Inspection, grant of lic, conditions of lic, Suspension, Cancellation, Appeal, Test License
Chapter – V	Import of MD-Application, Overseas Inspection, grant of lic, Test lic, Hospital use, Personal use
Chapter – VI	Labelling requirement
Chapter – VII	Clinical Investigation- Permission, Medical management, Compensation, Inspection
Chapter – VIII	Permission to import or manufacture medical device which does not have predicate medical device
Chapter –IX	Duties and Powers of Medical Device Officer, Medical Device Testing Officer and Notified Body
Chapter –X	Regulation of Laboratories for carrying test or evaluation
Chapter – XI	Sale of Medical Devices
Chapter – XII	Miscellaneous – Rejection of application, Debarment of applicant, Exemptions

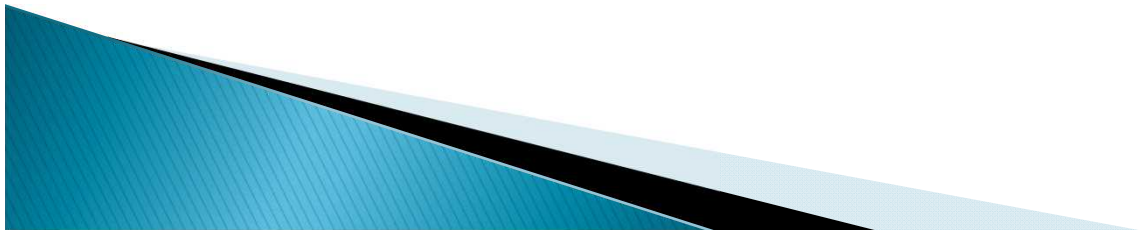
Proposed Medical Device Rules, 2017-Schedules

Schedule Number	Title
First	Classification of MD and IVD
Second	Fee
Third	Registration and functions of Notified Bodies
Fourth	Documents required for grant of mfg and Import licence
Fifth	Quality Management System
Sixth	Post Approval – Major and Minor Changes
Seventh	Requirements to conduct Clinical Investigation
Eight	Exemptions

Medical Device Rules, 2017 – Salient Points

New Definitions

- Medical Device
- Substantial Equivalence
- Predicate device
- Investigational Medical Device
- New *in-vitro* diagnostic
- Clinical Investigation
- Notified Body
- Clinical Performance Evaluation



Risk based classification.....

- **Medical devices shall be notified by the Central Government and classified by the CLA based on the classification rules specified in the *First Schedule* of the drafted rules.**

- **Following are the risk Classes and the classification criteria based on the severity of risk associated with the medical device.**

Risk Criteria	Risk Class
Low	Class A
Low-Moderate	Class B
Moderate-High	Class C
High	Class D

Scheme of proposed regulation

Device Class / Activity	Class A	Class B	Class C	Class D
IMPORT	Import Licence	Import Licence	Import Licence	Import Licence
MANUFACTURE	*Manufacturing License	Manufacturing License	Manufacturing License	Manufacturing License
CLINICAL INVESTIGATION FOR investigational DEVICES and new IVDs	For an Investigational medical device, the applicant shall need to obtain Permission from CLA to conduct clinical investigation of Class B, Class C and Class D And Clinical Performance Evaluation of new IVDs			
SALE	**Regulation as per Current D & C Rules**			
QMS Verification by	*Notified Bodies	Notified Body	CLA	CLA

* Licence will be issued without prior inspection...

Regulatory Authorities

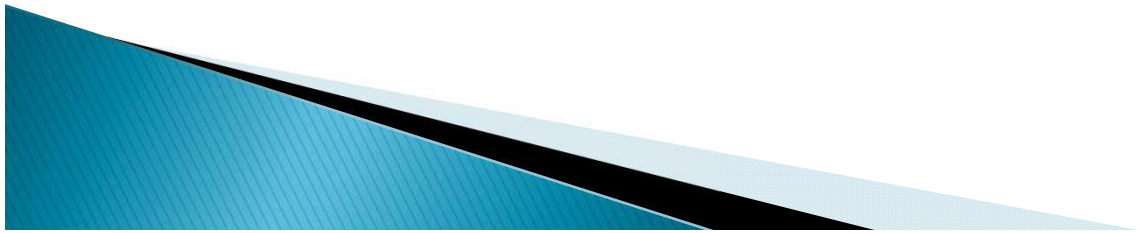
Device Class / Activity	Class A	Class B	Class C	Class D
IMPORT	CLA	CLA	CLA	CLA
MANUFACTURE	SLA	SLA	CLA	CLA
Permission to conduct CLINICAL INVESTIGATION	Permission from CLA			
SALE	SLA			
QMS Verification by	*Notified Body	*Notified Body	CLA	CLA

*Note: Notified Bodies shall be registered with Central Licencing Authority. Prior inspection shall not be required before the grant of manufacturing of Class A devices.

Licensing Authorities…..contd.

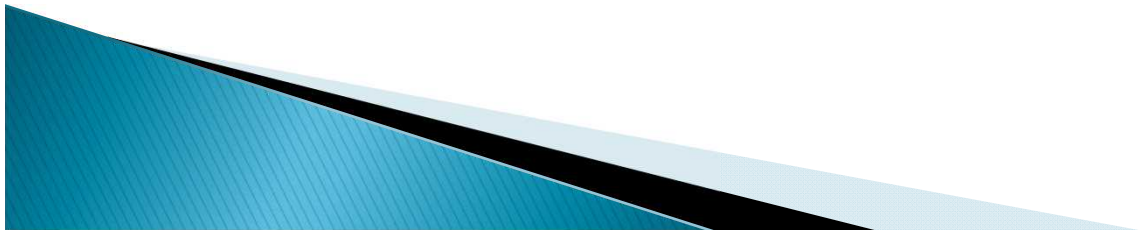
- Application for Import, Clinical Performance evaluation of new IVD and manufacture of Class C and Class D IVDs, test licence, Free Sale Certificate, and personal use will be submitted to CLA through online portal. Inspection of manufacturing site will be carried out by Drugs Inspectors.

- Application for sale, manufacture of Class A and Class B devices will be submitted to SLA through online portal. Audit of manufacturing site will be carried out by Notified Bodies.



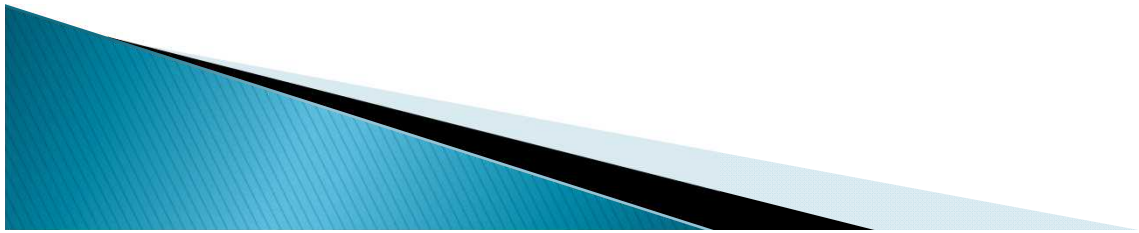
Scope of Notified Bodies

- Only Class A and Class B medical Devices
- To verify QMS conformance at manufacturing site where necessary by inspection
- Verification of Essential Requirements
- Verifying validation of manufacturing process through objective evidence
- conformity of material with defined specifications
- Responsibility for ensuring conformance to QMS and conditions of license/registration
- State Licensing Authority to audit at least 2% of the audits carried out and recommended for grant of license by of each Notified Body.



Registration & Regulation of Notified Bodies

- Registered with CDSCO.
- Accredited by National Accredited Body (such as NABCB).
- Procedures prescribed in schedules for registration of notified bodies.
- Schedule of fee to be charged by notified bodies.
- Duties, functions and obligations of notified bodies specified in the *Third Schedule* of the rules.



Technical Requirements for the applications

- For Class A types of devices a minimum set of requirements as specified in Part II (i) of the Forth Schedule.
- For Class B, Class C and Class D types of devices a minimum set of requirements as specified in Part II (ii) of the Forth Schedule.
- Appendix I of Part III of the Fourth Schedule specifies requirements for Site Master File.
- Appendix-II and Appendix- III of Part III of the Fourth Schedule specifies requirements for Device Master File.
- Clinical investigation of investigational medical devices as per the requirements of the Seventh Schedule.
- For new IVDs- Technical Data requirements has been specified in section (b) of Part IV of the Fourth Schedule.
- Performance Evaluation of IVDs to establish specification, specificity, sensitivity, etc. of all the IVDs shall be carried out at the medical device testing laboratory registered under rule 83.

Major policies of the Rules

- Licence shall remain valid, till it is suspended or cancelled from its date of issue, provided the applicant pays a licence retention fee in every five years.
- Manufacturer shall be audited periodically.
- No inspection prior to grant of manufacturing licence for Class A devices.
- Test licences shall be granted by Central Licencing Authority.
- Provisions for loan licence.
- For Regulators- Establishment or designation Govt. laboratories for testing.
- For Manufacturers- Testing laboratories registered under these rules.

Standards of medical devices

i. BIS or those set by Central Government

ii. Failing (i) by International Organisation for Standardisation (ISO) or International Electro Technical Commission (IEC)

iii. Failing both, manufacturers validated standards.

Clinical investigation

- Medical Devices which do not have a predicate device will undergo through a clinical investigation to establish safety
- Supervision by Ethics Committee as in case of Drugs.
- Application to CLA with Clinical Investigation Plan.
- Maintenance of investigation records.
- Waiver in case of National Emergency.
- Pilot Clinical investigation (to check feasibility on 3 to 5 patients)
- Pivotal clinical investigation (on 10 to 50 patients)

Exempted Medical Devices

- Class A devices exempted from clinical investigation.
- Custom made devices are exempted from all provisions.
- Medicated Dressings, Mechanical Contraceptives, bandages and disinfectants are exempted from provisions of Sale.
- Non-sterile components and raw material – exempted from import licence.
- Devices intended for charity – exempted from import licence

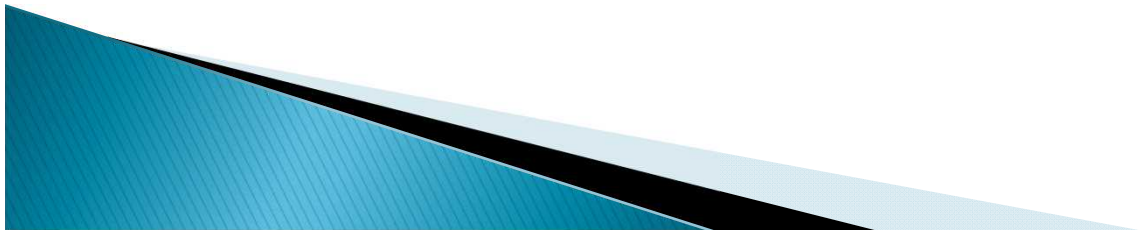
Implementation…..A way forward

- Commencement from January, 01, 2018
- Entire process of regulations shall be a single through online portal
- Guidance documents to the industry and patients will be issued
- To strengthen the regulatory system Medical Devices officers will be recruited for carrying out enforcement activities

Implementation…..A way forward

- Additional medical devices are to be notified under the provisions of the D&C Act, 1940.
- Classification of each of the devices will be made available on the CDSCO website
- Medical Devices Testing Centres for testing Critical to Quality parameters of finished devices

THANK YOU…



Overview of MD Regulation in Japan

2nd Japan-India Medical Products Regulation Symposium

April 2017

厚生労働省
Ministry of Health, Labour and Welfare

pmda

History of PAL(regulations on MDs)

(1889 The first regulations of Medicines was stipulated)

1930 The first regulation on Medical Devices (Appliance for contraception)

(1943 The establishment of the first Pharmaceutical Affairs Law(PAL). MDs were not included)

1948 Full revision of the First PAL. (MDs were included)

It is used to clear harmful medicines and devices . Like police

1960 Full revision of the PAL

This is the base of the PAL we used.

- Licensing system for manufacture/ import of each product

1979 Strengthen assurance of safety, efficacy and quality and help for side effects.

1993 Introducing Promotion of Research and Development.

1994 Improvement of Medical device regulations.

History of medical device regulations in Japan – recent big amendments (1/2)

Medical Device has been regulated in Japan since 1960, and there have been 2 big amendments for the regulations recently;

1.Amendment in 2005

① Introduction of Marketing Authorization Holder system
② Introduction of Registered Certification Body system
③ Introduction of medical device classification based on the GHTF classification rule
④ Introduction of STED and Essential Principles
⑤ Introduction of GCP as a ministerial ordinance
⑥ Introduction of QMS, instead of GMP

History of medical device regulations in Japan – recent big amendments (2/2)

Medical Device has been regulated in Japan since 1960, and there have been 2 big amendments for the regulations recently;

2.Amendment in 2014

① Amendment of Registered Certification Body system, including expansion of scope
② Improvement of regulations on manufacturer
③ Improvement of QMS inspection
④ Application of medical device regulations on SaMD (Software as a Medical Device)
⑤ Establishment of a new category, Regenerative Medicine Product

- Regulatory Authorities in Japan -

MHLW

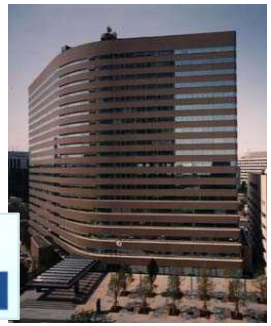
Ministry of Health, Labor and Welfare

- Final Authorization of applications
- Publishing Guidelines
- Advisory committee
- Supervising PMDA Activities

PMDA

Pharmaceuticals and Medical Devices Agency

- Scientific Review for Drugs & MD
- GCP, GMP Inspection
- Consultation on Clinical Trials etc.



