WHO Global Model Regulatory Framework for Medical Devices and IVDs

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Public confidence in medical devices including IVDs requires effective and efficient regulation built upon a sound legal and policy foundation, as well as GRP”

-World Health Organization Global Model Regulatory Framework for Medical Devices & IVDs

The Global Model Regulatory Framework

The GMRF includes three main sections:

Legal & Resource Framework

Setting up law and regulation & ensuring appropriate resources, tools and funding to sustain an effective and sustainable regulatory system.

Maturity Model

A maturity model to help regulatory authorities determine what to implement as resources can accommodate.

International Best Practice

What regulation should look like - based almost completely on international best practice established by the IMDRF.

This approach allows regulation to develop over time in a **risk-based** fashion, according to the **least burdensome** methods while maintaining focus and limited resources on areas with the highest risk to **patient safety** - all while developing along the same continuum - to arrive at the same **north star - IMDRF**.

The GMRF Acknowledges Implementing & Consistently Following GRPs is Critical to an Effective, Efficient Regulatory System

Scope of Oversight

The GMRF isn't just about regulations for the oversight of MD/IVDs - it includes a great deal about GRPs their necessity to develop a sound legal framework.

Inextricable Link

The GMRF recognizes that risk-based, global convergent regulation cannot exist independently of GRPs. They are inextricably linked that is why GRPs are included in the beginning of the section on Legal Framework - section 5.

Compliance & Trade

Without consistently following GRPs, regulation isn't risk-based or globally convergent—nor in full compliance with WTO trade obligations.

Roadmap For Sustained Success

"GRPs are critical to efficient performance of a regulatory system and, consequently, to the public's confidence in the system, while also setting clear requirements for regulated entities." - WHO GRP, page 269.

Why are Good Regulatory Practices so important?

Promoting Public Health

GRP is the **quality control mechanism** for the development of regulations, ensuring on a continuous and systematic basis, that government rules are relevant, of the highest quality, cost-effective, internationally aligned and least economically restrictive.

Accelerated Access

GRPs accelerate access to safe and effective MD/IVDs by allowing manufacturers to follow a **predictable, transparent and repeatable** process to design, develop, and maintain products globally to the same high standard.

Global Harmonization

When applied, ensures technical regulations are not prepared, adopted or applied with a view to or with the effect of creating unnecessary obstacles to international trade. Therefore, technical regulations shall **not be more trade-restrictive than necessary to fulfil a legitimate objective.**

Solid GRP Foundations Lead to Effective Regulation

"The NRA should adhere to Good Regulatory Practices (GRP), including allowing public comments on proposals, assessing regulatory impacts, providing reasonable transition periods, and adopting proportionate, least-burdensome requirements"

Transparent & Consistent Framework: Laws and guidelines must be written for MD and IVDs specifically to avoid complexity and delays.See GBT+ tool

Gap Assessment: A thorough assessment should precede the implementation of new regulatory requirements.

Implementation Planning: NRA should publish clear plans including awareness, feedback loops, and reasonable transition periods.

Performance Tracking: Use performance-based indicators to track progress and report to the public and legislature.

The GMRF on Seeking Stakeholder Input

Stakeholder engagement benefits Rulemaking.

Transparency

Stakeholder consultation can increase the **transparency** of the rulemaking process because stakeholders have access to the process itself.

Experience & Knowledge

Enables policy-makers to make use of the **stakeholder's expertise and local insights** to improve outcomes.

Familiarity & Compliance

Striving for consensus can help increase social acceptance, contributing to **greater compliance** and reduced enforcement costs.

Stakeholder Education

Promotes education on rulemaking and provides an opportunity for stakeholders to increase their regulatory **knowledge**.

Legitimacy

Increases **legitimacy** and improves conflict management, serving as **proof of successful governance**.

Credibility & Cohesion

Establishes **trust** and **credibility** by creating better ways to communicate and collaborate with stakeholders.

A Tiered Regulatory Approach

Ensuring clarity, stability, and technical flexibility as international standards evolve.

