Overview of medical device regulation in Japan

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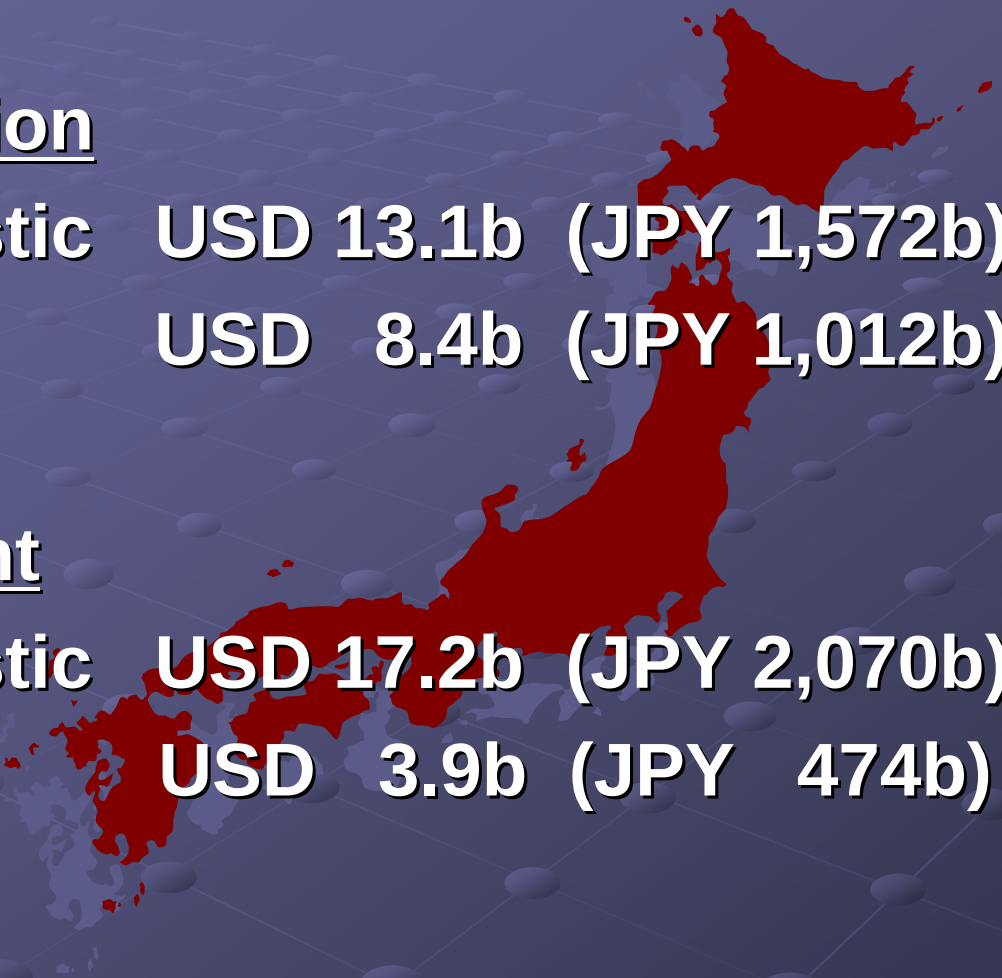
Topics

1. **Statistics on medical device production**
2. **Understanding of medical device requirements**
3. **Overview of Japanese Authorities**

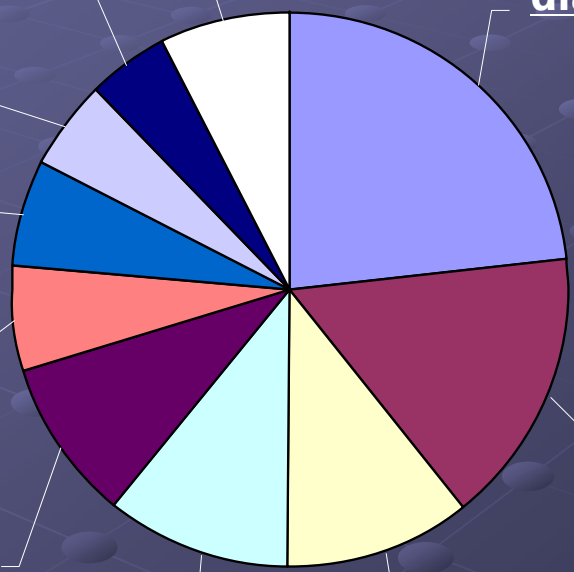
Production and shipment value of MDs



- **Production**
  - Domestic USD 13.1b (JPY 1,572b) 60.8%
  - Import USD 8.4b (JPY 1,012b) 39.2%
- **Shipment**
  - Domestic USD 17.2b (JPY 2,070b)
  - Export USD 3.9b (JPY 474b)

Ref. Statistics on Production by Pharmaceutical and Medical Device Industry (Economic Affairs Division, MHLW) (薬事工業生産動態統計年報)

Production values classified MDs



others (USD 0.99b, 8%)

ophthalmic and related devices (0.61b, 5%)

dental materials (0.70b, 5%)

medical specimen testing devices (0.79, 6%)

X-ray imaging related apparatus (0.82b, 6%)

Medical devices household use (1.23b, 9%)

Bio-phenomena monitoring/testing devices (1.41b, 11%)

