eCTD Implementation: Japan

Getting Ready for eCTD

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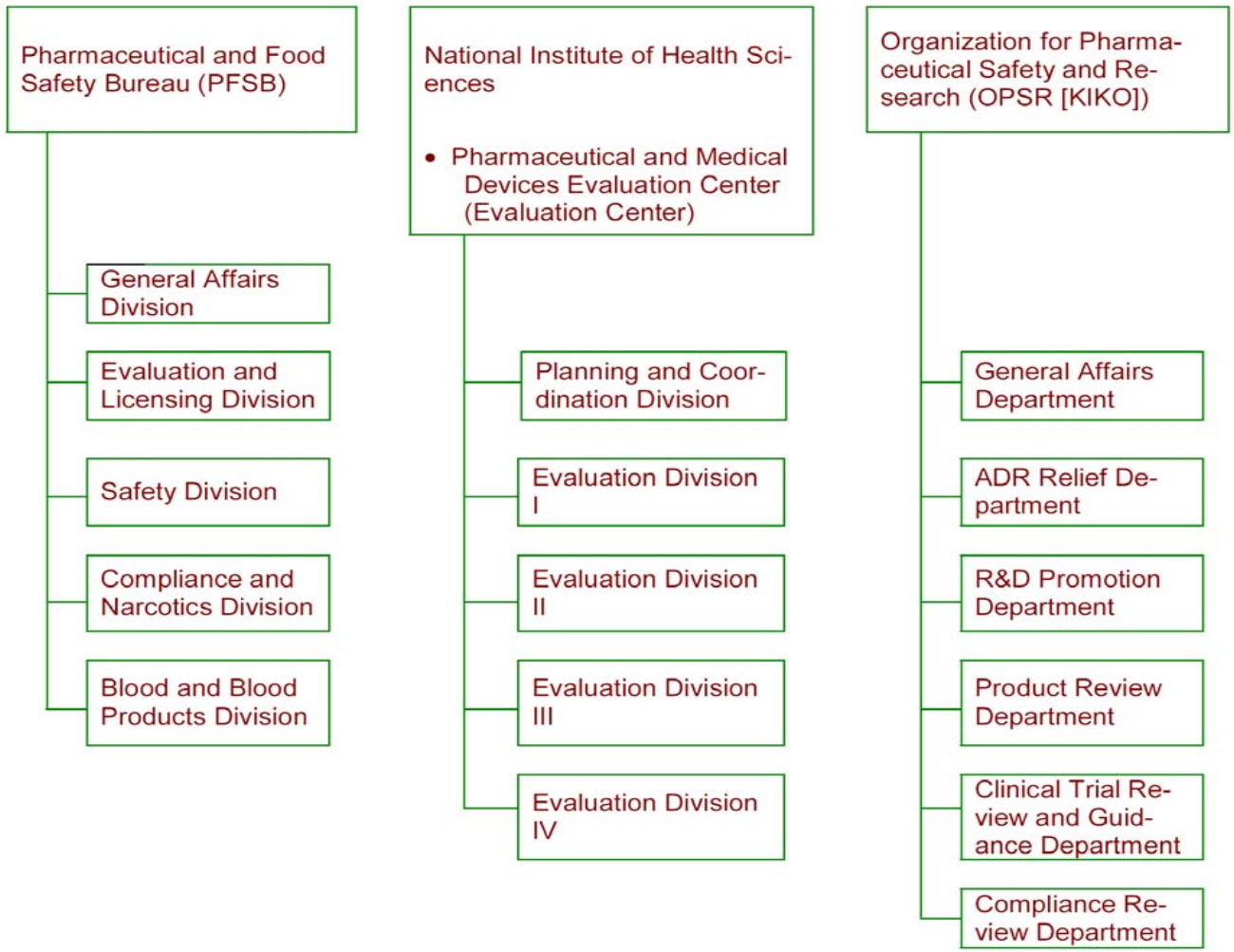
Overview

- Japan regulatory environment
- Historical perspective
- Current status
- Regional issues
- Information resources

MHLW Pharma Bureaus



MHLW - OPSR

- OPSR ("Kiko"):
  - http://www.kiko.go.jp/english/e_top.html
  - Established October 15, 1979
  - A Japanese quasi-government organization authorized by the Minister of Health, Labour and Welfare (MHLW)
    - Clinical study oversight
    - Protocol review
    - Reviews clinical data submitted with NDAs

