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DRAFT WORKING DOCUMENT FOR COMMENTS

Good regulatory practices for regulatory oversight of medical products

Please send your comments to **Dr Marie Valentin**, Technical Officer, Regulatory Convergence and Networks, Regulation and Safety (valentinm@who.int), with a copy to Mrs Carolyn Doucelin (doucelinc@who.int) by **11 September 2020**. Please use our attached Comments Table for this purpose.

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Good regulatory practices for regulatory oversight of medical products

Description of activity	Date
Concept Paper on Good Regulatory Practices.	October 2013
Concept development workshop – India.	July 2014
Draft development workshop – China.	October 2015
Public consultation of the first draft document.	May- December 2016
Internal consultation meeting.	July 2017
Presentation to 53rd Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP) on the way forward.	September 2018
Consultation with National Regulatory Authorities and regulatory organizations – Switzerland.	19 September 2019
Update on the proposed plan for a high-level document for Good Regulatory Practices to the 54th ECSPP.	14-18 October 2019
Development of the high-level Good Regulatory Practice high-level document.	Until 31 July 2020
Second public consultation.	Until 11 September 2020
Consolidation of comments received and revision of the working document by WHO.	September 2020
Presentation to the 55th ECSPP with a proposal for adoption.	12-16 October 2020

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Good regulatory practices for regulatory oversight of medical products

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Acronyms

APEC	Asia-Pacific Economic Cooperation
ASEAN	Association of Southeast Asian Nations
GGP	Good Governance Practices
GRP	Good Regulatory Practices
GRelP	Good Reliance Practices
GRevP	Good Review Practices
OECD	Organisation for Economic Co-operation and Development
QMS	Quality Management System
QRM	Quality Risk Management
WHO	World Health Organization
WLAs	WHO-Listed Authorities

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Executive summary

A fundamental role of government is to protect and promote the health and safety of the public, including the delivery of health care. A well-functioning health care system depends upon the availability and affordability of medical products that are safe, effective and of consistently assured quality.

The medical products sector is one of the most regulated of all industries as a consequence of the impact of the diverse range of medical products on health, the difficulty in assessing their quality, safety and efficacy, and the complexities associated with their development, production, supply and surveillance. It is therefore essential that the interests and safety of the public be entrusted to a regulatory body responsible for ensuring that only products in legal trade are available and that marketed products are safe, perform as claimed and are of assured quality.

Regulatory authorities have a duty to ensure that they regulate in a manner that achieves public policy objectives. A coherent legal framework should be established and implemented that provides the required level of oversight while also facilitating innovation and access to safe, effective and quality medical products. This also means building the necessary flexibilities and responsiveness to manage public health emergencies, address new technologies and practices and promote international regulatory cooperation.

Governments incur costs by establishing and maintaining regulatory systems to protect and promote the health of its citizens. Regulated parties incur costs in complying with regulation. However, additional impacts (health system, socio-economic and economic impacts) can accrue from inefficient regulatory systems - with potentially significant implications for disease morbidity/mortality, health care costs and the economy.

A sound legal framework, the adoption of international norms and standards and the recruitment and development of competent staff are necessary but not sufficient conditions to ensure 'good regulatory oversight'. These measures must be combined with good regulatory practices (GRP) that guide all individuals within organizations entrusted to regulate in the application of requirements and the formulation of decisions so that they are clear, consistent, impartial, proportionate, timely and based on sound science and legislation.

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GRP can be defined as a set of principles and practices that are applied to the development, implementation and maintenance of regulatory instruments – including laws, regulations and guidelines – in order to achieve a public health policy objective in the most efficient way.

The successful application of GRP is the hallmark of a modern, science-based and responsive regulatory system that translates the practice of regulation into desired outcomes. GRP provide a means of establishing and implementing sound, affordable and efficient regulatory oversight of medical products as an important part of health system performance and sustainability.

This document is intended to present Member States with widely-recognized principles of GRP. The principles presented in this document derive from an extensive review of public documents developed by governments and multi-lateral organizations on the subject, as well as many consultative workshops, benchmarking exercises and interactions with Member States. The nine principles presented in this document, such as, legality, consistency, independence, impartiality, proportionality, flexibility, clarity, efficiency and transparency, are relevant to all authorities responsible for the regulatory oversight of medical products, irrespective of resources, sophistication or regulatory model.

GRP serve as a foundation within a suite of related guidance documents on best regulatory practices. Taken together, this expanding set of guidance documents is intended to provide regulatory authorities comprehensive guidance on improving their performance. This document will be supplemented by practical 'how to' guides and tools designed to facilitate the implementation of GRP.

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1. Introduction

This document responds to requests from national authorities responsible for the regulatory oversight of medical products for guidance in addressing common gaps in regulatory practices identified during benchmarking exercises.

This document draws upon documents from multilateral bodies such as the Asia-Pacific Economic Cooperation (APEC), the Organisation for Economic Co-operation and Development (OECD), the World Bank and the Association of Southeast Asian Nations (ASEAN) *(1) (2) (3) (4) (5)* as well as guides published by a number of governments. The document also takes account of earlier World Health Organization (WHO) documents that touch on aspects of GRP *(6) (7) (8) (9) (10) (11) (12) (13) (14)* and from WHO experience in applying the WHO Global Benchmarking Tool (GBT) and promoting the various principles of good regulatory practices (GRP).

When the principles of GRP are properly implemented through the GRP enablers across the regulatory system, desired regulatory outcomes and impact can be achieved.

2. Background

A fundamental role of government is to protect and promote the health and safety of the public, including in the delivery of health care. A well-functioning health care system depends upon the availability and affordability of medical products that are safe, effective and of assured quality.

Medical products are essential to the prevention, diagnosis and treatment of disease and the consequences of substandard and falsified medical products can be therefore life-threatening. This reality is of particular concern as users of medical products are typically not in a position to judge their quality. It is therefore essential that the interests and safety of the public be entrusted to a regulatory body or bodies responsible for ensuring that only products in legal trade are available and that marketed products are safe, perform as claimed and are of assured quality.

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The regulatory oversight of medical product has become increasingly complex given the globalization of product development, production and supply, coupled with the rapid pace of technological and social change in a context of limited financial and human resources.

The importance of robust regulatory systems was recognized by the Sixty-Seventh World Health Assembly in endorsing Resolution WHA 67.20 Regulatory system strengthening for medical products. The Resolution notes that "effective regulatory systems are an essential component of health system strengthening and contribute to better public health outcomes", that "regulators are an essential part of the health workforce", and that "inefficient regulatory systems themselves can be a barrier to access to safe, effective and quality medical products" (*15*).

A sound system of oversight requires that regulatory authorities are supported by an effective framework of laws, regulations and guidelines, and that they have the competence, capacity and science-based knowledge to conduct their mandate in an efficient and transparent manner. The degree to which the regulatory framework fulfils policy objectives depends on the quality of its development and implementation processes.

GRP are critical to the efficient performance of the regulatory system and, consequently, to the public's confidence in the system. A sound regulatory framework, including the adoption of international norms and standards and the recruitment and development of competent staff, are necessary but not sufficient conditions to ensure 'good oversight'. These measures must be combined with GRP that guide all individuals from regulatory authorities to set appropriate requirements and formulate decisions that are clear, consistent, impartial, proportionate, timely and based on sound science.

3. Purpose

This document presents the high-level principles of GRP. The principles are intended to serve as a benchmark and thereby assist Member States in the application of good practices for the regulatory oversight of medical products. This document is also meant to assist Member States in prioritizing the functions of a regulatory system based on available resources, national goals, medical products policies and the medical product environment.