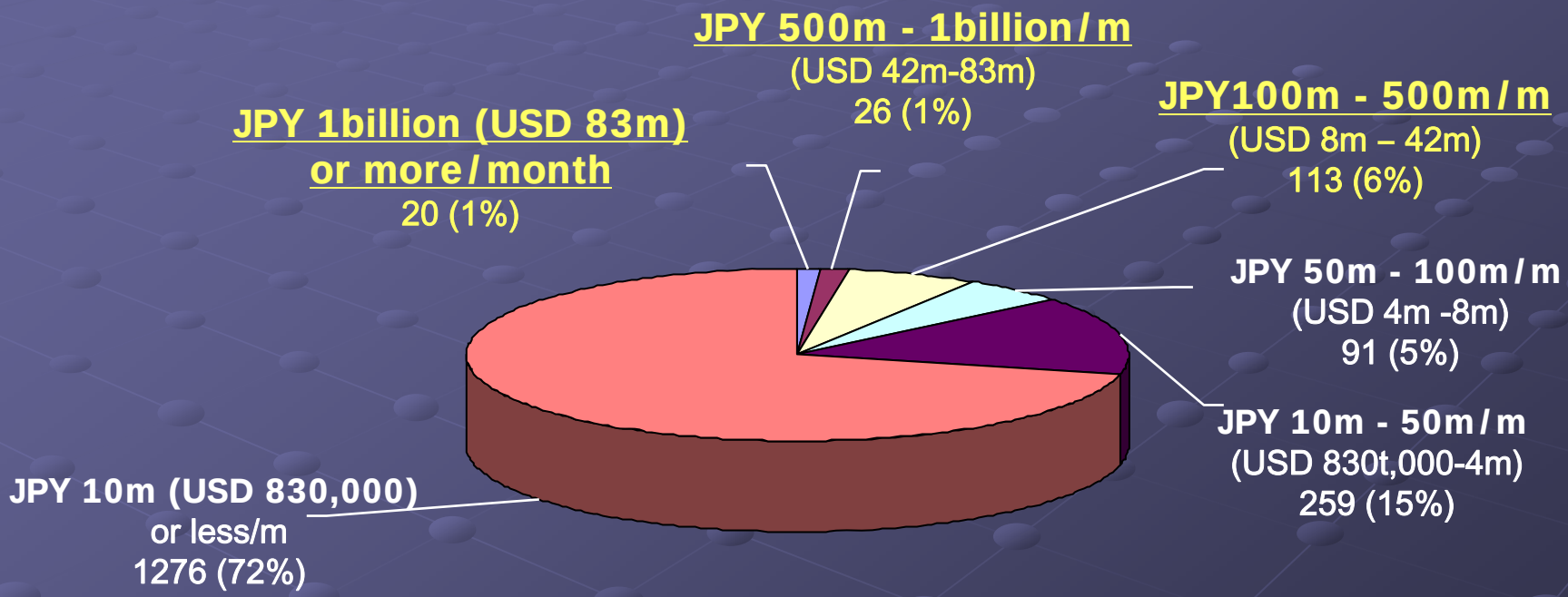
Bio-function substitute / assistive devices, artificial organs (1.41b, 11%)

surgical instruments and supplies (2.08b, 16%)

diagnostic imaging systems (USD 3.06b, 23%)

Total: USD 13.1b (JPY 1,572b)

Number of manufacturers by production scale



Top 3 classes contribute 90% of total domestic production

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Classification of Medical Devices

GHTF Classification	
Class A	extremely low risk X-Ray film
Class B	low risk MRI, digestive catheters
Class C	medium risk artificial bones, dialyzer
Class D	high risk pacemaker, artificial heart values

PAL classification		
Category	Pre-market regulation	Japanese MD Nomenclature
"General MDs" (Class I)	Self declaration	1,195
"Controlled MDs" (class II)	Third party Certification	1,785
"Specially Controlled MDs" (class III & IV)	Minister's Approval	737
		325

Japanese Medical Devices Nomenclature (JMDN) and MD classification

- Each MD has to fall under generic nomenclature (JMDN). JMDN is based on GMDN.

- Ministerial Notification #298 (July 20, 2004) shows lists of JMDN and their classification. Classification rule is based on GHTF document (SG1-N15:2006).
  (see also DG-PFSB Notification #0720022, July 20, 2004)

Example:
(JMDN) lumbar puncture kit, single use
(class) class II *

* **GHTF Classification Rule 6**.
All surgically invasive devices intended for transient use are in Class B

Prerequisites to bring MDs into the Japanese Market

Product

Minister's Approval (*syonin　承認*) (Art.14)
or Certification (*ninsyo　認証*) (Art.23-2)

