



Asian Harmonization Working Party

WORKING TOWARDS MEDICAL DEVICE HARMONIZATION IN ASIA

<http://www.ahwp.info>

REGULATORY RELIANCE AND RECOGNITION FOR MEDICAL DEVICE PREMARKET REGISTRATION

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Regulatory Reliance and Recognition – *The Way Forward*

Scope of presentation

CONSIDERATIONS:

- *Definitions*
- *Principles & Requirements*
- *Applications*
 - *Expediated Routes of Reviews*
- *Examples*

Definitions

For a more comprehensive list of definitions, please refer to:

https://www.who.int/medicines/areas/quality_safety/quality_assurance/GoodRegulatory_PracticesPublicConsult.pdf

Good Regulatory Practice (GRP) – points for consideration

- ❖ **Good regulatory practices (GRP) provide a means for establishing **sound, affordable and effective** regulation of medical products**
 - *A set of practices that are to be applied to the development, implementation and maintenance of controls*
 - *including laws, regulations and guidelines – in order to achieve a public policy objective*
 - *achieve a public policy objective*
- ❖ **REGULATIONS should be -**
 - *sufficiently flexible to allow for a rational response to changes e.g. new technologies, emergencies, shortages etc*
 - *language should be descriptive and not prescriptive*
- ❖ **Regulatory system** should provide the flexibility to apply good judgement within the regulatory framework.
- ❖ **inefficient regulatory systems** can be a barrier to access to safe, effective and quality Medical products

Regulatory Cooperation

- ❖ **A practice between NRAs** aimed at efficiently regulating medical products.
- ❖ **Or by agency or institution or on a government-wide basis.**
- ❖ Formal mechanisms can include the creation of
 - *joint institutions and treaties and conventions such as **MRAs**, or*
 - ***sharing of information, scientific collaboration, common risk assessment, joint reviews, and development of standards.***
- ❖ Can include work with international counterparts to build regulatory capacity or provide technical assistance building the improvement of international regulatory governance practices

Regulatory Convergence ; Regulatory Harmonization

Regulatory convergence:

- ❖ a voluntary process whereby the regulatory requirements in different countries or regions become more similar or “aligned” over time, which will result
 - *from the gradual adoption of internationally recognized technical guideline documents, standards and scientific principles, common or similar practices and procedures, or*
 - *In the establishment of appropriate domestic regulatory mechanisms that align with shared principles to achieve a common public health goal*

Regulatory harmonization

- ❖ the process by which technical guidelines are developed in order to be uniform across participating authorities in multiple countries

Regulatory Recognition

- ❖ **The routine acceptance** by the NRA in one jurisdiction of the regulatory decision of another NRA or other trusted institution.
- ❖ Recognition indicates that **evidence of conformity** with the regulatory requirements of country A is sufficient to meet the regulatory requirements of country B
- ❖ Recognition may be **unilateral or multilateral**,
- ❖ May be the subject of **a mutual recognition agreement**

Regulatory Reliance

- ❖ The act whereby the **NRA in one jurisdiction** may take into account and give significant weight to (totally or partially) **rely upon evaluations performed by another NRA or trusted institution in reaching its own decision**
- ❖ **A practice between NRAs** aimed at efficiently regulating medical products.

NOTE: The relying authority remains responsible and accountable for decisions taken, even when it relies on the decisions and information of others

Putting it in place

A Stepwise approach, harmonization, reliance, recognition

- **Reliance and recognition :**
 - *National responsibilities*
 - *International collaboration*
 - *Basic-level controls and their enforcement*
- **Publish law, including definition, and regulations with transition period**
 - *Establish medical device classification for regulatory purposes*
 - *Establish Essential Principles of safety and performance*
 - *Basic-level controls and enforcement – premarket*
 - *Establish a basis for reliance and recognition*
 - *Establish requirements for declaration of conformity*
 - *Establish requirement for manufacturers to have a QMS*
 - *Establish requirements for labels and labelling*
 - *Prohibit deceptive, misleading and false advertising*
 - *Establish provisions for exceptional premarket situations*