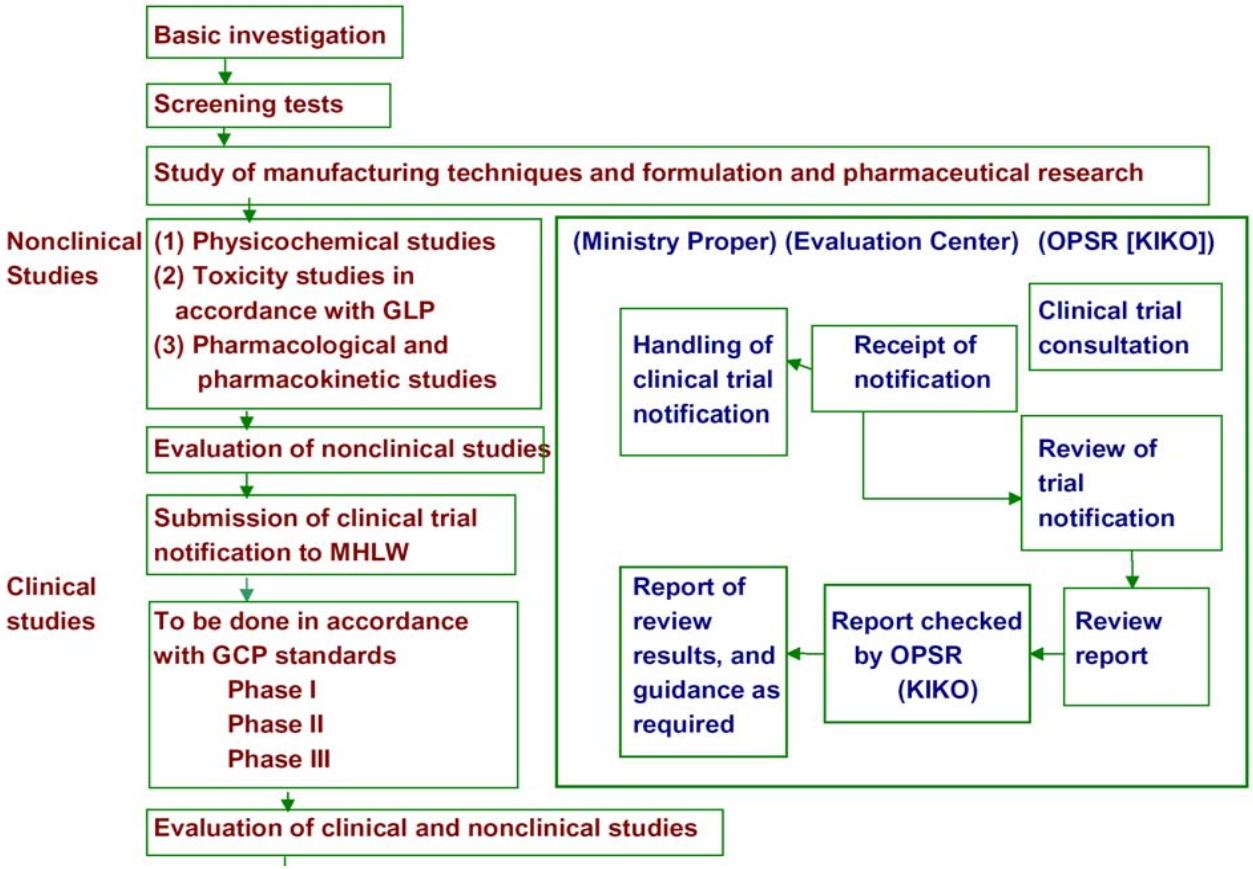
MHLW - PMDEC

- Established July 1st 1997 to speed up the review process
  - Evaluates quality, efficacy and safety of prescription drugs
  - review teams, made up of experts in various fields, work with OPSR (KIKO) to conduct reviews

