Medical Device Regulatory Convergence Project (MDRC)
Good Regulatory Practices & Technical Competencies
South African Health Products Regulatory Authority (SAPHRA) & Regulated Sector

Good Regulatory Practice and Global Model Regulatory Framework for medical devices including IVDs (GMRF) – revised

14 November 2023

Presenter's Name: Agnes Sitta Kijo
Title: Technical Officer, WHO HQ

Outline

World Health Organization

- Good Regulatory Practices Principles
- Global Model Regulatory Framework for medical devices including in vitro diagnostics

Access to medical products – a global challenge

Good health is impossible without access to medical products

Universal Health Coverage depends on the availability of quality assured affordable health technologies in sufficient quantities

Reasons for limited/insufficient access are numerous

- **World Health Assembly Resolution 67.20 in 2014**
  - ✓ recognized the importance of strong regulatory systems to a well-functioning healthcare system and the attainment of health-related United Nations Sustainable Development Goals and Universal Health Coverage.

Main challenges:

- Lack of national policy and long-term strategy
- Unclear vision and mission (what should be done and what should not)
- Insufficient commitment and engagement from political level (access and price vs. quality)
- Inadequate resources to establish and sustain regulatory oversight
- **Non implementation of Regulatory Practices**

Objectives of the WHO regulatory system strengthening programme

1

- build regulatory capacity in Member States consistent with good regulatory practices

2

- promote regulatory cooperation, convergence and transparency through networking, work-sharing and reliance

- **WHA Resolution 67.20 in 2014**
  - ✓ recognized the importance of strong regulatory systems to a well-functioning healthcare system and the attainment of health-related SDGs and UHC.

WHO GRP Guideline

Purpose

- High-level principles of GRP
- Serve as benchmarks
- Guide Member States in **prioritizing** their regulatory activities according to; resources, national goals, public health policies, medical products policies and the medical product environment
- Complemented by related guidance on:
  a) Good governance practices
  b) Good reliance practices
  c) Good review practices and
  d) Quality management systems for NRAs
  e) Global Model Regulatory Framework for medical devices incl IVDs

WHO Good regulatory practices in the regulation of medical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations: Fifty-fifth report. Technical Report Series, No. 1033, Annex 11; 2021.

Link: https://www.who.int/publications/i/item/55th-report-of-the-who-expert-committee-on-specifications-for-pharmaceutical-preparations

WHO GRP Guideline

Scope

- Principles and considerations in the development and use of the regulatory instruments
- Relevant to all regulatory authorities, irrespective of their resources, maturity or regulatory model.
- High-level GRP principles are equally applicable to supranational (e.g. regional), national and subnational regulatory systems

Audiences:
Institutions and policy-makers responsible for formulating health policies, laws, regulations and guidelines;
Regulatory networks and parties affected by or otherwise interested in regulatory frameworks, such as industry or other developers of medical products.

