APEC Harmonization Center

2011 AHC Workshop on Medical Devices:
"Implementation of GHTF Documents"

Understanding Japanese Medical Device Requirements

Japan's experience to implement international guidance documents

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APEC Asia-Pacific Economic Cooperation

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Unique Medical Devices Regulation of Japan

- 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) Third Party review system for some low risk medical devices

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Japan's experience to implement international guidance documents

Revision of PAL 2002 (enforced in 2005)

- GHTF classification rule
- GMDN
- STED
- Essential Principle
- GCP/GLP

Revision of PAL 2002

- GHTF documents such as MD Classification, the Essential Principles and STED were introduced into national legislation, the Pharmaceutical Affairs Law (PAL), by its revision 2002.
- Japan could transpose GHTF documents without major changes from their original forms after intensive and constructive discussion among interested parties.

  (Japan has been involved drafting process of GHTF documents under the policy that the GHTF document, in principle, should be enough to be introduced into national regulations in their original forms)

The revised PAL has been entered into force in 2005.

MD classification

- Because one of the purpose of PAL revision 2002 was to establish risk-based MD regulation, it was good opportunity to introduce GHTF MD classification into PAL.

- With full cooperation of industry, we sorted out four thousands of MDs into four classes. It was laborious but we've done it within 2 years after the publication of the revised law.

Classification of Medical Devices

Former Regulation	Current Regulation (From April 2005)		GHTF Classification	
Approval is not necessarily	"General MDs" (Class I)	Self declaration	Class A	extremely low risk X-Ray film
	"Controlled MDs" (class II)	Third party Certification (in principle)	Class B	low risk MRI, digestive catheters
Minister's Approval is needed	"Specially Controlled MDs" (class III & IV)	Minister's Approval	Class C	medium risk artificial bones, dialyzer
			Class D	high risk pacemaker, artificial heart values

MD classification(cont.)

- **(barrier, problems)**

  Much effort in both of industry and regulator was needed.

  Small groups of MDs were classified higher class by the GHTF rule and subject to more strict regulation compared to before.

- **(benefit)**

  This was a first step for multilateral harmonization.

  It is expected that it provides fundamentals for fast access to foreign market in future.

International Harmonization of Nomenclature

- Propose for adoption of nonproprietary names of MDs which is created in Japan to the GMDN secretariat
- In case of newly approved MDs requiring a new nonproprietary name, they will be assigned a new nomenclature and will be added to the most recent published list

GMDN

- GMDN was originally developed as ISO TS 20225(2001) from several nomenclature systems (ECRI, EDMA, FDA, MHLW, NKKN, and ISO 9999) by international collaboration in ISO/TC210/WG3
- It was originally assumed that Japan could introduce GMDN only with translation.
- It turned out that GMDN did not correspond to GHTF classification rule. Some nomenclatures cover multiple classes under the one nomenclature.
- Therefore, some of the GMDN nomenclatures were adjusted as JMDN to fit with classification systems in PAL, while basic structure of GMDN(2003 version) was preserved as much as possible.

Japanese Medical Devices Nomenclature (JMDN) and MD classification

- Each MD has to fall under generic nomenclature (JMDN). JMDN is based on 2003 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).

  (see also DG-PFSB Notification #0720022, July 20, 2004 and JMDN file. 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

Adoption of GMDN

- 3 digits were added after GMDN 5 digits code when GMDN was translated into JMDN
  - 1's digit show GHTF classification when divided
  - 10's digit show variation (when original GMDN was too broad and separated into JMDN)
  - 100's digit show other division for regulatory purpose (containing biological ingredients or drug substances)
- Only about 20 nomenclatures were added to JMDN in 5 years(ex. decorative contact lenses)

Example of adjustment of GMDN to JMDN

- Original GMDN in 2003
  - 37870"Drill attachment, surgical“
- Under JMDN, 3 digits were added to show classification
  - Class 1 : 37870001"Drill attachment, surgical, reusable“
  - Class 2 : 37870002"Drill attachment, surgical, single use“
- Later, GMDN 37870 became obsolete and divided into 9 new nomenclatures
  - 42981"Trephining power tool attachment“
  - 43555"Burring power tool attachment“
  - 43660"Wire-driving power tool attachment“

  And other 6 nomenclatures

GMDN(cont.)

- **(barrier, problems)**

  Much effort in both of industry and regulator was needed.

  JMDN stays same but GMDN is updated every 10 days. Difference becomes larger.

