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WHO GLOBAL MODEL REGULATORY FRAMEWORK FOR MEDICAL DEVICES INCLUDING IVDs (GMRF)…Good Regulatory Practices and Good Reliance Practices

Virtual Regional Workshop on Good Regulatory Practices and Medical Device Regulation

0900 – 1200 hrs (JKT), 28 February and 1 March 2023

28 March 2023

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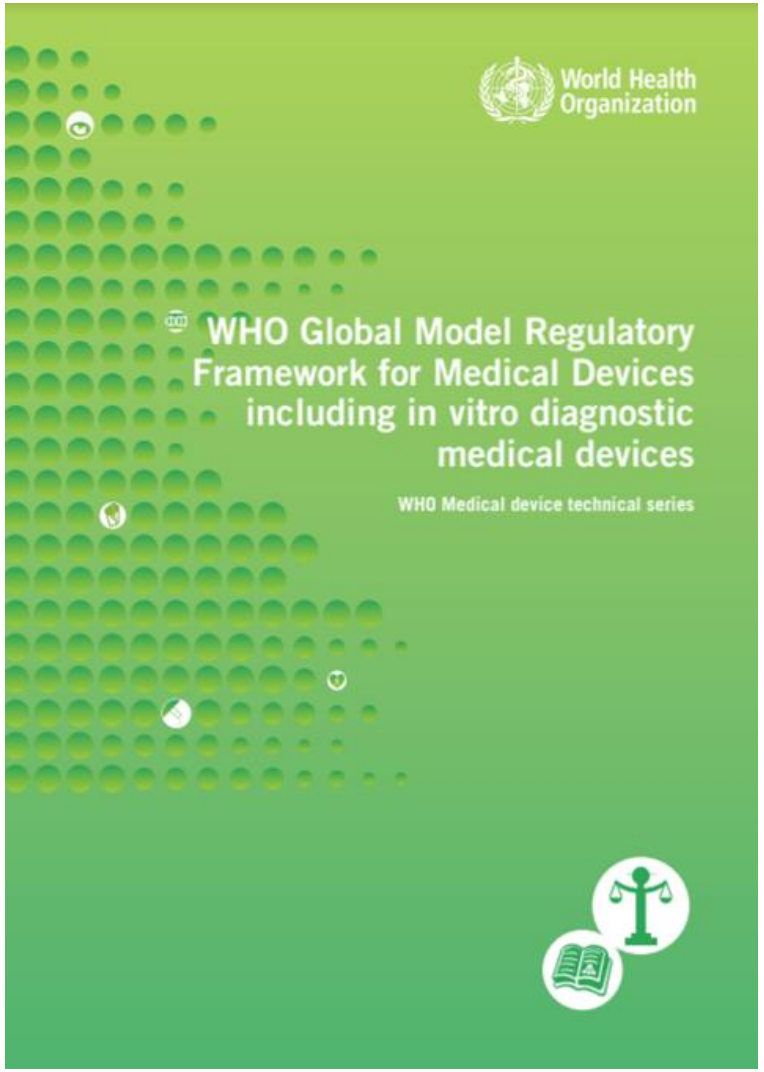
Why revise and update the GMRF



https://www.who.int/publications/i/item/9789241512350

- ✓ The WHO Global Model Regulatory Framework for Medical Devices including IVDs (GMRF) was published in 2017, developed in 2015-2016.
- ✓ Rapidly changing field, technologies are advancing in their nature and complexity e.g., Software as a medical device.
- ✓ Update of guidance such as post-market surveillance and market surveillance, Good Reliance Practice, Good Regulatory Practice and discussions during integration of medical devices indicators into the Global Benchmarking Tool.
- ✓ Experience with implementation including challenges experienced by regulators during the COVID-19 pandemic which clearly demonstrates the importance of safe, reliable, and appropriate quality medical devices including IVDs.
- ✓ Experience in the use of the GMRF teaches that countries would benefit more from a more expanded guidance.