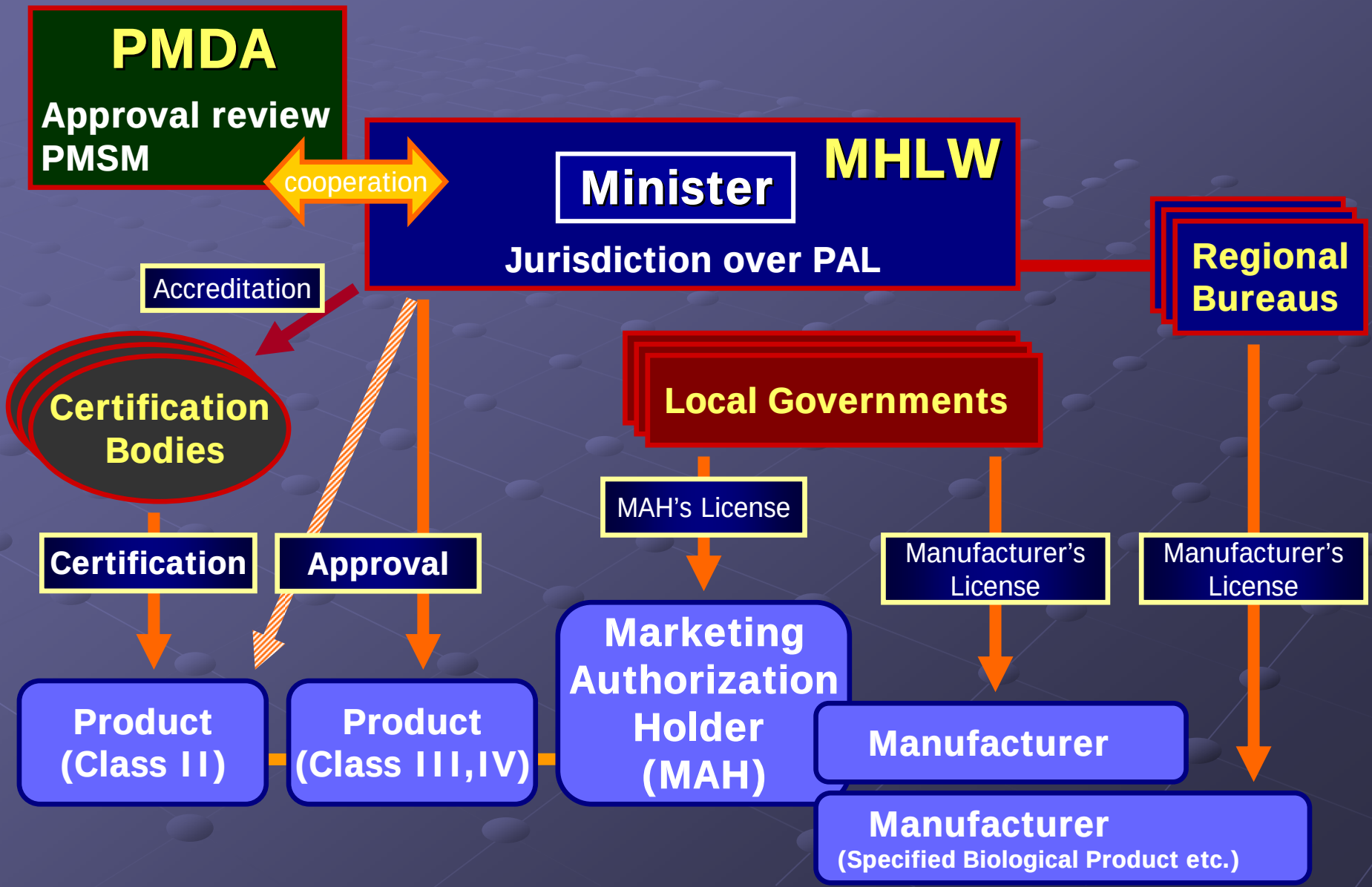
Company

License for Marketing Authorization Holder (*Seizohanbai-gyo-kyoka 製造販売業許可*) (Art.12)

Plant

License for Manufacturer (*seizo-gyo-kyoka　製造業許可*) (Art. 13)
or Status as Recognized Foreign Manufacturer (*gaikoku seizo-gyosya nintei　外国製造業者認定*) (Art. 13-3)

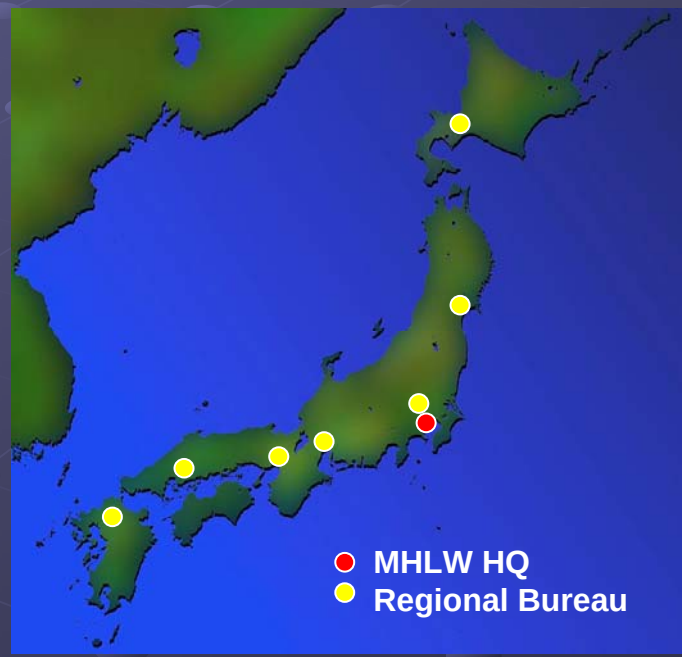
Authorities of MD regulation



MHLW HQ and Regional Bureau of Health and Welfare (RBHW)

- MHLW has 7 regional bureaus
- The Minister delegates part of his/her authority under the PAL to DGs of RBHW.

  For example, license for a manufacturer which produces MD regarded as a Specified Biological Products or radiological pharmaceuticals is issued by the DG of RBHW