- **(benefit)**

  It is expected that it provides fundamentals for international information exchange. (eg. adverse event reporting)

Risk Classification of Medical Devices

- Classify more than 4,000 nonproprietary names into four categories according to GHTF Rule, i.e. class A – D

- In Pharmaceutical Affairs Law, those into three categories as following

  1) Highly Controlled Medical Device (class C & D)
  2) Controlled Medical Device (class B)
  3) General Medical Device (class A)

Japanese Medical Devices Nomenclature (JMDN)

- JMDN is based on GMDN in Japanese
- Number of items for each class of JMDN

  Class A : 1195 items

  Class B : 1785 items

  Class C : 739 items

  Class D : 325 items

  In total : **4044 items**

Classification of Medical Devices (2)

Specially controlled MDs

Medical devices that in case of malfunctioning or if side effects occur, their potential risk to human life and health is significant.
Designated by the Minister after seeking the opinion of the Pharmaceutical Affairs and Food Sanitation Council (PAFSC) as those devices that require proper management.

Controlled MDs

MDs other than Specially controlled MDs that in case of malfunctioning or side effects occur, they have potential risk to human life or health.
Designated by the Minister after seeking the opinion of the PAFSC as what require proper management.

General MDs

MDs other than Specially controlled MDs and Controlled MDs, that in case of malfunctioning or side effects occur, their potential risk to human life and health is Almost insignificant.
Designated by the Minister after seeking the opinion of the PAFSC.

Class D

highly invasive; in case of malfunctioning, have potential to threaten life directly

Class C

in case of malfunctioning, risk to human life is relatively high

Class B

in case of malfunctioning, risk to human life is relatively low

Class A

even in case of malfunctioning, risk to human life is extremely low

Classify MDs grouped by each general nomenclature using GHTF classification rule

General nomenclatures are based upon GMDNs which are discussed within ISO TC210.

Classification of Medical Devices (3)

Among MDs, those which need expertise and technic for maintenance, repair and other management, unless it is done properly, prevention,diagnosis or treatment of disease could not be attained. The Minister designates above mentioned MDs as such after seeking opinion from the Pharmaceutical Affairs and Food Sanitation Council.

Among specially designated maintenance management required MDs, those which need assembly upon installation, and need management of assembly from viewpoint of prevention of damage to public health. Above mentioned MDs are designated by the Minister as such.

The Essential Principles

- The Essential Principles (EPs) were new requirement for Japanese industry and it was big challenge especially for small and medium companies. Therefore we took two step approach. Until April 2008, only “the General Requirements” are required. Then, “the Design and Manufacturing Requirements” will become obligatory.

- Industry has drafted around 400 checklists for conformity to EPs for class II (GHTF class B) MDs, product by product. They also drafted 38 checklists for class III, IV (GHTF class C, D) MDs as well.

- **(barrier)** EPs were new requirements and big challenges especially for SMEs.

- **(benefit)** EPs provide clear requirements for MDs.

Introduction of STED

Application Form
(Form22-3 of Ministerial Ordinance on PAL)

+

STED

+

Data set

Declaration of Conformity with EP

- In Japan, application for Brand-new MD approval should be filed with 1)Application form (*Shinseisyo*), 2)Summary of the products (*Shiryo-gaiyo*) and 3)Attachment (data sub set).

  The Summary is quite useful in a review process because it is not only a compilation of data but also an applicant's view on how the data support safety and performance of the device.

- February 2002, STED(PD) was introduced on a trial basis for new or improved MDs. Applicant might use STED as the Summary.

- From 2005, STED(PD) has been used mandatory for application.

Introduction of STED (cont.)

Application Form

STED(Data set)

Declaration of Conformity with EP

- In Japan, application for MD other than Brand-new MD approval/certification should be filed with

  1)Application form (Shinseisyo),

  2) Attachment (data set contains STED elements).

  - Designated Class II devices

    MHLW Notification by Director, OMDE, Yakushokuki-hatsu No. 0331008 March 31, 2005
  - Class III/IV devices which have approval standards

    MHLW Notification by Director, OMDE, Yakushokuki-hatsu No. 0401003 April 1, 2005
  - Generic(Me-too) devices

    MHLW Notification by Director, OMDE, Yakushokuki-hatsu No. 0327004 March 27, 2009

STED (cont.)

- **(barrier)**

  Many of Applicants were not accustomed to make and use STED. (eg. way of description)

- **(benefit)**

  It is expected that it provide fundamentals for fast access to foreign market in future.