Guidance document for regulating medical devices including IVDs

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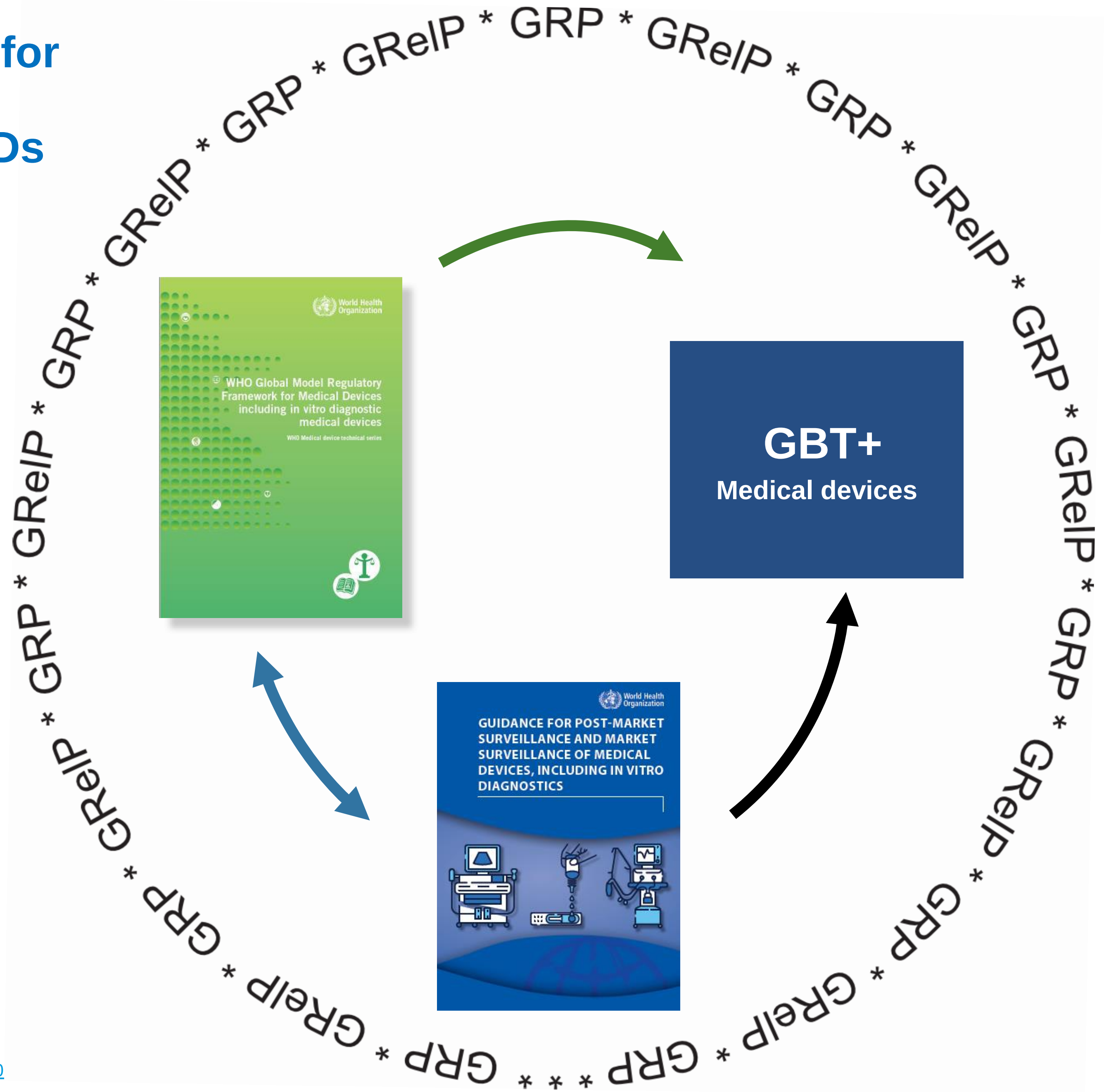