Laws

Establish authority, scope, principles, powers, and core obligations.

Implementing Regulations

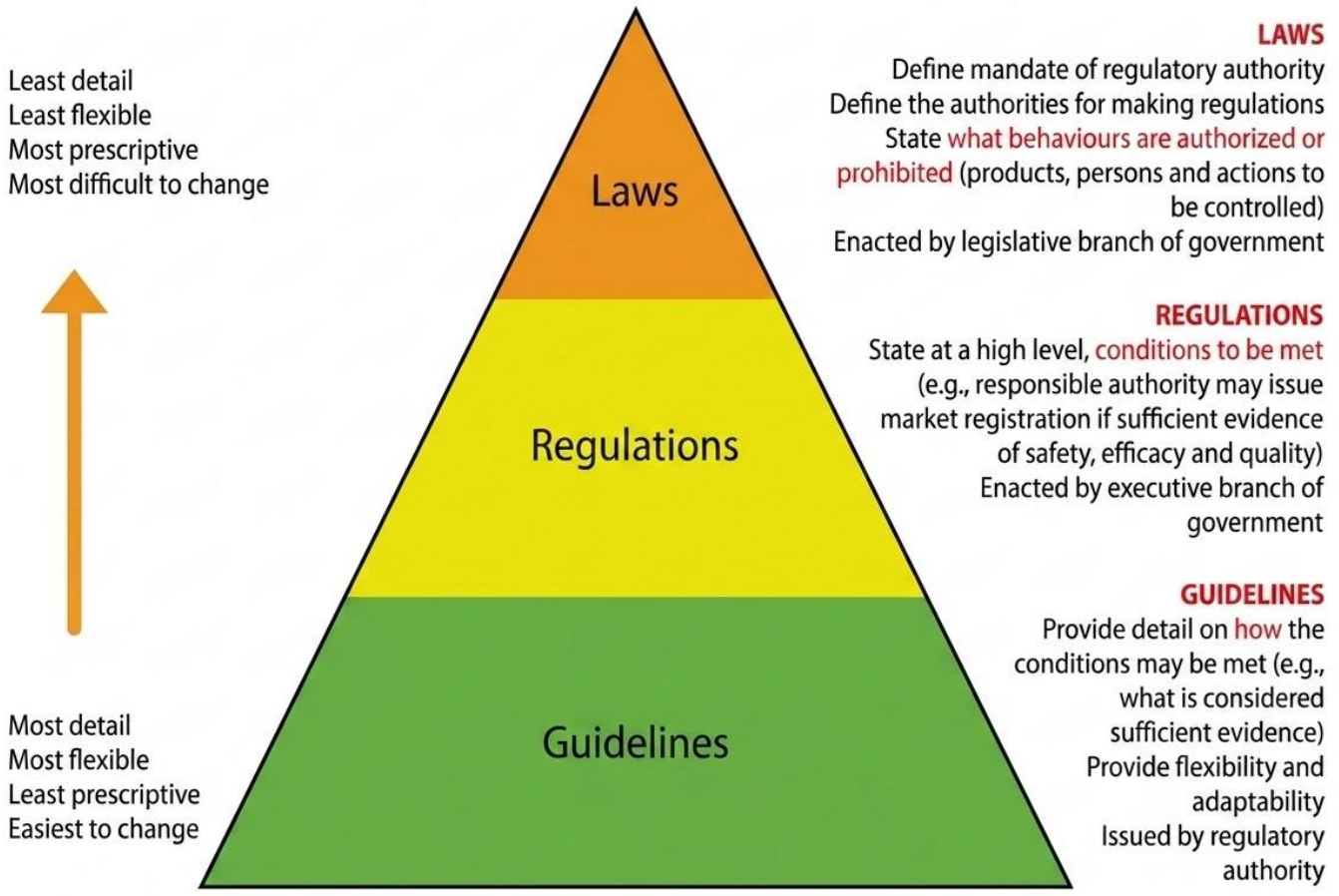
Define operational requirements: classification, conformity assessment, and postmarket controls.