- **(Challenge)**

  Japanese STED was introduced based on early STED(PD).

  → STED currently used in Japan basically corresponds with STED(FD).

Summary Technical Documentation (STED)

- GHTF STED is mandatory using
- Using GHTF Essential Principles (EPs)
- Conformity assessment providing the Check List for EPs providing the Technical Standard (TS)
- TS required International Standard or well used guidance documents

(Those slides originally made by Hiroshi Ishikawa, JFMDA)

Medical Device Registration Process

Authority		Tenpu-shiryo	Summary (Gaiyo)
MHLW	No TS	Prepared the documents according to the Notice (Data Sub set)	STED Form
	TS	STED Form	Not Required
Third Party	TS	STED Form	Not Required

Summary include summary of Test results and its report should be attached. GLP may be required, if Biological tests were generated.

How the STED may differ by classification ?

PMDA

Third Party

Application Form 22-3 “ Shonin Shinsei Syo ”	Application Form 64-1 “ Ninshou Shinsei Syo ”

Binding

+

“ Tenpu-Shiryo “
- STED
- Data Sub Set

No need
If provided TS

Local Government

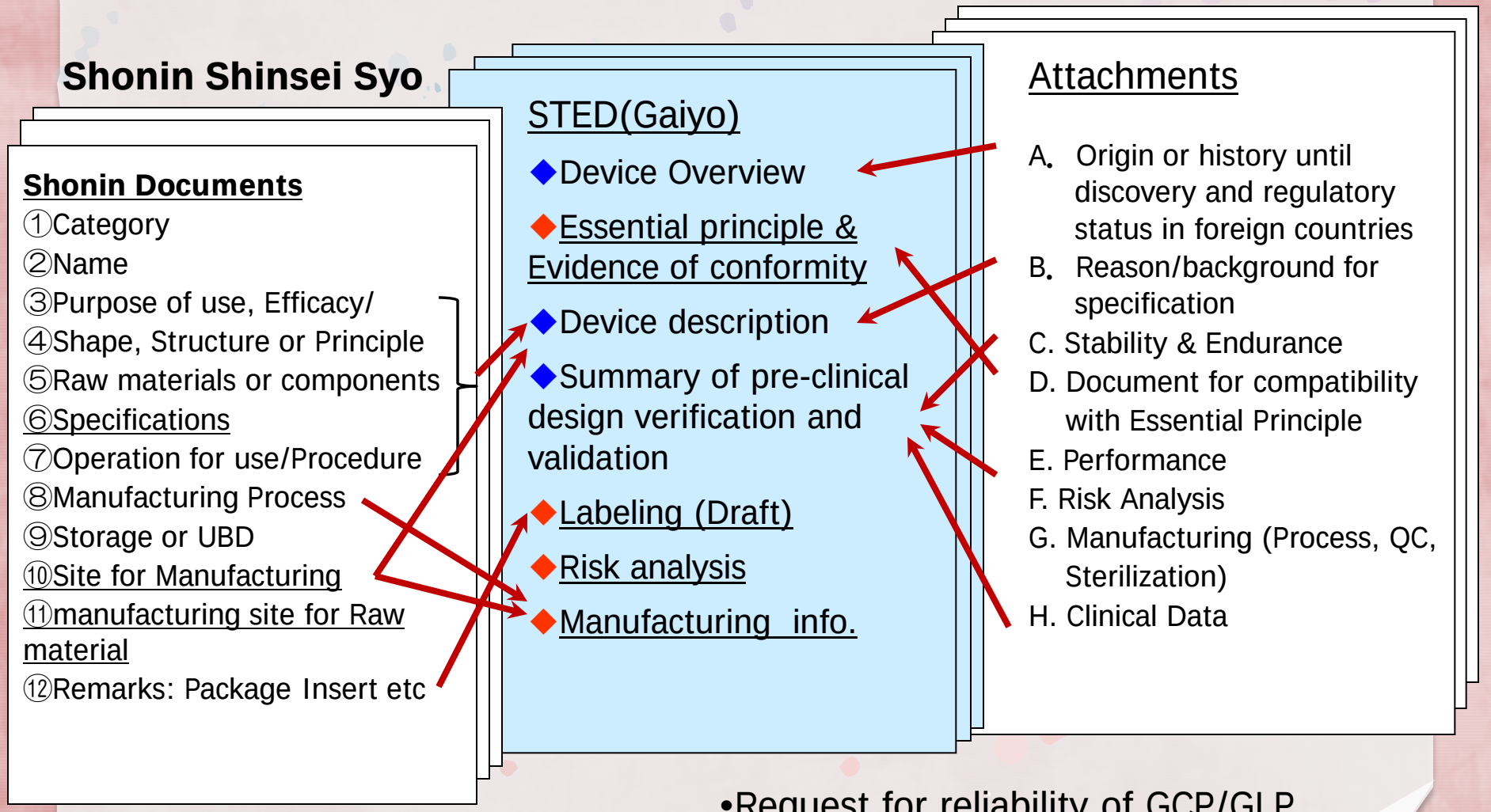
+

Third Party

Request for GMP Conformity Assessment 25-2
“ Tekigousei Cyousa “ 67-1

Set of Application Documents (Image)

- In case of High Risk exclude GMP conformity assessment -



- Request for reliability of GCP/GLP
- Request for compliance to GMP(ISO13485)

GLP / GCP

- Good Laboratory Practice (GLP) Ministerial Ordinance

  JGLP Ministerial Ordinance for MD was introduced in 2005 (8 years later from JGLP for drugs). JGLP for MD is based on OECD-GLP and almost same as JGCP for drug.

- Good Clinical Practice (GCP) Ministerial Ordinance

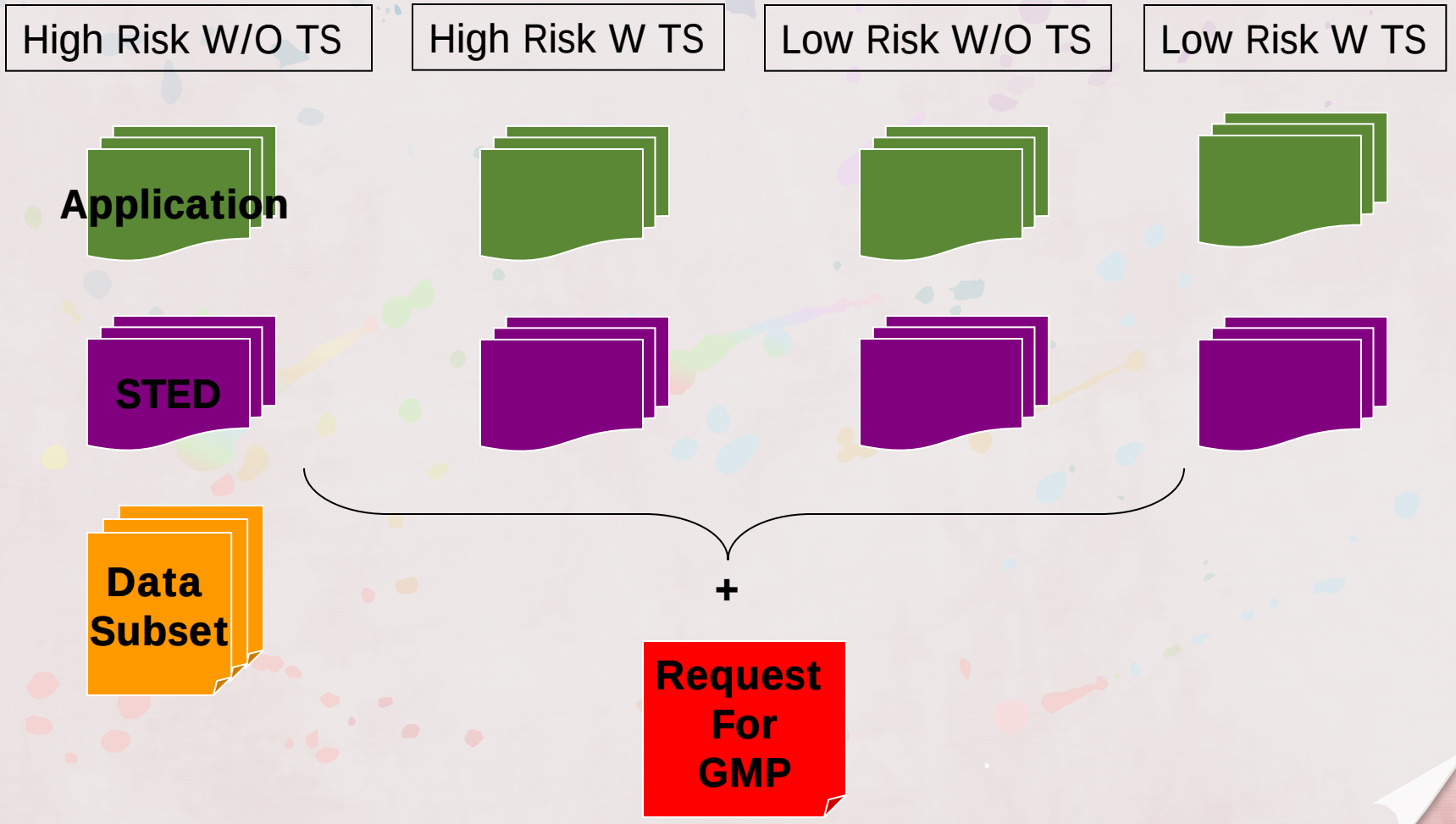
  JGCP Ministerial Ordinance for MD was introduced in 2005 (8 years later from introduction of ICH-GCP for drugs). JGCP for MD is based on ICH-GCP(ICH E6 guideline) and almost same as JGCP for drug.
  - Clinical trial sites had already been accustomed to JGCP for drug
  - ISO 14155:2003 (ISO GCP) was not well written (and now under revision)
  - ICH-GCP is also implemented in US for drug and medical device.