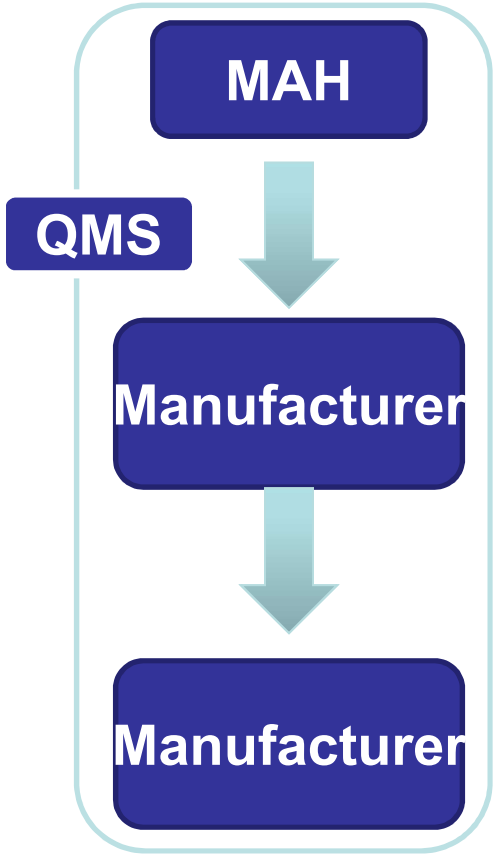
Scope of regulations on medical device/IVD marketing in Japan under PMD Act

Product	Minister's Approval for marketing or Certification by a Registered Certification Body or Marketing Notification
Company	License of Marketing Authorization Holder (MAH)
Manufacturing facility	Registration as a Manufacturer
Distributor	License/notification/self declaration of selling Medical devices
Repairer	License of repair Medical devices

Medical Device Regulations in Japan

Classification	Class I	Class II	Class III	Class IV
Category	General MDs	Controlled MDs	Specially controlled MDs	
Review regulation	Self-declaration	Third party certification	PMDA review (MHLW approval)	
Example		 	 	  
Post market safety (vigilance/surveillance)	PMDA and MHLW			

COMPANY/ MANUFACTURING FACILITY REGULATION



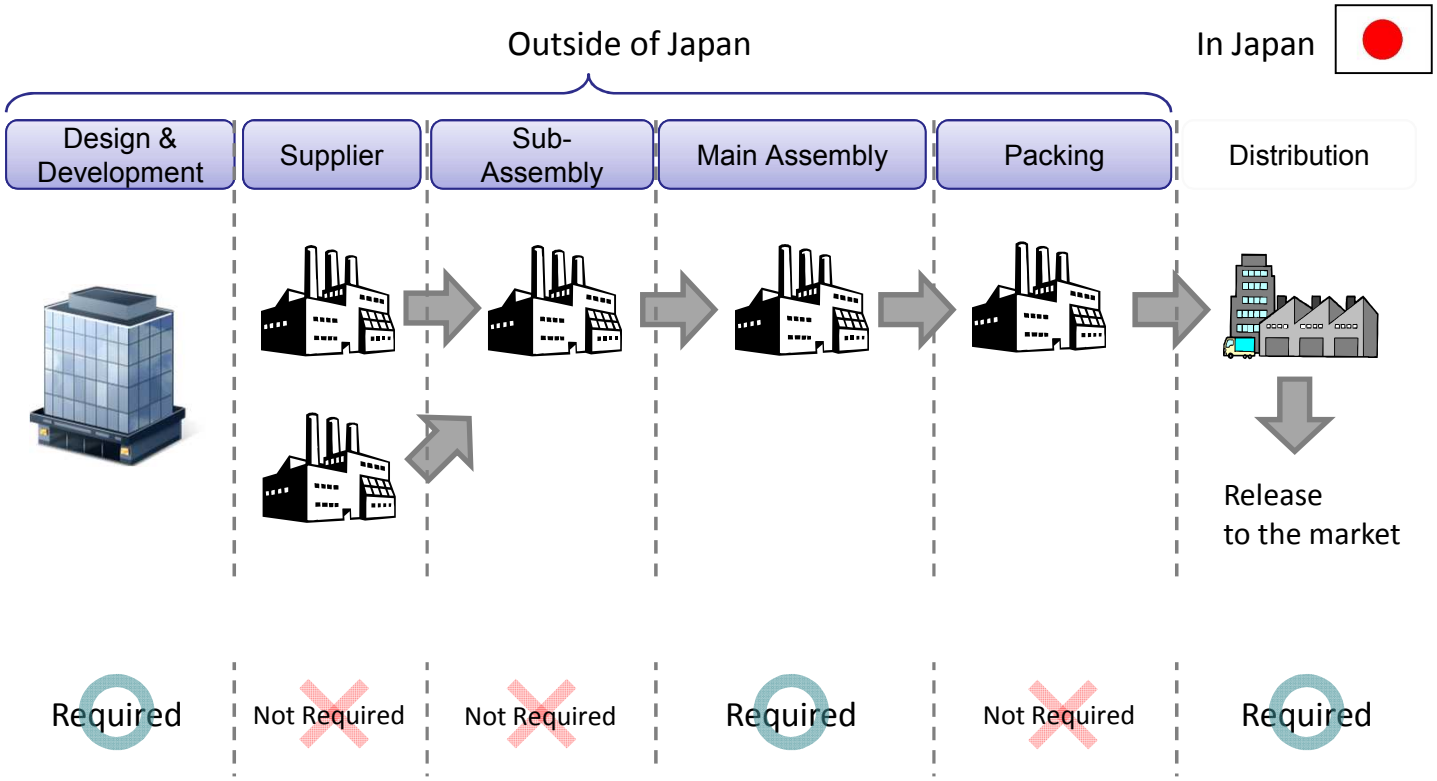
MAH License : From local government
Need for
1. Having marketing supervisor general, safety management supervisor and quality assurance supervisor
2. Having system for GVP
3. Having system for QMS

(They should follow QMS and GVP when they market products)

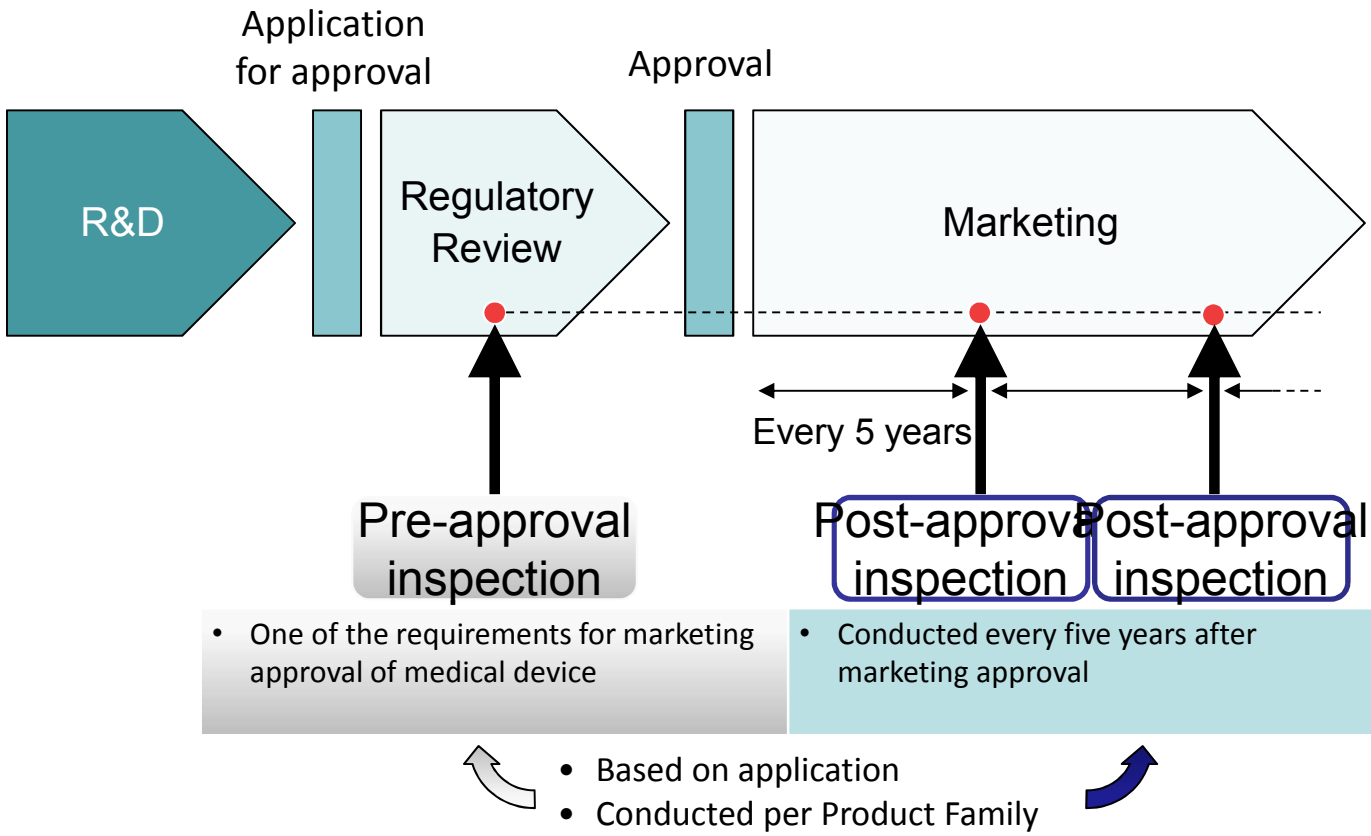
Manufacturer : JUST register
(They should follow QMS when they manufacture products)

Since 2014

Example of manufacturing site registration



Type of QMS Inspection



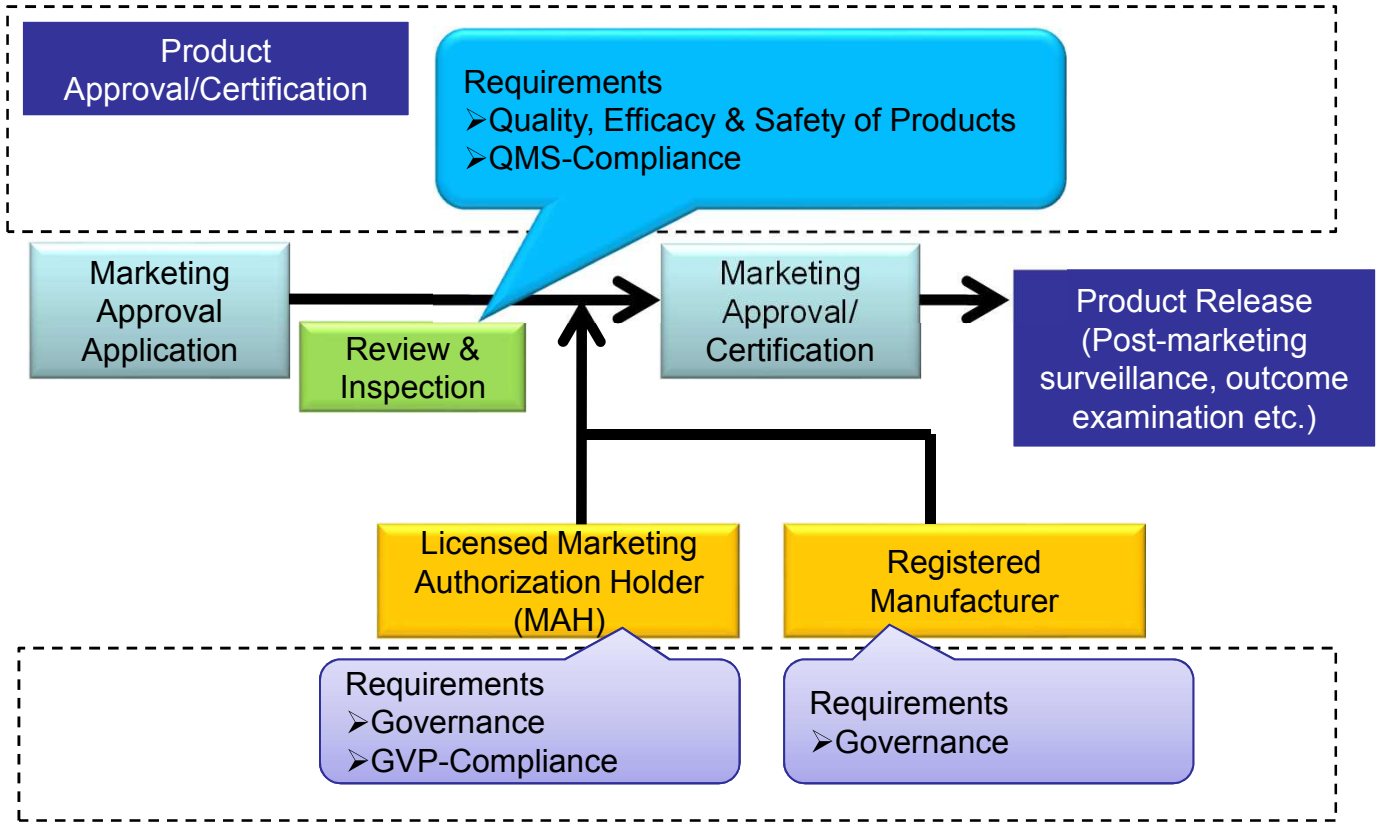
QMS Inspection Authority

Product		Inspection Authority
Medical Devices	• Class IV • New medical devices • Cell / Tissue-based medical devices	PMDA
	• Class III and Class II (without CS*)	PMDA
	• Class III and Class II (with CS*)	Registered certification body
IVDs	• New drugs • Radioactive drugs	PMDA
	• Products without CS*	PMDA
	• Products with CS*	Registered certification body