Guidance

Explains how regulated parties can comply with requirements in practice.

Fig. 5.1

Architecture of a regulatory framework (4)



What does the GMRF Recommend to Include in the Legislative Framework for MD/IVDs?

Not an exhaustive list:

- Define the **products** within their **scope** & **entities** subject to regulation.
- Delineate the **responsibilities of the NRA**.
- Establish its **enforcement powers**.
- **Define the responsibilities** of manufacturers, authorized representatives, importers, exporters and distributors - these will differ.
- Provide scope for **enforcement discretion**.
- Authorize the NRA to implement the principles of **reliance and recognition**

- .Allow the NRA to **respond to public health emergencies** in an appropriate and timely manner.
- Accommodate a **reasonable transition** period when new regulatory requirements are established.
- Where regulatory authority is delegated to an independent administrative agency **require clear lines of political oversight and accountability**

GRP & tiered approach to law, regulation and guidance ensures:

- Adequate **tools and trained resources**
- Clear oversight, authorities, and responsibilities to **effectively and consistently perform duties**.
- Flexibility to **adopt international best practice** when it is published to avoid technical barriers to trade
- Ability for regulators to **keep pace with technology** and maintain oversight while **supporting timely patient access**

Transition: Maturity Model advanced in the Global Model Regulatory Framework

Maturity Model Risk-Based Regulatory Framework: Basic

The GMRF advances a **stepwise approach from basic-level to expanded-level** regulatory controls, with **basic controls forming a critical foundation for success**.

Foundation for Growth

Basic-level controls form the foundation of the expanded-level regulatory controls.

Without effective implementation, expanded elements will be of limited value and difficult to manage.

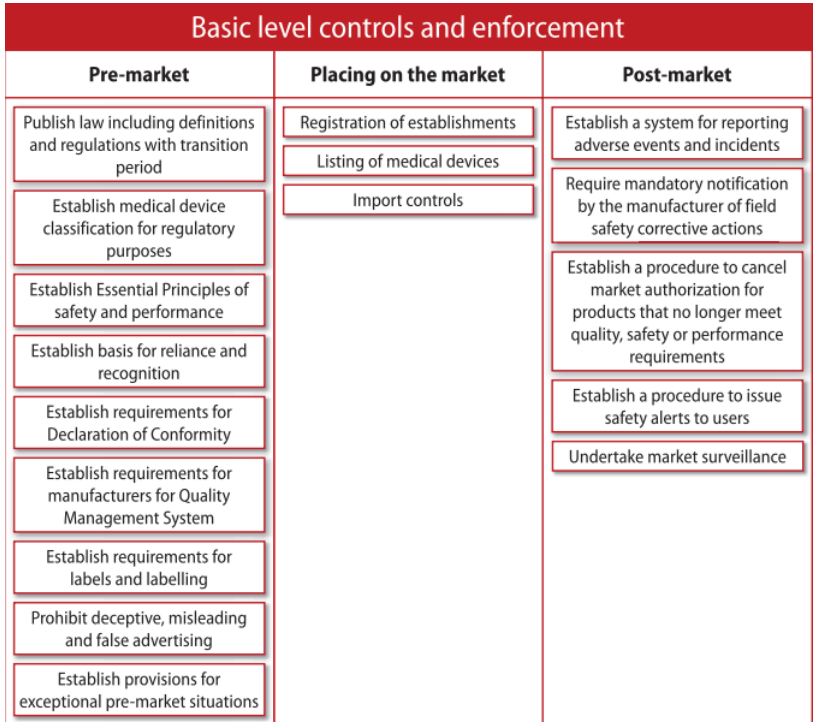
Continuity of Reliance

Implementation of **expanded-level** pre-market controls **does not mean a regulator should discontinue existing reliance practices.**

— Source: GMRF, page 223

Harmonization

GMRF **encourages countries to adopt internationally harmonized technical guidance** to promote global convergence and harmonization.