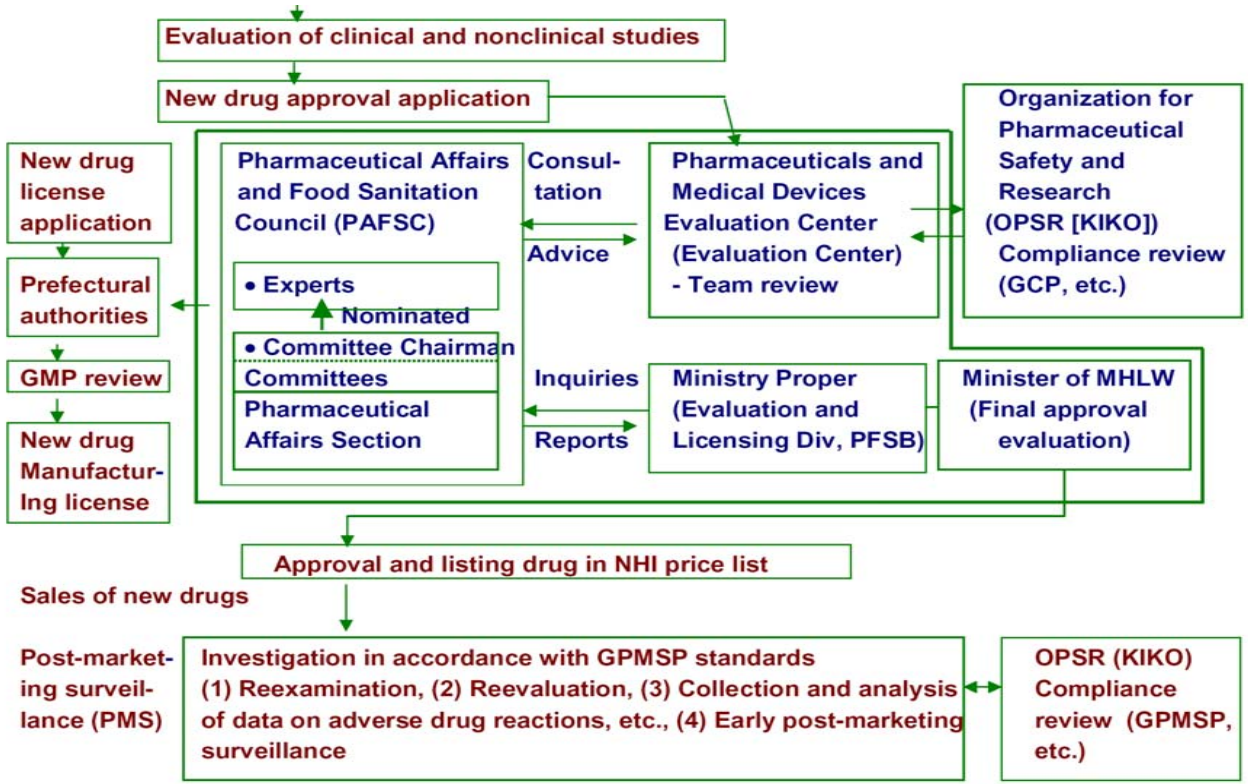
MHLW - PMDEC - cont'd

- Five divisions
  - Planning and Coordination Division
    - Office of General Affairs
    - Office of Information
  - Evaluation division I
    - antibiotics, chemotherapeutics, and anti-cancer drugs.
  - Evaluation division II
    - cardiovascular drugs, antiallergic drugs, and urogenital drugs.
  - Evaluation division III
    - biological products, blood products, radiopharmaceuticals, generic prescription drug products, over-the-counter (OTC) drugs, quasi-drugs, and cosmetics.
  - Evaluation division IV - *in vitro* diagnostics and medical devices