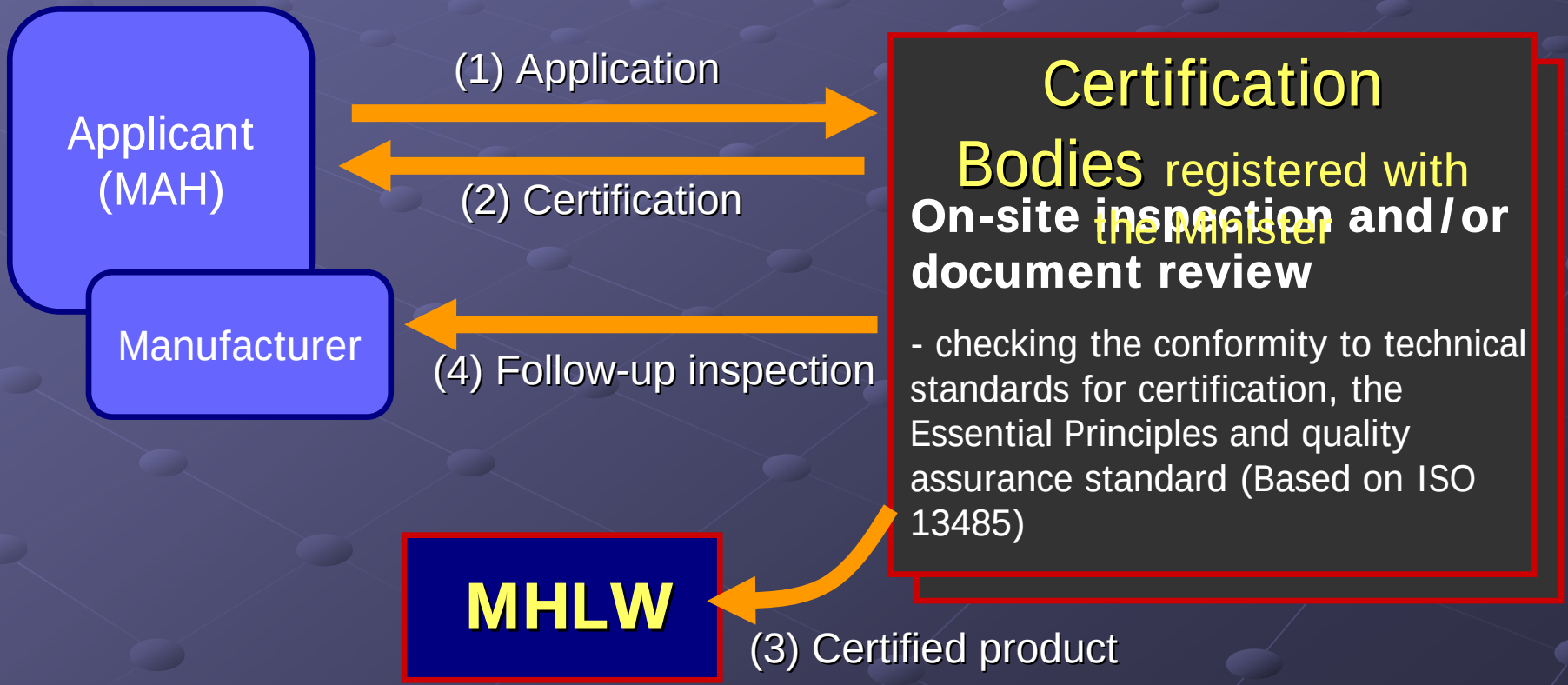


Pre-market regulation on products

Classes	Risk-based Classification	Technical Stds. for Certification	Type of regulation	Review	QMS
Class I	Extremely Low Risk		Self-declaration	MAH (report to PMDA)	* Some exception
Class II	Low Risk	Technical Stds.	3rd. Party Certification	Registered Certification Body	Inspection
		No Technical Stds.	**Minister's Approval**	**PMDA and MHLW**	
Class III	Medium Risk				
Class IV	High Risk				

Third-party Certification system in Japanese MD regulation

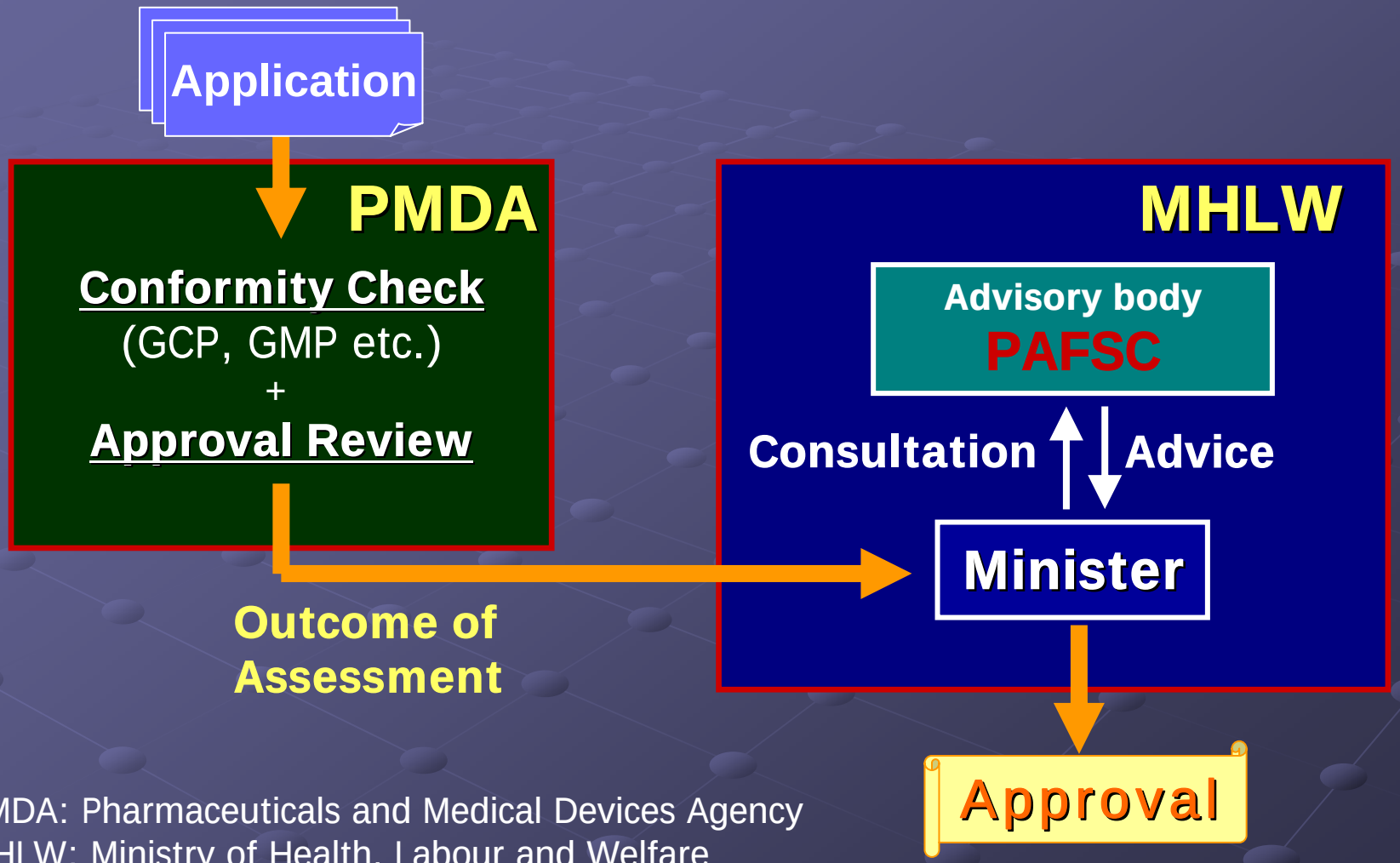
A Certification issued by a registered certification body is required for Class II MD and IVDD which have technical standards for certification before their marketing.



Registered certification body

- 14 private organizations.
  http://www.jaame.or.jp/jyusho/ninjyu_eng.html
- Compliance with ISO/IEC guide 62 and guide 65
- Independent from MAH and manufacturer
- Scope of certification service varies from the bodies.

