Medical Device Regulation in Japan

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Japan

Agenda

- Overview of Pre-market Regulation
- Third Party Certification for Class II Devices
- Approval Process for New / High Risk Devices
  - Clinical Trial Requirement
  - Acceptance of Foreign Clinical Data
- Update of Japanese MD Policy Issues
  - Regulation on Decorative, Non-corrective Contact-lenses
  - Action Program for Acceleration of MD Review
  - US-Japan Pilot Program regarding Collaborative Consultation and Review

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Prerequisites to Bring Medical Devices into the Japanese Market

Product

Minister's Approval (*shonin* 承認) (Art.14)
or 3rd party Certification (*ninsho* 認証) (Art.23-2)
or Marketing Notification (*todokede* 届出) (Art.14-9)

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)

Overview of Classification and Pre-market Regulation for 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 valves

PAL classification		
Category	Pre-market regulation	Japanese MD Nomenclature
General MDs (Class I)	Self declaration	1,195
Controlled MDs (class II)	Third party Certification	1,786 (835 for 3rd Party)
Specially Controlled MDs (class III & IV)	Minister's Approval	746
		330

(MHLW Ministerial Notification No.298, July 20, 2004)

Japanese Medical Devices Nomenclature (JMDN) and MD classification

- Each MD has to fall under generic nomenclature (JMDN). JMDN is based on an initial version of 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 and the latest JMDN. http://www.pmda.go.jp/operations/notice/2007/file/kiki-ippan.pdf)

