General Overview of the New PAL

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Shinichi TAKAE, MHLW of Japan

Medical Devices Regulation of Japan, EU and US

- EU : Notified Body Certification
  (All Medical Devices)

- Japan: Third Party Certification (Low Risk Medical Devices)
  Minister's Approval on basis of PMDA review
  (High Risk Medical Devices)

- US FDA: Approval or Pre-market clearance

  (Note) under pilot study of Third Party review system for some low risk medical devices

Major Points of Reform

1. Adoption of International Standards as Regulatory Basis
2. Risk Classification along with GHTF
3. Third Party Certification system
4. Marketing Approval instead of Manufacturing Approval
5. License system has been changed

Adoption of International Standards as Regulatory Basis

- Global Medical Devices Nomenclature (GMDN)
- Risk Classification of Medical Devices
- GMP regulation based on ISO13485:2003
- Summary Technical Documentation (STED)

Risk classification

Classify more than 4,000 nonproprietary names into Four Category in GHTF Rule, i.e. class 1 – 4

In Pharmaceutical Affairs Law,
those into Three categories as following

1) Highly Controlled Medical Device (class 3 and 4)
2) Controlled Medical Device (class 2)
3) General Medical Device (class 1)

Classification of Medical Devices

GHTF Classes	Classification of medical devices according to risk
Class A	extremely low risk to the human body e.g. X-Ray film
Class B	low risk to the human body e.g. MRI, digestive catheters
Class C	medium risk to the human body e.g. artificial bones, dialyzer
Class D	high risk to the human body e.g. pacemaker, artificial heart values

Former Regulation
Approval of manufacturing is not necessarily
Minister's approval for manufacturing

New Regulation (From April 2005)
Approval for marketing authorization is not required
Introduction of third-party certification system
Minister's approval for marketing authorization

Marketing Authorization Holder

Past (Transient Period)

- "Manufacture" approval and "manufacturing" permission for each product

Current (effective in April 2005)

- Approval for "marketing authorization" focused on marketing of each product
- Full freedom to outsource some or all the manufacturing process
- Reinforced post-marketing measures and clarify the MAH's responsibilities

Regulation on Manufacturing (License)

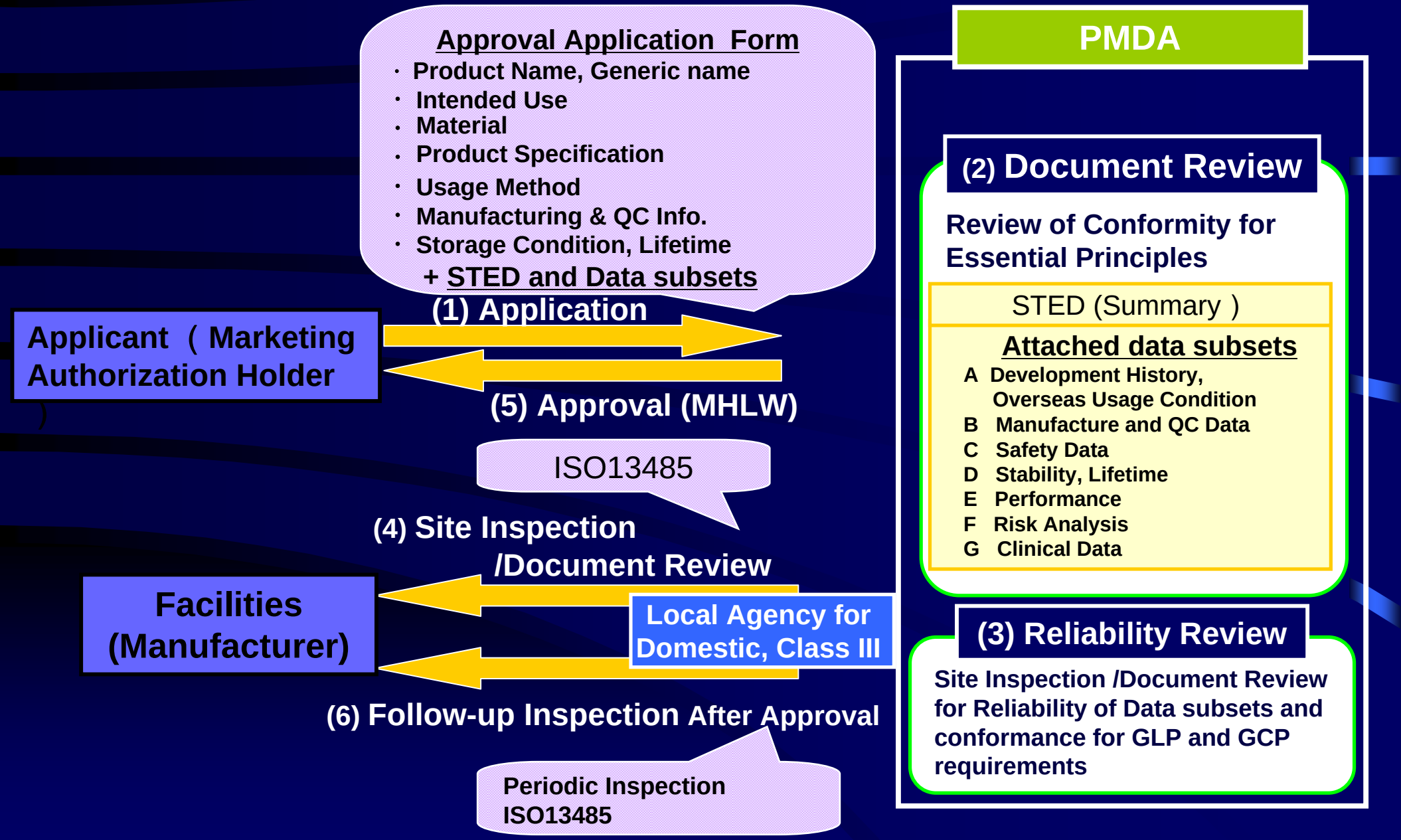
- Four Category for Manufacturing License