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This principles-based document will be supplemented by practical 'how to' guides and tools designed to facilitate the implementation of GRP within organizations responsible for the regulatory oversight of medical products.

This foundational document is complemented by a suite of related guidance on best regulatory practices, including but not limited to good governance practices (GGP) *(16)*, good reliance practices (GRelP) *(17)*, good review practices (GRevP) *(18)* and the implementation of quality management systems (QMS) for national regulatory authorities (NRAs) *(19)*. Taken together, this expanding body of work is intended to provide regulatory authorities with comprehensive guidance on improving performance.

4. Scope

This document is relevant to all regulatory authorities irrespective of resources, maturity or regulatory model. These GRP high-level principles are equally applicable to regulatory systems that are supranational (e.g. regional), national and/or subnational in nature, or involve multiple institutions charged with regulating certain products or activities within a country or jurisdiction.

This document presents principles and considerations in the development and implementation of regulatory instruments which underpin regulatory activities. Broader practices and attributes are presented that define well-performing regulatory systems for medical products.

This document is intended for a number of related audiences: institutions and policy-makers responsible for the formulation of health policies, laws, regulations and guidelines; institutions that, together, form national or supranational systems for regulatory oversight of medical products; regulatory networks and parties affected by or otherwise interested in regulatory frameworks; for example, industry or other developers of medical products.

5. Objectives

GRP provide a means of establishing sound and effective oversight of medical products as an important part of health system performance and sustainability. If consistently and effectively implemented, they

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can lead to higher quality regulation, improved regulatory decision-making and compliance, increased efficiency of regulatory systems, and better public health outcomes. They help to ensure that regulatory systems remain current as technologies and the systems in which they are used continue to evolve.

Within the context of an increasingly complex and interconnected regulatory environment, GRP are also an important enabler in promoting trust between regulatory authorities and thereby facilitating international cooperation and the adoption of more effective and efficient approaches to ensuring the quality, safety and efficacy of medical products within the global regulatory community.

The ultimate aim of GRP is to serve and protect public health and patients' interest, respecting all applicable ethical principles.

6. Key considerations

The medical products sector is one of the most regulated of all industries as a consequence of the impact of the diverse range of medical products on health and society, the difficulty in assessing their quality, efficacy and safety, lessons learned from public health tragedies, and the complexities associated with developing, producing, supplying and monitoring medical products to ensure they consistently perform as intended. This has led many countries to put into place an increasingly sophisticated set of laws, regulations and guidelines that control all aspects of the medical product life-cycle.

While providing the necessary authorities, prohibitions and tools necessary to fulfil publicly entrusted mandates, regulatory authorities have a duty to ensure that they regulate in a manner that achieves public policy objectives. This means establishing and implementing a coherent regulatory framework that provides the required level of oversight and control while also facilitating the innovation and access to safe, effective and quality medical products. It also means building the necessary flexibilities and responsiveness to manage public health emergencies, address new technologies and best practices, and promote international regulatory cooperation.

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Increasingly, policy makers and regulatory authorities must adopt modern and responsive models of regulation that consider resource constraints in the face of the challenges posed by scientific development, globalization, rising public expectations and public health emergencies.

Weak or inefficient regulatory systems can be a barrier to access to safe, effective and quality medical products and a threat to public health. At the same time, countries strengthen regulatory capacity regulatory systems need to be science-based, respect international standards and to adopt an approach that leverages the work of other trusted regulatory authorities and institutions whenever possible. Towards this end, countries are encouraged to formulate and implement policies and strategies that promote convergence, harmonization, information and work-sharing, and reliance as part of GRP *(17).* An ongoing initiative at WHO aims at establishing and implementing a framework for evaluating NRAs and regional regulatory systems as well as designating those that meet a specific standard as WHO-Listed Authorities (WLAs) *(20).*

For reasons of public health protection noted earlier in the document, the need for regulatory controls over medical products is fully acknowledged. The issue is more *how* to regulate in an effective, efficient and transparent manner, such that the interests of the health care system are served. The consistent application of GRP in all aspects of oversight is essential in ensuring that these interests are met and providing the foundation on which a well-performing, respected regulatory system is built.

GRP can be defined as a set of principles and practices that are applied to the development, implementation and maintenance of regulatory instruments – including laws, regulations and guidelines – in order to achieve a public health policy objective in the most efficient way.

GRP is about instilling a culture of best practices across institutions responsible for regulatory oversight to ensure that regulation is fairly, consistently and effectively applied.

7. Overview of regulatory system for medical products

Definitions are essential to a common understanding of concepts. While a more extensive set of terms is provided in the Glossary, an elaboration of the terms *regulatory framework*, *legal framework,*

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regulatory authority, *regulatory system*, and *regulatory outputs* is provided below to ensure a proper understanding of their usage in this document.

Components of the regulatory framework

In this document, the terms "law" and "regulation" are used for the components of the legal framework (binding legislation). It is acknowledged that other terms may be used in different jurisdictions, such as "act" (instead of law) or "ordinance" (instead of regulation).

Laws are generally used to set out at a high level the roles and responsibilities of institutions;, in this case, the regulatory authority, the ministry of health and other relevant organizations. They define the products, persons and activities that are to be regulated and state what is permitted and what is not. More importantly, laws authorize the institution to make lower level (or subordinate) regulations.

Regulations are a diverse set of instruments by which governments place requirements on enterprises and citizens. The *regulations* usually state at high level the conditions to be met and detail the requirements defined in the laws.

For instance, a law may prohibit the manufacturer, importation or sale of a medical product in the absence of specific authorisation. The regulations would set out the conditions for obtaining authorisation; for example, the need to provide certain types of information - such as clinical trial and manufacturing and control data - that would allow the regulatory authority to establish the quality, safety and efficacy of a medical product.

Guidelines (and other guidance documents) provide further detail on how the regulated stakeholders can comply with the laws and regulations. Guidelines may also provide details on the processes that enforce the respective legislation (laws and regulations). Within a regulatory framework for medical products, these documents are usually non-binding and are generally more detailed and scientific in nature. This makes them appropriate for describing approaches generally considered suitable for satisfying regulatory requirements but unsuitable to be embedded into legislation.

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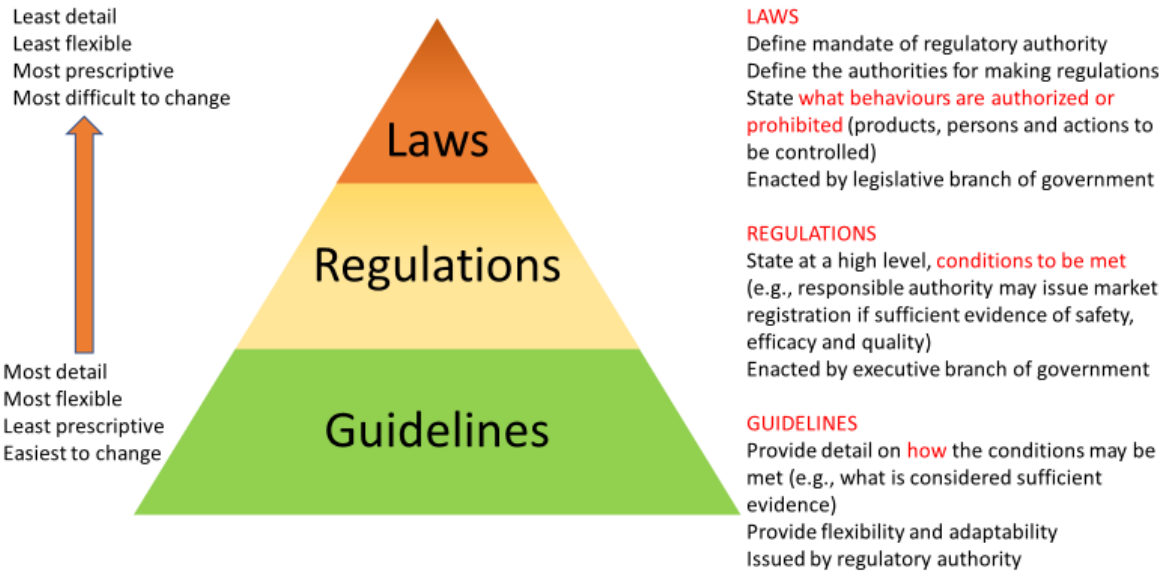