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

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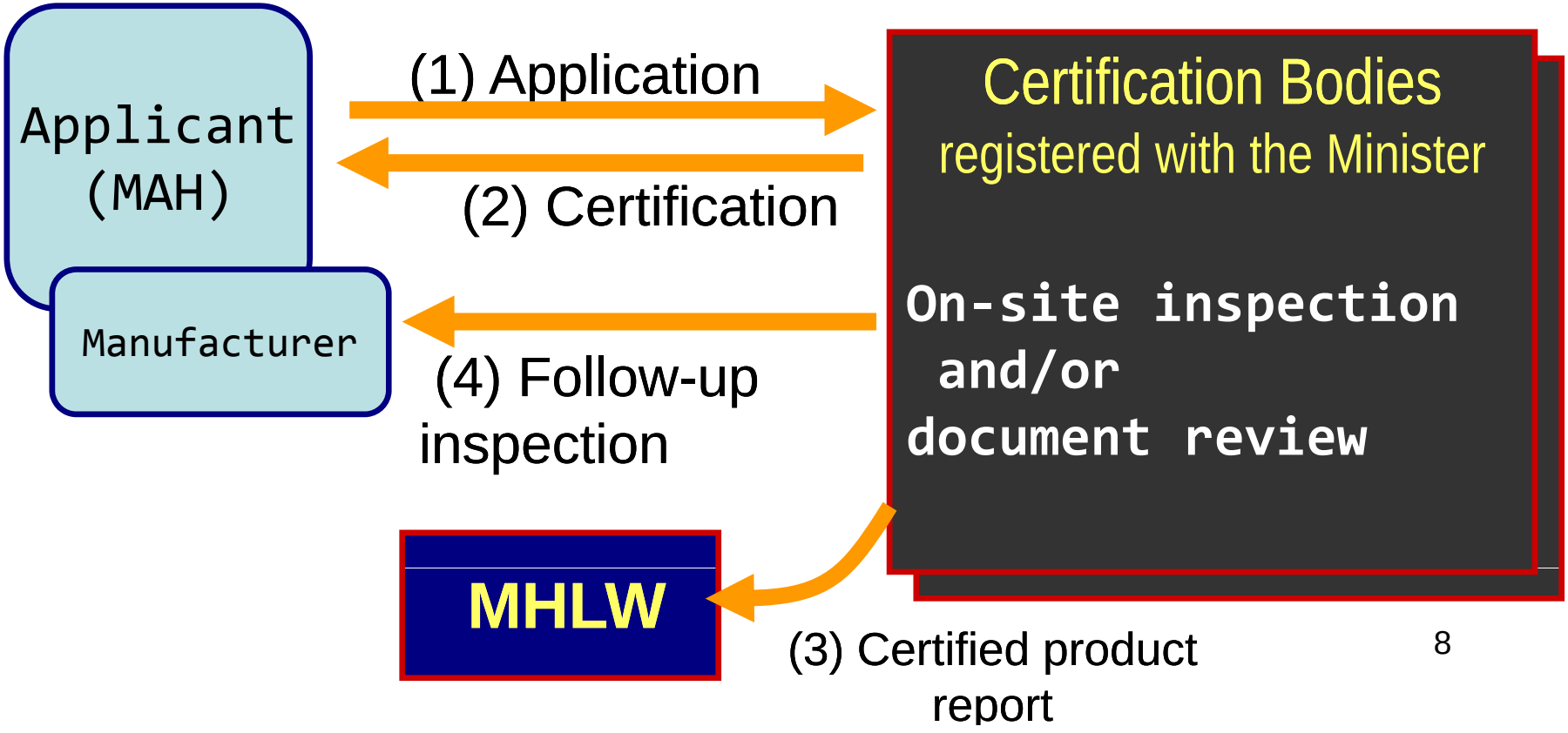
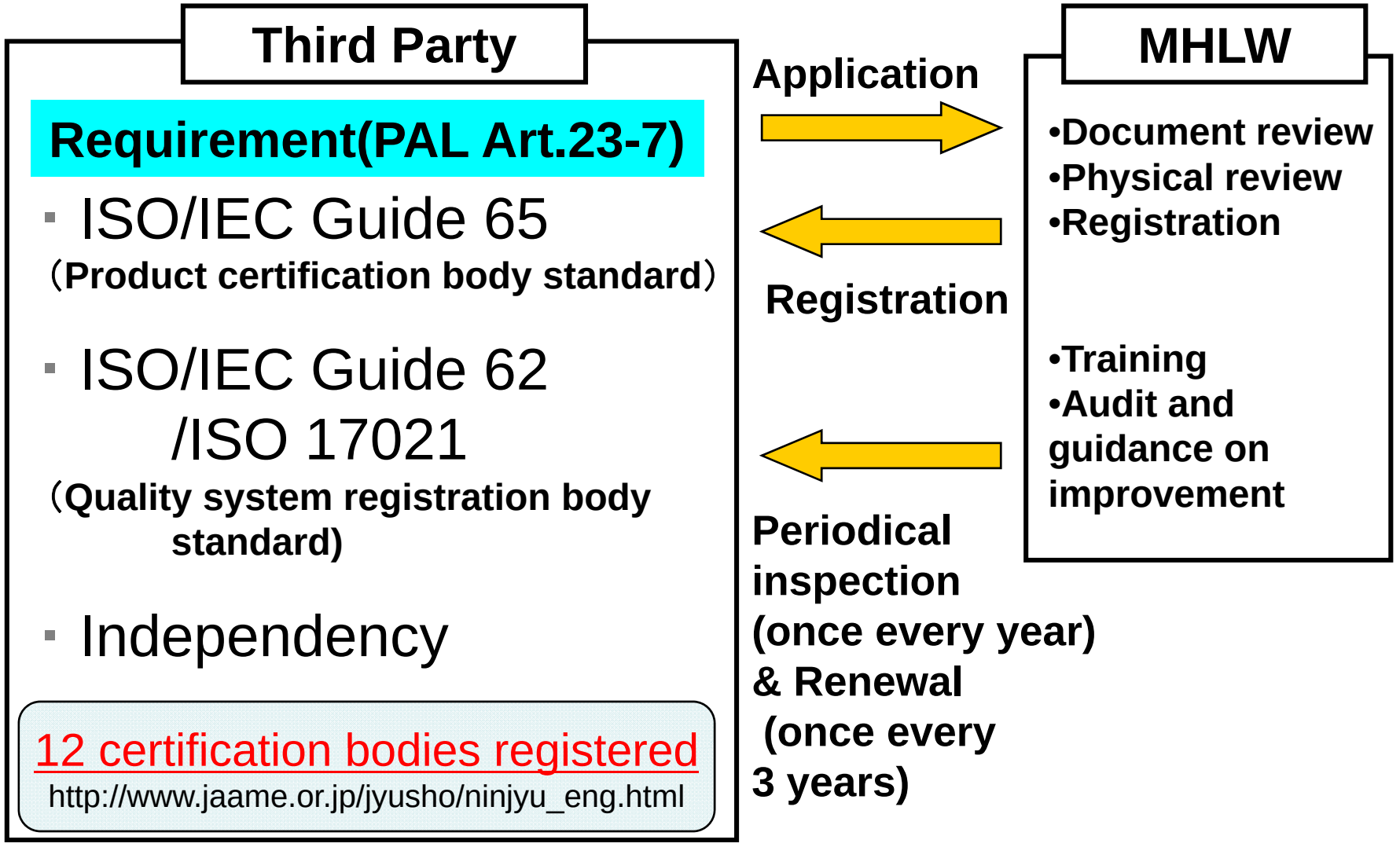
Third-party Certification System in Japanese Medical Device Regulation

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.