GMRF https://www.who.int/publications/i/item/9789241512350
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GBT+ https://www.who.int/tools/global-benchmarking-tools/evaluation-of-national-regulatory-systems-of-medical-devices-in-vitro-diagnostics
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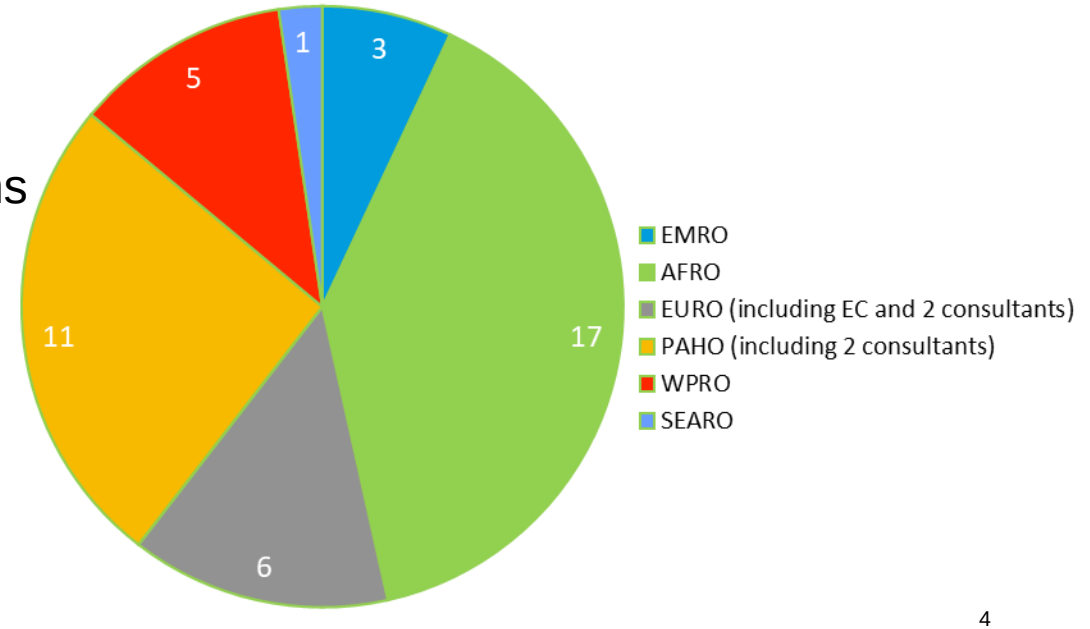
GMRF Working group and experts

GMRF Working group: 47 countries/jurisdictions, entities and consultants/experts

- Regulators on medical devices from NRAs
- International harmonization initiatives:
  - IMDRF (International Medical Device Regulators Forum)
  - GHWP (Global Harmonization Working Party)
  - AMDF (African Medical Devices Forum)
  - West African Health Organization (WAHO)