*CS : Certification Standards

PRODUCT REGULATION

Approval/Certification system in Japan



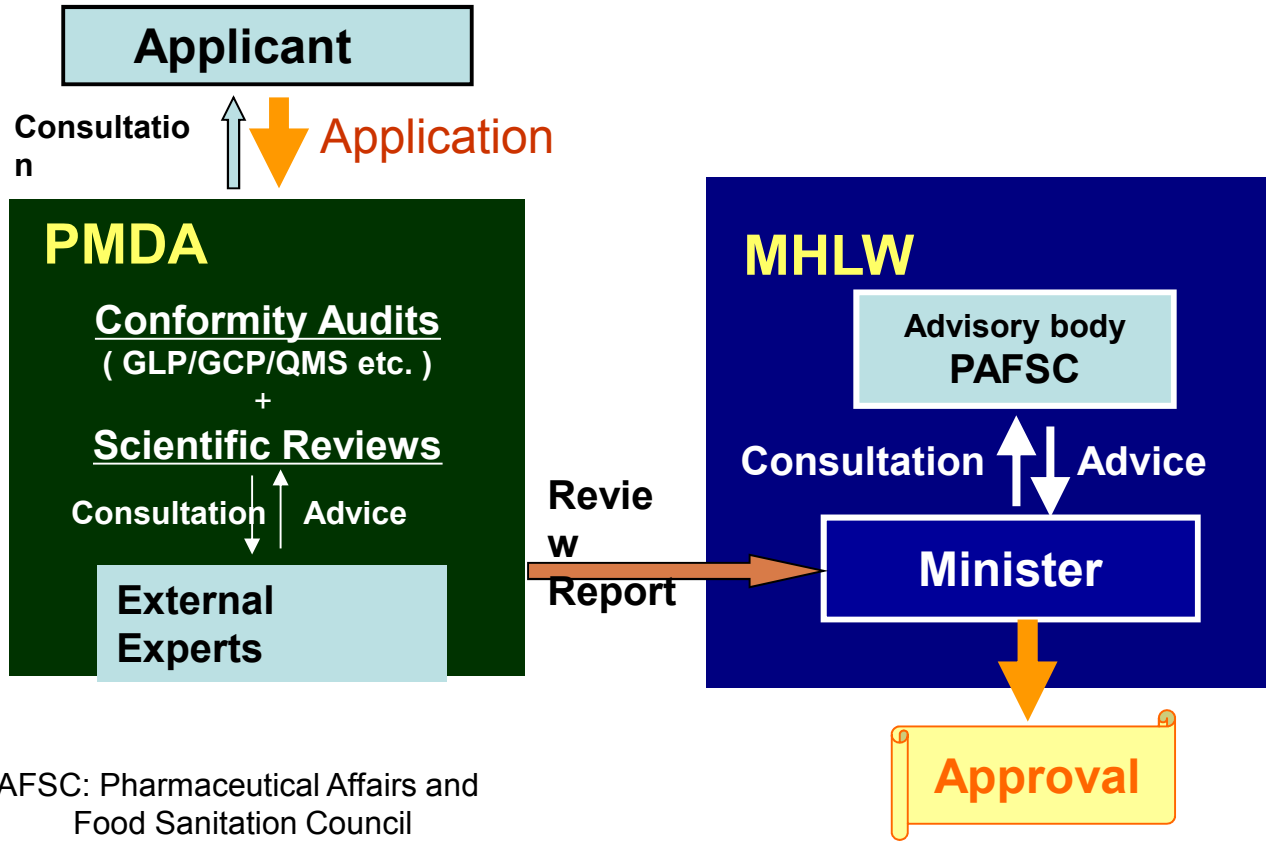
Regulation according to Risk Based Classification of Medical Device in Japan

As of March, 2016

GHTF Classification		Classification in Japan		
		Category	Pre-market regulation	# of JMDN*
Class A	extremely low risk X-Ray film	General MDs (Class I)	Self declaration	1,195
Class B	low risk MRI, bronchial catheters	Controlled MDs (class II)	Third party Certification	1,972
Class C	medium risk artificial bones, dialyzer	Specially Controlled MDs (class III & IV)	Minister's Approval (Review by PMDA)	771
Class D	high risk pacemaker, artificial heart valves			350

*JMDN: Japanese Medical Device Nomenclature

Outline of brand-new medical device approval review process



PAFSC: Pharmaceutical Affairs and Food Sanitation Council

Review Time of Brand-new Medical Devices

Priority items

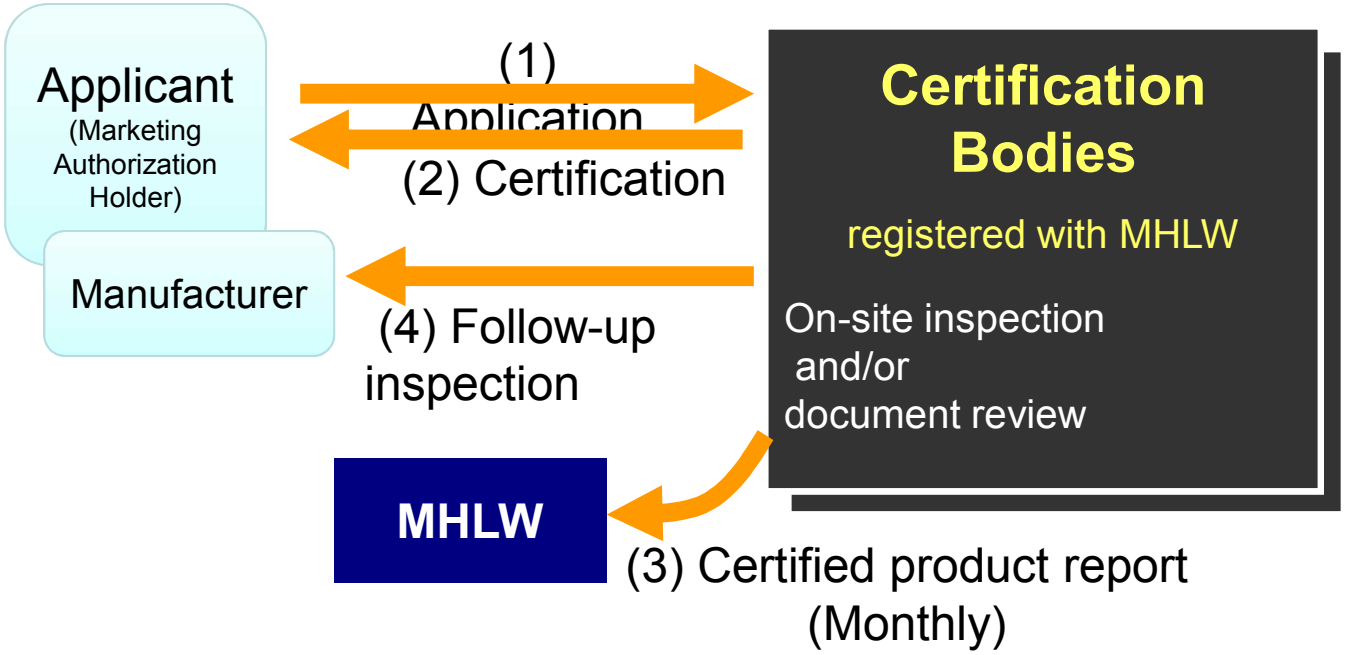
FY	2010	2011	2012	2013	2014	2015
Target (months)	16 (50th percentile)	15 (50th percentile)	13 (50th percentile)	10 (50th percentile)	10 (60th percentile)	10 (60th percentile)
Performance (months)	15.1	4.3	9.3	9.0	8.8	7.9
#	3	6	5	14	5	8

Normal items

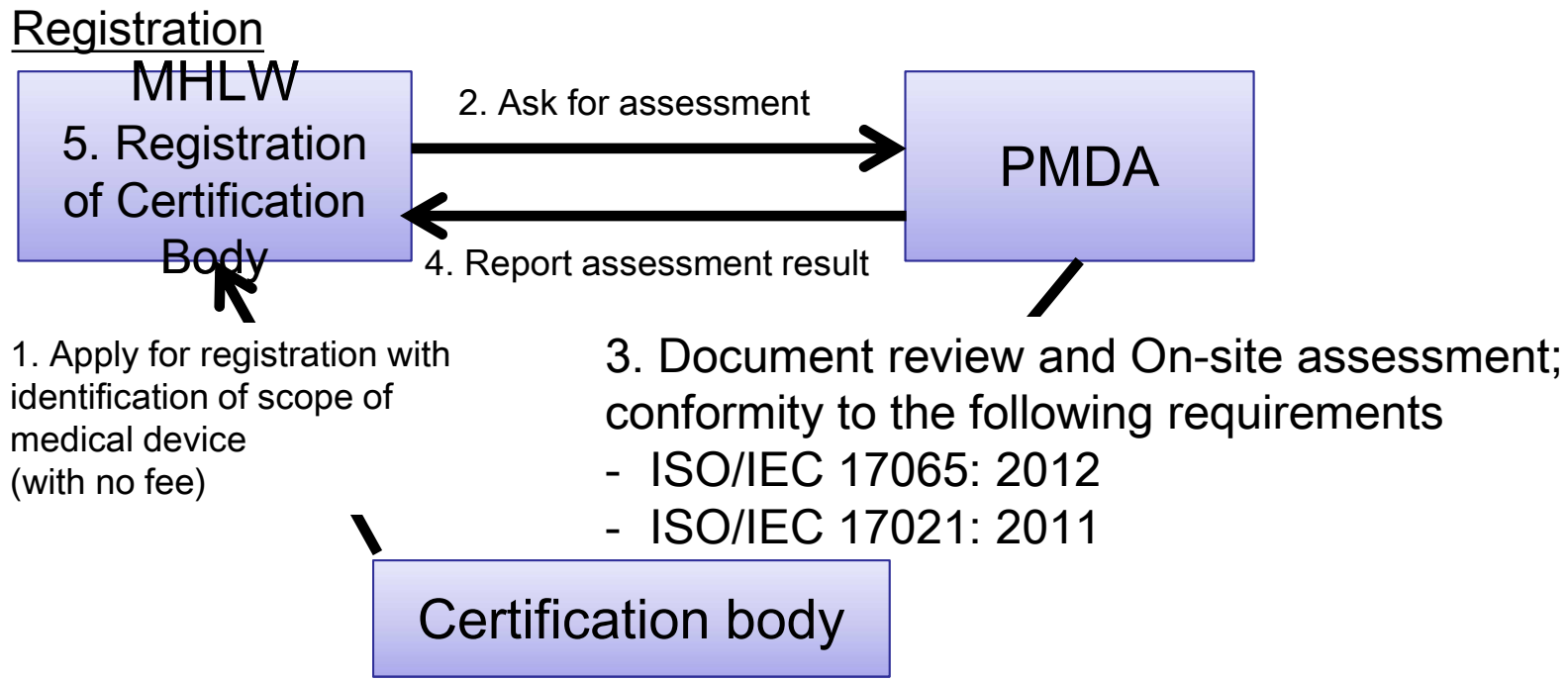
FY	2010	2011	2012	2013	2014	2015
Target (months)	21 (50th percentile)	20 (50th percentile)	17 (50th percentile)	14 (50th percentile)	14 (60th percentile)	14 (60th percentile)
Performance (months)	16.5	9.7	12.7	6.3	5.6	10.1
#	15	27	41	80	62	48

Third party certification process in Japan

A Certification issued by a registered certification body is required for Class II/III MDs/IVDs that have technical standards for certification before their marketing.