Third Party Registration



Third Party Certification Standards

Standard for Products

Technical Standard for each MD (PAL Art. 23-2)
=JIS(Japanese Industrial Standards) plus Indication

Most JIS are harmonized with ISO/IEC

+

Essential Principles (GHTF EP for all MD, PAL Art.41(3))
=Detail explanation to apply for each MD is shown
in notification with quotation of Technical Standard

Standard for Quality Management System

Quality Management System Ministerial Ordinance
= based on ISO 13485

Third Party Certification

Application

STED(*) document to explain conformity to
Technical Standard and Essential Principles
(*Summary Technical Documentation, GHTF SG1N11)

Evaluation/Certification

Conformity to Technical Standard and Essential Principles
Conformity to Quality Management System

- On-site inspection and/or document review upon certification
- Follow-up inspection after certification

Future Direction of Third Party Certification System

- Currently 835 (/ 1786) class II medical devices are designated for third party certification.

- In principle, all Class II medical devices are expected to be transferred to the third party certification system (to be implemented by FY 2011).

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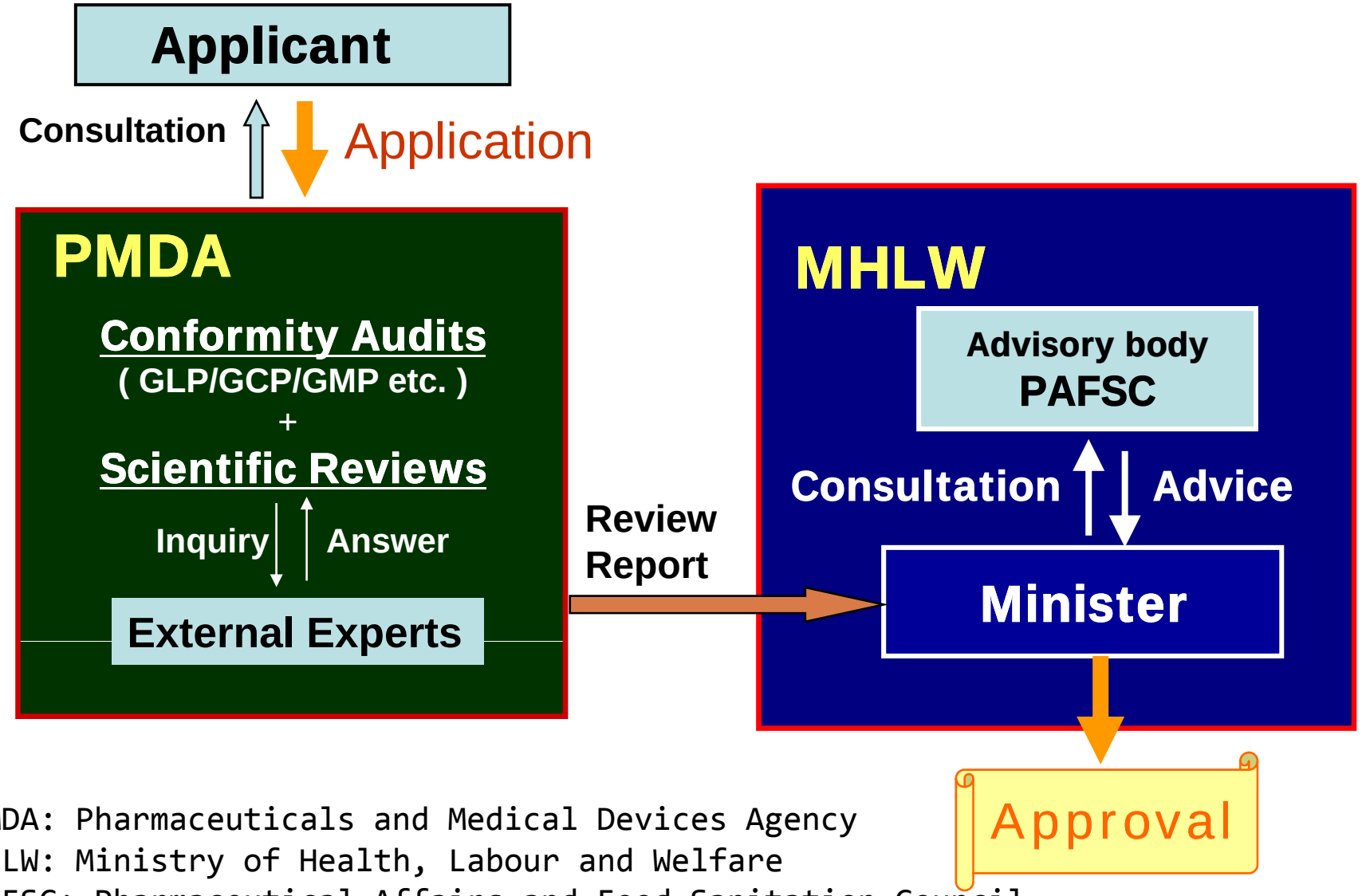
Outline of Approval Review Process