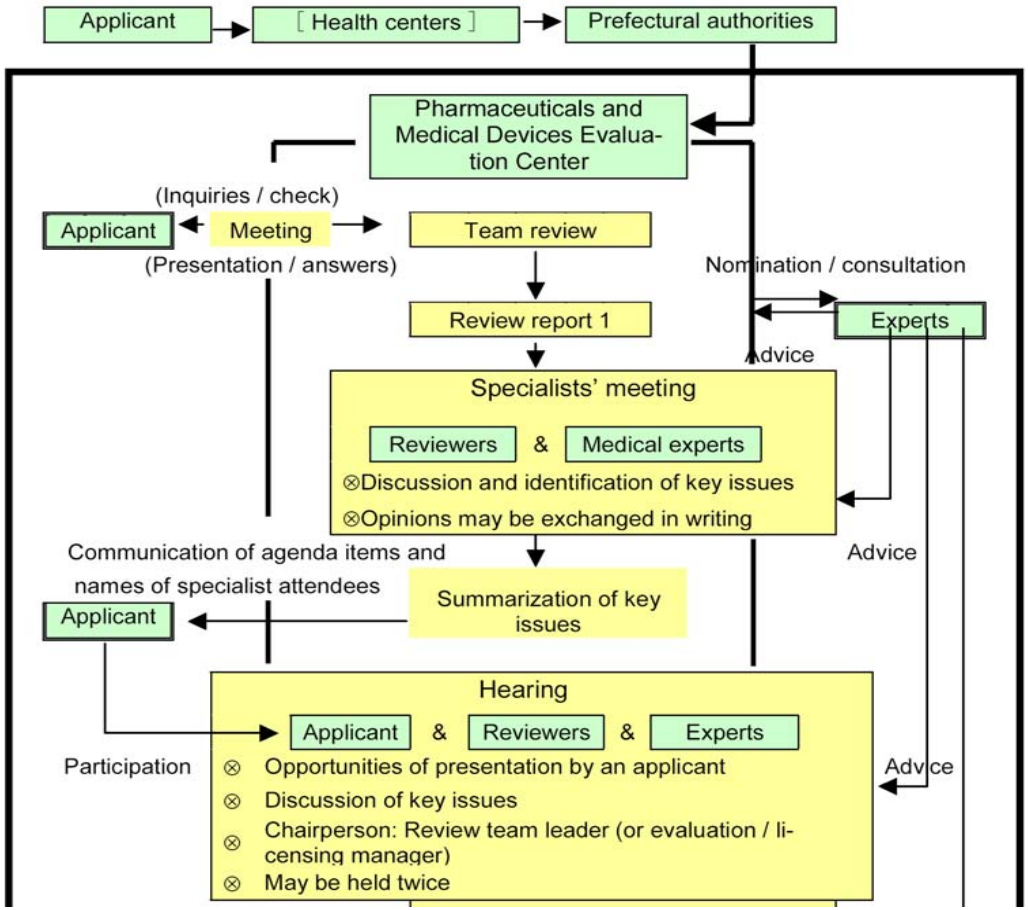
Development & Approval Process



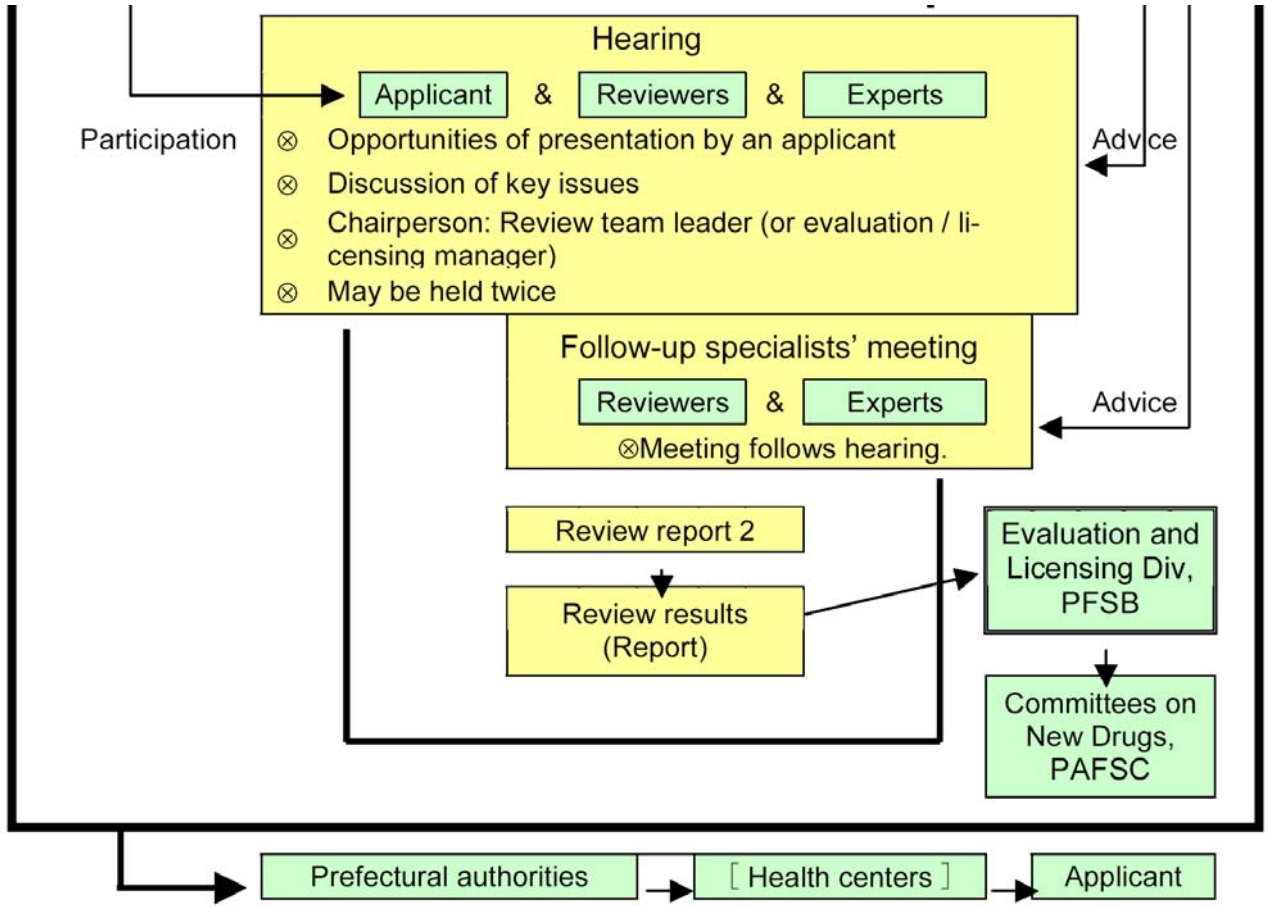
Development & Approval Process – cont'd



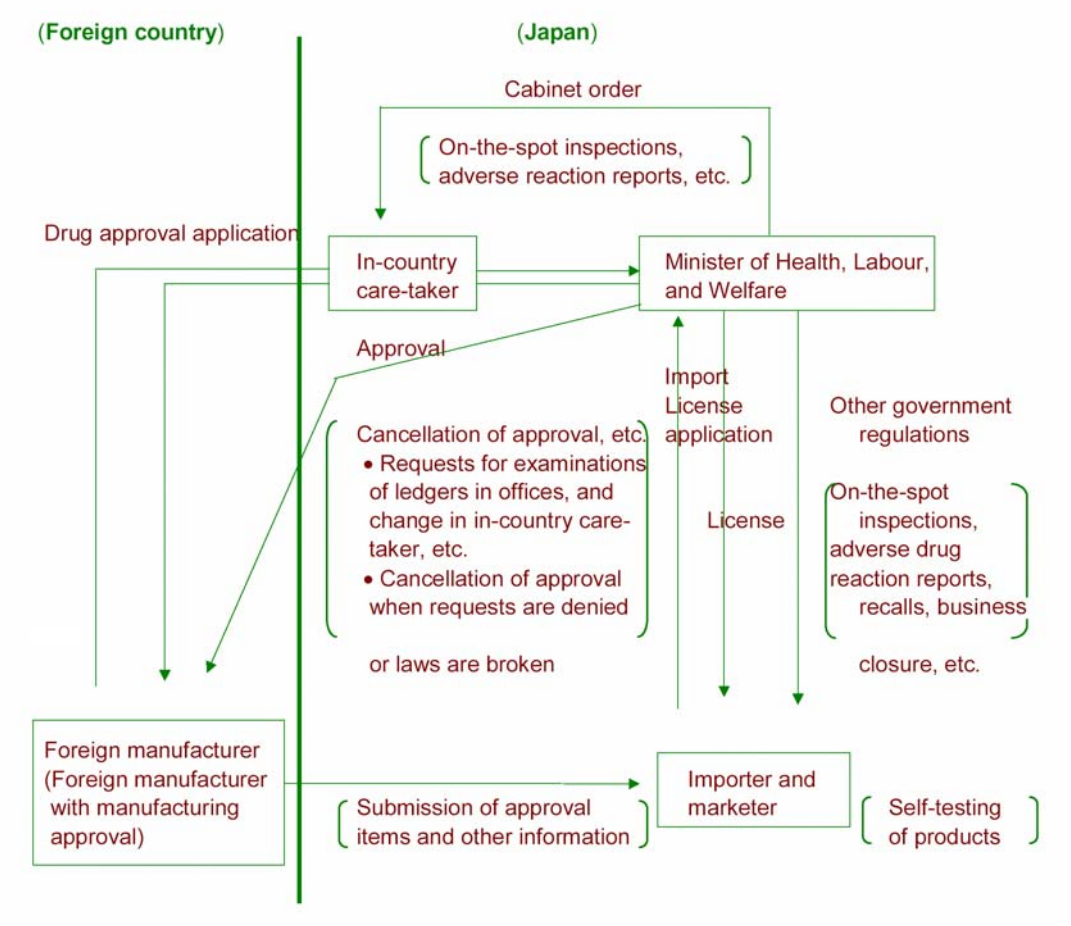
Review Process 1



Review Process 2



Foreign Company Submissions



Guidance Documents - JPMA

- "Pharmaceutical Administration and Regulations in Japan" February, 2002
  - Click here to view or download
  - Comprehensive (106 pages) – updated biannually
  - All relevant regulations and procedures described
  - Recent changes outlined – to comply with ICH

Guidance Documents - MHLW

- No. 357: "Guidelines for Paper Compliance Reviews for New Drugs"
- N0. 481 and No. 666: "Approval Reviews of New Drugs"
- No. 663: "Handling of Data to be Attached to Approval Applications for Drugs"
- No. 899: *Organization of NDA Dossier….ICH CTD* in English on NIHS web

Historical Perspective

- Review Philosophy
  - Review process focuses on Gaiyo (summary)
  - CRFs not required
  - Datasets submitted on paper
- Existing E-submission Standards/Regulations
  - NDA Registration Form – SGML on floppy disk
  - Package insert SGML plus PDF
  - Safety reports
  - E-Signature Law – April 2001
    - "Law Concerning Electronic Signatures and Certification Services"