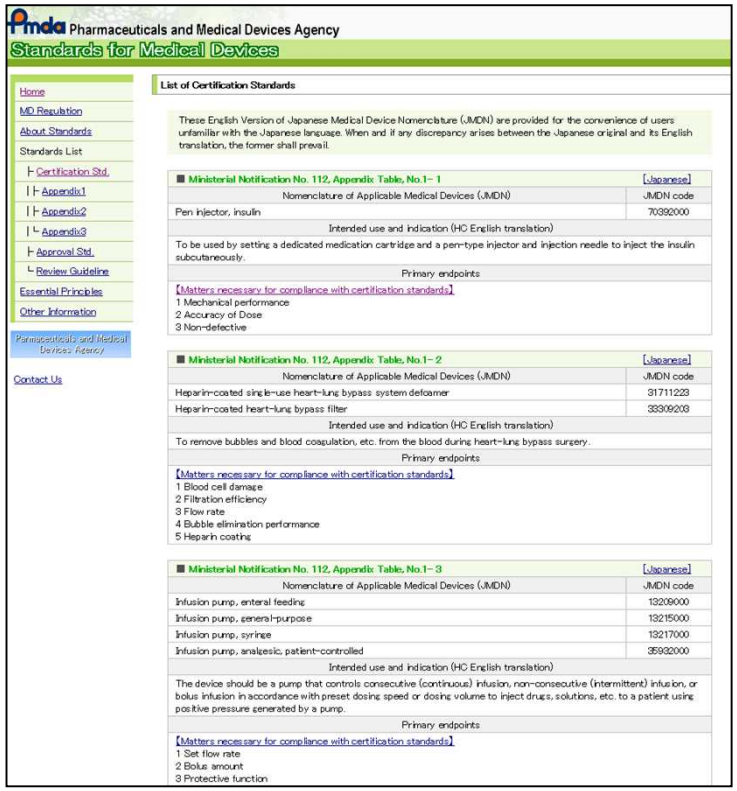
Registration and Supervision of certification body



Supervision of registered certification body

- PMDA perform annual on-site surveillance.
- Registration has to be renewed every 3 years.

(Reference) List of Certification Standards for Third Party Certification



Pmda Pharmaceuticals and Medical Devices Agency

Standards for Medical Devices

Home
MD Regulation
About Standards
Standards List
- Certification Std.
  - Appendix1
  - Appendix2
  - Appendix3
- Approval Std.
- Review Guideline

Essential Principles
Other Information
Pharmaceuticals and Medical Devices Agency
Contact Us

List of Certification Standards

These English Version of Japanese Medical Device Nomenclature (JMDN) are provided for the convenience of users unfamiliar with the Japanese language. When and if any discrepancy arises between the Japanese original and its English translation, the former shall prevail.

■ Ministerial Notification No. 112, Appendix Table, No.1- 1 [Japanese]

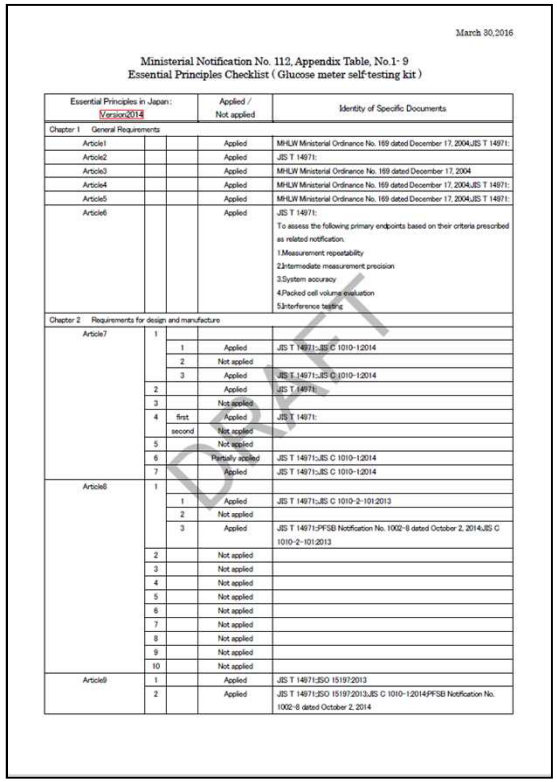
Nomenclature of Applicable Medical Devices (JMDN)	JMDN code
Pen injector, insulin	70392000
Intended use and indication (HC English translation)	
To be used by setting a dedicated medication cartridge and a pen-type injector and injection needle to inject the insulin subcutaneously.	
Primary endpoints	
【Matters necessary for compliance with certification standards】 1 Mechanical performance 2 Accuracy of Dose 3 Non-defective	

■ Ministerial Notification No. 112, Appendix Table, No.1- 2 [Japanese]

Nomenclature of Applicable Medical Devices (JMDN)	JMDN code
Heparin-coated single-use heart-lung bypass system defoamer	31711223
Heparin-coated heart-lung bypass filter	33309203
Intended use and indication (HC English translation)	
To remove bubbles and blood coagulation, etc. from the blood during heart-lung bypass surgery.	
Primary endpoints	
【Matters necessary for compliance with certification standards】 1 Blood cell damage 2 Filtration efficiency 3 Flow rate 4 Bubble elimination performance 5 Heparin coating	

■ Ministerial Notification No. 112, Appendix Table, No.1- 3 [Japanese]

Nomenclature of Applicable Medical Devices (JMDN)	JMDN code
Infusion pump, enteral feeding	13209000
Infusion pump, general-purpose	13215000
Infusion pump, syringe	13217000
Infusion pump, analgesic, patient-controlled	35932000
Intended use and indication (HC English translation)	
The device should be a pump that controls consecutive (continuous) infusion, non-consecutive (intermittent) infusion, or bolus infusion in accordance with preset dosing speed or dosing volume to inject drugs, solutions, etc. to a patient using positive pressure generated by a pump.	
Primary endpoints	
【Matters necessary for compliance with certification standards】 1 Set flow rate 2 Bolus amount 3 Protective function	



March 30,2016

Ministerial Notification No. 112, Appendix Table, No.1- 9
Essential Principles Checklist (Glucose meter self-testing kit)

Essential Principles in Japan: Version2014			Applied / Not applied	Identity of Specific Documents
Chapter 1 General Requirements				
Article1			Applied	MHLW Ministerial Ordinance No. 169 dated December 17, 2004,JIS T 14971:
Article2			Applied	JIS T 14971:
Article3			Applied	MHLW Ministerial Ordinance No. 169 dated December 17, 2004
Article4			Applied	MHLW Ministerial Ordinance No. 169 dated December 17, 2004,JIS T 14971:
Article5			Applied	MHLW Ministerial Ordinance No. 169 dated December 17, 2004,JIS T 14971:
Article6			Applied	JIS T 14971: To assess the following primary endpoints based on their criteria prescribed as related notification. 1.Measurement repeatability 2.Intermediate measurement precision 3.System accuracy 4.Packed cell volume evaluation 5.Interference testing
Chapter 2 Requirements for design and manufacture				
Article7	1			
		1	Applied	JIS T 14971:,JIS C 1010-1:2014
		2	Not applied	
		3	Applied	JIS T 14971:,JIS C 1010-1:2014
	2		Applied	JIS T 14971:
	3		Not applied	
	4	first	Applied	JIS T 14971:
		second	Not applied	
	5		Not applied	
	6		Partially applied	JIS T 14971:,JIS C 1010-1:2014
	7		Applied	JIS T 14971:,JIS C 1010-1:2014
Article8	1			
		1	Applied	JIS T 14971:,JIS C 1010-2-101:2013
		2	Not applied	
		3	Applied	JIS T 14971:PFSB Notification No. 1002-8 dated October 2, 2014,JIS C 1010-2-101:2013
	2		Not applied	
	3		Not applied	
	4		Not applied	
	5		Not applied	
	6		Not applied	
	7		Not applied	
	8		Not applied	
	9		Not applied	
	10		Not applied	
Article9	1		Applied	JIS T 14971:ISO 15197:2013
	2		Applied	JIS T 14971:ISO 15197:2013,JIS C 1010-1:2014:PFSB Notification No. 1002-8 dated October 2, 2014

DRAFT

Number of Certification Standards

As of March, 2017

For class II MDs	935
For class III MDs	11

Class III MD Certification Standards for	Issued on
Pen type infector for insulin	25 November 2014
Blood filter and bubble eliminator for artificial cardiopulmonary circuit with heparin	25 November 2014
Infusion pumps	25 March 2015
Manual type lung resuscitator	30 September 2015
Electrosurgical unit with substances	18 November 2015
Monitors such as Arrhythmia monitoring system	18 November 2015
Non-absorbed thread	24 December 2015
CPAP	24 December 2015
Self Measuring device for blood glucose	30 March 2016
Navigation system for neurosurgery	18 November 2015

Number of approvals of Medical Devices

		FY2010	FY2011	FY2012	FY2013	FY2014
Medical devices (total)		1,634	1,227	1535	1,347	1,235
Priority review items (included in total)		3	6	5	14	5
Breakdown	Band-new MDs	18	33	46	94	67
	Others (e.g. Improved MDs w/wo clinical data, Me-too MDs)	1,616	1,194	1,489	1,253	1,168

Number of certifications by registered certification bodies

Certification (including partial change certification)	**2,298**	**2,369**	**2,350**	**2,417**	**2,276**

Recent measures taken related to medical device regulations in Japan

Implementation of PMD Act; Revision of Pharmaceutical Affairs Law (PAL)

The PMD Act came into force on 25 November 2014 for the purpose of:

1. Strengthening safety measures regarding drugs and medical devices
2. Revising medical device regulations based on its characteristics
3. Introducing cellular and tissue therapeutic product regulations based on its characteristics

According to the revision:

a. Some Class III Medical Devices undergo certification
b. Software as a Medical Device (SaMD) is newly regulated
c. Manufacturer is required to be registered, instead of to be licensed
d. More efficient QMS inspection system is introduced

Establishment of new international regulatory harmonization strategies by MHLW and PMDA

International Regulatory Harmonization Strategy by MHLW and *PMDA International Strategic Plan 2015 by PMDA* have been published on 26 June 2015.
Based on the *mutually complementary* strategies, the following measures will be taken:

A) Promotion of Regulatory Science

Guidelines related to medical device regulations in Japan will be prepared and internationally announced.

B) Establishment of Training Center for regulatory matters

PMDA will provide regulators outside Japan with training for capacity building.

C) Active commitment to IMDRF as well as advancement of bilateral collaboration

Official Participation in MDSAP

Japan made an announcement on the *official participation in MDSAP Pilot* on 23 June 2015.
Further information will be provided in a timely manner.

Shown at right is the press release on the official participation in MDSAP Pilot in Japan
(written in Japanese).

You can find the announcement in English here;
http://www.fda.gov/MedicalDevices/InternationalPrograms/MDSAPPilot/ucm452243.htm

ひと、くらし、みらいのために
厚生労働省
Ministry of Health, Labour and Welfare

Press Release

平成 27 年 6 月 23 日
【照会先】
医薬食品局医療機器・再生医療等製品担当参事官室
参事官　磯部　総一郎（内線 2911）
調整官　近藤　英幸　（内線 2787）
（代表電話）03(5253)1111
（直通電話）03(3595)2419

Medical Device Single Audit Program Pilot に正式参加します

～国際協力の下、医療機器の品質確保を推進～

医療機器の品質確保に関する国際協力活動として、2014年1月から米国、カナダ、オーストラリア及びブラジルにより「MDSAP（Medical Device Single Audit Program（医療機器単一調査プログラム））Pilot」が試行的に運用されています。本日、米国ワシントンDCで行われるMDSAPフォーラムの場で、日本も正式メンバーとして本プログラムに参加することを表明します。今後とも本活動の下で、より一層の医療機器の品質確保を徹底してまいります。

Implementation of Strategy of Sakigake

An *innovative MD/IVD for patients in urgent need of innovative therapy* may be designated as a Sakigake Product if;

1) its premarket application will be filed in Japan firstly or simultaneously in some countries including Japan, *AND*
2) prominent effectiveness can be expected.

Once an MD/IVD is designated, its developer can enjoy such benefits as:

A) Prioritized Consultation by PMDA

B) Pre-application substantive review

C) Prioritized Review
(12 months → 6 months [MD])

D) Review Concierge assigned by PMDA

Designation of Sakigake products

As of 28 February 2017, 7 more products (3 medical devices, 1 IVD and 3 regenerative medicines) have been designated as Sakigake products.