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

Responsibilities of MHLW & PMDA

[MHLW]

Planning basic policy, enforcement of administrative measures, such as approval, administrative order, etc. which are based on the law

ex. ・Final judgment on approval
・Directions of withdrawal and issuance of emergency safety information
・Safety measures for emergent and significant cases

Responsibilities of MHLW & PMDA

[PMDA]

Implementation of work, such as review, examination, data analysis, etc. before administrative measures

ex. ・Scientific review of Pharmaceuticals and Medical Devices
GLP/GCP/GMP/QMS inspection,
Clinical trial consultation

・Collection, examination, analysis, assessment and provision of ADR information

Application Dossier

- GHTF-based STED is required.
- Essential Principles from GHTF was introduced in Japanese regulation (PAL Art.41(3)) and any device shall be in conformity with the EPs.

See
•Notification by DG-PFSB, *Yakusyoku-hatsu* #0216002, February 16, 2005
•Notification by Director, OMDE, *Yakusyokuki-hatsu* #0216001, February 16, 2005
•Notification by Director, OMDE, *Yakusyokuki-hatsu* #0216003, February 16, 2005
→ http://www.pmda.go.jp/operations/shonin/info/iryokiki/iryokiki-list.html (Japanese)

Clinical Trial Requirement
(1) General Guidance

- A guidance for clinical data requirement was revised for more flexibility in August 2008.
  (Notification by Director, Office of Medical Device Evaluation, *Yakusyokuki-hatsu* #0804001, August 4, 2008)