Figure 1: Architecture of a Regulatory Framework

Components of the regulatory system

A *regulatory authority* is a public institution(s) or governmental body/bodies authorized by law to independently exercise regulatory powers concerning the development, production, marketing and surveillance of medical products. Although the term implies that a single organization is responsible for all regulatory functions, indeed these functions may be undertaken by one or more institutions reporting to the same or different senior official. The regulatory authority plays a critical role in ensuring the quality, safety, efficacy and performance of medical products as well as the relevance and accuracy of product information.

The *regulatory framework* is the collection of laws, regulations, guidelines and other regulatory instruments through which a government and a regulatory authority controls particular aspects of a specific activity.

The *legal framework* is the part of the *regulatory framework* that refers to (binding) pieces of legislation, such as laws and regulations.

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365 *Regulatory outputs* are the results or products coming from the regulatory authority
366 (e.g. inspection/assessment reports, decisions, product label, and so on).
367
368 The term *regulatory system* is used to describe the combination of the institutions, processes,
369 regulatory framework and resources which, taken together, are integral to the effective regulatory
370 oversight of medical products in a given country or multi-country jurisdiction. GRP should be
371 considered and applied for the whole regulatory system.
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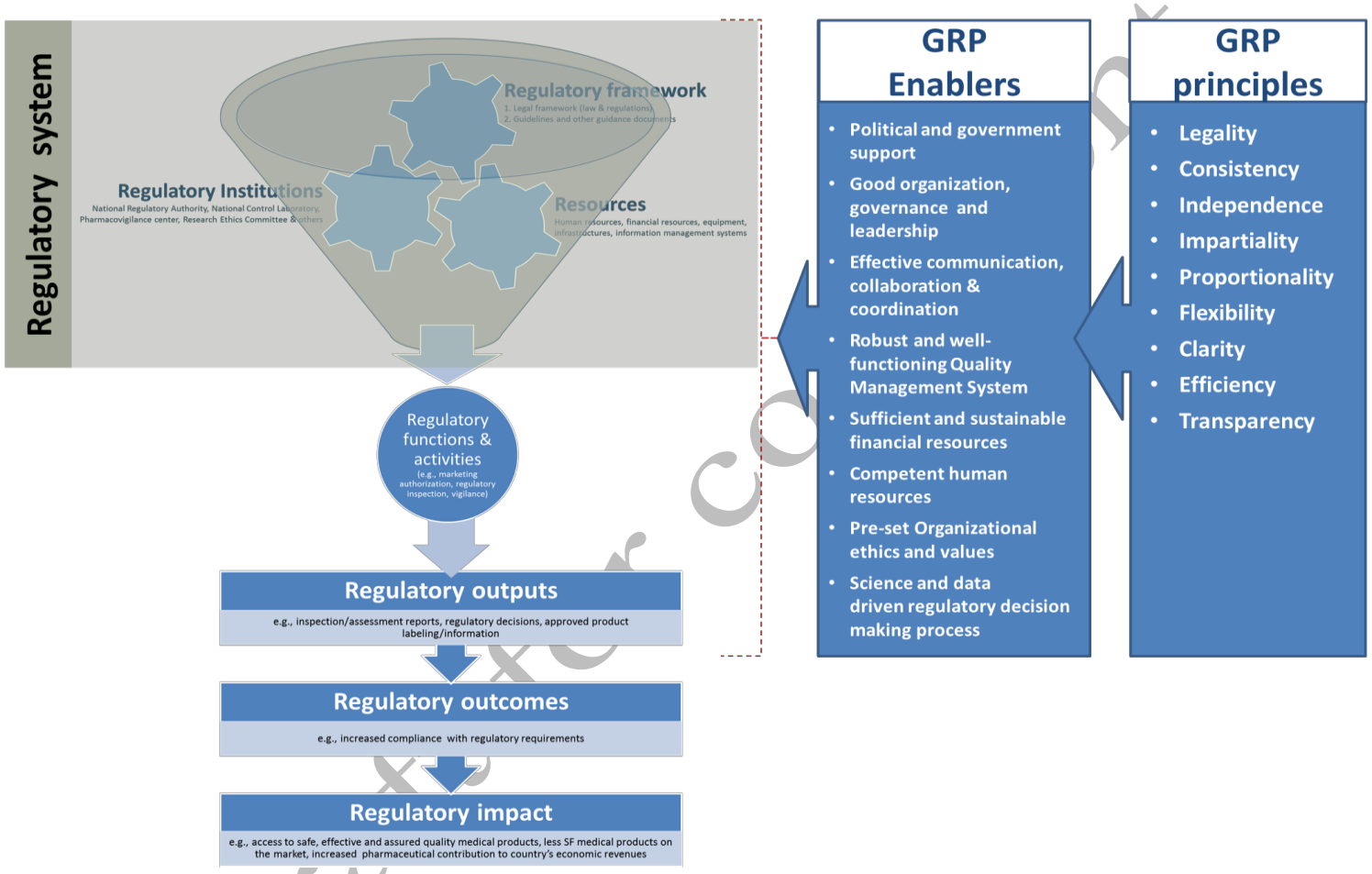


Figure 2: Principles and enablers of Good Regulatory Practices (GRP) and Components of the regulatory system

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When looking at the overall regulatory system, three main components (inputs) can be seen as the main contributors to regulatory functions and activities: (1) regulatory framework composed of legal framework (laws and regulations) along with guidelines and other guidance documents, (2) regulatory institutions which may be represented by one or more entities including the national regulatory authority (NRA), the national control laboratory, pharmacovigilance centre(s), research ethics committee(s) and others, and (3) all types of resources including human and financial resources, infrastructure and equipment and information management systems. There are several regulatory outputs depending on the concerned functions and activities (e.g. regulatory and marketing authorization inspection/assessment reports). The concepts and principles of GRP cover and address the overall regulatory system as explained above. For the purpose of application and implementation of GRP, several enablers are essential (see 10. *Enablers for Good Regulatory Practices*). When the principles of GRP are properly implemented through the enablers, a desired regulatory outcome and impact can be achieved.

WHO classifies the spectrum of regulatory activities according to seven common regulatory functions applicable to the regulation of all medical products: clinical trials oversight, registration and marketing authorization, vigilance, market surveillance and control, licensing establishments, regulatory inspection and laboratory testing *(21).* In addition, a number of non-common functions apply to certain medical products, such as official lot release for vaccines and other biologicals.

The term *regulatory authority* implies that a single organization is responsible for all regulatory functions. This is not always the case. For example, different organizations may be legally responsible for the regulation of medicines and vaccines as compared to medical devices. Even when one body is responsible for all regulatory functions, aspects critical to certain functions may lay outside the authority, such as those performed by pharmacovigilance centres that have a formal relationship with the authority in collecting adverse event reports. Certain regulatory functions may also be undertaken by third parties, as in the case of auditing organizations in relation to medical devices.