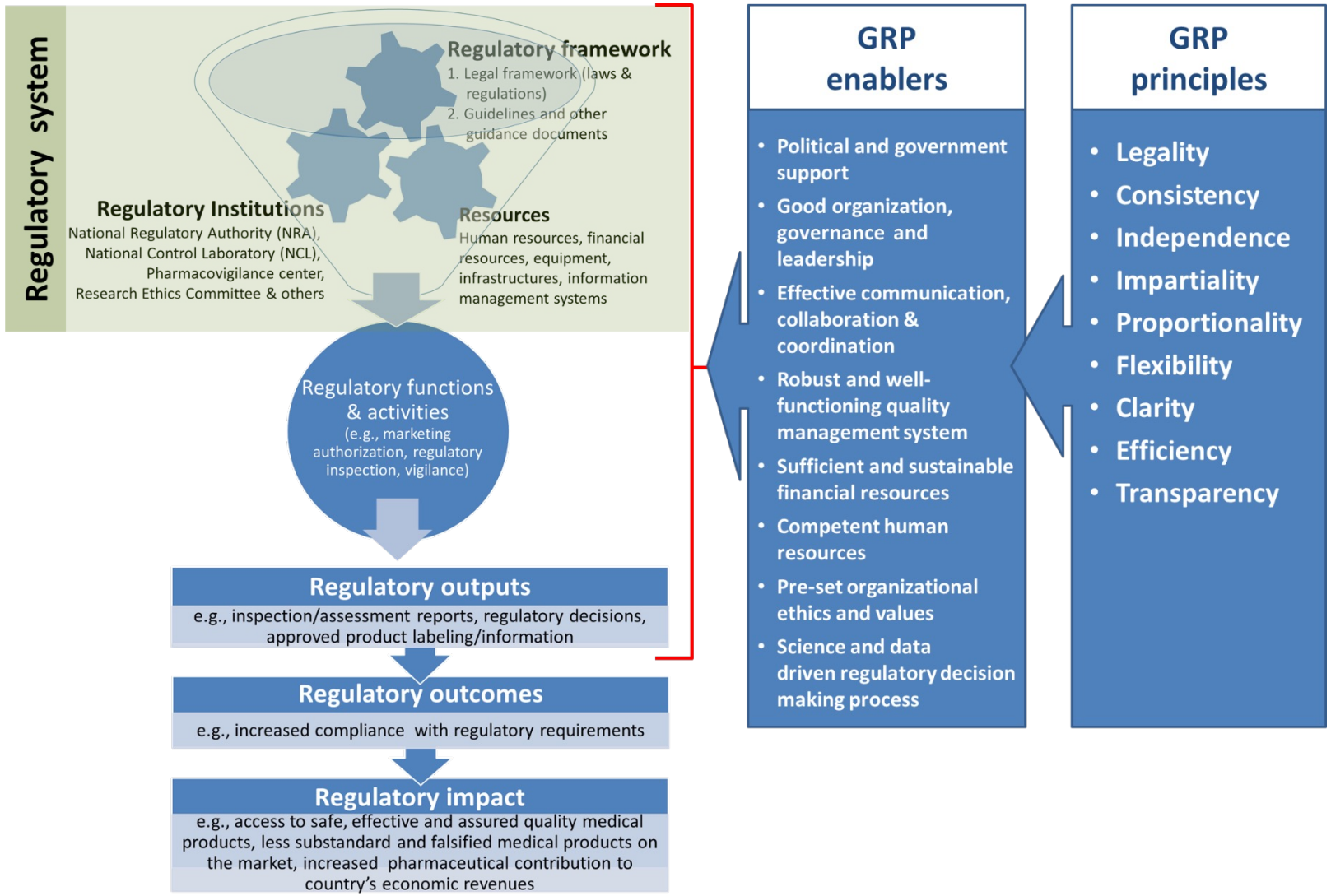
WHO GRP Guideline

Objectives

- Ensure sound and effective regulation of medical products
- Higher-quality regulation, better regulatory decision-making and compliance
- More efficient regulatory systems and better public health outcomes
- Up to date regulatory systems
- Promote trust among regulatory authorities and other stakeholders
- Facilitate international cooperation

The ultimate aim of GRP is to serve and protect public health and patients' interests, with respect for all applicable ethical principles

Principles and enablers of GRP and components of a regulatory system



Nine high-level GRP principles

World Health Organization

Legality	Consistency	Independence
Impartiality	Proportionality	Flexibility
Clarity	Efficiency	Transparency

GRP main principles

World Health Organization

Legality

Regulatory systems and the decisions that flow from them must have a sound legal basis

- Authority, scope and flexibility to safeguard and promote health
- Delegation of power and responsibilities
- support and empower international cooperation
- Possibility to review regulatory decisions and sanctions
- Scope and lines of authority of involved institutions
- Accountable

Impartiality

All regulated parties should be treated equitably, fairly and free from bias

- No conflicts of interest or unfounded bias
- Impartial operations
- No engagement in the activities that must be regulated
- Science and evidence-based decision-making

Clarity

Regulatory requirements should be accessible to and understood by users

- Understandable language
- Terminology consistent with international norms
- Consultation, education and training
- Proper interpretation of regulations
- Clear process and basis for taking regulatory decisions and enforcement

GRP main principles

Consistency

Regulatory oversight of medical products should be consistent with existing government policies and legislation and be applied in a consistent and predictable manner

- Fit coherently into the national legal and policy framework
- Complementary and not conflicting
- Consistent implementation and enforcement

Proportionality

Regulatory oversight and regulatory decisions should be proportional to the risk and to the regulator's capacity to implement and enforce the decisions.