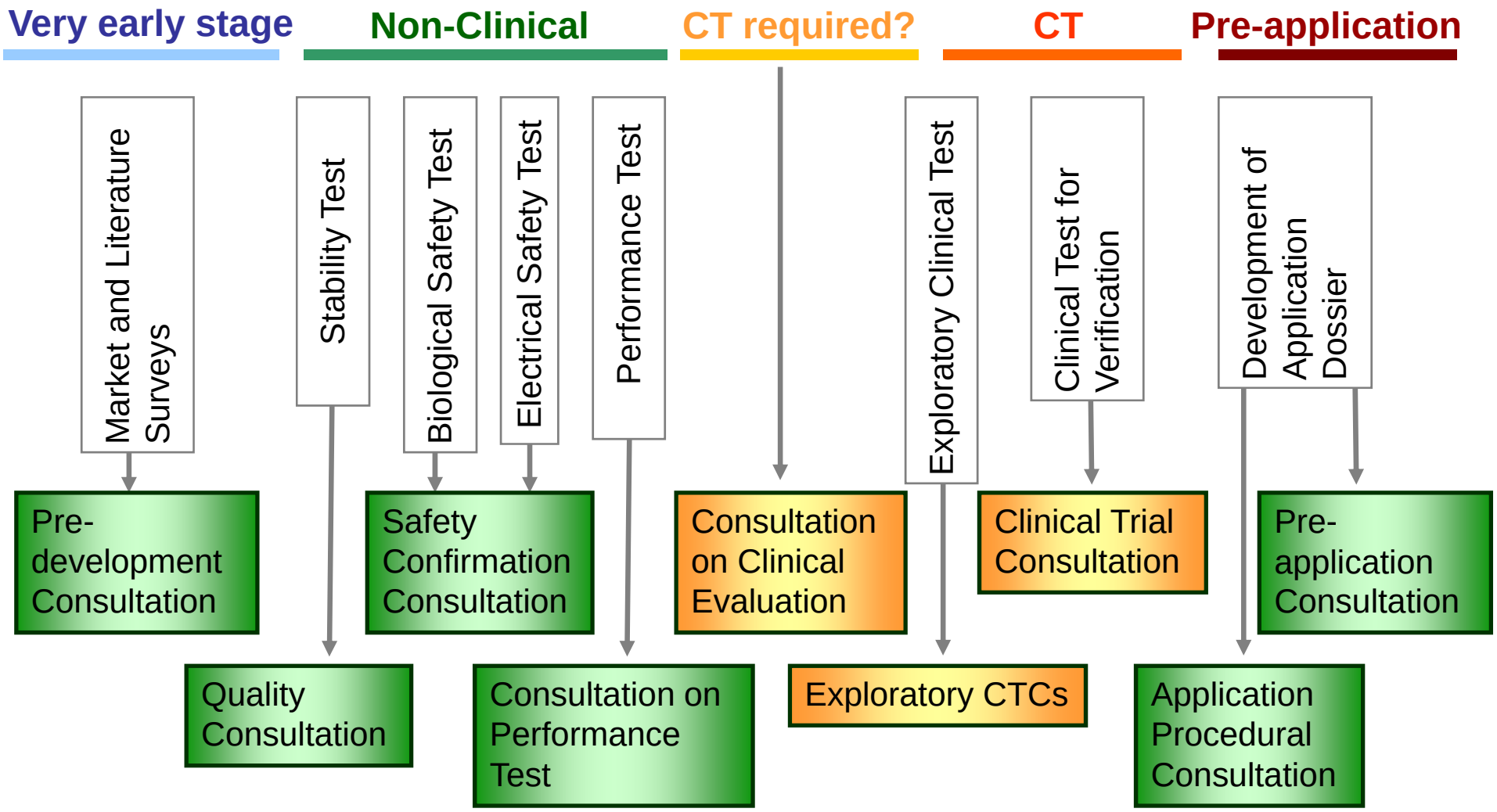
→ Clinical data is necessary to demonstrate clinical safety and efficacy unless they can be assessed only with pre-clinical data and literature. For brand new device, in principle, clinical trial data is required

→ MHLW/PMDA strongly recommend use of PMDA's clinical evaluation consultation to determine if clinical trials are required.

(FYI) PMDA's Consultation Menu

expanded since 2007

http://www.pmda.go.jp/operations/shonin/info/consult/taimen.html (Japanese)



(FYI) PMDA's Consultation

Number of consultation for medical devices

FY2004	FY2005	FY2006	FY2007	FY2008
8	30	42	72	76

Area of consultation for medical devices in 2008

Pre-development Consultation	11
Quality Consultation (Biologics)	1
Quality Consultation (Non-Biologics)	1
Consultation on Performance Test	2
Consultation on Clinical Evaluation	12
Application Procedural Consultation	6
Clinical Trial / Pre-application Consultation	43
Total	76

CT required?

(Source: PMDA Annual Report FY2008)

Clinical Trial Requirement
(2) Guidance for Specific Products

Guidance for specific products to show when clinical data are not required

- Therapeutic laser products
  - (Notification by Director, Office of Medical Device Evaluation, *Yakusyokuki-hatsu* #1008001, October 8, 2008)
- Surgical implants
  - (Notification by Director, Office of Medical Device Evaluation, *Yakusyokuki-hatsu* #1128001, November 28, 2008)
- Contact lenses
  - (Office Memo, Office of Medical Device Evaluation, July 13, 2009)

Clinical Trial Requirement
(3) Approval Standards

- If approval standards exists, pre-market approval review are conducted by assessing conformity to them
- Clinical data is not necessary if new products meet approval standards
- In principle, approval standards are based on international standard

- Approval standards offer clear direction to manufacturers and contribute to faster review by reviewers.