Regulatory activities may also be undertaken at a supranational (e.g. regional), national and/or subnational level. Examples include the supranational evaluation of certain products for the purpose of granting a marketing authorization valid across multiple countries, or the GMP inspections of multi-source medicines performed at the state level.

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8. Principles of good regulatory practices

There is no universal model for the regulatory oversight of medical products. Each approach will reflect national health policies and priorities, the country's level of socioeconomic development, the availability of resources and infrastructure, the health system, the national legal system, the research and development capacity, as well as the local production capacity. Nonetheless, as in other regulated sectors, there is a growing international consensus on best practices that may be applied to regulatory oversight.

A review of public documents *(1) (4) (5) (22)* on GRP reveals common themes that should be adopted by all institutions responsible for or involved in the regulatory oversight of medical products. These principles apply equally to the development and implementation of regulatory oversight and to daily regulatory business.

GRP are guided by overarching principles. There are nine principles which are listed below and are described in this section, together with considerations relevant to the regulatory oversight of medical products.

Further elaboration of the principles, practices and examples is foreseen in supplemental 'how to' guidance complementing this document.

Principles of Good Regulatory Practice	
Legality	Regulatory systems and the decisions that flow from them must have a sound legal basis.
Consistency	Regulatory oversight of medical products should be consistent with existing government policies and legislation and be applied in a consistent and predictable manner.
Independence	Institutions executing regulatory oversight of medical products should be independent.
Impartiality	All regulated parties should be treated equitably, fairly and free from bias.
Proportionality	Regulation and regulatory decisions should be proportional to risk and the regulator's capacity to implement and enforce.

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Flexibility	Regulatory oversight should not be prescriptive but rather allow for flexibility in responding to a changing environment and unforeseen circumstances. Responsiveness in a timely manner to public health emergencies should be built into the regulatory system.
Clarity	Regulatory requirements should be accessible to and understood by users.
Efficiency	Regulatory systems should achieve their goals within the required time and at reasonable effort and cost. International collaboration promotes efficiency by allowing the best use for resources.
Transparency	Regulatory systems should be transparent; requirements and decisions should be made known, and input sought on regulatory proposals.

8.1 Legality

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

Key elements:

- The regulatory framework should provide the necessary authorities, scope and flexibilities to safeguard and promote health.
- The delegation of power and responsibilities to different levels of the regulatory system should be clear and explicit.
- Regulatory frameworks should support and empower regulatory authorities to contribute to and benefit from international cooperation.
- Systems should be in place to ensure that regulatory decisions and sanctions can be reviewed.
- Regulatory framework should afford for the integrity of the regulatory system with clear scope and lines of authority of institutions forming the regulatory system.
- A legal framework must hold the regulatory authority accountable to the public, those regulated and the government for their actions and decisions.

The principle of legality means that the regulatory system is structured so that all regulatory actions and decisions are based on clear legal authority, thus respecting the “rule of law”.

A regulatory body exists to achieve objectives deemed by the government to be in the public interest. It must operate within and in accordance of the powers conferred by the legal framework *(23)*. The law or act establishing the regulatory authority should be clear on the objectives of the enabling legislation, the powers of the authority, the scope of products and general activities the authority is mandated to regulate, and the provisions for making regulations.

The delegation of power and responsibilities to different levels of the regulatory system should be explicit and clear. When more than one institution or level of government is involved in the regulation of medical products, the functions and responsibilities of the various institutions should be clear and complementary (see *9.2 Consistency*).

Given the need for *all* regulatory authorities to cooperate to manage increasingly complex and cross-jurisdictional issues, it is essential that a modern legal framework for medical products supports and encourages such cooperation in all its forms - including convergence, harmonization, information- and work-sharing, reliance and recognition. Ideally, this would take the form of explicit provisions in law and/or regulations, with further operational detail provided in policies and procedural guidance. At a minimum, the legal framework should not *prohibit* all forms of regulatory cooperation, including the use of assessments and decisions of other trusted regulatory authorities and institutions in performing its own work. Cooperation does not alter the sovereign responsibility and accountability of each regulatory authority to protect the health and safety of its citizens but allows for the exchange of good practices and may help save resources and avoid duplication.

Legislation has to be in place to control and perform all required regulatory activities under common and non common regulatory functions. Policies, guidelines and procedures cannot compensate for the absence of legislation.

A legal framework should support the integrity of the regulatory system with clear authority, power, roles and responsibilities of institutions forming the regulatory system. Conflict in organizational authority or responsibilities should be avoided.

All regulatory authorities must be accountable to the public, those regulated, and the government for their actions and decisions as part of good governance and accountability frameworks. Within the context of GRP, accountability means that regulatory authorities are: (i) responsible for acting according to certain standards and commitments; (ii) answerable for their actions; and (iii) willing to face the consequences when standards or commitments are not met.

Regulatory actions and decisions should be consistent with authorities and controls provided for by the legal framework. Processes should therefore be put in place for the review of regulatory decisions. This includes internal appeal mechanisms and the right to judicially appeal decisions of regulators –

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including on the grounds of procedural fairness and due process – in addition to scientific and administrative grounds.

8.2 Consistency

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

Key elements:

- The regulatory framework for medical products should fit coherently into the national legal and policy framework.
- New regulations should complement, and not conflict with, existing regulatory instruments.
- Regulatory requirements should be consistently implemented and enforced across medical product sectors and stakeholders.

Regulatory oversight of medical products must be performed in the context of, and in ways coherent with, the national legal framework, general government policies and public health policy objectives. This also includes any treaties, conventions and regional or international agreements to which the country is a party as well as any supranational legislation having an effect on constituent Member States.

Overlap and conflicts with existing laws and regulations should be avoided since this causes confusion and the duplication of mandates, unnecessary regulatory burden and the likelihood of noncompliance. Manufacturers, importers, distributors and other stakeholders should be able to consistently identify which authority is responsible for what.

This is especially important where the regulation of medical products is decentralized – when, for instance, there may be central and state/provincial-level authorities. Effective systems of mutual consultation, cooperation and coordination between the different levels of government should be put in place in order to promote the national uniformity of regulatory requirements while respecting local responsibilities. It is essential that all the different regulatory functions and activities are efficiently integrated allowing for the uniformity of the regulatory system.

The same considerations are equally important when more than one institution or department within the same level of government is responsible for different, or the same, regulatory functions and products – a situation which is not uncommon. The problems associated with unclear or conflicting

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mandates and requirements can and do result from complex regulatory systems, compounded by challenges in effective communication and coordination.

In all instances, formal mechanisms should be established to ensure proper coordination during the drafting and execution of the regulatory instruments and the ongoing operations of bodies charged with the regulatory oversight of medical products.

Consistency in regulatory actions and decisions means that the same or similar circumstances should lead to the same or similar outcomes. It is therefore important for the regulatory system to build an institutional memory to keep records of decisions made in order to offer similar and fair treatment to future similar situations. Consistency is supported when the regulatory framework provides for appealing regulatory decisions through an impartial appeals process. The enforcement of such, and corrective measures, should also be consistent across sectors.

Consistency is also supported by having sufficient and clear regulatory guidance based, whenever possible, on international guidelines; the orientation and training programmes for staff; and regular discussions with regulated parties and other key stakeholders that serve as mechanisms for the identification and resolution of issues.