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Maturity Model Risk-Based Regulatory Framework: Expanded

Once the basic-level regulatory controls have been implemented effectively and efficiently, the regulatory authority may consider implementing more advanced controls.

(a) Legal Basis

The law should provide the **legal basis** for such expanded-level regulatory controls.

(b) Effective Enforcement

The regulatory authority **must have effectively enforced** the basic-level regulatory controls.

(c) Resources

Additional resources (financing and technical expertise) **must be available** for this purpose.

Implementation Principle

Enacting and enforcing a limited set of requirements is preferable to attempting a larger range without proper enforcement.

Source: GMRF pages 235-36

Expanded level and enforcement		
Pre-market	**Placing on the market**	**Post-market**
Create oversight of clinical investigation	Perform in-country quality management systems audits	Establish processes for review of manufacturer's post-market surveillance
Appoint and have oversight of conformity assessment bodies (CAB)	Perform review of submissions for compliance with Essential Principles	Require mandatory and timely reporting of adverse events and incidents by manufacturers
Adopt standards		Inspection of registered establishments
Adopt medical device nomenclatura system		Provide for testing laboratories
Control advertising and promotion		

Transition: Key Regulatory Topics in Global Model Regulatory Framework

MD & IVD Risk Classification

Core Principles

Regulatory controls should be **proportional to the level of risk** associated with a MD/IVD. The level of regulatory control should increase with increasing degree of risk, taking account of the benefits off/ered by use of the device. At the same time, the imposition of regulatory controls should not place an unnecessary burden on regulators or manufacturers.[1]

Medical Devices (MD)

WHO GMRF & IMDRF explain that medical devices are classified based on:

- The **manufacturer's intended purpose** and design factors, including the duration of contact (transient, short-term, or long-term), the degree of invasiveness, whether the device delivers medicinal products or energy, and whether it has local versus systemic biological effects

GMRF Page 196, Principles of Medical Devices Classification, GHTF/SG1/N15:2006

In Vitro Diagnostics (IVD).

IVDs do not usually come into direct contact with the patient, as such, their risk is determined by the impact of an inaccurate test result. Classification based on the:

- Intended use and indications for use **as specified by the manufacturer**;
- Technical, scientific or medical expertise of the intended user;
- Importance of the information to the diagnosis (sole determinant or one of several),

GMRF Page 205; Principles of In Vitro Diagnostic (IVD) Medical Devices Classification, IMDRF/IVD WG/N64 , 2021.

1. Principles of In Vitro Diagnostic (IVD) Medical Devices Classification, IMDRF/IVD WG/N64FINAL:2021 (formerly GHTF/SG1/N045:2008), page 9

Classification Continued

Core Framework

GMRF and IMDRF separate medical devices and IVDs into groups or classes A, B, C and D.