- Adequate to achieve the objectives without being excessive
- Proportionate to the risk
- Do not exceed the national capacity to implement and enforce
- Benefit–risk evaluation and continuous monitoring

Efficiency

Regulatory systems should achieve the intended results within the required time and
at reasonable effort and cost

- Achieve the public health goals
- Effective use of resources and information from other authorities
- Most efficient and least burdensome means of achieving regulatory purposes
- Evaluation of the total burden and resources
- Explore ways of improving efficiency
- Alignment of regulatory requirements
- Contribution of regulated entities
- Performance-based indicators

GRP main principles

World Health Organization

Independence

Institutions responsible for regulation of medical products should be independent

- Operate in an independent and authoritative manner
- Discharging its duties independently from politicians, government and regulated entities
- Improper and undue influence of stakeholders on Regulatory activities and decisions
- Appropriate and clear funding
- The independence of the leadership

Flexibility

Regulatory oversight should be flexible to respond to a changing environment and unforeseen circumstances.

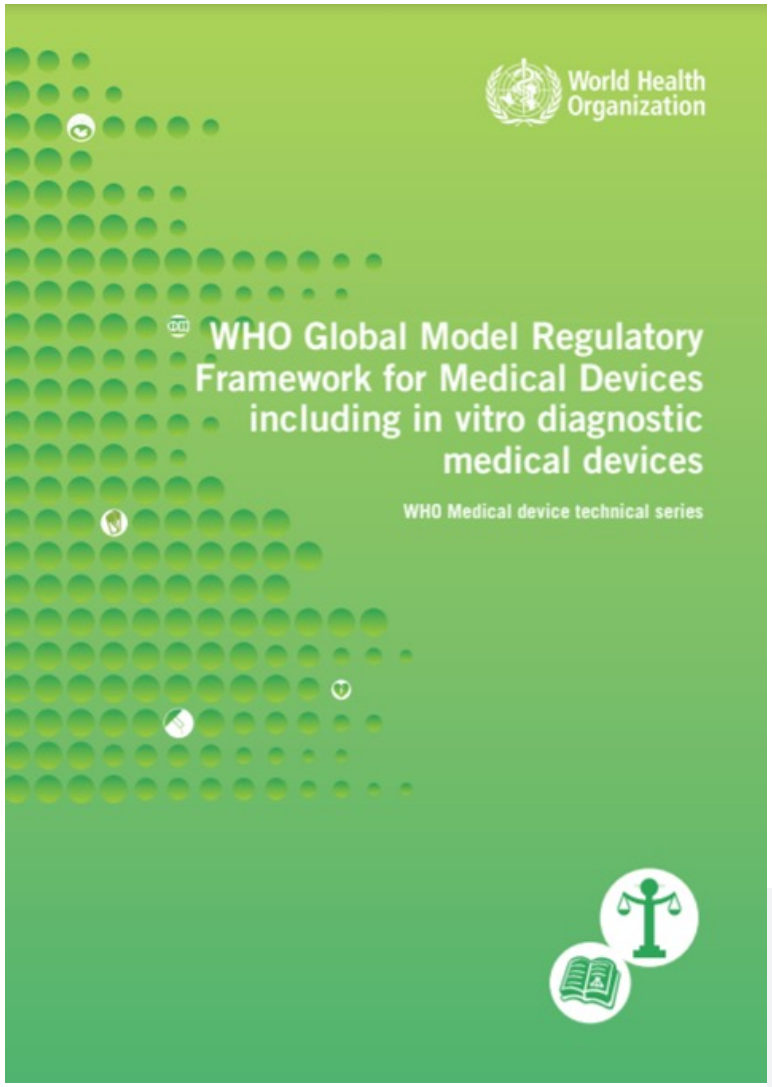
- Sufficient flexibility to reflect or respond to changes
- Timely responses to urgent situations
- Performance based
- Alternative approaches
- Flexibility for applying good judgement

Transparency

Regulatory systems should be transparent; requirements and decisions should be made known, and input should be sought on regulatory proposals.

- Investment and a culture of openness, supported by government policy, commitment and action
- Stakeholders should be consulted
- Access to regulations and decisions
- disclosure should be consistent with national laws on access to information.