Outline of Approval Review Process



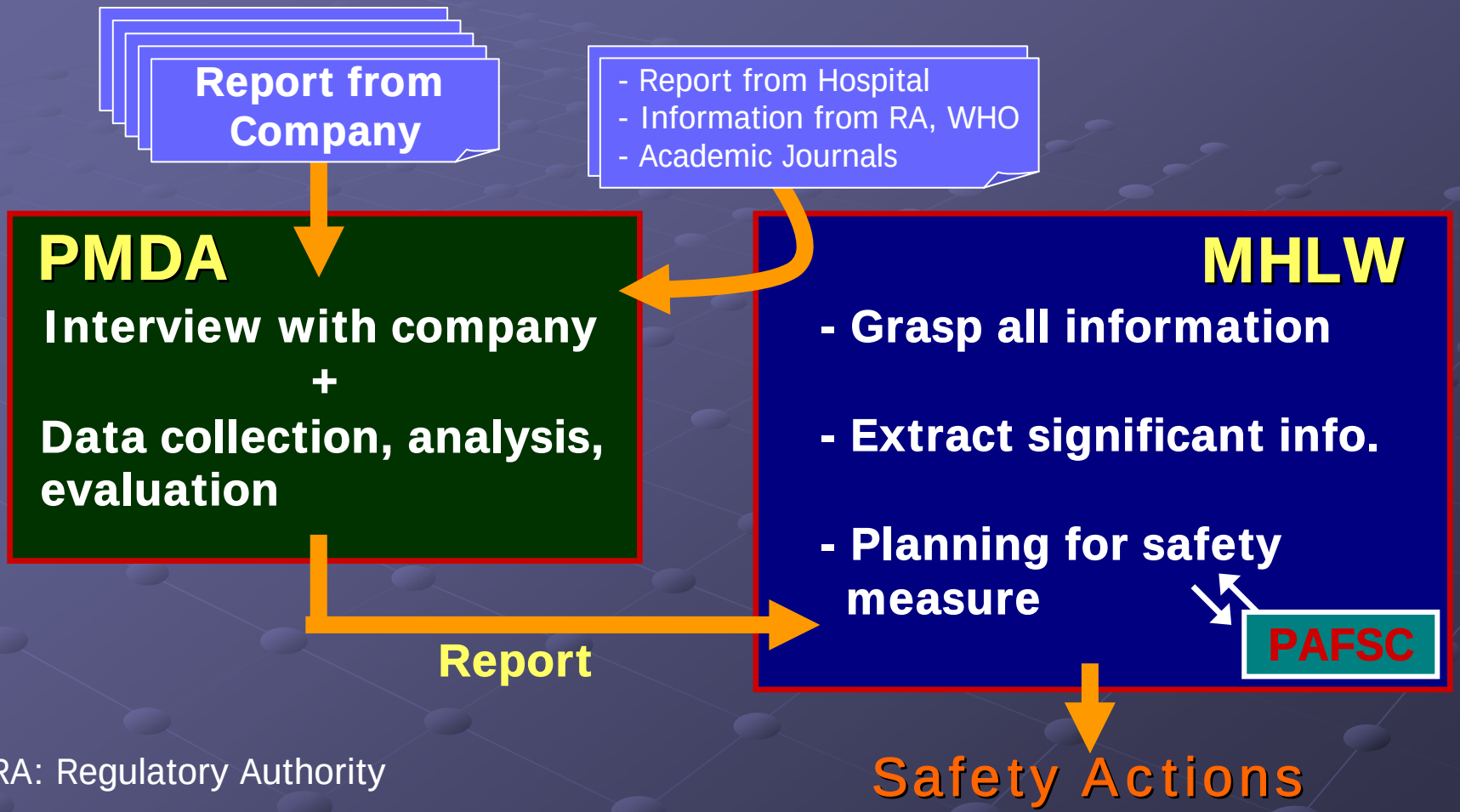
PMDA: Pharmaceuticals and Medical Devices Agency
MHLW: Ministry of Health, Labour and Welfare
PAFSC: Pharmaceutical Affairs and Food Safety Council

What is PMDA?

- Pharmaceutical and Medical Device Agency (PMDA) was established in 2004 as an independent agency in Japanese administration.

- PMDA has 3 major tasks
  - Relief system for sufferers from ADR
  - Approval review and related operations
  - Post-marketing safety measures in cooperation with MHLW

(FYI) Outline of Post-Marketing Safety Measure



RA: Regulatory Authority

Clinical data

Class IV	In principle, clinical data is required for approval review
Class III	In principle, clinical data is required only in cases which listed in the Notification* (* Notification #0216001 of Director of Office of Medical Device Evaluation, Feb. 16, 2005)
Class II	Clinical data may be required for approval review

Note: Even in those cases shown above, clinical data is **not** required if the MD is a me too MD or a MD which has applicable approval standards.

License and requirements for MAH

License for MAH (Art.12)

- The license for MAH is required to market MDs in Japan according to the classification of MDs which the company deals.

- The authority of the Minister to issue a MAH license is delegated to the Heads of Prefectures. (Art.81)

- Licenses are valid for 5 years, renewable.

Classification of MD	Type of license needed
Highly controlled (class III, IV)	Type 1 MAH license
Controlled (class II)	Type 2 MAH license
General (class I)	Type 3 MAH license

License and requirements for MAH (Cont.)

Requirements for MAH (Art.12-2)

- To comply with **the standards of quality control** of a medical device in the application. (Good Quality Practice; GQP)