No.	Product name	Expected performance/effectiveness
MD 3	**Artificial tracheal** (made of polypropylene mesh and collagen sponge)	Aiding reconstruction of tracheal while maintaining intratracheal structure after partial removal.
MD 4	**Boron neutron capture therapy (BNCT) system** (Neutron irradiation system for BNCT)	Selective destruction of tumor cells marked by boron agents, without damaging normal cells.
MD 5	**UT-Heart** (Software program to aid prediction of effectiveness of cardiac resynchronization therapy)	Higher accuracy of prediction of effectiveness of cardiac resynchronization therapy for patients with serious heart failure.
IVD 1	**Cancer-related gene panel examination system** (Diagnostic system for DNA sequencer)	Collective examination of cancer-related genes to aid decisions on cancer treatment strategies

No.	Product name	Expected performance/effectiveness
RP4	**CLS2702C/D** (Oral mucosa-derived esophageal cell sheet)	Shorter re-epithelialization period after extensive endoscopic submucosa dissection (ESD) in esophageal cancer.
RP5	**Dopamine neural precursor cell derived from non-autologous iPS cell** (Therapeutic stem cell for Parkinson's disease)	Novel therapy by inducing dopamine discharge to mitigate neural symptoms of patients with Parkinson's disease.
RP6	**Pluripotent progenitor cell derived form human (allogeneic) adult bone marrow** (Stem cell suspension derived from adult marrow)	Novel therapy for improving functional impairment caused by acute brain infarction.

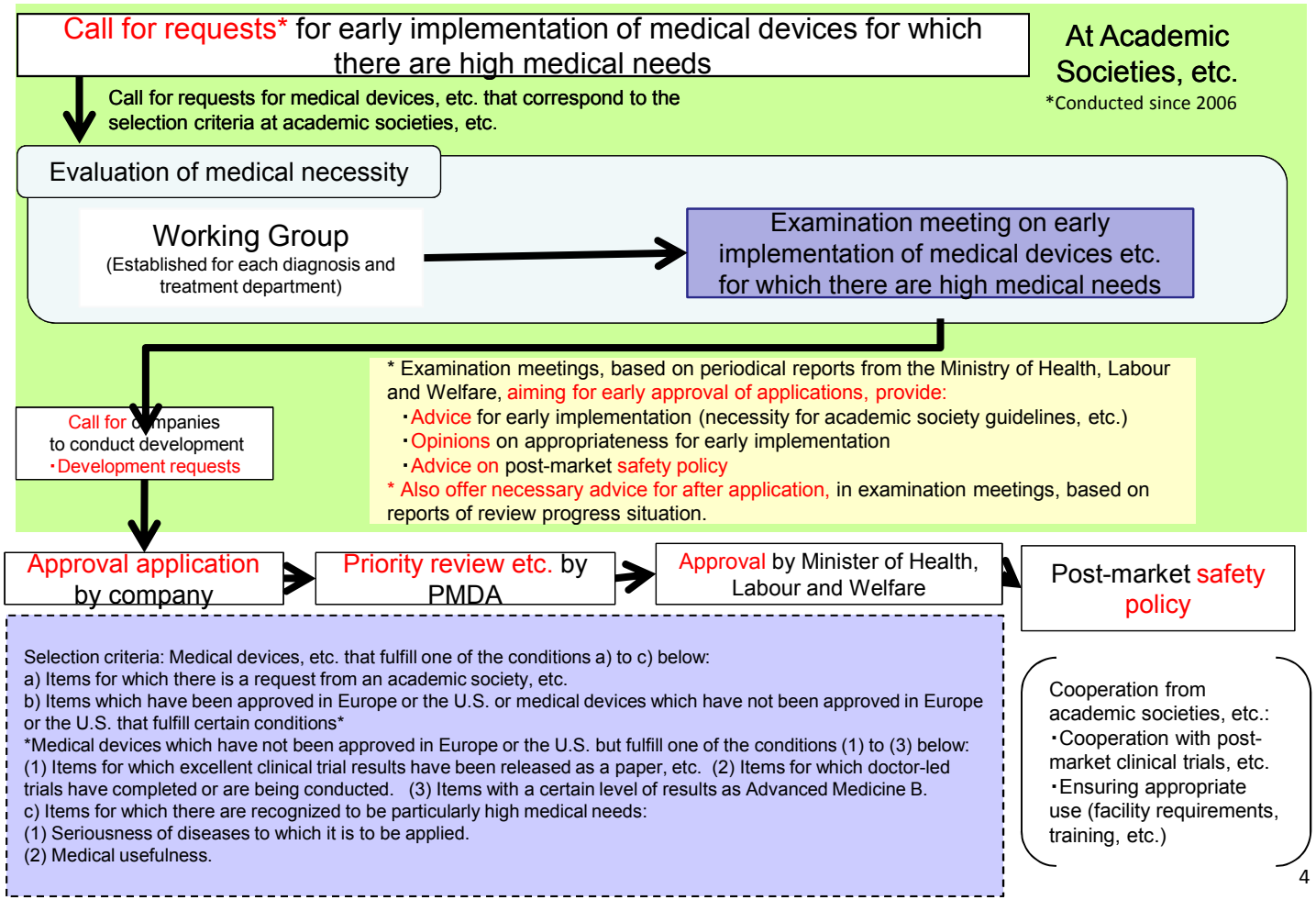
✧ Meanwhile, the absorbing barrier for adhesion prevention (MD2) which was designated last year will be withdrawn, due to the termination of development by the manufacturer.

(Reference) Designation of Sakigake products in 2016

The following 5 products under development have been designated as Sakigake products since 10 February 2016.
If a pre-market application for the products is filed, a priority review is applied.

No.	Product name	Expected performance/effectiveness
MD1	**Titanium Bridge** (Hinge-type plate with titanium)	Adduction-type spasmodic dysphonia
MD2	**Absorbing barrier for adhesion prevention** (Trehalose solution)	Reduction of postoperative adhesion prevention by Intraperitoneal injection
RP1	**STR01** (Autologous bone marrow-derived stem cells)	Improvement of neurological symptoms and functional impairment due to spinal cord injury
RP2	**G47Δ** (Recombinant herpes virus)	Glioma
RP3	**Autologous intracardiac stem cells**	Improvement of heart function in children with congenital heart disease

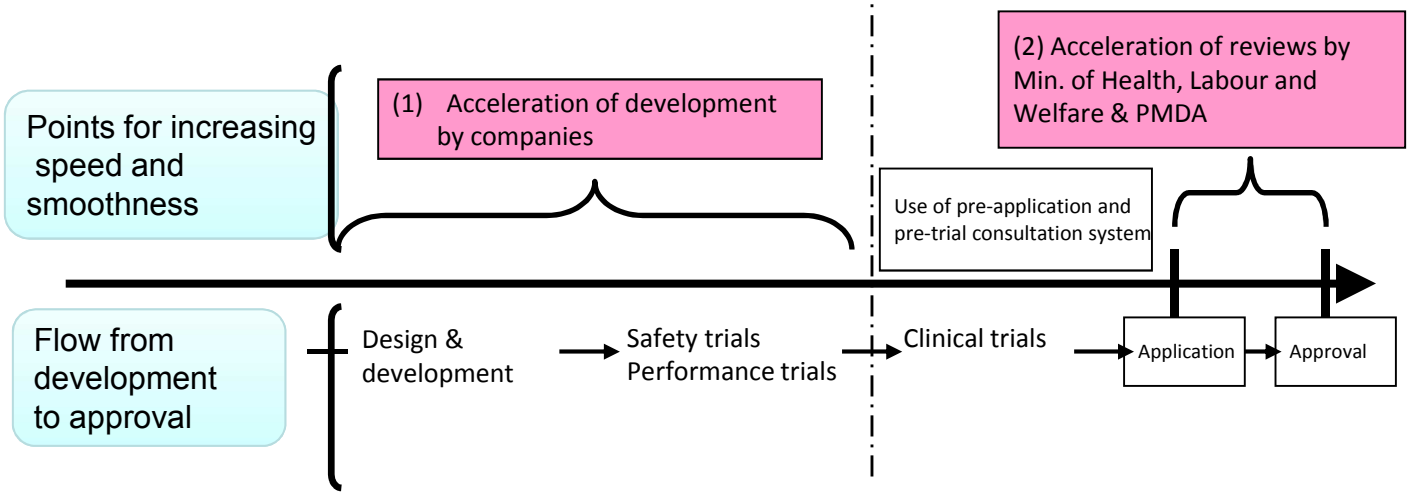
Examination relating to the early implementation of medical devices for which there are high medical needs



Next-generation medical devices and regenerative medicine, etc. product evaluation criteria

Objective:

To seek to accelerate approval reviews and improve efficiency of product development by preparing in advance and releasing the technology evaluation criteria, etc. to be used in reviews for next-generation medical devices with high medical needs and practical applicability, to enable to rapid provision to the medical workplace of medical devices and regenerative medicine products that use diverse cutting-edge technologies including IT, biotechnology, etc.



Evaluation criteria released until now (1/2)

Field	Evaluation criteria classification	Medical device review management office notification name
Active in vitro medical devices	Clinical evaluation of next-generation high performance artificial hearts	Pharmaceutical and Food Safety Bureau 0404002, issued on Apr. 4, 2008.
Critical limb ischemia	Clinical evaluation of medical devices for treatment of critical limb ischemia	Pharmaceutical and Food Safety Bureau 0529 No. 1, issued on May 29, 2013.
Tailor-made medical diagnostic devices	DNA judgment diagnostics using DNA chips	Pharmaceutical and Food Safety Bureau 0404002, issued on Apr. 4, 2008.
	Diagnostic equipment based on RNA profiling	Pharmaceutical and Food Safety Bureau 1120 No. 5, issued on Nov. 20, 2012.
Navigation medicine	Diaplasis support equipment	Pharmaceutical and Food Safety Bureau 0118 No. 1, issued on Jan. 18, 2010.
	Joint surgery support equipment	Pharmaceutical and Food Safety Bureau 0118 No. 1, issued on Jan. 18, 2010.
	Computerized surgery support equipment for application to soft tissue	Pharmaceutical and Food Safety Bureau 0528 No. 1, issued on May 28, 2010.
	Custom-made orthopedic implants, etc. made from 3D laminated structure technology using patient image data	Pharmaceutical and Food Safety Bureau Council 0925 No. 1, issued on Sep. 25, 2015.
Regenerative medicine	Cell sheets for cell therapy for serious heart failure	Pharmaceutical and Food Safety Bureau 0118 No. 1, issued on Jan. 18, 2010.
	Cell sheets for corneal epithelium	Pharmaceutical and Food Safety Bureau 0118 No. 1, issued on Jan. 18, 2010.
	Cell sheets for endothelium of cornea	Pharmaceutical and Food Safety Bureau 0528 No. 1, issued on May 28, 2010.
	Articular cartilage regeneration	Pharmaceutical and Food Safety Bureau 1215 No. 1, issued on Dec. 15, 2010.
	Cell sheets for periodontal tissue treatment	Pharmaceutical and Food Safety Bureau 1207 No. 1, issued on Dec. 7, 2011.
	Self-iPS cell derived retinal pigment epithelial cells	Pharmaceutical and Food Safety Bureau 0529 No. 1, issued on May 29, 2013.
	Same-type iPS cell derived retinal pigment epithelial cells	Pharmaceutical and Food Safety Bureau Council 0912 No. 2, issued on Sep. 12, 2014.
	Nasal cartilage regeneration	Pharmaceutical and Food Safety Bureau Council 0925 No. 1, issued on Sep. 25, 2015.
	Articular cartilage regeneration using human cartilage cells or somatic stem processing	Pharmaceutical Safety and Environmental Health Bureau 0630 No. 1, issued on Jun. 30, 2016.
	Articular cartilage regeneration using human (same-type) iPS cell processing	Pharmaceutical Safety and Environmental Health Bureau 0630 No. 1, issued on Jun. 30, 2016.

Evaluation criteria released until now (2/2)

Field	Evaluation criteria classification	Medical device review management office notification name
Neural function modification equipment & activity function recovery equipment	Neural function modification equipment	Pharmaceutical and Food Safety Bureau 1215 No. 1, issued on Dec. 15, 2010.
	Activity function recovery equipment	Pharmaceutical and Food Safety Bureau 0529 No. 1, issued on May 29, 2013.
In vitro materials	Custom-made bone connecting material implants for orthopedic use	Pharmaceutical and Food Safety Bureau 1215 No. 1, issued on Dec. 15, 2010.
	Custom-made artificial hip joints for orthopedic use	Pharmaceutical and Food Safety Bureau 1207 No. 1, issued on Dec. 7, 2011.
	Custom-made artificial knee joints for orthopedic use	Pharmaceutical and Food Safety Bureau 1120 No. 5, issued on Nov. 20, 2012.
	Spine implants to maintain mobility and stability	Pharmaceutical and Food Safety Bureau Council 0912 No. 2, issued on Sep. 12, 2014.
	3D laminated structure technology using orthopedic implants	Pharmaceutical and Food Safety Bureau Council 0912 No. 2, issued on Sep. 12, 2014.
Computer diagnostic support equipment	Computer diagnostic support equipment	Pharmaceutical and Food Safety Bureau 1207 No. 1, issued on Dec. 7, 2011.
Cardiac catheter ablation	Cardiac catheter ablation equipment	Pharmaceutical and Food Safety Bureau Council 0925 No. 1, issued on Sep. 25, 2015.
Stents	Bio-absorbable heart stents	Pharmaceutical Safety and Environmental Health Bureau 0630 No. 1, issued on Jun. 30, 2016.