The application of a well-functioning quality management system that spans all regulatory activities *(24)* is critical for achieving regulatory consistency. This includes, among others, the adoption of a process approach involving the systematic definition and management of regulatory processes, and their interactions, so as to achieve the intended results in accordance with the quality policy and strategic direction of the organization.

Performance based indicators, internal reviews and external audits can also play an important role in ensuring consistency in the application of regulations and regulatory operations.

8.3 Independence

Institutions executing regulatory oversight of medical products should be independent.

Key elements:

- The regulatory system must operate, and be seen to operate, in an independent and authoritative manner, discharging its duties independently from politicians, government and regulated entities.

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- Regulatory activities and decisions should avoid improper and undue influence from stakeholders (also known as regulatory capture).
- The appropriate funding and clarity on funding processses is essential.
- Independence of leadership should be put in placein order to support independent behaviour while in employment and upon exiting.

525

526 According to an OECD publication entitled *Creating a culture of independence (20)* "regulatory agencies
527 (authorities) often find themselves under various pressures from different stakeholders and interest
528 groups which can subject them to different forms of influence. To ensure they conduct their activities
529 correctly and achieve the right policy outcomes they must take on board legitimate interests and
530 protect themselves from inappropriate or undue influence*".*

531

532 Good governance and anti-corruption measures *(16)* should be built into the regulatory framework to
533 avoid actual or perceived conflicts of interest, unfounded bias or improper influence by stakeholders
534 (also known as regulatory capture). To maintain public confidence, the regulatory authority must
535 operate, and be seen to operate, in an independent, authoritative and impartial manner, discharging
536 its duties independently of those regulated entities (e.g. independence from researchers and
537 industries).

538

539 For regulators that are funded through fees, an appropriate cost-recovery mechanism is essential to
540 set the "right" fee and avoid a regulator that is under-funded, captured by industry or undermined by
541 the executive. It can be easier to influence a regulator funded through general government revenues
542 by reducing the resources at its disposal. Annual appropriations can make it easier to influence the
543 regulator than multi annual appropriations that are less susceptible to short-term shocks, such as
544 political/electoral imperatives. Adequate safeguards can protect the budget process from being used
545 to unduly direct the regulator.

546

547 The nomination and appointment of the regulator's leadership should be based on transparent and
548 accountable processes. Clear conflict of interest rules should be in place to support independent
549 behaviour while in employment and upon exiting.

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8.4 Impartiality

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

Key elements:

- Regulatory activities and decisions should avoid conflicts of interest or unfounded bias.
- The regulatory system must operate in an impartial manner.
- The regulatory authority should not be engaged in activities it regulates nor be at a hierarchal level that is subordinate to institutions that perform regulated activities.
- Regulatory decision should be science- and evidence-based and the decision-making process should be robust, according to defined criteria.

Regulatory instruments must be written so that regulatory activities and decisions made on the basis of such instruments are legitimate, evidence-based and ethical. Public and private bodies, domestic and foreign entities should all be regulated equitably using the same principles and framework so that *competitive neutrality* is achieved.

The regulatory authority must operate in an impartial manner, discharging its duties independently of those regulated entities (see *9.3 Independence*).

This principle also extends to researchers and other experts sitting on scientific and advisory committees convened to provide recommendations to the regulatory authority on matters related to regulatory policy or the authorisation of medical products. Declarations of interest have to be completed and reviewed, and rules for withdrawal need to be defined prior to discussions to maintain the integrity and impartiality of the committee and its recommendations.

Furthermore, the regulatory authority should not be engaged in the activities it regulates nor be at a hierarchal level that is subordinate to those institutions that perform regulated activities, including the procurement of medical products by a ministry of health or other government institution.

Regulators can avoid actual or perceived influence by being open and transparent about their decisions and decision-making process. This will help ensure impartiality, better regulatory outcomes and increased public confidence in the use of the regulated products.

Regulatory activities and decisions should be science-driven, evidence-based and predictable. While there will always be a need for good regulatory judgement and discretion in enforcement, actions and

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decisions should be based on regulatory requirements and on the evidence or circumstances of the situation (also supports *9.2 Consistency*).

8.5 Proportionality

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

Key elements:

- Regulatory oversight should be adequate to achieve the objectives without being excessive.
- Regulatory measures should be proportionate to the risk of the product or activity or service.
- Regulation should not exceed the national capacity to implement and enforce the regulation.
- The assessment of medical products should be based on a benefit/risk evaluation and continuous monitoring of the benefit/risk profile through a robust vigilance system.

The principle of proportionality means that an action does not go beyond what is needed to achieve an intended objective. This principle should be applied to all elements of a regulatory system. Regulation should be created only when necessary and should be adequate to the aim being pursued without being excessive. The content and form of regulation should be appropriate to both the issue being addressed and the risk it poses. For instance, extensive pre-clinical and clinical studies are needed to support the safety and efficacy for the marketing authorization of a new medicine, whereas, limited safety/efficacy studies, usually in a form of a single in vivo bioequivalence study or, where appropriate, in vitro studies, are sufficient for generic medicines.

Regulatory enforcement and inspection regimes should also be proportionate to the risk and severity of the infraction with an aim to reduce or mitigate the health risk posed by the infraction. A proportionate, risk-based approach allows the regulator to allocate resources where the need is greater. It also ensures that the cost of complying with regulation is proportionate to the nature of the risk.

The principle of proportionality also applies to the policies and processes by which regulation is made. The regulation-making process should be flexible and proportionate to the complexity and/or impact of the problem that it addresses. For instance, a rigorous cost/impact analysis may be required for a new complex regulatory framework but not for simple regulations or where the policy alternatives are limited.

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Regulation should not exceed national capacity to implement and enforce the regulation. "If there are no strategies, facilities and resources for implementation and enforcement, legislation on its own will achieve nothing. A law with modest aims and objectives that is properly enforced is preferable to a more comprehensive one that cannot be implemented"(*12).* Furthermore, the lack of resources or ability to implement and enforce represents a liability for the government.

The assessment of medical products should be based on a benefit/risk evaluation. All the demonstrated benefits from the medical products should be weighed against the identified risks in order to determine if the benefit outweighs the risks. Regulatory systems should have appropriate vigilance processes in place in order to monitor the benefit/risk profile and to take any regulatory actions if required.

8.6 Flexibility

Regulatory oversight should allow for flexibility in responding to a changing environment and unforeseen circumstances.

Key elements:

- The regulatory system, including regulatory frameworks, should provide sufficient flexibility to reflect/respond to changes in the regulated environment, including evolving science and technology.
- The regulatory system should be prepared and provide for timely response to urgent situations, including public health emergencies and shortages of medical products.
- The language of regulation should be performance-based whenever possible, allowing for alternative approaches that achieve the same result.
- The regulatory system should provide the flexibility to apply good judgement.

Flexibility is essential to ensure that regulatory frameworks and regulatory systems remain "fit for purpose". This requires the appropriate design and use of regulatory instruments.

In developing a meaningful, understandable and enforceable regulatory framework, there is a need to provide sufficient detail to ensure clarity. At the same time, the regulatory framework should allow flexibility to respond to new technologies and innovation, to changes in the regulated environment and to enable a timely response to unforeseen public health threats. It should provide for the regulator's administrative and enforcement discretion – that is, the flexibility to apply good judgement within the regulatory framework. This discretion must be subject to the appropriate controls and oversight. Flexibility in regulatory oversight should also be risk-based and must not compromise the ability to ensure the quality, safety and efficacy and performance of the product *(19)*.