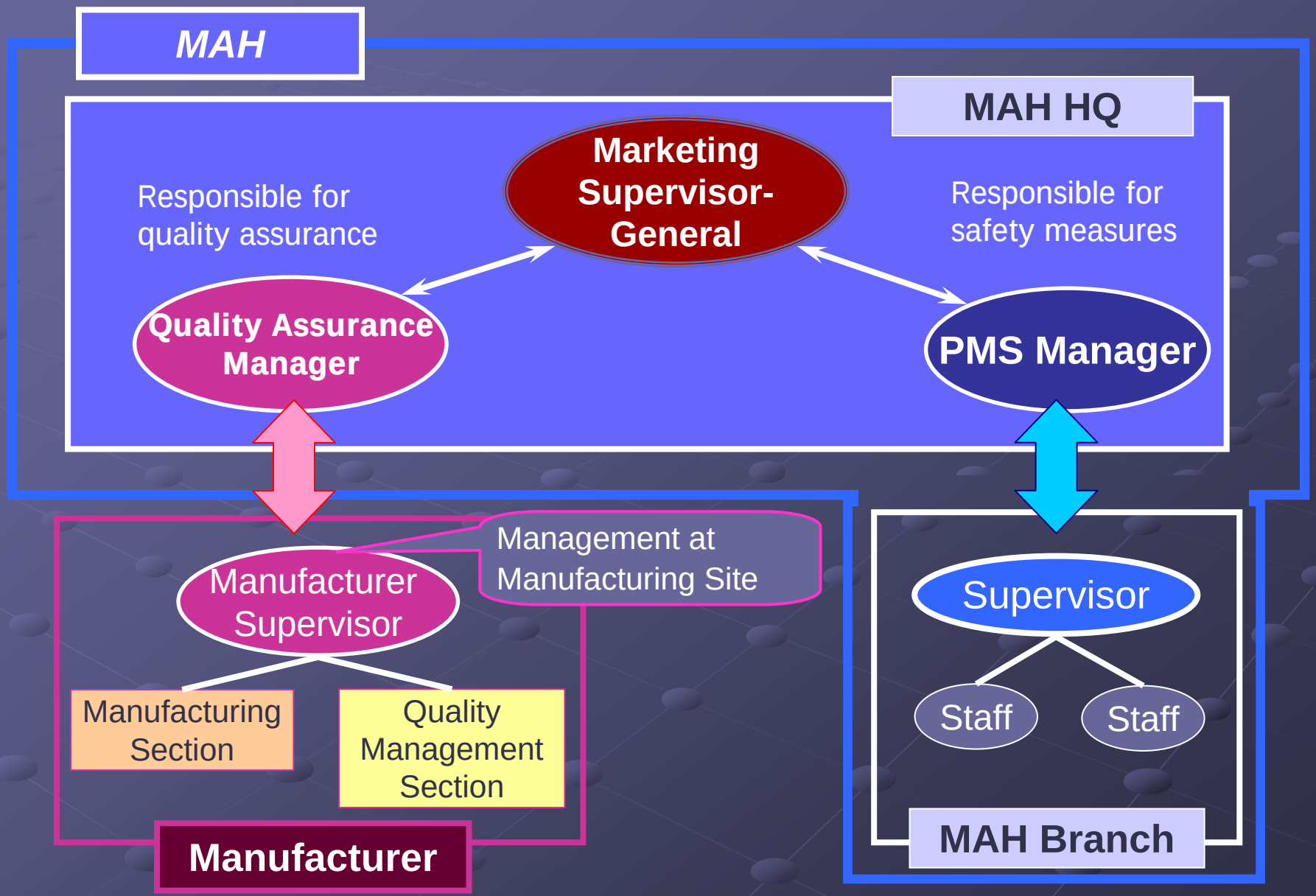
- To comply with the standards of **post-marketing safety management** of a medical device in the application. (Good Vigilance Practice; GVP)

GQP includes standards concerning
-Shipping control
-Supervision of manufacturer
-Handling of defective products etc.

GVP includes standards concerning
-Organization and staffs engaged in PMSM
-Collection of safety information
-Internal audit etc.

MAH has full responsibility for its products placed in the market

Typical Corporate Organization of a MAH



For companies outside Japan

Approval given to foreign company (Art.19-2)

- A foreign company, not a Japan branch, can directly obtain the Minister's approval to place its product in the Japanese market. It shall appoint a MAH in Japan as a legal representative ("Designated MAH").

- Not the foreign company (foreign approval holder) itself but the Designated MAH can sell the products in Japan.

- If the foreign approval holder has changed the Designated MAH, it shall notify the Minister of the change within 30 days through the Head of the Prefecture.

License for Manufacturer

License for Manufacturer (Art.13)

- The authority of the Minister to issue a Manufacturer license is delegated to the Heads of Prefectures and the Heads of Regional Bureau of Health and Welfare. (Art.81 and 81-4)

- Licenses are valid for 5 years, renewable.

category	operation	authority
"General"	1) All/Part of processes of manufacturing and quality management for general MDs	Head of Prefecture (Except for manufactures of Specific Biological Products etc. Their licenses are issued by Head of RBHW)
"Biological"	2) All/Part of processes of manufacturing and quality management for MDs designated by the Minister (eg. Biological product)	
"Sterilization"	3) Sterilizing process other than 1) and 2)	
"Packaging etc."	4) Only packaging, labeling and storage	

For plant outside Japan

Accreditation of Foreign Manufacturer (Art.13-3)

- The Minister can give a foreign plant the Accreditation of Foreign Manufacturer. Four categories of the Accreditation, same as the License for Manufacturers, are valid for 5 years, renewable.

- Application for the Accreditation should be submitted to the PMDA.