Basic level controls and enforcement

Premarket	Placing on the market	Postmarket
<ul style="list-style-type: none">• Publish law, including definition, and regulations with transition period• Establish medical device classification for regulatory purposes• Establish Essential Principles of safety and performance• Establish basis for reliance and recognition• Establish requirements for declaration of conformity• Establish requirement for manufacturers for a QMS• Establish requirements for labels and labelling• Prohibit deceptive, misleading and false advertising• Establish provisions for exceptional premarket situations	<ul style="list-style-type: none">• Registration of establishments• Listing of medical devices• Import controls	<ul style="list-style-type: none">• Establish a system for vigilance reporting• Require mandatory notification by the manufacturer of field safety corrective actions• Establish a procedure to withdraw unsafe medical devices from the market• Establish procedure to issue safety alerts to users• Undertake market surveillance

Source: WHO

Table of Contents (ToC)

- The comprehensive **table of contents** is a complete list of all documents in the dossier, arranged by Module, and with location references for each document. Specify the titles of studies in the **table of contents**, indicating the type of study and topic in the title.



<http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-190321-nivd-dma-toc-n9.pdf>

Table of Contents (ToC) – Dossier Submissions

- The Regulated Product Submission (RPS) - the objective of establishing a internationally agreed, comprehensive harmonized file structure for premarket medical device submissions
- PURPOSE :
 - *To create a comprehensive submission structure that can be used as a harmonized international electronic submission format to the NRA for market authorization.*
 - *To minimize regional divergences and indicating where regional variation exists.*

Table of Contents (ToC) – Dossier Submissions

Essential Principles Requirement is a principle component in the ToC harmonized dossier

- **IMDRA** guidance document provides a harmonized Essential Principles, covering
 - *Common set of fundamental design and manufacturing requirements of medical devices /IVDs to ensure safety and performance as intended and are met.*
- Worldwide adoption of this common set will have significant benefits to manufacturers, users, patients/consumers, and to Regulatory Authorities.
- It will reduce differences between jurisdictions and decreases the cost of gaining regulatory compliance and
- allows patients earlier access to new technologies and treatments.
- Adoption of this document's recommendation will support global convergence of regulatory systems
 - *There will be a consistent , economic and effective approach to the control of MDs and the interest of public health*
 - *There will be a balance between the responsibilities of RAs to safeguard the health of their citizens and avoid placing unnecessary burdens upon the industry.*

Current dossiers templates

- Many jurisdictions (apart from the GHTF founding members) use the STED or CSDT template.
- Co-relation and mapping of the 2 templates example:-

CSDT AND STED – COMPARISON

- STED is GHTF format (Australia, Canada, EU, Japan, USA)
- STED and CSDT are similar.

ASEAN AMDD CSDT		STED General Medical Device	
Sect.	Heading	Sect.	Heading
		9.0	Essential Principles
3.0	Executive Summary	6.0-6.2	Device Description and Product Specification
4.1	Essential Principles	6.3	Reference to similar and previous generations
4.2	Device Description	11.0-11.8	Product Verification & Validation
4.3	Design Verification and Validation	7.0	Labeling
4.4	Labeling	10.0	Risk Analysis & Control Summary
4.5	Risk Analysis	8.1	Device Design Stages
4.6	Manufacturer's Information	8.2-8.3	Manufacturing Information
AMDD Annex 6: Declaration of Conformity		13.0	Declaration of Conformity

Table 1: Overview of Differences Found between the CSDT and STED

	CSDT	STED
Executive Summary	<p>An executive summary shall be provided with the CSDT, which shall include the following information:</p> <ul style="list-style-type: none"> • an overview, e.g., introductory descriptive information on the medical device, the intended uses and indications for use of the medical device, any novel features and a synopsis of the content of the CSDT; • commercial marketing history; • intended uses and indications in labelling; • list of regulatory approval or marketing clearance obtained; • status of any pending request for market clearance; and • important safety/ performance related information. 	No requirement for an Executive Summary in STED
Reference to similar and	CSDT does not call for information on previous generations of device.	Where relevant to demonstrating conformity to the Essential Principles, and

Current dossiers – Mapping CSDT with the ToC (OF IMDRA)

3. TABLE 1 – SUMMARY OF SUBMISSION REQUIREMENTS

Legend:

F	Full evaluation route
A	Abridged evaluation route
E	Expedited evaluation route
I	Immediate registration route