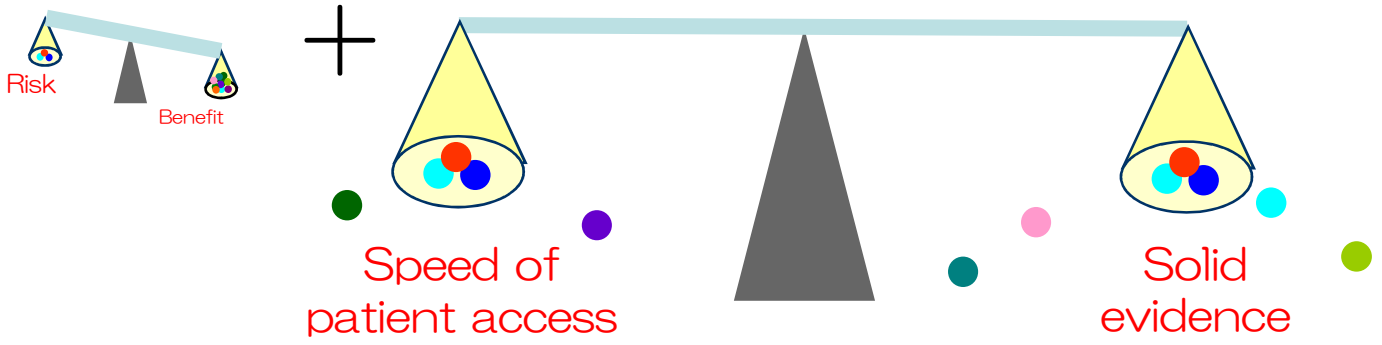
Release of next-generation medical devices evaluation criteria:
(Notifications addressed to each Prefecture's Director of Health and Safety after public comment and reporting to the Pharmaceutical and Food Safety review committee) http://dmd.nihs.go.jp/jisedai/tsuuchi/index.html

Concept of reviews: New Thinking

It is demanded to reconsider the balance between patient's timely access to MDs and considerable amount of time required to conduct clinical trials in order for much more robust evidence.

As well as the balance of risk and benefit in reviews, examination is also required regarding the balance of what should be required in pre- and post-market stage.

⇒ Guidance on the number of cases for clinical trials, Fast Break Scheme for innovative medical devices.



<Support for accelerated approval for innovative Medical device ~Importance of approval system encouraging medical venture~>

Fast Break Scheme for Innovative MD (Draft)

Innovative MDs created by medical venture enterprises are expected to have extremely effective and safe profile, however, these MDs tend to target extremely few patients. In that case, the development might be stagnated because of difficulties in collecting cases for clinical trial.

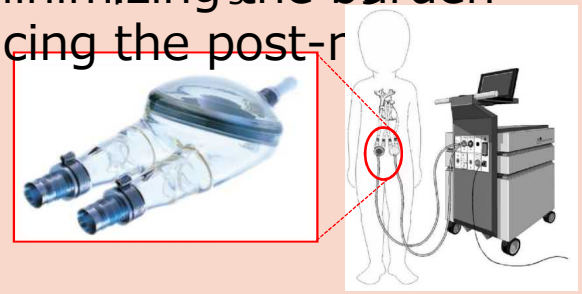
Considering such a situation and our mission to introduce innovative MDs to the public the government should construct the scheme which accelerate the approval the innovative MDs by minimizing the burden regarding clinical trials and enhancing the post-r surveillance.

From the Report by Conference for promotion of venture candidate drug/ medical innovations

Subjects to be solves

- The scope of the scheme
- Premarket review with limited number of clinical cases, overseas data and literature
- Post-market safety monitoring system which enables accelerated approval …etc.

Examples of target of Fast Track MD



EXCOR Pediatric (Ventricular assist device for pediatric)

Single-use Medical Device (SUD) Reprocessing

- Backed by the high interest in SUD reprocessing, currently carried out in an orderly manner in such countries like the US and Germany etc., Japan is now studying its appropriate implementation, since it could give great benefits of saving materials, reducing wastes and suppressing medical costs.
- After organizing a Study Group in FY 2015, the following investigations have been conducted, in order to identify the issues and to develop implementation guidelines.
  1) **Actual regulatory situations (US, Germany, UK)**
  2) **Domestic needs for reprocessed SUD**

- Relevant regulations will be streamlined in FY 2017 for the proper implementation of SUD reprocessing, and studies are on-going to establish criteria for the quality of reprocessed SUD, and for the reprocessing quality control.

Thank you!

厚生労働省
Ministry of Health, Labour and Welfare

pmda

Third party certification system and Certification standard in japan

Katsuhisa Ide

Division of Standards for Medical Devices

Office of standards and Guidelines Development

The 2nd Japan-India Medical Products Regulation Symposium 2017

Today's Agenda

1. *Introduction*
   a. PMDA, Office of Standards and Guidelines Development
2. *Utilization of Standards in review process in Japan*
   a. Framework for Certification Standards, Approval Standards and Review Guideline
   b. Certification Standards
   c. Approval Standards and Review Guideline
   d. Process of development for Certification Standards ,etc.
3. *Our Website for Standards regarding Medical Devices*

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3. *Our Website for Standards regarding Medical Devices*

Who We are ?

Date of establishment: April 2004

Who we are :

PMDA (Pharmaceuticals and Medical Devices Agency) is a Japanese regulatory agency, working together with the Ministry of Health, Labour and Welfare.

Our obligation is to protect public health by assuring the safety, efficacy and quality of pharmaceuticals and medical devices.

Please refer to the following website for details
https://www.pmda.go.jp/english/index.html)

PMDA Organization

- Office of Review Administration
- Office of Review Management
- Office of Standards and Guidelines Development※
- Office of Medical Devices I-III
- Office of Vaccines and Blood Products
- Office of Cellular and Tissue-based Products
- Office of Generic Drugs
- Office of OTC/Quasi-drugs
- Office of New Drug I-V
- Office of Non-clinical and Clinical Compliance

※ We focus on developing standards and guidelines

PMDA Organization

Office of Standards and Guidelines Development

Division of Pharmacopoeia and Standards for Drugs

- Secretariat of Japanese Pharmacopoeia Expert committees
- Registration of Master Files for Drug Substances

Division of Standards for Medical Devices

- Secretariat of Committees for Certification and Approval Standards
- Cooperation to establishment of JIS, ISO and IEC standards
- Open these standards to the public in a timely manner.

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Framework of Standards in Japanese regulation

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<tr><th colspan="2" rowspan="2">GHTF Classification</th><th colspan="3">PMD Act classification</th></tr>
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e.g.,
X-ray film</td><td>General MDs
(Class I)</td><td>Self declaration
Approval of the product is not required, but marketing notification is necessary.</td><td>1,196</td></tr>
<tr><td>Class B</td><td>Low risk
e.g., MRI, digestive catheters</td><td>Controlled MDs
(class II)</td><td>Third party Certification
Certification by a registered certification body is required.
・Certification Standard</td><td>1,974
(1,518 for 3rd Party)</td></tr>
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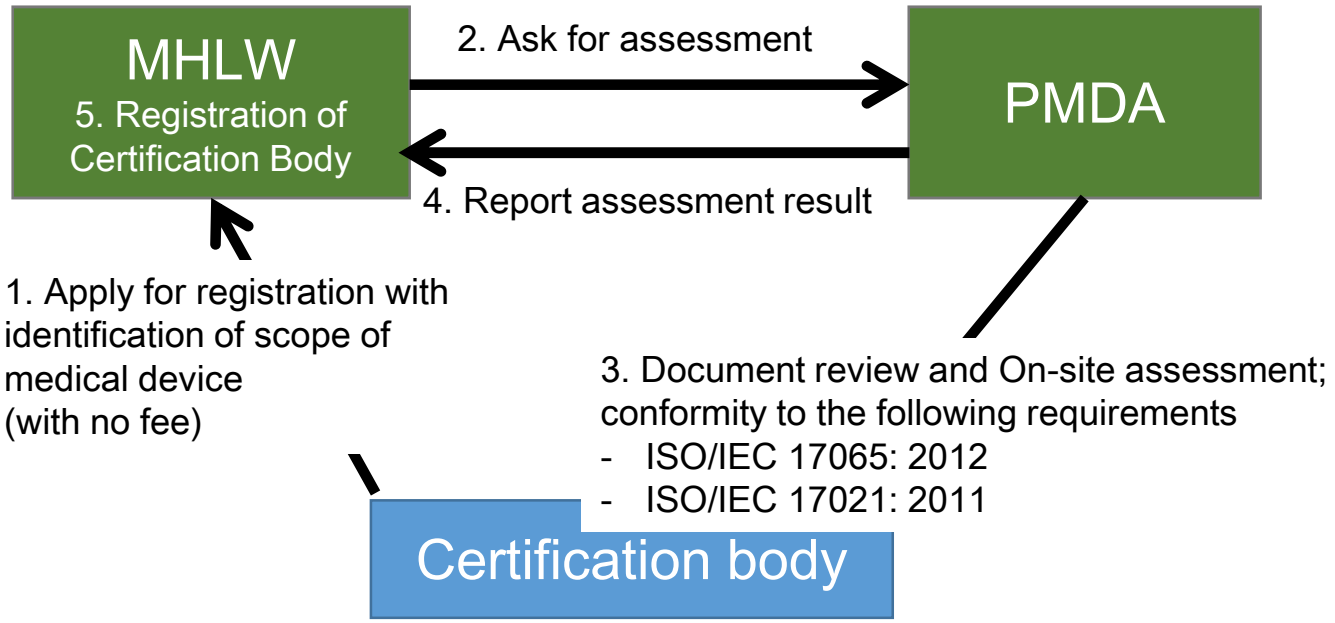
e.g., pacemaker</td><td>354</td></tr>
</table>

As of March, 2017

How we control the quality of certification body

Registration



Supervision of registered certification body

- PMDA perform annual on-site surveillance.
- Registration has to be renewed every 3 years.

Certification Standards

◆ *Certification Standards (Third party Certification)*

The “Certification Standards” are specified by the MHLW.
Registered third-party certification bodies※ utilize these standards to confirm the conformity of Class II or III medical devices to the technical requirements.

※ Third-party certification bodies are requested to satisfy ISO/IEC 17021 and ISO/IEC 17065

1) Regarding Class II medical devices

⇒ ***935*** Certification Standards have already been developed which cover ***1518*** of ***1974*** Class II products**. (77%)**

2) Regarding Class III medical devices ***<New Activities since 2014>***

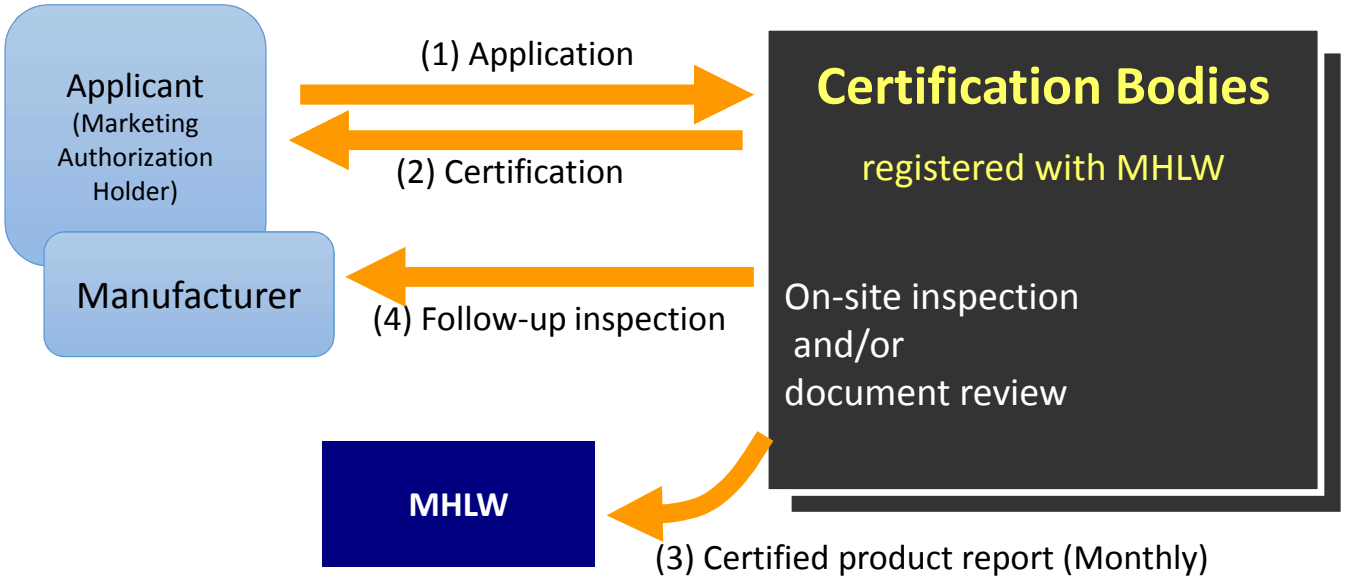
⇒ The scope of third party certification was expanded to class III

⇒ 11 Certification Standards have already been developed which cover 43 Class III JMDNs.