(PMDA website)
http://www.pmda.go.jp/english/operations/pdf/application.pdf

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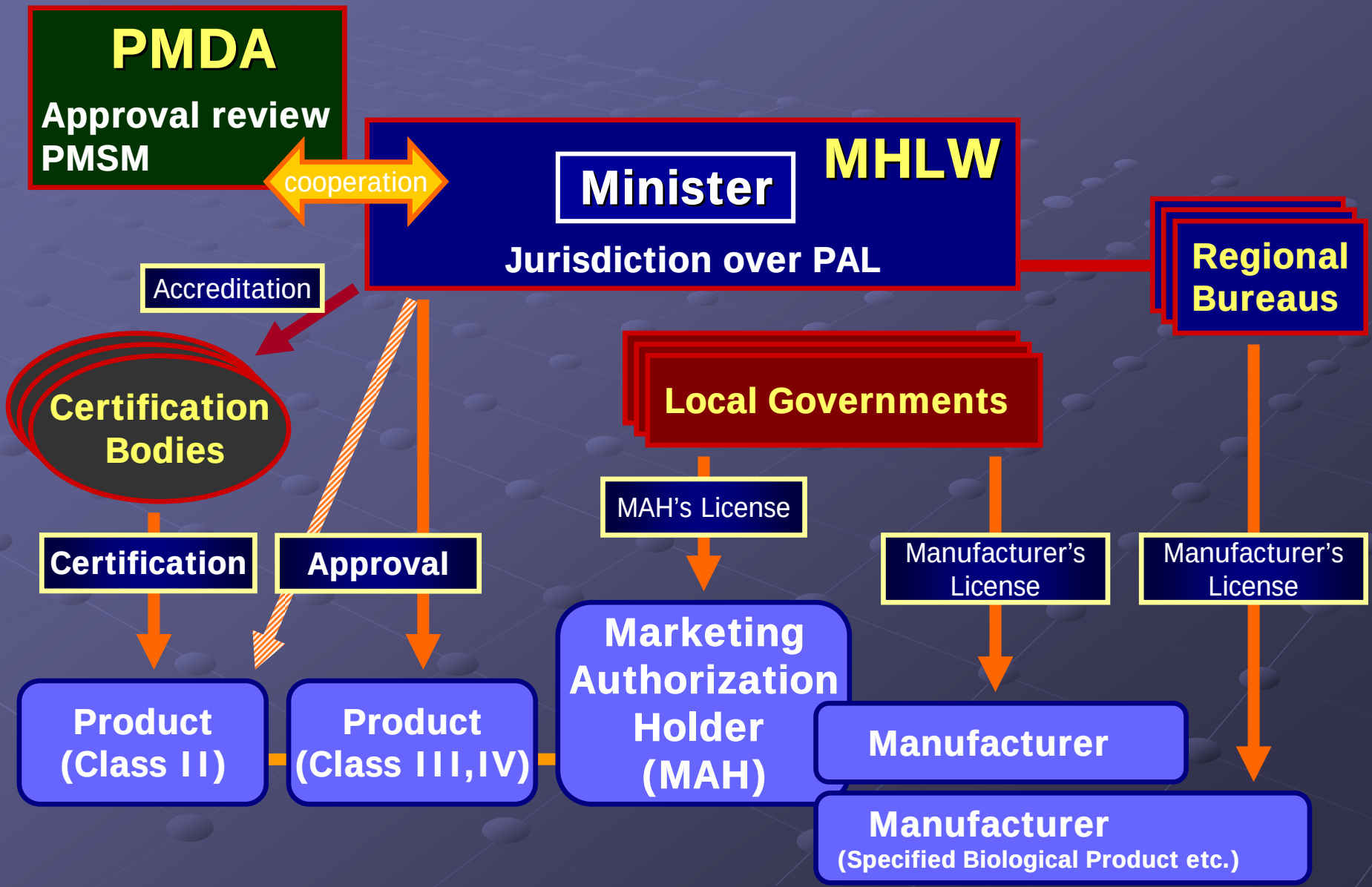
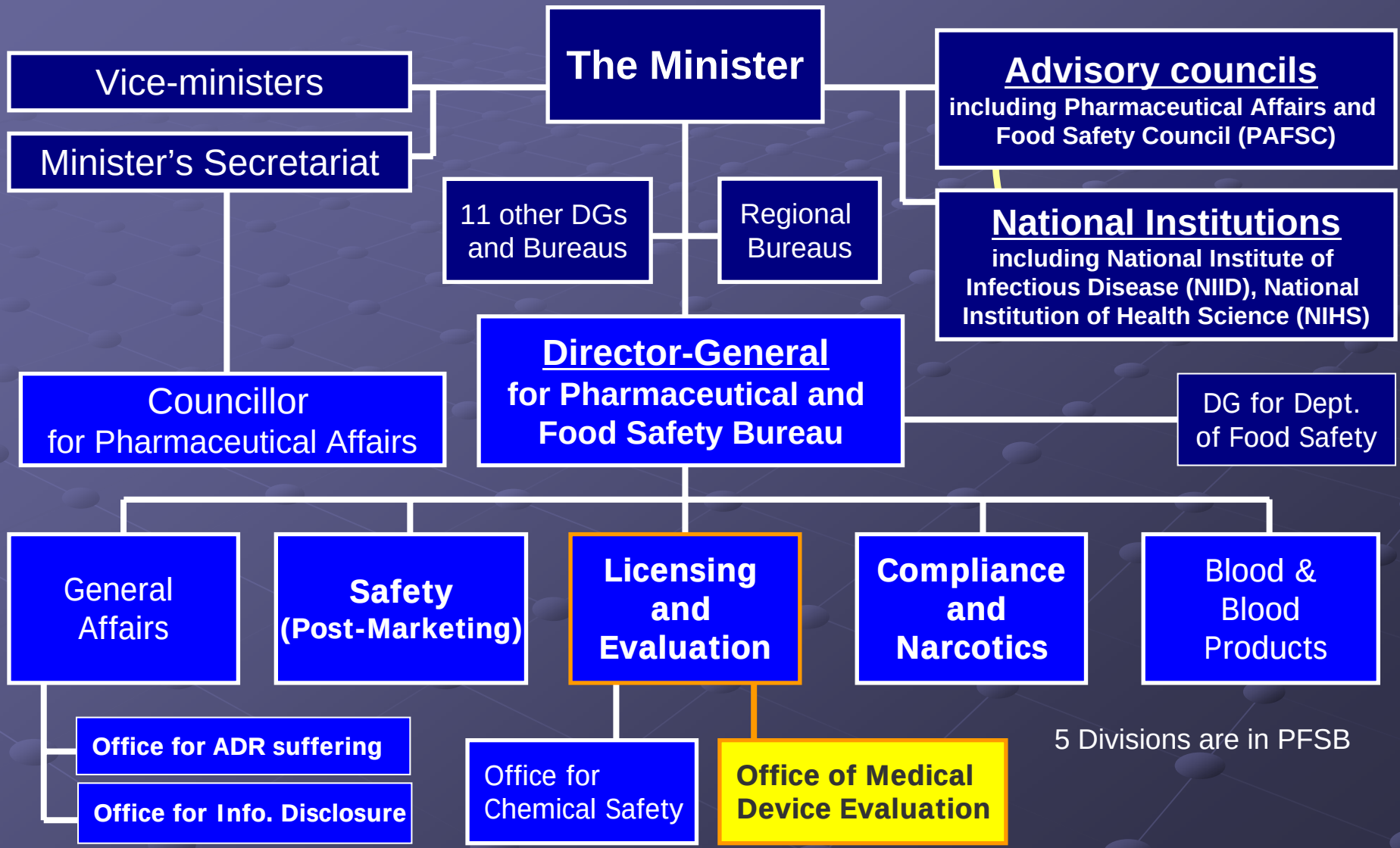
Authorities of MD regulation



Ministry of Health, Labour and Welfare (MHLW)

- **Ministry of Health, Labour and Welfare (MHLW)** holds jurisdiction over the Pharmaceutical Affairs Law. The Minister is supported by Pharmaceutical and Food Safety Bureau (PFSB) of the Ministry.