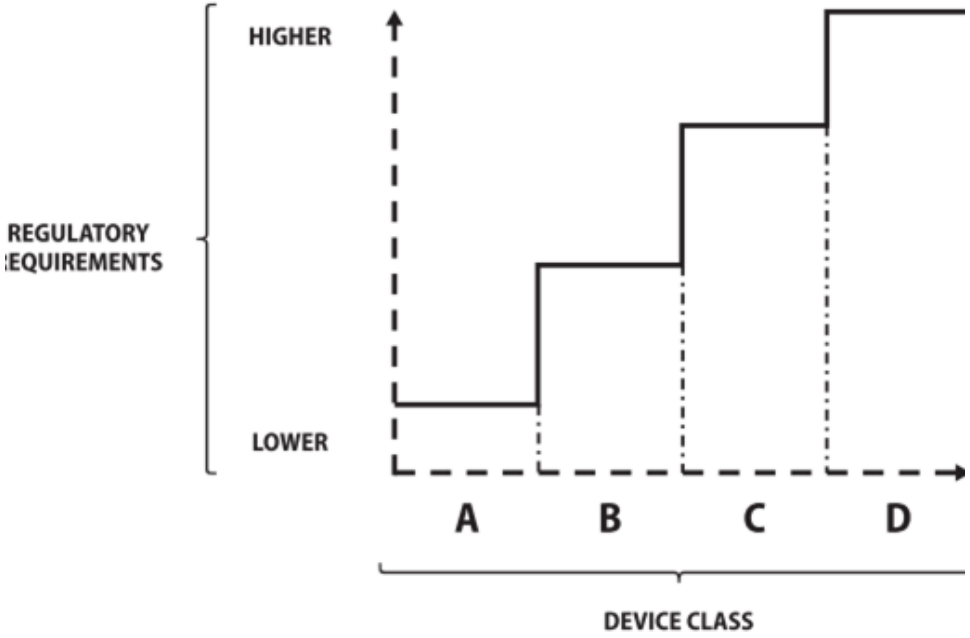
GMRF page 198

Dynamic Reclassification

Reclassification is appropriate as experience and knowledge increase.

- **To Higher Risk:** If scientific evidence shows existing controls are insufficient for safety and performance.
- **To Lower Risk:** If less rigorous controls provide reasonable assurance of safety and performance.

GMRF page 198



The manufacturer determines the classification, which is then reviewed by the regulator.

Key Takeaway

Flexibility and following Good Regulatory Practices (GRP) allow changes based on sound scientific evidence.

Regulatory Controls Increase with Product Risk

Classification Recommendations — Framework from GMRF and IMDRF based on risk levels.

Medical Devices (MD)

Examples of Risks by Class:

Class A: Surgical retractors, tongue depressors (Low Risk)

Class B: Hypodermic Needles, suction equipment

Class C: Lung ventilator, bone fixation plate

Class D: Heart valves, implantable defibrillator (High Risk)

Source: GHTF Principles of Medical Devices Classification, page 10

In Vitro Diagnostics (IVD)

Examples of Risks by Class:

Class A: Chemistry analyzer; culture media (Low Risk)

Class B: Vitamin B12; pregnancy self-testing; test strips

Class C: Blood glucose self-testing, PSA screening, Rubella

Class D: HIV Blood donor screening; HIV Blood diagnostic

Source: Principles of IVD Medical Devices Classification, page 11

Getting this classification approach correct is essential to the success of the entire regulatory system – because the risk classification guides many downstream processes including **Conformity Assessment, evidence requirements, and inspections.**

Where there is divergence in classification approach, it creates technical barriers to trade and unnecessarily slows patient access.

Conformity to Essential Principles

Standards & Consensus

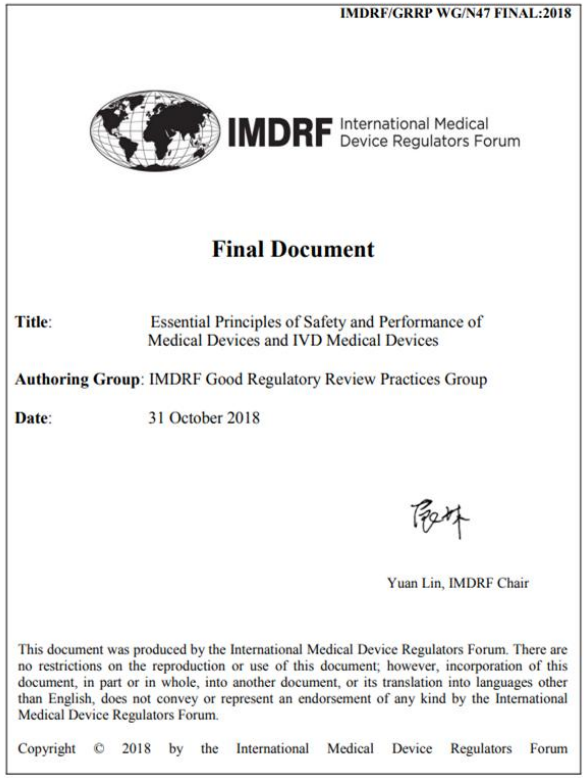
GMRF recommends the NRA encourage manufacturers to **apply international recognized consensus standards** to demonstrate conformity with IMDRF Essential Principles.