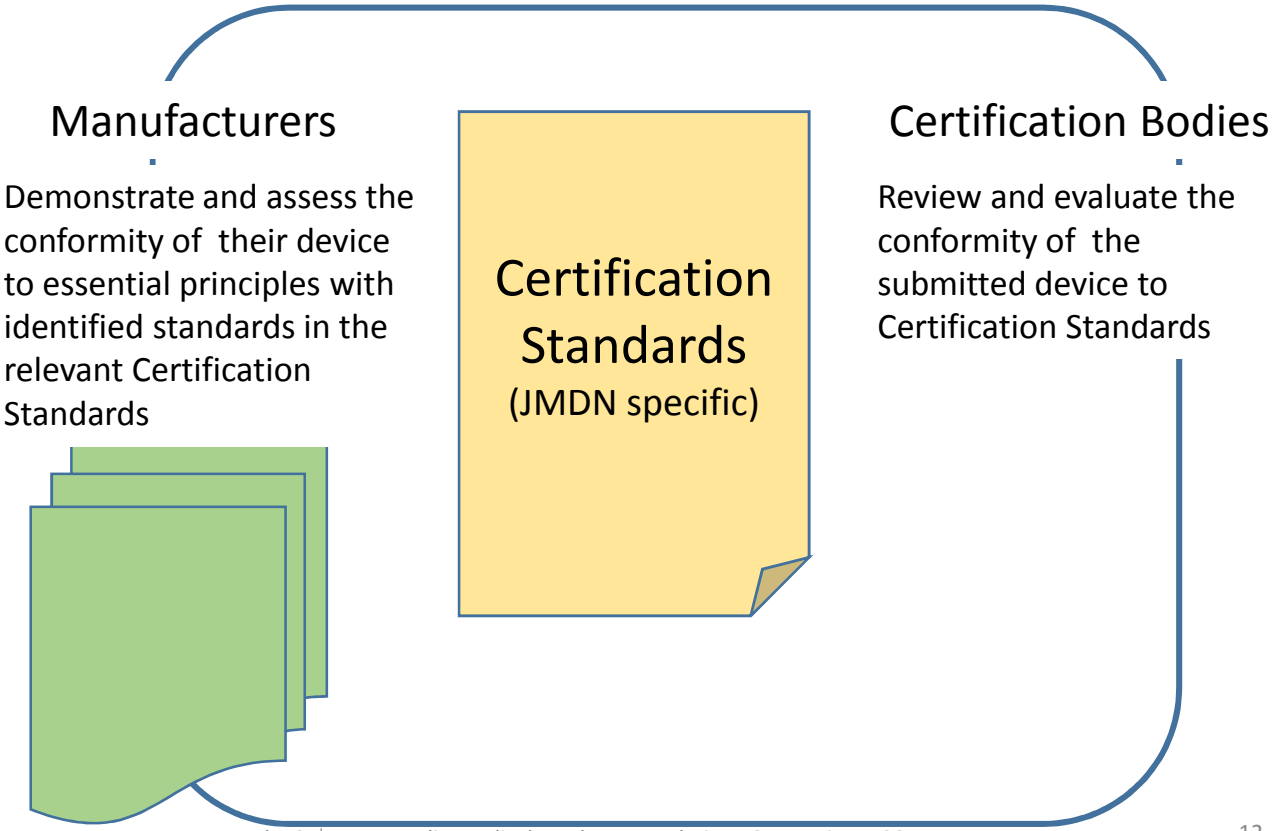
※ As of March.2017

Third party certification process in Japan

A Certification issued by a registered certification body is required for Class II/III MDs/IVDs that have **technical standards for certification** before their marketing.



How we control the quality of submissions and review of Third Party Certification



Certification Standards (Class II)

◆*Structure of Certification Standards*

1. JMDN

Certification Standards are Notified by the MHLW .
Related applicable Japanese Medical Device Nomenclature (JMDN) are also listed.

2. Technical standard

Japanese Industrial Standard (JIS) is cited in principle.
Together with the EP check list including applicable standards to be used for conformity assessment.

3. Scope of Purpose of use and effect

The purpose of use and effect for a medical device are determined based on its definition given in the relevant technical standards.

◆*Compliance with Essential Principles*

All medical devices are required to satisfy the essential principle that align with those defined in GHTF/SG1/N68:2012. A checklist of conformity to the Essential Principles is basically defined and published notification.

◆*Substantially Equivalent to Existing Product*

Products subject to compliance with Certification Standards are limited to those which have substantially equivalent to existing controlled medical devices

Certification Standards (Class II)

Certification Standard is consisted of
JIS and purpose of use and effect.

◆ *Structure of Certification Standards*

No.	Nomenclature of Applicable Medical Devices (JMDN)	Certification Standard	
		JIS	**Purpose of use and effect**
1	1. X-ray system, diagnostic, general-purpose, mobile, analogue 2. X-ray system, diagnostic, general-purpose, portable, analogue 3. X-ray system, diagno general-purpose, por digital 4. X-ray system, diagno general-purpose, stationary, analogue 5. X-ray system, diagnostic, general-purpose, stationary, digital 6. X-ray system, diagnostic, general-purpose, mobile, digital	T 0601-1-3 Z 4751-2-54	To provide the imaging information of human body for medical care used with the scintillation effect, photo-effect or ionization effect that X-ray went through a body has.

JIS required by technical requirement
JIS T 0601-1-3 is based on IEC 60601-1-3:2008 (IDT)
JIS Z 4751-2-54 is based on IEC 60601-2-54:2009 (MOD)

Certification Standards (Class II)

◆*Essential Principles Checklist*

A checklist of conformity to the Essential Principles is basically published as notification.

Essential Principles of Safety and Performance of Medical devices	Applicable	Method of Conformity	Identity of Specific Documents
1.General requirements			
(Design) Clause 1 Medical devices should be designed and manufactured ・・・・・・	Applicable	Show the conformity with recognized standard included requirements Show risk management is conducted according to recognized standard	Ordinance on Standards for Manufacturing Control and Quality Control of Medical Devices and *In Vitro* Diagnostic Reagents（MHLW Ministerial Ordinance No. 169 in 2004） JIS T 14971:「Medical devices -- Application of risk management to medical devices」
（Risk management） Clause 2 The solutions adopted by the manufacturer ・・・・・・	Applicable	Show risk management is conducted according to recognized standard	JIS T 14971:「Medical devices -- Application of risk management to medical devices」
:			
(Effective for medical devices) Clause 6 All known and foreseeable risks, and ・・・・・・	Applicable	verify the effective to conduct risk analysis. Show the conformity with recognized Standard to verify the effective	JIS T 14971:「Medical devices -- Application of risk management to medical devices」 JIS Z 4751-2-54:2012:「Particular requirements for the basic safety and essential performance of X-ray equipment for radiography and radioscopy 203.6.3.2.101 , 203.6.4.3, 203.6.4.7., etc.

Certification Standards (Class II)

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and ・・・・・		Show the conformity with recognized Standard to verify the effective	JIS Z 4751-2-54:2012:「Particular requirements for the basic safety and essential performance of X-ray equipment for radiography and radioscopy 203.6.3.2.101 , 203.6.4.3, 203.6.4.7., etc.

Identity of Specific Documents

MHLW Ministerial Ordinance No. 169 is based on ISO 13485：2003

JIS T 14971 is based on ISO 14971:2007 (IDT)

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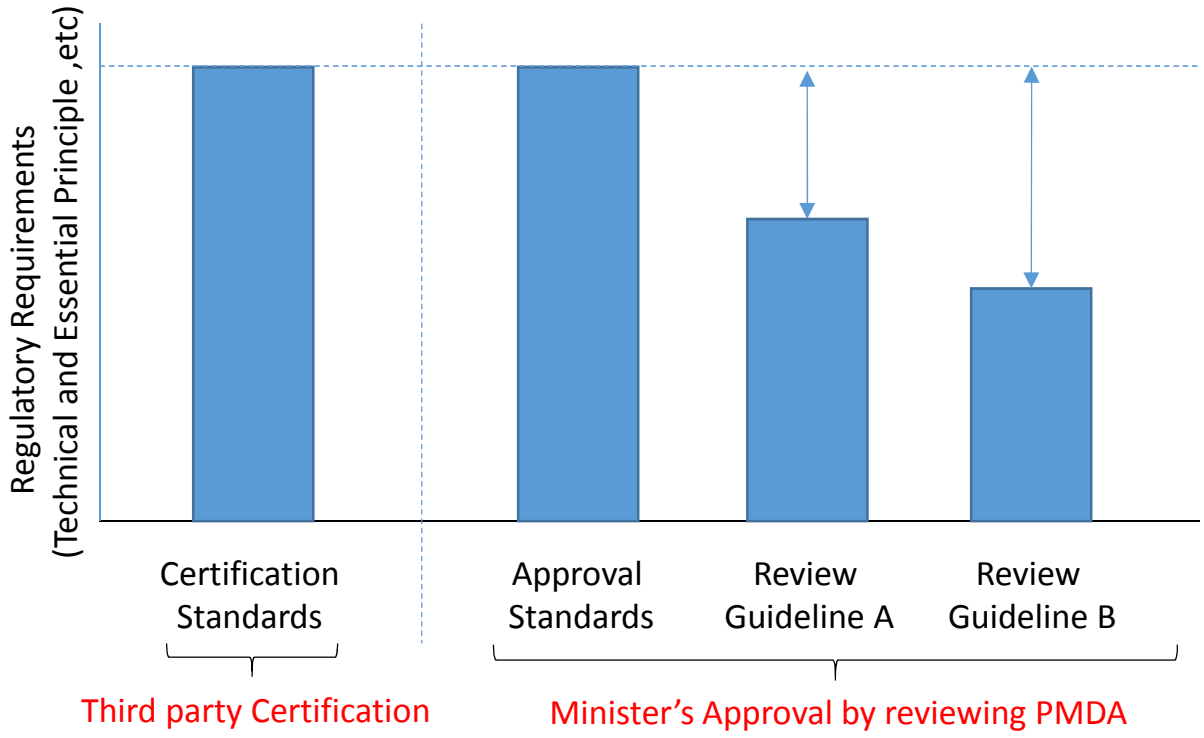
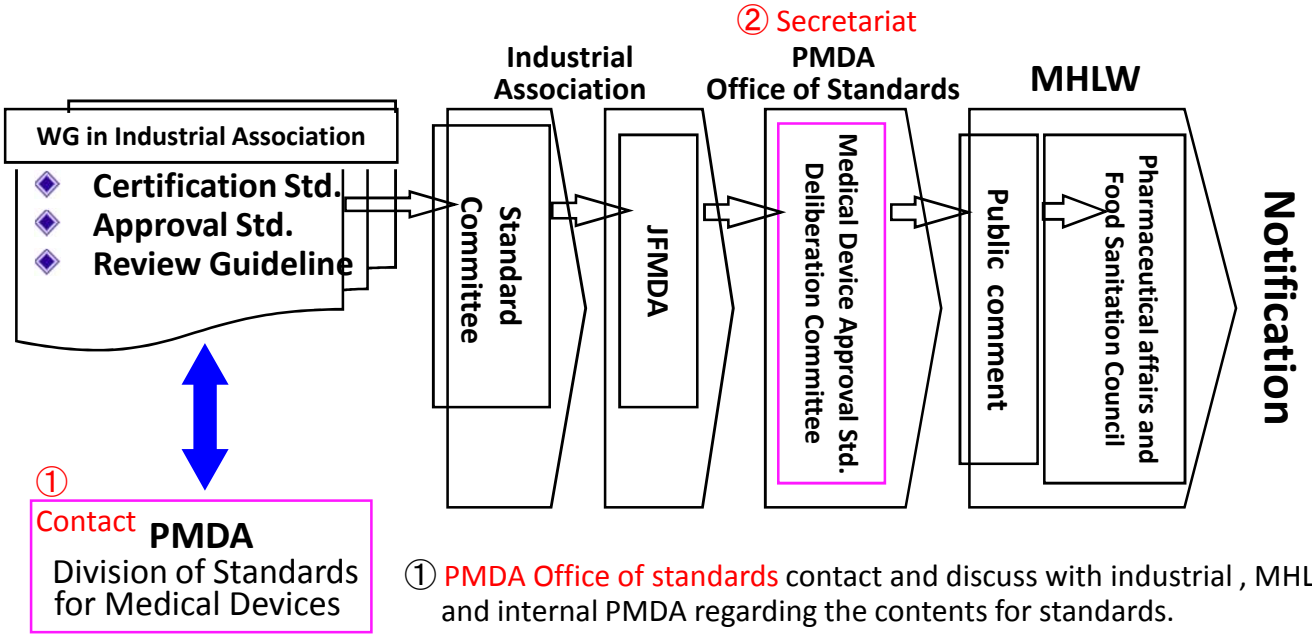


Process for Certification Standards, etc..