Experts on specific topics from NRAs, consultants and institutions



Process of revision of the GMRF

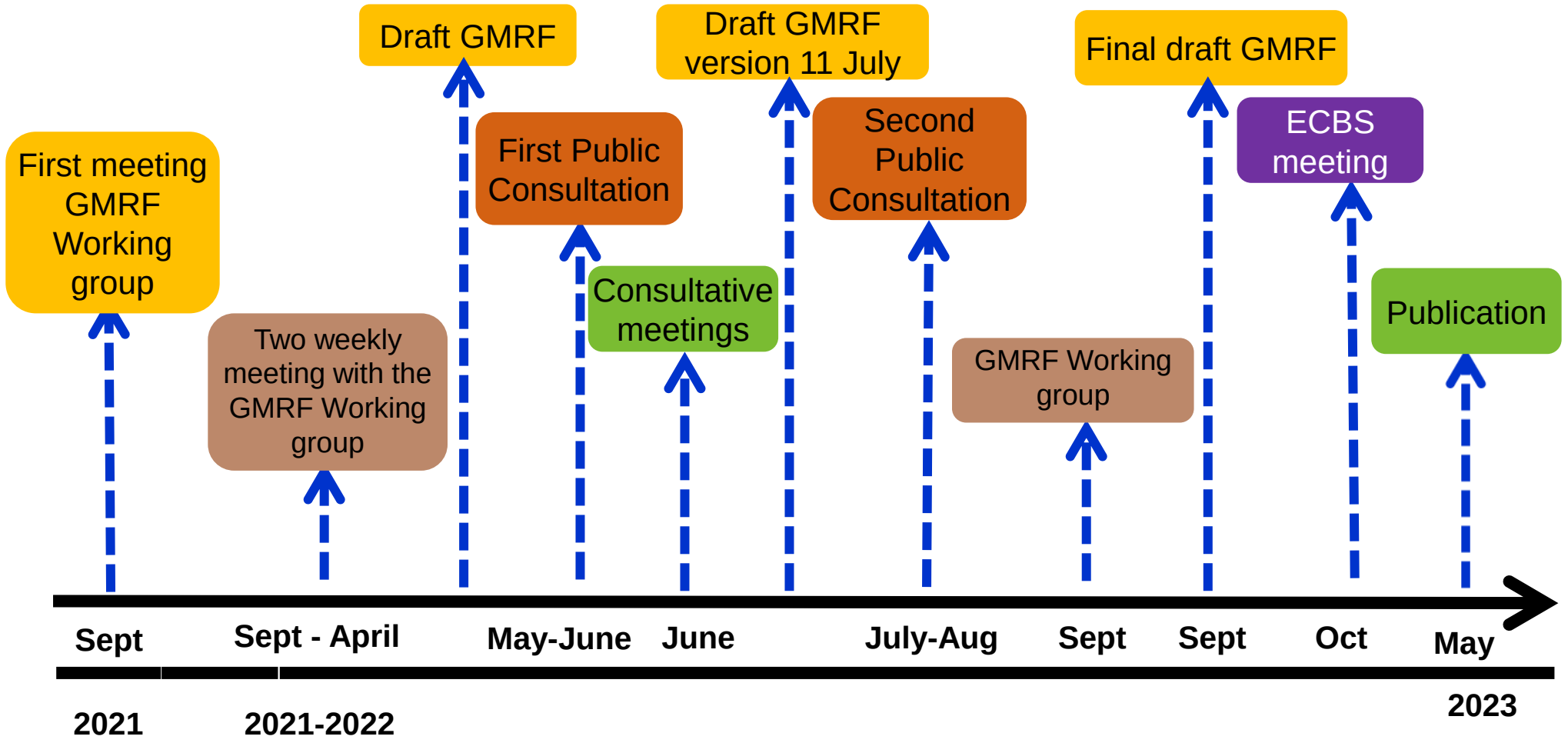


Table of contents

Expanded and new topics (I)

Chapter 2 Definition, classification, essential principles, and conformity assessment of medical devices