Organization Chart of MHLW and PFSB



MHLW and Local Governments

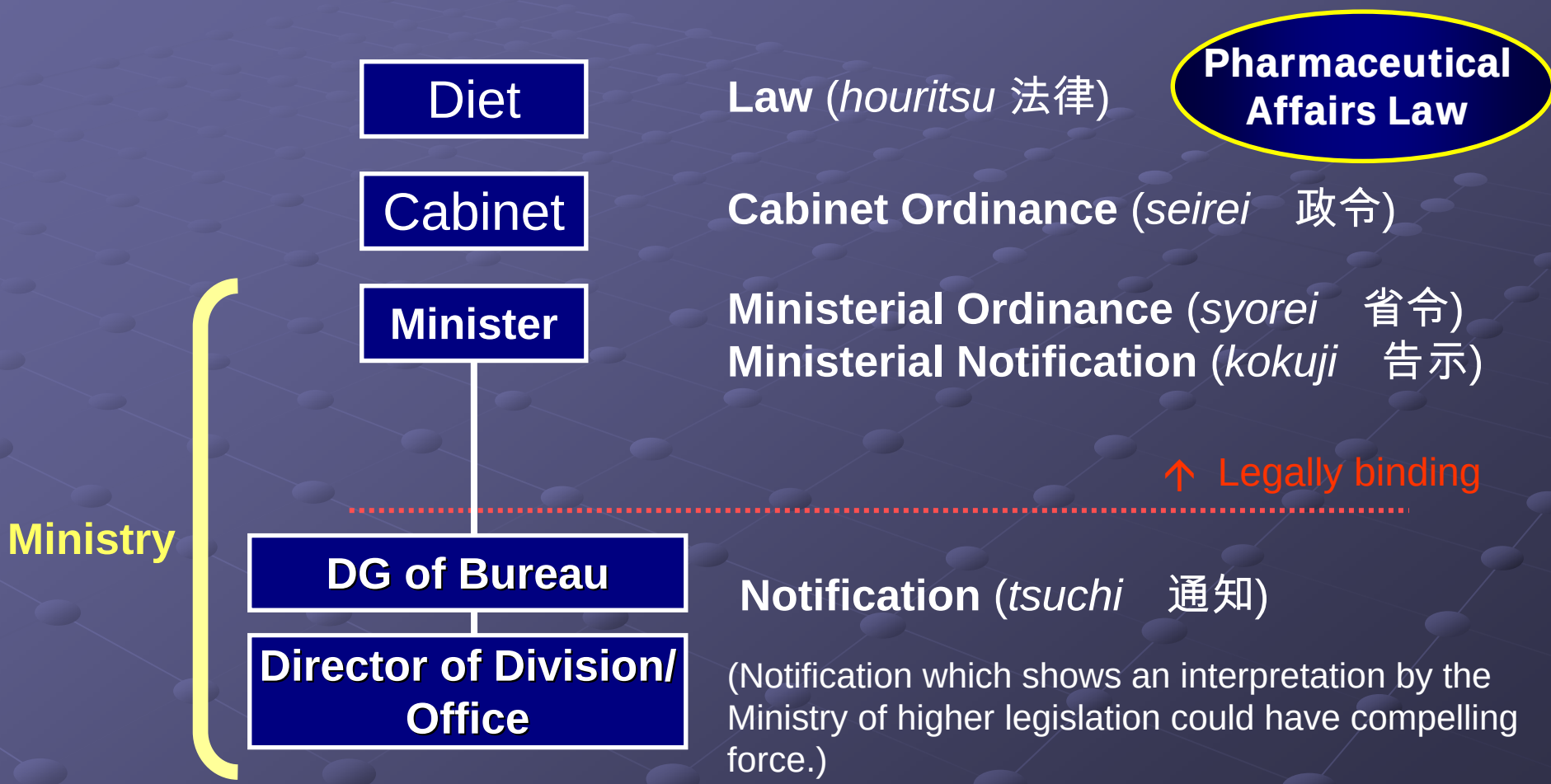
- Along with MHLW, local governments bear a responsibility of implementation of PAL.

  (eg.) licensing for pharmacies, wholesalers, drug sellers or device sellers, law enforcement and inspection.

- The Minister delegates part of his/her authority under the PAL to the heads of local governments.

  For example, license for MAH or license for manufacturer is issued by the head of prefecture with some exception (eg. License for a manufacturer of Specified Biological Product).

(FYI) Hierarchy of legislation



Key pharmaceutical legislation

Law	Pharmaceutical Affairs Law (PAL, 1960)
Cabinet Ordinance	Cabinet Ordinance on PAL, 1961 Cabinet Ordinance on PAFSC, 2000
Ministerial Ordinance	Ministerial Ordinance on PAL, 1961 GCP for pharmaceuticals, 1997 Good Vigilance Practice (GVP), 2004 Good Quality Practice (GQP), 2004 etc.
Ministerial Notification	Standards of pharmaceuticals (eg. JP) Certification standards for class B devices Classification of medical devices List of orphan designation etc.
Notification	Information on application procedures Guidelines for clinical evaluation etc.

(FYI) Numbering rule of Notifications (from 2002)

Example:

“Notification on establishment of the Approval Standards for Implantable Cardiac Pacemaker etc.”
(Notification of DG-PFSB（医薬食品局長通知） #0302004, 2nd of March, 2007)

#0302 004
M M D D #

→It means that it is 4th Notification issued by the DG on March 2.
→Information on publication year is needed to specify the Notification.

* In this case, “etc.” means pacemaker leads, pacemaker adapter.

Thank you!

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