1) All/Part of Processes for Manufacturing and Quality Management
2) All/Part of Processes for Designated MDs
3) Sterilizing Process other than 1) and 2)
4) Only Packaging, labeling and storage

Regulation on Marketing

- Minister's Approval
  for MDs other than General MDs and Designated Controlled MDs (PMDA evaluation)
- Certificate by Registered Assessment Body
  for Designated Controlled MDs (Class 2)
  ("Designated MDs" means MDs to be Certificated by Assessment Standards by Third Party)
- No approval nor certificate
  for General MDs (Class 1)

Medical Device New Approval Process



New Submission Categories for MD

- **No Standards-Clinical Data** — **(equivalent to Present "New Medical Devices" and "Improved Medical Devices (with Clinical Data)")**
- **No Standards-No Clinical Data** — **(equivalent to Present "Improved Medical Devices (without Clinical Data)")**
- **Standards-No Clinical Data** — **(equivalent to Present "me-too" Medical Devices")**

Low risk MDs with Standards are to be submitted to Third Party Accreditation Bodies for Certification

Third Party Certification System

1. From Minister's Approval to Third Party Certification (Low Risk MD with Certification Standards)

2. Acceptance of International Notification Standards for Certification bodies

ISO Guide 65 Product Certification

ISO Guide 62 Quality System Certification

Certification Process of Individual Product under the Third Party Certification System (Medical Devices)

Applicant

(Marketing Authorization Holder)

(1) Application

(2) Certification

(4) Follow-up Inspection After Certify

Objection

ISO13485

(3) Certified product report

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Third Party Certification Body

Evaluation

Conformity to Medical Device's Essential Principles

- -Verification of conformity to performance standards
- -appropriateness of risk management
- -Verification of chemical, physical, and biological characteristics
- -Verification of removal of infection and monocontamination
- -Appropriateness of labeling, package insert, etc.

Conformance to Quality assurance standard (ISO)

- -Appropriateness of design control
- -Appropriateness of manufacturing control etc

Evaluation

Primarily on site inspection
Specific evaluation method, including document review, will be considered by referring to the method employed by EU NB.

Judgment for the conformity assessment to a performance standard

Meet the JMDN(GMDN) definition

↓ **YES**

Meet the JIS standard which described the conformity to performance standard

- Within the scope or range which is described in the relevant JIS
- Performance is to meet the relevant JIS
- All components should be included.
- Within the scope of the fundamental view of an incidental function

↓ **YES**

Within the scope of performance which are shown in the conformity performance standard

↓ **YES**

Meet the proper Conformity Performance Standard

→ **Third Party Certification MD**

It is obviously required to assess essential principal

Conformity Assessment Technical Standard

382 Standards have been established.

So far 382 new application for MDs and 18 for IVDs are certified by Third Party.

Third Party Accreditation

Third Party

Requirement

- ISO/IEC Guide 65
  (Product certification body standard)
- ISO/IEC Guide 62
  (Quality System Registration Body Standard)
- Independency
  - **Parent Company must not be a MD manufacturer**
  - **More than half of the executive or board member should not be a MD manufacturer**
  - **Represented person should not be a executive , board member or staffs of the MD manufacturer**

(1) Application

3 year duration

(2) Accreditation

(3) periodical inspection (once every year)

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Duties

(1) Document review
(2) Physical review
(3) Accreditation

(4) Training
(5) Audit and guidance on improvement

Application will start from 15 Sept. 2004, and pilot study will start the fall in 2004

Thank you for your attention

Pass a baton to Ishikawa-san