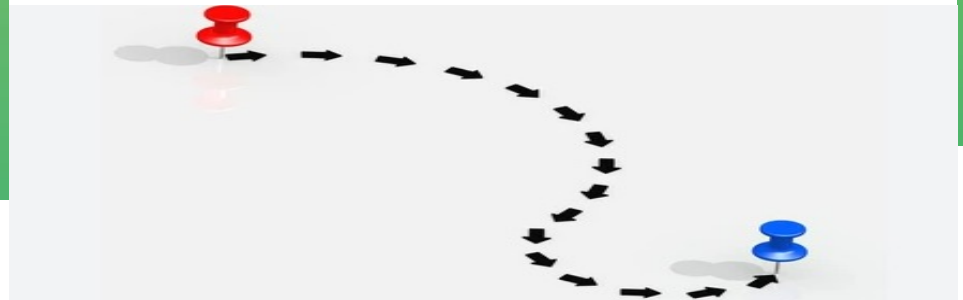
Why revise and update the GMRF



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

Published first in 2017

- *Revised in 2022*
- *Triggers for revision: rapidly changing field, updated guidance documents, Integration of sub indicators in the GBT plus MDs tool, experience with implementation, COVID 19 pandemic.*



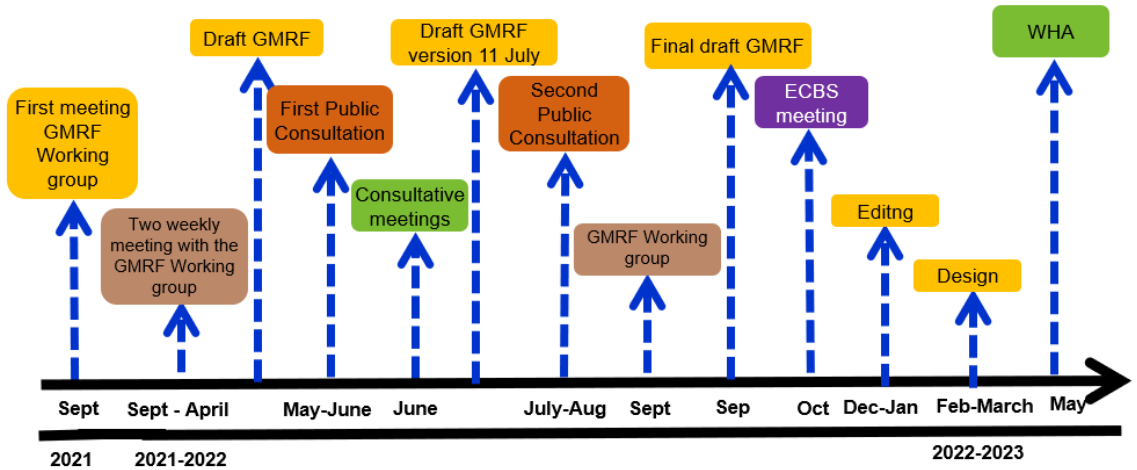
WHO Expert Committee on Biological Standardization: seventy-sixth report (WHO Technical Report Series, No. 1045)

Revision of the Global Model Regulatory Framework for medical devices

New Table of contents

- Chapter 1-3. Introduction, Purpose and scope and Terminology
- Chapter 4. Definition, classification, essential principles, and conformity assessment of medical devices
- Chapter 5. Enabling conditions for effective regulation of medical devices including IVDs
- Chapter 6. Establishing a stepwise approach to regulating medical devices
- Chapter 7. Regulatory pathways *New*
- Chapter 8. Additional topics
- Chapter 9. Implementation *New*

WHO Model Regulatory Framework for medical devices including In vitro diagnostics was successfully revised and endorsed during the 76th meeting of the WHO Expert Committee on Biological Standardization (ECBS) which was held from 24 to 28 October 2022 – Final editing and design of the revised Model and publishing during the WHA in May 2023.



* ***Chapters have been expanded from 5 chapters in the 2017 version to 9 chapters in the revised version***

WHO Expert Committee on Biological Standardization: seventy-sixth report (WHO Technical Report Series, No. 1045)

Expanded and new topics

Chapter 4 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.
- Classification: allocate resources and impose controls proportionate to the potential for harm associated with medical devices.