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Responsiveness is an extended principle of flexibility, however slightly different. Responsiveness is time-bound and temporary in nature due to the fact that it addresses urgent situations such as public health emergencies, serious shortages of medical products with no alternatives, unmet medical needs and rare disorders, and the use for compassionate and donation purposes. Regulatory systems should be well prepared and equipped with the necessary regulatory instruments to respond to and manage these unforeseen situations. Flexible and responsive provisions are critical for providing the authority with the ability to make decisions based on best available science and benefit/risk considerations, often in the face of less-than-complete information (e.g. compassionate use, emergency use authorization or listing). The lack of necessary regulatory tools and the flexibilities they afford can pose real and significant impediments to public safety, particularly in times of public health emergencies.

During times when regulatory responsiveness is urged, a regulatory authority should consider the prioritization of its activities using a risk-based approach. The involvement of policy and decision-makers, as well as regulatory collaboration and coordination within the international regulatory community, significantly contributes to regulatory responsiveness.

Flexibility and responsiveness within regulatory framework should aim to accommodate continuing evolution in science and technology. The language of the regulations that support the law should normally be performance-based rather than prescriptive *(6)*, thus allowing regulated parties to use alternative approaches that achieve the same outcome.

Guidelines and other guidance documents are the most detailed, most flexible and most amendable of the regulatory framework instruments. These attributes allow the regulatory framework to respond to new risks in a timely manner and allow for the possibility that an unforeseen technology may be used in a future medical product. Unlike laws and regulations, guidelines in themselves usually do not have the force of law. However, guidelines are very effective if appropriately anchored to the regulation and used to describe how compliance with the regulation may be achieved. They should also allow for other scientifically justified approaches to compliance. Alternate approaches to the principles and practices described in a guidance may be acceptable provided they are supported by adequate scientific justification. The flexibility and amendable attributes that guidelines offer is lost if such detailed texts are put into regulation.

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In circumstances where science is rapidly evolving and not sufficiently mature to justify the development of regulatory guidelines, 'points to consider' type documents can provide useful principles-based guidance and definitions that promote best practices, a common regulatory understanding, international convergence, and prepare the ground for eventual guidelines. Existing international guidelines and standards should always be considered when new guidance documents are being developed.

The regulation of medical products is complex and ever-evolving. New technologies and practices will continue to pose challenges to regulatory systems and redefine the boundaries of what can and should be regulated. Prior to the possible development of regulations designed to deal with new technologies or address certain practices, regulators will often need to generate the necessary regulatory flexibility through the appropriate interpretation of existing legislation and regulations.

8.7 Clarity

Regulatory requirements should be accessible to and understood by users.

Key elements:

- Regulatory instruments should be written in language that is understood by users.
- Terminology should be defined and consistent with international norms whenever possible.
- Consultation, education and training on new requirements contribute to clarity and compliance.
- Guidelines and *good guidance practices* are instrumental to proper interpretation of regulations.
- The process and basis for taking regulatory decisions and enforcement actions should be clear.

The compliance with and consistent application of regulatory requirements and processes require a clear understanding of what is expected. Both the regulator and the regulated party should understand the conduct that is expected and the consequences of non-compliance.

Proposed regulatory instruments should be written in language that can be understood by intended users. This will require the collaboration of regulatory programme personnel and legal drafters, taking into consideration the objectives of the legal instrument, the intended audience and other potentially impacted stakeholders, as well as feedback from internal and external consultations. Clear, unambiguous and precise instruments that are drafted in a language and form consistent with other

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laws and regulations reduce the potential for disputes or misinterpretation and also promote compliance.

As an initial step in the process, the authority drafting medical product regulations should conduct a review to identify areas that lack clarity and resolve any inconsistencies – whether within the regulation itself or between regulations. This also serves as an opportunity to review the "regulatory stock" – the accumulated body of applicable regulations – to identify the need for future updating and better integration of regulatory requirements with a view to eliminating inconsistencies, redundancies and complexity or adapting to new requirements.

Providing interested parties, including the public, the opportunity to be informed of and contribute to the process of regulatory development and regulatory impact analysis is critical to improving the quality and language of the regulatory instrument, promoting a clear understanding of what is intended, and increasing the likelihood of buy-in and future compliance. The means by which interested parties can contribute should be made clear.

Regulatory impact analysis is a valuable tool for systematic assessment of the expected effects of regulatory proposals. It is usually undertaken by the policy analysts of the regulatory departments, agencies or ministries that sponsor the proposal and is primarily aimed at assisting decision-makers in their consideration of a recommended proposal. The product of the regulatory impact analysis process is a document that summarizes the regulatory proposal, the potential alternatives and the implementation aspects and impacts of the proposal.

Terminology should be defined whenever possible to avoid ambiguity or misinterpretation. Where possible, terminology should be consistent with established international norms, standards and harmonized guidelines. As noted, international standards and guidelines are particularly important as vehicles to promote a common regulatory language, convergence and international cooperation.

The principle of clarity is equally important and applicable to the development of regulatory and administrative guidelines which are instrumental in interpreting and providing operational clarity to regulations. Guideline development should follow good guidance practice to ensure that guidelines are written in a clear and concise manner and are consistent with other guidelines and the underlying

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regulations. This includes the use of standard templates and formats, writing style guides, editors, and experts with a good knowledge of the regulatory framework.

Draft guidelines, as with regulations, should be subject to internal and external consultation. Consultation will help confirm if language is clear or if it requires some refinement to improve comprehension. Plain language and simple sentence structure should be the goal as well as to give illustrative examples where possible.

Education, awareness sessions and training, along with clear timelines for the adoption of new regulations and guidelines, should also be considered as tools to promote clarity and compliance when introducing or amending regulations and guidelines, particularly when complex in nature.

Regulations and supporting guidelines should be reviewed periodically to ensure that they still reflect the authority's current practices and expectations, are adapted to the scientific and technological developments, and are aligned with current international standards and guidelines, where applicable. When reviewing and revising any guideline, one must consider the consequential changes in other existing guidelines that will need simultaneous revision.

From an operational perspective, the process and basis for taking regulatory decisions and enforcement actions should be clear and accessible to those directly impacted or otherwise affected (see 7.9 Transparency).

In summary, clarity is essential in all aspects of regulatory oversight (requirements, procedures, decisions and communications) if regulatory programmes are to have the desired effect.

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8.8 Efficiency

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

Key elements:

- Efficient regulatory oversight are those that achieve the intended public health goals.
- A sound regulatory framework, competent staff and the effective use of resources and information from other authorities are the key elements of an efficient regulatory system.
- Policy-makers should seek the most efficient and least burdensome means of achieving their regulatory purposes and confirm actual effectiveness once implemented.
- In considering a regulatory approach, the total burden and resource needs of cumulative regulation should be evaluated.
- Regulatory authorities should continually explore ways of improving efficiency in fulfilling their mandate.
- Alignment of regulatory requirements with other countries and international collaboration promote efficiency.
- Regulated entities play a critical role in contributing to the efficiency of regulatory systems.
- The efficiency of regulatory instruments and regulatory operations should be assessed using performance-based indicators.

An efficient regulatory system must be science- and evidence-based, apply the principles of risk assessment and management, and embed a strategy of international regulatory cooperation into daily business. A regulatory system that is unable to make sound decisions in a timely and consistent fashion is not effective. This is not only a matter of having sufficient resources but also having the right resources and using them effectively, irrespective of size. In this context, lack of integrity of the overall regulatory system is a barrier to regulatory efficiency.

Less resourced regulatory systems can be as effective as more resourced systems if risk-based and if advantage is taken of the work and decisions of other regulatory authorities while focusing resources on essential, value-added activities which only the regulatory authority is in a position to perform *(17)*.