Pre-Market Evaluation by Class

Regulations specify evaluation extent based on device class (IMDRF Guidance). **Class A and B typically do not require pre-market authorization or inspection**.

QMS Assessment & Risk

NRA **assessment degree depends on MD/IVD risk class**. Higher risk classes are subject to regulatory assessment. (GMRF page 202)



IMDRF/GRRP WG/N47 FINAL:2018

IMDRF International Medical Device Regulators Forum

Final Document

Title: Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices

Authoring Group: IMDRF Good Regulatory Review Practices Group

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IMDRF Essential Principles of Safety and Performance of Medical Devices and IVD Medical Devices

GMRF and IMDRF Risk-Based Conformity Assessment Guidelines

Conformity assessment element	Class A	Class B	Class C	Class D
Quality management system (QMS)	Regulatory audit normally not required, except where assurance of sterility of accuracy of the measuring function is required.	The NRA should have confidence that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to market authorization.	The NRA should have confidence that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to market authorization.	The NRA should have confidence that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to market authorization.
Technical documentation	Pre-market submission normally not requested.	Not normally reviewed pre-market. The NRA may request and conduct a pre-market or post-market review sufficient to determine conformity with essential principles.	The NRA will undertake a review sufficient to determine conformity with essential principles prior to the device being placed on the market.	The NRA will undertake an in-depth review to determine conformity with essential principles, prior to the device being placed on the market.
Declaration of conformity	Submission normally not requested.	Review and verify compliance	Review and verify compliance	Review and verify compliance

General Rules from IMDRF and WHO:

- Class **A and B** regulatory audit and pre market submission and **review not normally required**.
- Class **C and D are reviewed** but the level of evidence and scrutiny for class D is higher than that of class C.

NOTE: Reliance should not be needed for class A and B because they should not require a review by the authority.

NOTE: Reliance (e.g., Recognition or an Abridged Assessment; MDSAP) is recommended by the WHO no matter the regulatory maturity of the authority.

What do you NOT see in the Conformity Assessment Guidance?

No mention of a Certificate of Free Sale (FSC) or Certificate to Foreign Government (CFG).

In fact, the GMRF does not mention FSC or CFG a single time.

The Challenge

Some agencies require a CFG to show authorization in the same country where the product is manufactured. This is restrictive and unrealistic because:

- Manufacturing locations are diversified.
- Launch decisions are independent of production sites.

Requiring both authorization AND production in the same country is an unrealistic barrier.

IMDRF Recommendation

Countries should strive to eliminate CFG or FSC requirements.

While some jurisdictions may need to change regulations or even laws, the IMDRF vision is clear: removing these administrative hurdles is a critical step for modern regulatory frameworks.

Doing so will also help regulators align to the WHO GMRF and the GBT+.

WHO Risk-Based Testing Recommendations

In-Country Clinical Investigations

"In-country clinical investigations... should not generally be a requirement." Page 239.

Lot Verification Testing

"...the Committee agreed that... such a requirement should be based on an assessment of risk." Page 22.

Acceptance of External Clinical Data

"...the NRA may consider the acceptance of data from clinical investigations conducted outside its jurisdiction, provided that... data are adequate and... obtained in accordance with applicable standards..." Page 201-02.

Risk-Based Verification for High-Risk IVDs

"Countries may implement a system of risk-based lot verification of high-risk IVDs (Class D), either before distribution... or before they are put into service." Page 207.

Risk-Based Regulations & Public Health Goals

"The costs of doing business – both direct and indirect – may influence whether medical devices are introduced to a particular market."

Cost Factors

Direct Costs
Example: User fees

Indirect Costs
Regulatory burden of local compliance

The Impact of Non-Harmonization

"If costs are disproportionately high or requirements are not harmonized, manufacturers may be discouraged, impeding national public health goals."

Source: GMRF page 215

Thank you!!

Gracias!!