What is Technical Standard ?

- JIS： Translated International Standard or other recognized standard, whichever *used as internationally.*
  - Translated in Japanese
  - Such as IEC or ISO: IEC60601, ISO13485, 14971

- If there is no such standard, then alternatively using *Guidance Documents* which NCA issues or Industry Standard such as NEMA Standard etc.

Image of Documents



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

YES

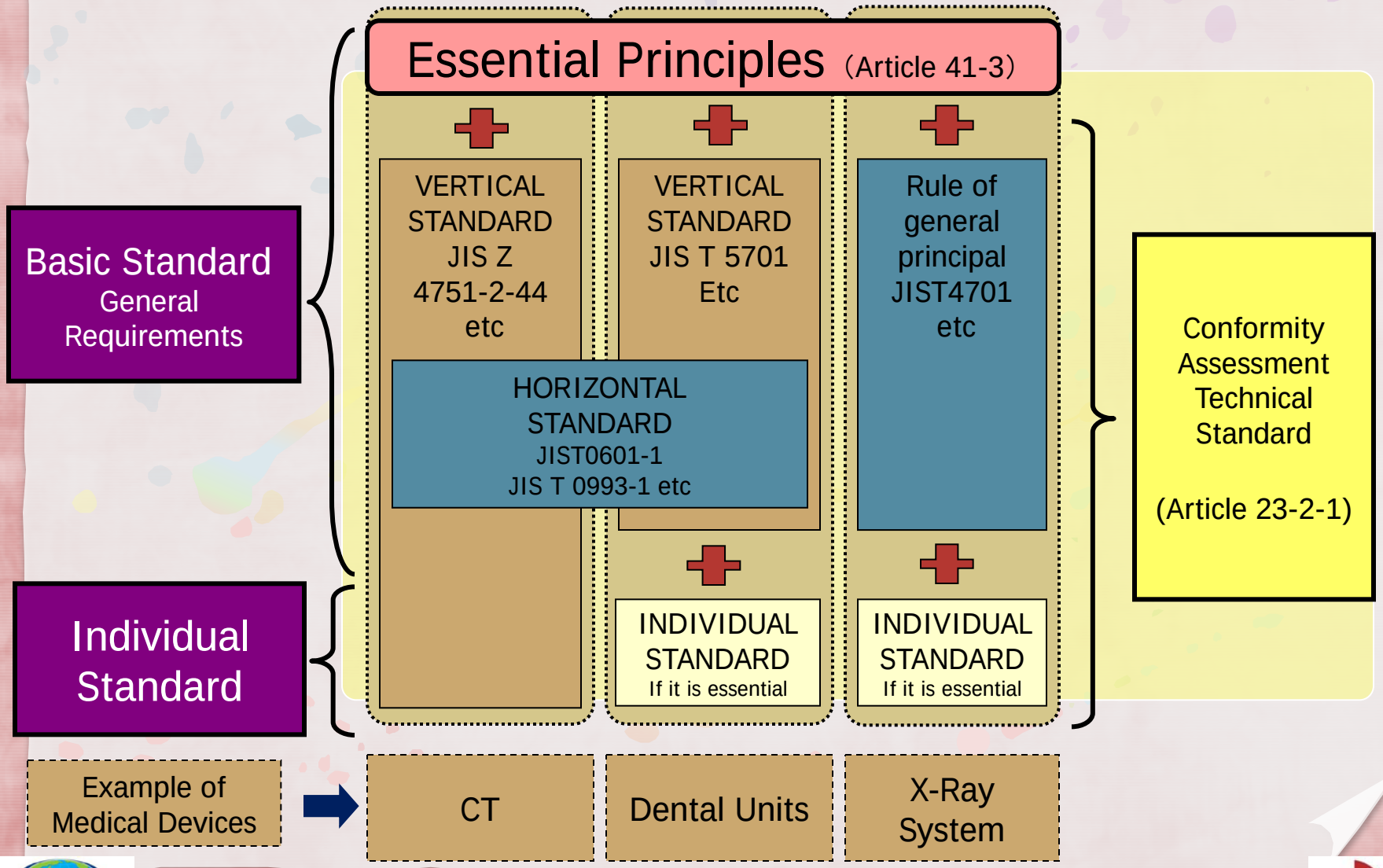
Within the scope of performance which are shown in the conformity performance standard