      - Validity of electronic documents
      - Accreditation of certification services
      - Provides for "technology watch"

Current Status – CTD/eCTD

- 5 CTDs Received as of February 2003
  - 2 accompanied by eCTDs
    - 1) Modules 1 and 2 only for test purposes
    - 2) complete eCTD by an applicant
  - Testing viewing tools

Current Status – CTD/eCTD

- CTD Format required by July 2003
  - Must be a paper submission
- eCTD acceptance
  - Can be submitted now together with paper
    - this is encouraged to help reviewers gain experience
    - Contact e-submission@nihs.go.jp
  - Review system will be prepared during the first half of FY 2003
    - Operational by second half of FY 2003 or first half of FY 2004

Current Status – Module 1

- Approval of draft expected in March 2003
- To be posted for public comment
  - In Japanese only
- Simple XML DTD

Module 1 Content

- 1. Module 1: Regulatory information such as application forms and information on attached documentation:
  - (1) Table of Contents
  - (2) Approval application (copy)
  - (3) Certificates [Declarations of those responsible for collection and compilation of data for approval applications, GLP and GCP related data, contracts for co-development (copies), etc.]
  - (4) Patent status
  - (5) Background of origin, discovery and development
  - (6) Data related to conditions of use in foreign countries, etc.
  - (7) List of related products
  - (8) Package insert (draft)
  - (9) Documents concerning non-proprietary name
  - (10) Data for review of designation as poison, powerful drug, etc.
  - (11) Draft of basic protocol for post-marketing surveillance
  - (12) List of attached documentation
  - (13) Other

CTD Language Requirements

	Japanese Req'd	English Allowed
Module 1	Yes	1.1.3 Certificates
Module 2	Yes	Tables & Figures
Module 3	TOC Only	Content
Module 4	TOC Only	Content
Module 5	TOC	Content
Module 5	5.3.7 Patient Listings and Tab.	If derived from an English DB *

* Must be accompanied by comprehensive English – Japanese glossaries

Japan e-Sub Problem Areas

- Language issues (for foreign submissions)
- Font support
  - Licensing issues
  - Special font sets
- Acrobat – Japanese version
  - Requires more computing power
- IT environment
  - Slow technology adoption
  - MHLW IT budget

Resources

- Japan
  - www.jouhoukoukai.com
  - www.kiko.go.jp
  - www.nihs.go.jp
- Global
  - www.ectd.com
  - www.reg123.com

Thank you

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