	MEDICS Application Form - Dossier & Supporting Document(s)	Reference technical documents		Class B			Class C & D			
		IMDRF nIVD ToC	CSDT TR-01	F	A	I	F	A	E	I
1	Letter of authorization									
	<ul style="list-style-type: none"> Letter of Authorization of Registrant by the Product Owner for all the products to be registered, using the latest template as per GN-15 Annex 1 Letter of Authorization template 	CH1.13 Letter of Authorization	NA	✓	✓	✓	✓	✓	✓	✓
2	Annex 2 List of Configurations									
	<ul style="list-style-type: none"> A copy of Annex 2 for GN17 and GN18 List of Configurations, including the complete list of configurations of medical devices subject to the submission. This is to be submitted in a Microsoft Excel file. 	CH1.05 Listing of Device(s)	4.2 Device Description	✓	✓	✓	✓	✓	✓	✓
3	Proof of reference agency's approval(s)									
	<ul style="list-style-type: none"> Copies of approval letter(s) from each reference agency. For CE marked devices, the EU declaration of conformity by the product owner must be submitted, in addition to the EC certificate issued by the notified bodies. 	CH1.07 Free Sale Certificate/ Certificate of Marketing authorization	3. Executive Summary		✓	✓		✓	✓	✓
4	Proof of marketing history in the reference agencies jurisdictions e.g. invoice with date, proof of sale or a declaration on marketing history									
	<ul style="list-style-type: none"> Invoice with date, proof of sale or a declaration on Marketing history as per Annex 2 of GN-15, to be completed by the local Applicant 	NA	NA			✓ (This required for Class B)			✓ (This required for Class C & D)	✓
5	Declaration of no safety issues globally									
	<ul style="list-style-type: none"> Safety declaration on template as per Annex 3 of GN-15, to be completed by the local Applicant 	NA	NA			✓			✓ (This required for Class C & D)	✓
6	Executive Summary									
	<ul style="list-style-type: none"> Introductory descriptive information on the medical device, the intended use and indications for use of the device. 		3. Executive Summary	✓	✓	✓	✓	✓	✓	✓

■ What's Next ?

Principles/parameters to consider for good governance in regulatory reliance, recognition practices

- To decide whether to use either the reliance or recognition option, NRA must have
 - *Have clear understanding of the regulatory system that applies within the country where the medical device is manufactured. (Export only MD-may have less reg requirements like labelling)*
 - *note that sometimes devices may have different configurations for different markets; these may vary in aspects such as the intended use, site of manufacture, power supply, labelling language and applied quality control,*
 - *Note , specifically for IVDs, market access review is complex, due wide variance in classification and scrutiny of IVDs in many countries. (e.g. in the EU Directive, independent assessment could mean that most IVDs bearing a CE mark are self-assessed by the manufacturer)*

In general, where a NRA relies upon information from a counterpart in another jurisdiction, it must first establish confidence in the counterpart authority and reach agreement on the exchange of confidential information

Examples: Countries practising Regulatory -Reliance, Recognition (some info)

- Australia (Therapeutic Goods Authority - TGA)
- Singapore (Health Sciences Authority - HSA)
- Thailand (Thai Food and Drug Authority - TFDA)
- Malaysia (Medical Device Authority – MDA)
- Vietnam (Dept of Medical Equipment & Construction – DMEC)

EU-Australia MRA (Mutual Recognition Agreements) on conformity assessment.

■ Background on the MRA

- *Both the European Union and Australia recognise and accept the technical competence of each other's conformity assessment bodies (CABs) to certify products for compliance with the regulatory requirements of the other Party, largely eliminating the need for duplicative testing or re-certification when the goods are traded.*
- *Came into force in **1999** and was the first fully operational MRA of its type in the world*
- To be amended the current EU-Australia MRA and came into force on **1 January 2013**.

EU-Australia Amended MRA

- **Changes in place (AMENDED MRA)**
- **Contributory Factor - The new EU Medical Device Regulations, in May 2017 and with full application of the MDR coming into effect on the 26th May 2020.**
 - *simplifying the administration of the MRA,*
 - *A number of amendments in which the MRA applies e.g.*
 - *A 'rule of origin' clause (which stipulates that only those products manufactured in the European Union or Australia are covered by the MRA) has been removed and replaced with a more specific clause in the medical devices with*
 - *Activities such as repairing, reconditioning, refurbishment, labelling, packaging, quality control inspections alone, or sterilisation alone, will be specifically excluded from the definition of 'manufacture'.*
- Radioactive medical devices of lower risk classes will be included in the MRA.
- Exclude a number of high risk medical devices from the MRA, MD with medicines, barrier contraceptives until confidence building activities are carried out by both Parties
- Others