Chapter 5 Enabling conditions for effective regulation of medical devices including IVDs

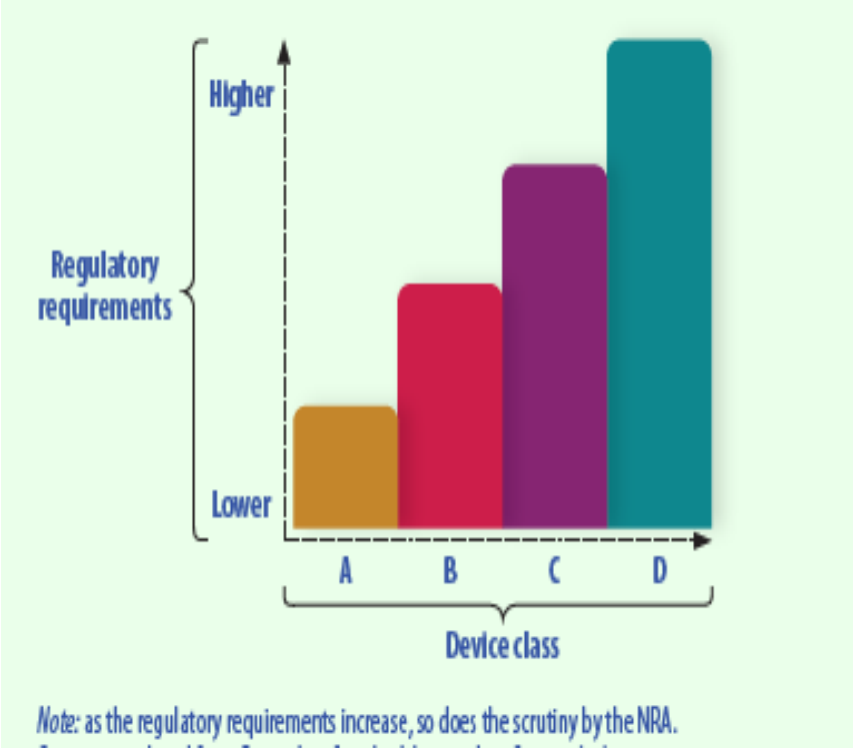
- Good regulatory practice: concept more explicit throughout the GMRF
- Good reliance practice: moved from Chapter 4; more explicit throughout the GMRF