Regulatory oversight cannot be considered efficient if it creates unjustified barriers to access, trade and international regulatory cooperation. The successful establishment of effective regulatory controls on medical products depends on a number of factors as previously described, including:

- The analysis of options that includes the results of consultation with stakeholders. Regulations are more likely to be effective if those impacted have provided input.
- Regulations that are proportional to perceived risk.

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- Early-stage planning for implementation and the practicalities of future enforcement. Application and enforcement should not be after-thoughts.

When new regulatory instruments are being developed and subjected to regulatory impact analysis, the regulatory authority should develop "strategies for education, assistance, persuasion, promotion, economic incentives, monitoring, enforcement, and sanctions" *(24).* The authority must decide which compliance strategies will be established and whether or not consumer awareness and market forces can reasonably be used, in addition to the threat of penalties. The role of civil society in monitoring adherence to regulation should also be considered, if appropriate.

Co-regulation may also be considered in certain circumstances. In such situations, a government would issue regulations and enter into a non-statutory agreement with a body to develop and administer a compliance program. While a government works with and through the body in regulating the activity, it has not delegated its oversight of the activity.

The use of third parties can also be considered by regulatory authority to conduct their activities, a model prevalent in the regulation of medical devices; for example, the use of recognized auditing organizations to conduct audits of manufacturers' quality managements systems to an international standard and applicable regulatory requirements. Regulatory resources are directed at establishing and maintaining oversight of audit organizations, providing more effective use of limited regulatory resources *(25).*

A government incurs costs by establishing and maintaining regulatory systems. Industry and other regulated parties incur costs in complying with regulation; for example, in undertaking studies, preparing application dossiers, maintaining records and paying fees – the cost of doing business.

Additional costs accrue from inefficient regulatory systems. If the cost of complying with regulation is disproportionately high, companies may decide against placing products on the market. For instance, a mandatory requirement to conduct local clinical trials as a condition for marketing authorisation could be a disincentive to enter a market, especially if trials conducted elsewhere reflect the patient profiles of the intended market and demonstrate safety and efficacy of the product. Similarly, lengthy product review times translate into lost revenue and unnecessary delays in the availability of products for patients – with potentially significant negative implications in terms of morbidity/mortality, health care costs and the economy (healthy economies require healthy people).

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Inefficiency also costs regulatory authorities in terms of sub-optimal impact for available resources, reputation, job satisfaction and time spent addressing complaints related to performance. Regulatory frameworks reflecting the principles of proportionality, flexibility and consistency are more likely to be effective. They allow for resources to be allocated to the regulatory activities where they are most needed.

International collaboration. Regulatory frameworks that are consistent and aligned with those of other countries and regions encourage the investment needed to bring appropriate and affordable products to that market. Internationally consistent frameworks also enable the regulatory authority to participate in work-sharing networks and other forms of regulatory cooperation (including convergence, harmonization, information- and work-sharing, reliance and recognition). When properly anchored in the regulatory framework, reliance on the work of other authorities eliminates or reduces the inefficient duplication of regulatory evaluations of medical products and the inspection/audit of facilities.

Regulatory authorities should continually explore the means of improving efficiency while maintaining standards for evaluating the quality, safety and efficacy/performance of medical products. For example, this could include the introduction or refinement good review practices *(18)* and a quality management system *(19)*; greater and more effective use of information technology; consultations with industry on common deficiencies and how best to address them; risk-based criteria for scheduling and conducting inspections; addressing gaps in guidance; performance measurement; and – as highlighted above – regulatory cooperation and reliance.

Industry also plays a critical role in contributing to the efficiency of regulatory systems. As an example, high quality applications for marketing authorization reduce the overall review time by reducing the number of deficiencies and review cycles. Similarly, a manufacturer with a good compliance record should not require the same frequency and depth of inspection as a poorly performing manufacturer. Consultations and training can be effective complements to enforcement actions in achieving the desired level of compliance.

As part of the regulatory impact analysis process, policy-makers should seek the most efficient and least burdensome means of achieving their regulatory purposes at a minimum reasonable cost, including non-regulatory options. In considering a regulatory approach, there should be consideration of the total burden and resource needs of cumulative regulation.

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Periodic performance assessments should evaluate the *actual* efficiency of regulatory instruments that are implemented in order to ensure that the foreseen benefits have been achieved and, if so, what the direct and indirect costs are.

8.9 Transparency

Transparency is the hallmark of a well-functioning regulatory system and essential to building public trust and enabling international cooperation.

Key elements:

- Transparency requires investment and a culture of openness, supported by government policy, commitment and action.
- The process of developing new or revising existing regulatory instruments should include stakeholder consultation.
- Regulatory requirements, processes, fees, assessments, decisions and actions should be accessible as much as possible.
- The regulatory authority's disclosure policies should be consistent with national laws on access to information.

*"*Informed opinion and active co-operation on the part of the public are of the utmost importance in the improvement of the health of the people*."* - World Health Organization Constitution

Transparency is a hallmark of a well-functioning regulatory system. It is in the interests of patients, consumers, governments, health care workers and manufacturers as it increases the level of public trust and confidence in the regulatory oversight of medical products. Transparency in regulatory requirements and actions allows for better-informed investment decisions in the public and private sectors and discourages discriminatory, corrupt or abusive practices.

Transparency means that all affected and potentially interested parties – domestic, foreign, public and private – have meaningful opportunities to be informed of new or amended regulations and guidelines and to make their views known before they are enacted.

Transparency means that, once adopted, medical product regulations and guidelines are readily available and accessible to stakeholders and the general public. Relevant laws, regulations and guideline documents should be posted on the authority's website. Additionally, national industry and professional associations will often work with regulatory authorities to disseminate new regulatory texts or to provide opportunities for the exchange of relevant information.

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The assessments, decisions (positive and also, when possible, negative ones) and actions of the regulatory authority should be documented and made publicly available. Such information is important to a broad range of stakeholders - including industry, researchers, health professionals, patients and consumers - who will use the information for a variety of purposes. It is also an essential element to building trust and confidence in the regulatory system.

Regulated parties should be able to access the full product assessment or site inspection reports that pertain to them. In addition to providing an insight into the basis for comments and decisions, it also serves as an educational tool that can help improve regulatory compliance and the quality of future submissions. This practice can also be beneficial to the regulatory authority by fostering a culture of transparency and accountability at the operational and management level. Furthermore, it can lead to higher quality reports by ensuring that reports clearly explain how such assessments led to decisions.

Transparency requires investment and a culture of openness that, in turn, must be supported by government policy, commitment and action. While it may not be possible for all regulatory authorities to implement the full range of measures that define an optimally transparent regulatory system, a step-wise approach can be adopted. Given the prevalence of smart devices and the internet, efforts could be directed towards establishing and maintaining an up-to-date, searchable public website that contains certain basic information, including:

- Information on the regulatory authority – roles, responsibilities, organization, and contact information.
- Access to laws, regulations, guidelines and procedures necessary to satisfy regulatory requirements and improve the safety and quality of medical products.
- A searchable product registry of approved, suspended and withdrawn products.
- Product information for health care professionals and patients.
- Licensing status of manufacturing sites.
- Health advisories, safety information, quality or substandard and falsified medical product alerts, recalls and other time-sensitive information of public health interest.
- Performance targets/results and annual reports.
- Proposed new regulatory instruments, including comment periods and how to provide input.