YES

Meet the proper Conformity Performance Standard

Third Part Approval MD

Examples for Third Party Certification Using Standards



MHLW's adoption of GHTF Products (SG1)

Title	Description	MHLW Regulation	Remarks
N020R5	Essential Principles	PAL, Notice	Approval Criteria Reflected in PAL
N009R6, etc.	Labelling	PAL, Ordinances	
N011R17	STED	PAL, Notifications on Data Submitted	Used in PMDA
N015R22	Classification, GMDN	PAL, Notice, Notification on Clarification	Basis of MD Regulation
N044R4	Standards	PAL, Notice and Notification on Standards, JIS	MHLW cooperates with JIS Committee JIS being revised

MHLW's adoption of GHTF Products (SG2)

Title	Description	MHLW Regulation	Remarks
N7R1, N32R5	Minimum/Universal Data Set	Notification 421 (1997/3/27) Notification 0317006 (2005/03/17)	ICH compatible
N36R7	Trend Report	Notification 0317006 (2005/03/17)	MHLW/PMDA Officials respects the Doc.
N8R4, etc.	Handling of Vigilance Report	N/A	MHLW/PMDA Officials respects the Doc.
N20R10, etc.	NCA Report Exchange	N/A	MHLW cooperates with other NCARs ADR Warnings issued based on NCAR
N21R8, N33R11	Adverse Event Reports/ Guidance, Timing	PAL, MHLW Ordinance	ICH compatible

MHLW's adoption of GHTF Products (SG3)

Title	Description	MHLW Regulation	Remarks
N99-8,9,10, N15R6	Quality System •Guidance •Design Control •Process Validation •Risk Management	PAL, MHLW Ordinance ("QMS Ordinance")	ISO 13485 compatible

MHLW's adoption of GHTF Products (SG4)

Title	Description	MHLW Regulation	Remarks
(99)28, N9924R3, N26R1, N30R6	Regulatory Auditing Requirements Strategy	Notification #1130004 (2006/11/30) "GMS/QMS Audit Manual"	Auditees know how Audit is made.

MHLW's adoption of GHTF Products (SG5)

Title	Description	MHLW Regulation	Remarks
N2:2007, N3:2010	Clinical Evaluation, Clinical Investigation	Notification #0804001 (2006/08/04)	When is clinical investigation undertaken?

Stepwise Enforcement of Amended Pharm. Affairs Law Amendment (2003)

2003

Biologics(-related MD)

Clinical Trials (Doctor-Sponsored)

2004

PMDA established

2005

Marketing Authorization (from Manufacture Authorization)

New Classification of MDs

Safety Measures for MDs strengthen

Accreditation of Foreign Manufacturer

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 Technical Standards by Third Party)

- No approval nor certificate

  for General MDs (Class 1)

Overview of PAL Regulation

GHTF Classes	Risk-based Classification	Pharm. Affairs Law.			QMS
		Class	Mkt. Auth.	Sales	
Class A	Extremely Low Risk (X-Ray films)	General	NA	NA	
Class B	Low Risk (MRI, digestive catheters)	Controlled	3rd. Party Certification	Regist-ration*	Inspection
Class C	Medium Risk (artificial bones, dialyzer)	Specially Controlled	MHLW's Approval	License (Pre-fecture)	
Class D	High Risk (pacemaker, artificial heart values)				

* Some exception

Thank you for your attention!!