- Currently 34 approval standards in total.

http://www.pmda.go.jp/operations/shonin/info/iryokiki/iryokiki-list.html
(Japanese)

Acceptance of Foreign Clinical Data

- MHLW/PMDA have accepted foreign clinical data for years if it is good enough to evaluate a device's clinical safety and efficacy on Japanese population under Japanese medical practice/environment.

Number of devices approved after review with clinical trial data

	FY2004	FY2005	FY2006	FY2007	FY2008
Foreign clinical data only	11	33	22	20	26
Both foreign and Japanese clinical data	1	1	2	4	2
Japanese Clinical data only	8	16	18	24	14

(Source: PMDA Annual Report FY2008)

Acceptance of Foreign Clinical Data

- MHLW published guidance on handling of foreign clinical data in 2006.

  (Notification by Director, Office of Medical Device Evaluation, *Yakusyokuki-hatsu* #0331006, March 31, 2006)

  → http://www.pmda.go.jp/english/services/reviews/file/0331006No.pdf

(Points)

- The CT has to be done in a country/jurisdiction which has good quality GCP standards as Japanese device GCP. The CT should be compliant with the local GCP.
- The trial sites have to be ready for accepting GCP inspection by Japanese authorities.
- If there are differences between Japanese and local GCPs, an applicant should submit a list of differences and its opinion on influence of the differences on reliability and

  quality of the data.

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Regulation on
Decorative, Non-corrective Contact-lenses

Decorative, non-corrective contact-lenses

- Will be regulated as medical devices on and after November 4, 2009.
- Can be distributed only by licensed marketing authorization holders (MAH) and distributers on and after November 4, 2009.
- Can be distributed without approvals until November 3, 2010 if

1) a MAH submits a notification to MHLW for each product, and

2) the labeling of the product states that this product is not yet approved.

Action Program for Acceleration of MD Review (issued on Dec. 2008)

1. **Qualitative improvement of reviewers by increasing the number & substantial training system**
   - **The number of medical devices reviewers will be increased from 35 (FY2008) to 104 (FY2013).**
2. **Introduction of 3-track review system : Brand-new (Shin), Improved (Kairyo) & Me-too (Kohatsu) MDs**
   - **3- track review system will be introduced with specific review team for each classification (phased operation from FY2011)**
   - **Introduce substantially equivalent review system for Me-too (Kohatsu) MDs (start from FY2009)**
   - **Introduce advance/previous data estimation system for Brand-new MDs (start from FY2010)**
3. **Stipulation of approval review criteria**
4. **Miscellaneous**

US-Japan Pilot Program regarding Collaborative Consultation and Review

- **FDA and MHLW announced the launch of pilot program regarding collaborative consultation and review on June 15, 2009**
- **This collaboration would permit the regulatory review staff of both MHLW/PMDA and FDA to discuss the contents of an individual submission in order to gain valuable regulatory information pertaining to device development and clinical trial design.**
- **The pilot does not affect each Agency's ability to make its decision independently.**

Advantages of the Pilot Program

- **Regulators work together with sponsor toward solutions**
  - **e.g. 3-way teleconferences (US and Japanese Regulators & sponsor) as appropriate – usual MHLW/PMDA consultation fees apply**
  - **e.g. Regulators can help design of the clinical trials which can be accepted by both agencies, in order to eliminate redundant clinical trials.**
- **Sharing of scientific and regulatory views expected to enhance (not hinder) review process**

Inclusion Criteria for the Pilot Program

- New device in the cardiovascular /endovascular field
- Similar development status in the US and Japan.
- A single (or similar) clinical trail protocol in the US and Japan.
- Must have early consultations with PMDA and FDA/CDRH when planning clinical trials
- Providing the same information to MHLW/PMDA and US FDA.

For Detailed Information

- Pilot Program Regarding Medical Device Collaborative Consultation and Review of Premarketing Approval, (June 15, 2009)
  http://www.fda.gov/InternationalPrograms/HarmonizationInitiatives/ucm167858.htm

- “Pilot program on exchanging information between MHLH/PMDA and US FDA regarding medical device consultation and review”, Notification from Director of the OMDE (*Yakusyokuki-hatsu* #0615001, June 15, 2009)
  http://wwwhourei.mhlw.go.jp/hourei/doc/tsuchi/T090623I001.pdf

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