The findings of all audits or oversight reviews of the performance and functioning of the regulatory authority should be made public. Such reviews are an important element of public accountability, as is

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the establishment and ongoing reporting of performance against regulatory targets and the publication of annual reports.

As it fulfils its responsibilities, the regulatory authority will necessarily create or come into possession of proprietary or confidential information. Examples include personal identifiable information from clinical trials or reports of adverse events, specifications of medical product compounds or materials, and key manufacturing processes. Measures should be established to prevent the inappropriate disclosure of such specific information. There should be a mechanism to address instances when the proprietary nature or confidentiality of the information is in dispute.

In general, national law and regulation should favour transparency and public access in both the process and the criteria of regulatory decision-making. The regulatory authority's disclosure policies should be consistent with the national laws on public access to government information or "freedom of information". Procedures and contact points to obtain information held by the regulatory authority should be accessible and clear.

Transparency is a key enabler to adopting new, more efficient ways of conducting regulatory operations. It is incumbent upon regulators to practice transparency in regulatory operations and decisions as a fundamental principle of GRP but also towards building trust and maximizing opportunities for cooperation and reliance as part of a shared regulatory community responsibility.

9. Enablers for good regulatory practices

An enabling environment will facilitate a successful implementation of GRP. The non-exhaustive list of GRP key enablers include:

9.1 Political and government-wide support

A sustained support at the highest political and government levels, including policy makers, is essential for the proper implementation of the concept and principles of GRP.

GRP should form an integral part of government-wide policies on regulatory system and, in addition, be backed by strong political support.

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9.2 Effective organization and good governance supported with leadership

The structure and line of authority among and within all institutions of the regulatory system should be well defined. The integrity of the overall regulatory system is critical to the effective and efficient performance of all institutions composing the regulatory system. If more than one institution is involved in the regulatory system, the legislation or institutional regulation should provide for clear coordination and avoid an overlap of the regulatory activities. Leadership is critical for setting and carrying out the organizational vision, mission, policies and strategies which in turn significantly contribute to organizational efficiency.

9.3 Inter-and-intra-organizational communication, collaboration and coordination

Adequate and effective communication plays a fundamental role for exchanging information within and outside the institutions forming the regulatory system. When regularly communicating both internally and externally, regulatory authorities remain more transparent and accountable. Communicating correct information prevents the potential misunderstandings and dissemination of misleading information to patients and the public. Communication is a powerful tool for collaboration and coordination with relevant stakeholders at national and international levels which in turn feed into an effective and efficient use of resources and better regulatory outcomes.

9.4 A robust and well-functioning quality mangement system

QMS (*19*), which includes the application of quality risk management (QRM) principles, is a valuable tool that helps regulatory authorities to achieve greater credibility for their decisions, and greater stability and consistency in their operations. QMS contributes to systematic planning, control and improved quality in all processes throughout all regulatory functions and ensures a comprehensive approach for all.

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9.5 Sufficient and sustainable financial resources

Investment in regulatory systems is critical to a well-functioning health care system. Securing financial resources to effectively carry out the regulatory mandate and to continuously improve the performance of regulatory activities is an essential enabler for regulatory system independence, impartiality, consistency and efficiency. The financial resources of all institutions of the regulatory system should be sustainable, apart from donors' or philanthropic entities donations.

9.6 Competent human resources

An array of knowledge and the skills of regulatory staff contribute to the development, implementation and maintenance of a regulatory system for medical products. Personal and career development policies and measures (e.g. training programmes, competitive remuneration schemes) are critical for regulatory authorities to attract and recruit competent staff and, in addition, to retain staff in the service.

9.7 Pre-set organizational ethics and values

Regulatory activities should abide by ethical principles, organizational values, and professionalism. All regulatory staff should be made aware and be trained on the ethics and values as set by the regulator authorities (e.g. code of conduct). A system should be established, within or external to the regulatory system, to manage situations of departure from the organizational ethics and values.

9.8 Science- and data-driven decision-making process

Regulatory decisions, along with their making process, should be based on scientific foundations and accurate data rather than intuitions or arbitrariness. Science-based decisions provide for the consistency and predictability of regulatory outcomes.

The above-listed enablers do not work in a stand-alone mode. Rather, they work in harmony to realize the application and implementation of GRP; for example, the sufficient and sustainable financial resources contribute to the recruitment, development and maintenance of competent human resources. Similarly, financial resources shall be managed following good governance practices.

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10. Implementing good regulatory practices

WHO Member States are encouraged to implement GRP in their regulatory systems with due consideration to their legal and regulatory system realities. Transparent and predictable processes should aim to develop high-quality regulatory oversight that achieves intended objectives while also minimizing negative impact and costs.

At the same time, there should be sufficient flexibility to allow the processes to be applied proportionately to the scope, magnitude and complexity of the issue. Sustained support at the highest levels, along with adequate resourcing, is essential.

Further guidance will be developed to assist Member States both in establishing new regulatory systems for medical products and in updating existing ones.

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Glossary

The definitions given below apply to the terms as used in this document. They may have different meanings in other contexts. Readers are also encouraged to consult related WHO guidances for a more complete set of definitions relevant to best regulatory practices (see References).

public health emergency. A public health emergency (the condition that requires a governor to declare a state of public health emergency) is defined as "an occurrence or imminent threat of an illness or health condition, caused by bioterrorism, epidemic or pandemic disease, or (a) novel and highly fatal infectious agent or biological toxin that poses a substantial risk of a significant number of human facilities or incidents or permanent or long-term disability (WHO/DCD, 2001). The declaration of a state of public health emergency permits a governor to suspend state regulations and change the functions of state agencies (*26*).

quality management system (QMS). An appropriate infrastructure encompassing the organizational structure, procedures, processes and resources and systematic actions necessary to ensure adequate confidence that a product or service will satisfy given requirements for quality.

recognition. The acceptance of the regulatory decision of another regulator or other trusted institution. Recognition should be based on evidence of conformity that the regulatory requirements of the reference regulatory authority is sufficient to meet the regulatory requirements of the relying authority.

regulatory convergence. A voluntary process whereby the regulatory requirements in different countries or regions become more similar or "aligned" over time. The process results from the gradual adoption of internationally recognized technical guideline documents, standards and scientific principles, common or similar practices and procedures, or the establishment of appropriate domestic regulatory mechanisms that align with shared principles to achieve a common public health goal *(27)*.

regulatory cooperation. A practice between regulatory authorities aimed at the efficient and effective regulation of medical products. Regulatory cooperation can be practised by an agency or institution or on a government-wide basis. The range of formal mechanisms include the creation of joint institutions and treaties and conventions such as mutual recognition agreements, while less formal practices include the sharing of information, scientific collaboration, common risk assessment, joint

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reviews and inspections and the development of standards. Regulatory cooperation may also include work with international counterparts to build regulatory capacity or provide technical assistance, thus contributing to the improvement of international regulatory governance practices *(28) (29) (30) (31)*.

regulatory harmonization. The process whereby technical guidelines are developed in order to be uniform across participating authorities in multiple countries *(32)*.

regulatory impact analysis. The process of examining the likely impacts of a proposed regulation and alternative policy options to assist the policy development process *(33)*.

regulatory stock. The collection or inventory of accumulated regulations.

regulatory system. The combination of institutions, processes and the regulatory framework through which a government controls the particular aspects of an activity *(34)*.

reliance. The act whereby the NRA in one jurisdiction may take into account and give significant weight to assessments performed by another NRA or trusted institution, or to any other authoritative information in reaching its own decision. The relying authority remains independent, responsible and accountable regarding the decisions taken, even when it relies on the decisions and information of others.

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