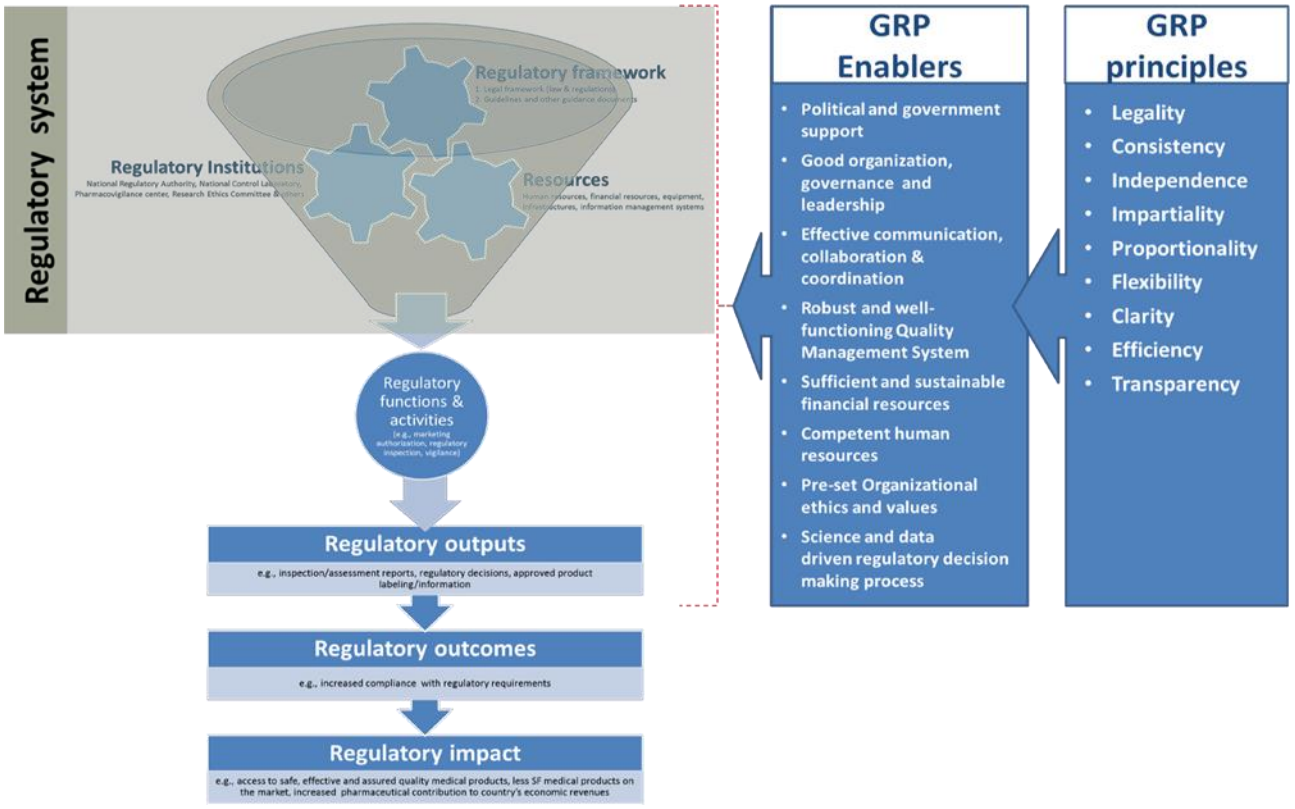
- Companion diagnostics: expanded and added in section 6.
- Alignment of definitions with updated IMDRF definitions e.g. medical device definition, adverse event.

Expanded and new topics (II)

Chapter 3 Enabling conditions for effective regulation of medical devices including IVDs

- Good regulatory practice: concept more explicit throughout the GMRF
- Good reliance practice: moved from Chapter 4; more explicit throughout the GMRF

Good regulatory practice: Chapter 3.2- 3.7



Elements of Good regulatory practice: Chapter 3 and Chapter 7

Legal requirements

Funding the regulatory authority

Stakeholder involvement

Conflict of interest and impartiality

Regulatory competencies and resources (human resources)

Implementation and monitoring plan

https://apps.who.int/iris/bitstream/handle/10665/340323/9789240020900-eng.pdf

WHO Good Reliance Practices – Key concepts

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Recognition (vs. reliance): more formalized approach to reliance, i.e. recognizes the decisions of another regulatory authority, system or institution, with no additional assessment. Usually requires formal and binding legal provisions.