Chapter 4.2 Medical devices classification and classification rules

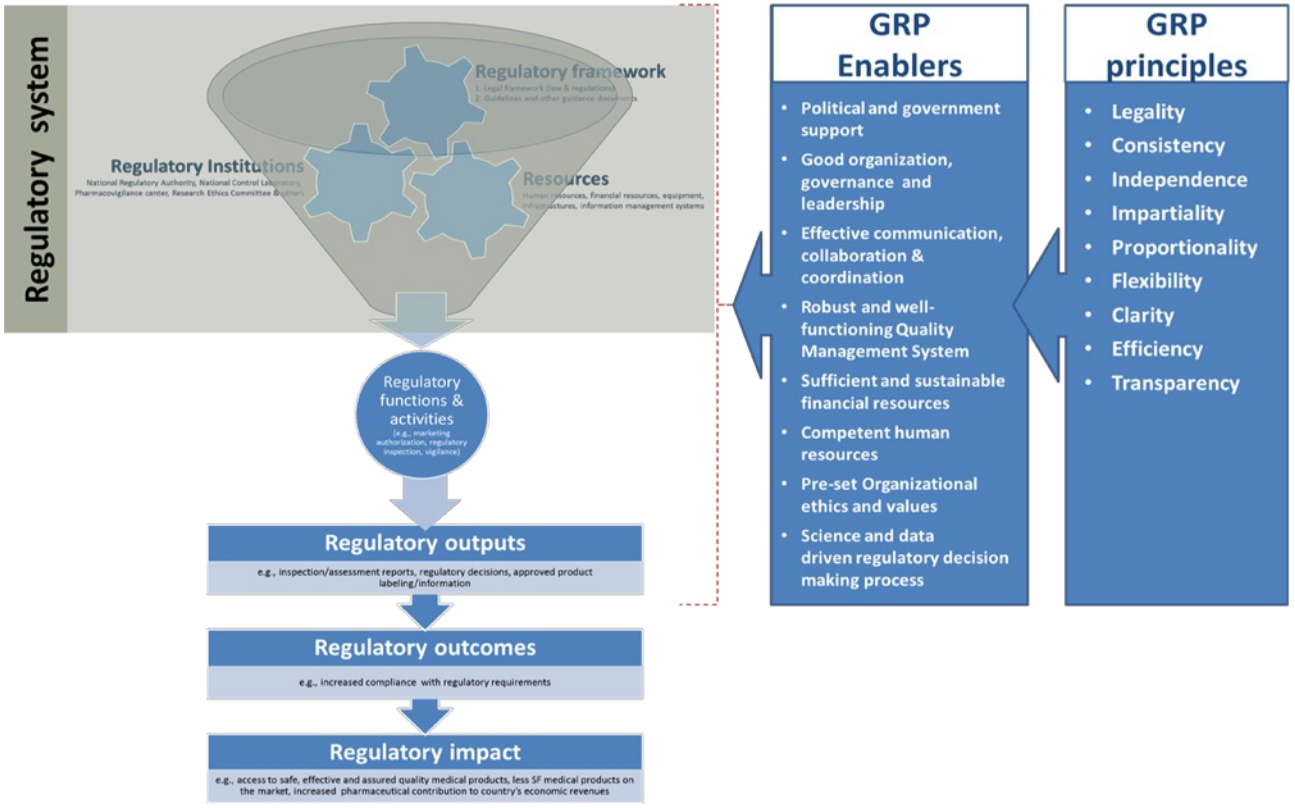
Classification system

Regulatory controls

- ✓ Four classes A, B, C and D
- ✓ Set of risk-based classification rules
- ✓ Specifying separately the different conformity assessment procedures that should apply to each group of devices



Good regulatory practice: Chapter 3.2- 3.7



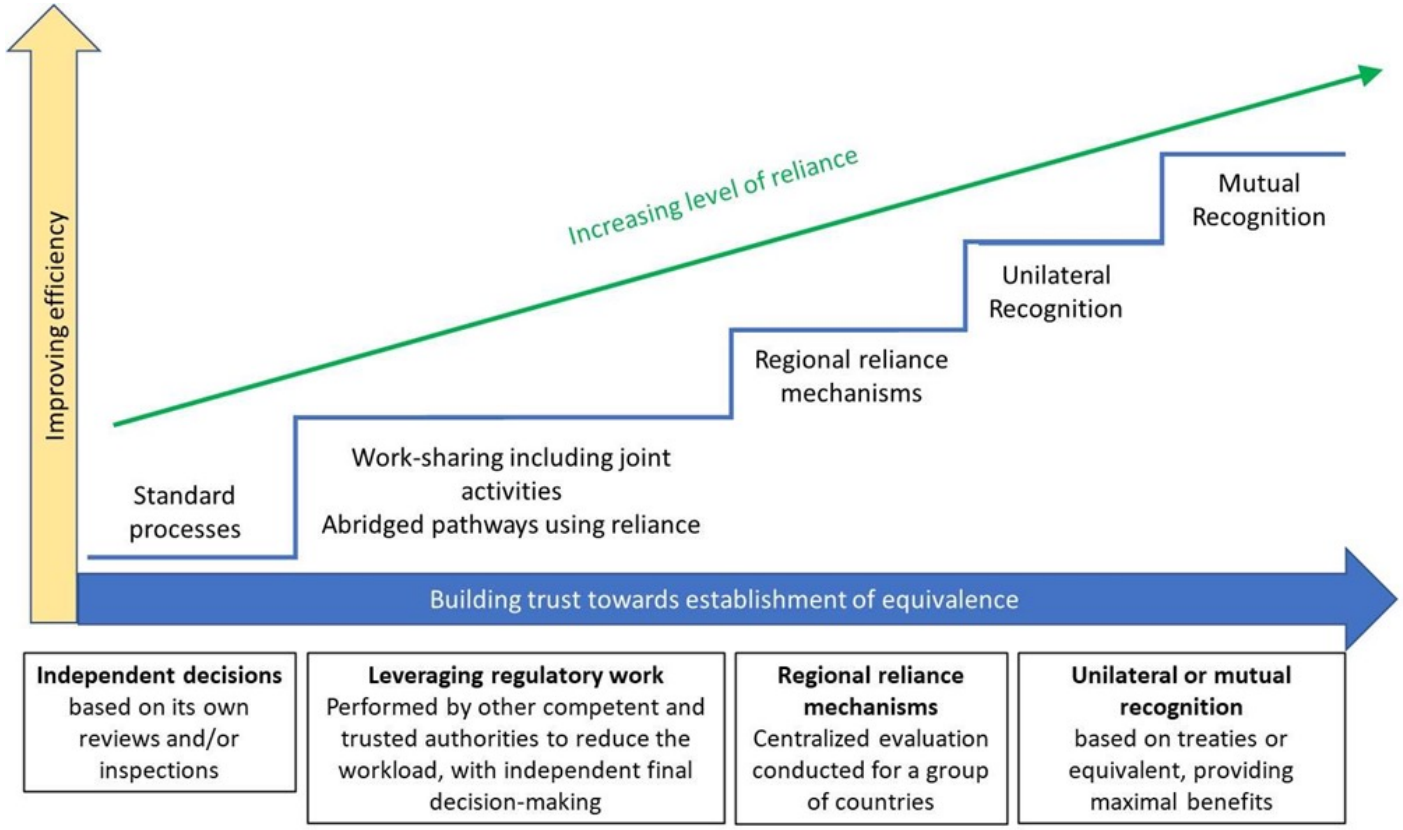
https://apps.who.int/iris/bitstream/handle/10665/340323/9789240020900-eng.pdf