(link <https://www.tga.gov.au/medical-device-amendments-eu-australia-mra-conformity-assessment-come-effect-1-january-2013>)

Example of the of Regulatory Reliance:

- Singapore (HSA) / Thailand (TFDA) / Vietnam and Malaysia

Types of registration submission routes

- Abridged, Expedited and Immediate evaluation (Singapore)
- Concise evaluation route (Thailand)

Reference NRAs :

- Australia Therapeutic Goods Administration (TGA) Device Registration Licenc
- Health Canada (HC) Device Registration Licence
- Japan Ministry of Health, Labour and Welfare (MHLW)
- US Food and Drug Administration (US FDA) 510K clearance, PMA approval
- *European Union Notified Bodies (EU NB) via EC certificates*

For Singapore, further info on types of EC certificates available on HSA website

Approvals from EU and TGA will qualify as independent reference regulatory agency's approval only if the devices have been reviewed and approved by the respective agencies and the devices are not registered based on the Mutual Recognition Agreement (MRA)

HSA Evaluation Route Class B (Example)

Abridged

- (i) A medical device that has obtained at least one reference regulatory agency approval for a labelled use *identical* to that intended for marketing in Singapore at the point of submission will qualify for the abridged evaluation route.

Immediate

- (ii) As abridged requirement PLUS
- (iii) Marketed for at least three years **Or** the medical device has been marketed in Singapore for 3 years (w evidence)
- (iv) **No safety issues globally associated with the use of the medical device(s) when used as intended by the product owner, in the last three years (details defined in Website)**
- (v) No prior rejection/withdrawal

Alternative to (ii) and (iii)

- *Approvals by at least two of HSA's independent reference regulatory agencies for a labelled use identical to that intended for marketing in Singapore;*

HSA Evaluation Route Class C & D (Example)

- (i) Full Evaluation Route (no prior approval fm recogized RAs)
- (ii) Abridged Evaluation Route
- (iii) Expedited Evaluation Route
 - a. Expedited Class C Registration (ECR)
 - b. Expedited Class D Registration (EDR)
- (iv) Immediate Class C Registration (ICR) Evaluation Route [solely for Standalone Medical Mobile Application]

For more details, please refer to HSA Website,

Thai FDA Evaluation Route for Medical Devices (Example)

■ Concise Evaluation Route

■ QUALIFICATION

- To qualify for Concise Evaluation, a medical device must be registered (through full evaluation) and marketed for **more than one year** without any serious adverse events in 2 of 5 reference markets listed below; or
- in 1 of the markets for at least three years.

1. Australia: Therapeutic Goods Administration (TGA)
2. Canada: Health Canada (HC)
3. European Union: Notified Body (EU NB)
4. Japan: Japan Ministry of Health, Labour and Welfare (MHLW)
5. USA: Food and Drug Administration (FDA)

For more details, please refer to TFDA Website,

Malaysia MD Authority Route for Medical Devices

Simplified Verification Assessment (SV)

■ **QUALIFICATION**

Premarket submissions for Class B, C and D can qualify for SA Route if the local or foreign manufacturer have obtained prior medical device registration approval from at least one of the five GHTF countries –

1. Canada: Health Canada (HC)
 2. European Union: Notified Body (EU NB)
 3. Japan: Japan Ministry of Health, Labour and Welfare (MHLW)
 4. USA: Food and Drug Administration (FDA)
 5. Australia TGA
- The SV route is a much simpler pathway of assessment vs the full conformity extensive assessment

For more details, please refer to MDA Website,

Vietnam DMEC (MOH)

– FAST Track Evaluation Route for Medical Devices

According to the new Decree passed in Vietnam early 2019, MoH will allow

- A **Fast Track route** for all MD product licenses for Class B, C, D, with the following qualifications :

- The MD have been registered in at least two (2) of the GHTF countries: Japan, United States, Canada, Australia, EU countries.
- The medical device has been sold in Vietnam prior to the 31 December 2018, and:
- The medical device has been available for sale in Vietnam for at least three (3) years within five (5) years of the submission date
- No notifiable safety/operation issues of the medical device have been reported

For more details, please refer to Vietnam DMEC (MOH) Website,

Main Source References:

WHO Guidelines – Good Regulatory Practice / Model Regulatory Framework

IMDRF Guidance Documents

HSA Singapore – Guidance Documents



Thank You for listening

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