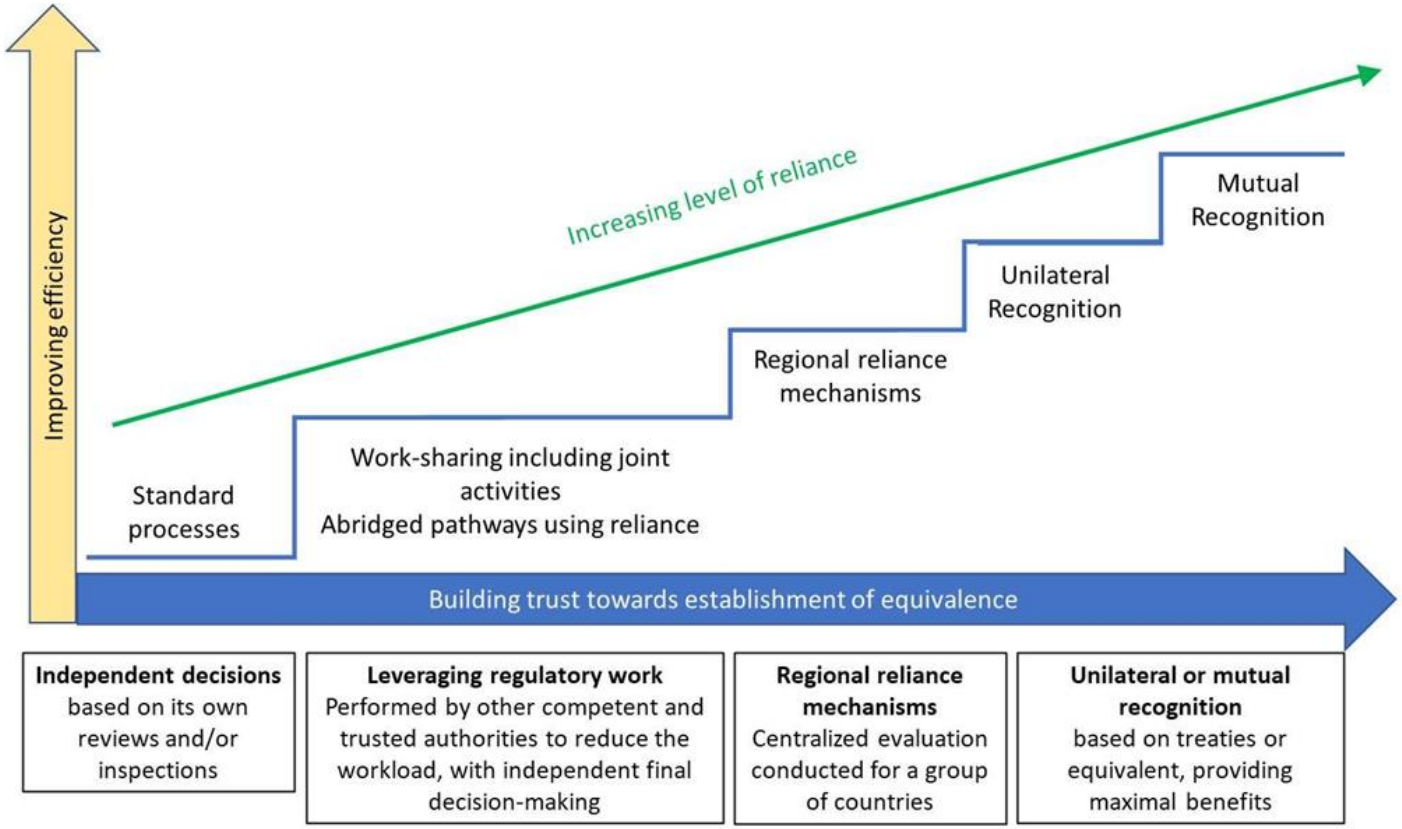
Unilateral vs. mutual: unilaterally/without reciprocity or mutual recognition based on binding mutual agreements or treaties.

Life cycle approach: to apply across the full life cycle of medical products and all regulatory functions (e.g. important for vigilance and post-authorization activities).

Risk-based approach: NRA to define own strategy (e.g. based on type and source of products evaluated, level of resources and expertise available, public health needs and priorities of the country, and opportunities for reliance) .

Regional reliance mechanisms: assessment for medical products can be conducted centrally based on a regional regulatory system for a group of countries (binding or not).

Key concepts of reliance: Chapter 3.9



Examples of reliance

CRP

WHO EUL

MDSAP

THAI FDA and HAS Singapore

https://apps.who.int/iris/bitstream/handle/10665/340323/9789240020900-eng.pdf

Expanded and new topics

Chapter 4 Establishing a stepwise approach to regulating medical devices

- Local production: policy, national strategy to support local manufacturers and no double standards with foreign manufacturers.
- Regulatory testing: no routine testing pre-market. Keep lot verification.