① PMDA Office of standards contact and discuss with industrial , MHLW and internal PMDA regarding the contents for standards.

② PMDA Office of standards hold a Deliberation Committee as secretariat. Academia, consumer(medical doctor), industrial attends as a delegate.

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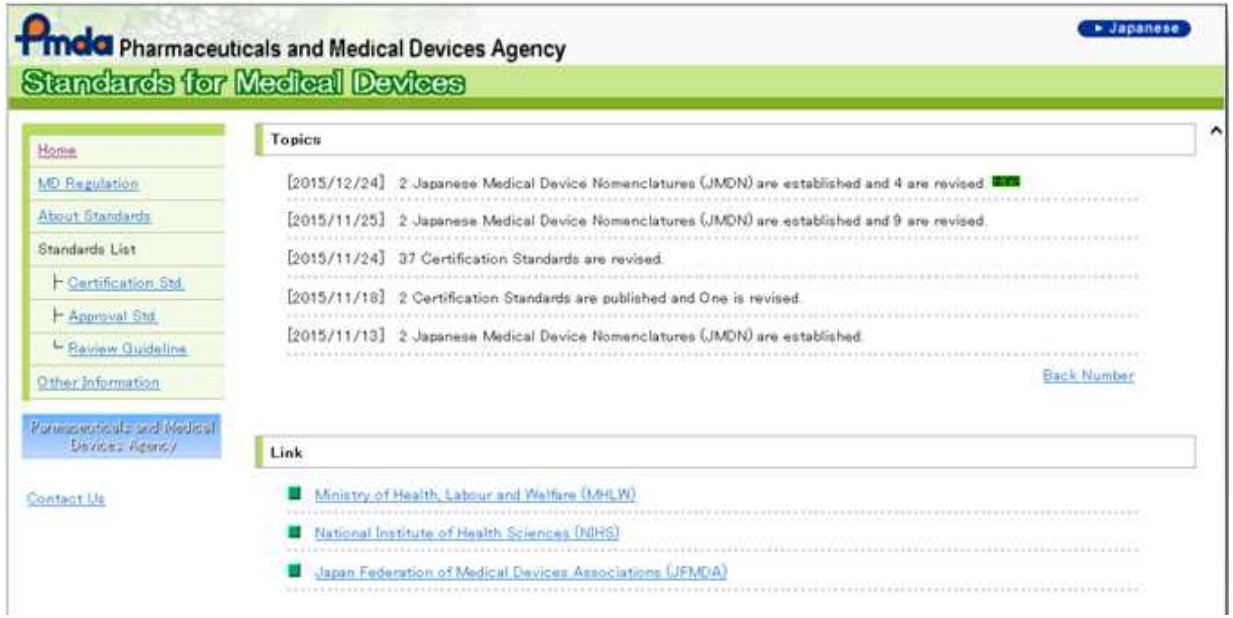
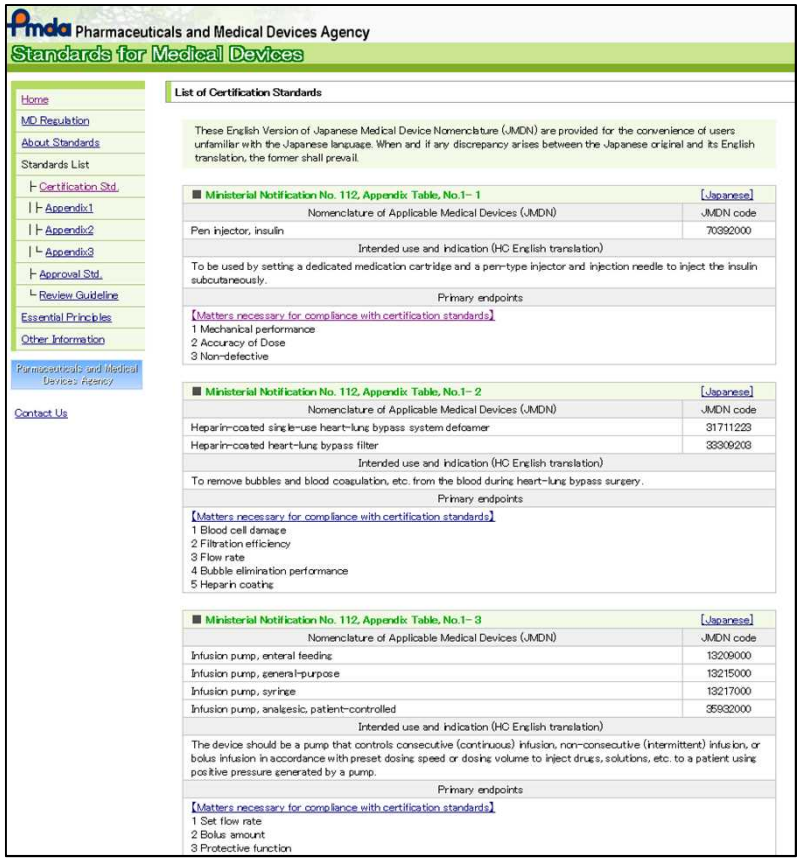
Our website for standards for Medical Devices

We open these standards to the public by English.

Please visit our Website : **http://www.std.pmda.go.jp/stdDB/index_e.html**



List of Certification Standards



Pharmaceuticals and Medical Devices Agency

Standards for Medical Devices

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Pharmaceuticals and Medical Devices Agency

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List of Certification Standards

These English Version of Japanese Medical Device Nomenclature (JMDN) are provided for the convenience of users unfamiliar with the Japanese language. When and if any discrepancy arises between the Japanese original and its English translation, the former shall prevail.

Ministerial Notification No. 112, Appendix Table, No.1- 1 [Japanese]

Nomenclature of Applicable Medical Devices (JMDN)	JMDN code
Pen injector, insulin	70392000

Intended use and indication (HC English translation)

To be used by setting a dedicated medication cartridge and a pen-type injector and injection needle to inject the insulin subcutaneously.

Primary endpoints

【Matters necessary for compliance with certification standards】
1 Mechanical performance
2 Accuracy of Dose
3 Non-defective

Ministerial Notification No. 112, Appendix Table, No.1- 2 [Japanese]

Nomenclature of Applicable Medical Devices (JMDN)	JMDN code
Heparin-coated single-use heart-lung bypass system defoamer	31711223
Heparin-coated heart-lung bypass filter	33309203

Intended use and indication (HC English translation)

To remove bubbles and blood coagulation, etc. from the blood during heart-lung bypass surgery.

Primary endpoints

【Matters necessary for compliance with certification standards】
1 Blood cell damage
2 Filtration efficiency
3 Flow rate
4 Bubble elimination performance
5 Heparin coating

Ministerial Notification No. 112, Appendix Table, No.1- 3 [Japanese]

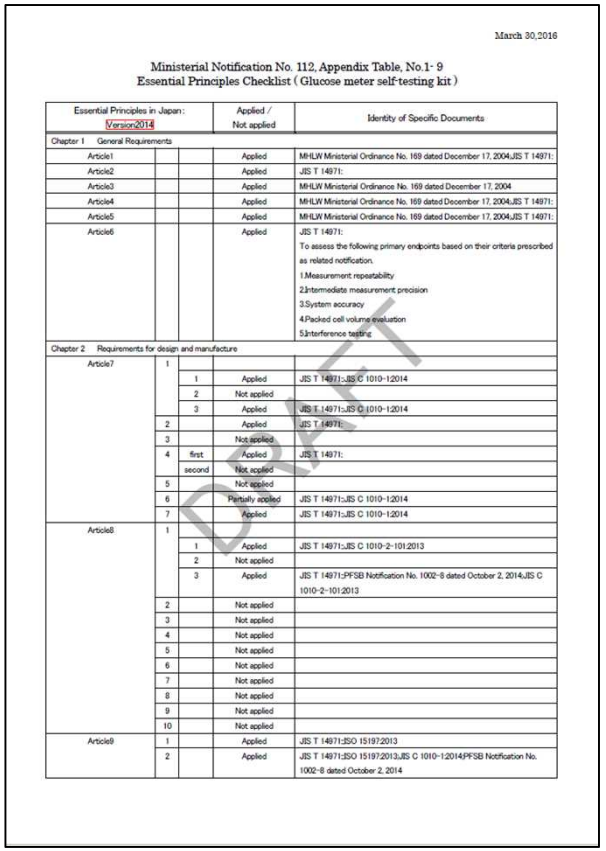
Nomenclature of Applicable Medical Devices (JMDN)	JMDN code
Infusion pump, enteral feeding	13209000
Infusion pump, general-purpose	13215000
Infusion pump, syringe	13217000
Infusion pump, analgesic, patient-controlled	35932000

Intended use and indication (HC English translation)

The device should be a pump that controls consecutive (continuous) infusion, non-consecutive (intermittent) infusion, or bolus infusion in accordance with preset dosing speed or dosing volume to inject drugs, solutions, etc. to a patient using positive pressure generated by a pump.

Primary endpoints

【Matters necessary for compliance with certification standards】
1 Set flow rate
2 Bolus amount
3 Protective function



March 30,2016

Ministerial Notification No. 112, Appendix Table, No.1- 9
Essential Principles Checklist (Glucose meter self-testing kit)

Essential Principles in Japan: Version2014			Applied / Not applied	Identity of Specific Documents
Chapter I General Requirements				
Article1			Applied	MHLW Ministerial Ordinance No. 169 dated December 17, 2004,JIS T 14971:
Article2			Applied	JIS T 14971:
Article3			Applied	MHLW Ministerial Ordinance No. 169 dated December 17, 2004
Article4			Applied	MHLW Ministerial Ordinance No. 169 dated December 17, 2004,JIS T 14971:
Article5			Applied	MHLW Ministerial Ordinance No. 169 dated December 17, 2004,JIS T 14971:
Article6			Applied	JIS T 14971: To assess the following primary endpoints based on their criteria prescribed as related notification. 1.Measurement repeatability 2.Intermediate measurement precision 3.System accuracy 4.Packed cell volume evaluation 5.Interference testing
Chapter 2 Requirements for design and manufacture				
Article7	1			
		1	Applied	JIS T 14971:,JIS C 1010-1:2014
		2	Not applied	
		3	Applied	JIS T 14971:,JIS C 1010-1:2014
	2		Applied	JIS T 14971:
	3		Not applied	
	4	first	Applied	JIS T 14971:
		second	Not applied	
	5		Not applied	
	6		Partially applied	JIS T 14971:,JIS C 1010-1:2014
	7		Applied	JIS T 14971:,JIS C 1010-1:2014
Article8	1			
		1	Applied	JIS T 14971:,JIS C 1010-2-101:2013
		2	Not applied	
		3	Applied	JIS T 14971:PFSB Notification No. 1002-8 dated October 2, 2014,JIS C 1010-2-101:2013
	2		Not applied	
	3		Not applied	
	4		Not applied	
	5		Not applied	
	6		Not applied	
	7		Not applied	
	8		Not applied	
	9		Not applied	
	10		Not applied	
Article9	1		Applied	JIS T 14971:ISO 15197:2013
	2		Applied	JIS T 14971:ISO 15197:2013,JIS C 1010-1:2014,PFSB Notification No. 1002-8 dated October 2, 2014

DRAFT

As a summary

Summary

- Use International Standards for regulatory purposes
- Regarding low risk devices with Certification Standards, the review is conducted by third party instead of PMDA.
- As for some of high risk devices, Approval Standards or Review Guideline for review process are notified by MHLW.
- All medical devices has to conform the Essential Principle (EP) and those EP using International Standards as well as JIS
- JIS is mostly based on ISO and IEC

  →It can be said the translation version of ISO/IEC.

Summary

Utilization of international Standards in regulation may make win-win-win situation for both Industries-regulators-patients.

- *Reduce duplication*
- *Enhance Transparency*
- *Save preparing time/cost*
- *Reduce review time*
- *Ensure Safety and Efficacy*

Example1
Challenge! Revision of ISO for Asian environment

- Revision of ISO22674:2006 Dentistry metallic materials for fixed and removable restoration and appliances *(JIS T6118, 6116, 6122, 6004 etc.)*

～ISO/TC106(Dentistry) SC2 prosthodontic materials/2013 International meeting Korea～

Norway Germany Canada USA Thailand Japan China etc.

Cf. Specified performance of EP CL /CS

○Test methods

2006： Linear thermal expansion (8.8) 'btw 25 and 500℃ for each specimen'

↓

Replace 25～500 with 50～500*

Reason: Since the starting temp. is often higher than 25 in Asian country in Summer.

There is no significant difference in the calculated coefficient of the evidence data.

→25～500 or 50～500

Thank you very much

URL http://www.pmda.go.jp

http://www.std.pmda.go.jp/stdDB/index_e.html