Elements of Good regulatory practice:

Chapter 3 and Chapter 7

- Gap analysis
- Stakeholder involvement – Good organization, governance and leadership
- Conflict of interest – Impartiality
- Regulatory competencies – science and data driven regulatory decision making process/ competent human resources
- Implementation and monitoring plan

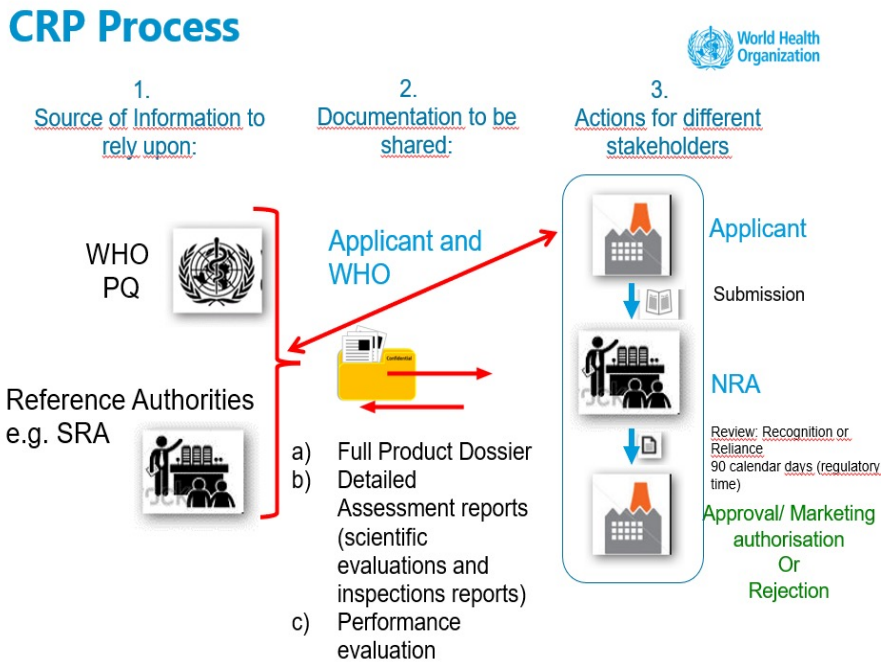
Key concepts of reliance: Chapter 3.9



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

Examples of reliance

- Collaborative Registration Procedure (CRP)



Expanded and new topics

Chapter 6 Establishing a stepwise approach to regulating medical devices .....cont

Local production: Chapter 6.3.3.4) policy, national strategy to support local manufacturers and no double standards with foreign manufacturers.

Regulatory testing: Chapter 6.3.3.5

- No routine testing pre-market
- Manufacturer is responsible
- Testing may be justified in case of
  - ✓ suspected products such as SF
  - ✓ adverse event
  - ✓ post-market according to risk based testing 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

World Health Organization

	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.

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.

World Health Organization

www.who.int/medicines

Thank you for your attention!

World Health Organization