Local production: Chapter 4.3.3.4

- Can contribute to better access
- Technology transfer needed
- Adopt international standards
- Impartial technical support to manufacturers
- Consistency of requirements
- Timely market authorizations
- Regional initiatives for reliance and recognition

Regulatory testing: Chapter 4.3.3.5

- No routine testing pre-market
- Manufacturer is responsible
- Testing may be justified in case of
  - ✓ suspected products such as SF
  - ✓ adverse event
  - ✓ post-market on risk based plan
  - ✓ lot verification
  - ✓ law enforcement

Expanded and new topics

Chapter 5 Regulatory pathways

- Regulatory pathway according to risk class: routine assessment and renewal period.
- Regulatory pathway based on reliance: applying reliance routinely.
- Regulatory pathway for emergency use authorization or derogation: preparedness and importance of reliance.
- Regulatory pathway for combination products: the need for a single regulatory pathway.
- Regulatory pathway for borderline products.
- Regulatory pathway for donated medical devices.

Regulatory pathway according to risk class: Chapter 5.1

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Regulatory pathway :according to risk class: Routine assessment

	A	B	C	D
Preparatory stage: collecting evidence of the safety and performance of the medical device	Device classification is determined according to the classification rules.			
	Registration of establishment (manufacturer, authorized representative and/or importer or distributor)*			
	Preparation and maintenance of the technical documentation according to requirements			
	Evidence of effective implementation of QMS and declaration of conformity	ISO 13485 certificate or inspection/audit from an accredited organization is required.		
Market authorization procedure	Listing submission to the regulatory authority	Submission of technical documentation/dossier to the Authority/CAB (including clinical evidence and evaluation)		
	Usually**, no review is required. Only notification to the regulatory authority is required.	Usually, administrative review only	Technical review	In-depth technical review
		Review is conducted, including a technical and administrative review. Novel and high-risk products may also be subject to an Expert Panel consultation.		
				In-depth review of clinical evidence (may require clinical investigation)
Approval	NRA lists the medical device.	NRA issues market authorization when all requirements are fulfilled or sends notice of deficiencies or rejection.		

* Overseas manufacturer shall assign a local authorized representative.
** Except for Class A devices that are sterile or have a measuring function: regulatory audit can be considered.

Regulatory pathway :according to risk class: Reliance

	A	B	C	D
Preparatory stage: collecting evidence of the safety and performance of the medical device	Device classification is determined according to the classification rules.			
	Registration of establishment (manufacturer, authorized representative and/or importer or distributor)*			
	The applicant assesses sameness** of the products, submits application and other relevant documentation based on requirements of the reference institution.			
	Evidence for an effective QMS implementation and declaration of conformity	Upon manufacturer consent, reference regulatory authority or other trusted institution exchange assessment reports with the relying NRA.		
Market authorization	Usually***, no review is required. Only notification to the regulatory authority is required.	Relying NRA conducts abbreviated assessment of the shared reports based on national requirements.		
Approval	NRA lists the medical device.	NRA issues market authorization when all requirements are fulfilled or sends notice of deficiencies or rejection.		

* Overseas manufacturer shall assign an authorized representative.
** For sameness check at a minimum name of the product, regulatory version, product code, design, labelling and packaging, intended use, IFU, manufacturing site and QMS certificate ISO 13485. Reference: Good Regulatory Practice.
*** Except for Class A devices that are sterile or have a measuring function: regulatory audit can be considered.

Expanded and new topics

Chapter 6 Additional topics

- Reprocessing of single-use medical devices: only in dire and exceptional situations.
- Software as a Medical Device (SaMD) and Software in a medical device (SiMD): framework for assessing SaMD.
- Companion diagnostics: framework for specific type of IVD.
- Collaborative Registration Procedure: specific form of work sharing and reliance.
- Emergency use listing: practice of EUL by WHO as an example for WHO Member states.

Chapter 7 Implementation

- Involving stakeholders in the regulatory process: important part of GRP.
- Developing a road map: systematic planning and follow up.
- Regulatory capacity building: important part of GRP.

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Thank you