



ประกาศสำนักงานคณะกรรมการอาหารและยา

เรื่อง แนวปฏิบัติในการกำกับดูแลผลิตภัณฑ์ยาที่ดีตามมาตรฐาน

WHO Good Regulatory Practices in the Regulation of Medical Products

เพื่อเป็นการคุ้มครองผู้บริโภคและส่งเสริมการกำกับดูแลผลิตภัณฑ์ยาตลอดวงจรชีวิต รวมถึงให้มีแนวทางการพิจารณาอนุญาตเป็นไปอย่างมีประสิทธิภาพ และมีการปฏิบัติงานเป็นมาตรฐานไปในแนวทางเดียวกัน เพื่อประโยชน์ที่ผู้ป่วยจะได้รับผลิตภัณฑ์ยาที่มีคุณภาพ ความปลอดภัย และมีประสิทธิภาพในการรักษาอย่างรวดเร็ว

เลขาธิการคณะกรรมการอาหารและยาจึงวางแนวปฏิบัติในการกำกับดูแลผลิตภัณฑ์ยาที่ดีตามมาตรฐาน WHO Good Regulatory Practices in the Regulation of Medical Products ขององค์การอนามัยโลก เพื่อเป็นกรอบหลักการ และใช้เป็นแนวปฏิบัติในการจัดทำข้อกำหนดกฎหมายการกำกับดูแลผลิตภัณฑ์ยาให้เป็นมาตรฐานเดียวกันในทุกระดับ ตามแนบท้ายประกาศนี้

ทั้งนี้ ตั้งแต่บัดนี้เป็นต้นไป

ประกาศ ณ วันที่ ๒๔ พฤษภาคม พ.ศ. ๒๕๖๔

(นายไพศาล คั่นคุ้ม)

เลขาธิการคณะกรรมการอาหารและยา

Annex 11

Good regulatory practices in the regulation of medical products

Background

A fundamental role of government is to protect and promote the health and safety of the public, including by delivering health care. A well-functioning health care system requires available, affordable medical products that are safe, effective and of assured quality. As medical products are essential in the prevention, diagnosis and treatment of disease, the consequences of substandard and falsified medical products can be life threatening. This is a concern, as users of medical products are not usually in a position to judge their quality. The interests and safety of the public must therefore be entrusted to a regulatory body or bodies that ensure that only products in legal trade are available and that marketed products are safe, perform as claimed and are of assured quality.

The regulation of medical products has become increasingly complex with the globalization of product development, production and supply and the rapid pace of technological and social change in the context of limited financial and human resources. The importance of robust regulatory systems was recognized by the Sixty-Seventh World Health Assembly when it endorsed 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” (23).

A sound system of oversight requires that regulatory authorities be supported by an effective framework of laws, regulations and guidelines and that they have the competence, capacity, resources and scientific knowledge to deliver their mandate in an efficient and transparent manner. The extent to which a regulatory framework fulfils its policy objectives depends on the quality of its development and implementation. GRP 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. A sound regulatory framework, including international norms and standards, and the recruitment and development of competent staff are necessary but not sufficient conditions to ensure “good oversight”. All individuals in regulatory authorities should be guided by GRP in setting appropriate requirements and formulating decisions



that are clear, transparent, consistent, impartial, proportionate, timely and based on sound science. Regulated parties and other stakeholders also play important roles in ensuring a clear, efficient regulatory environment so that quality-assured medical products are available to patients.

Acknowledgements	271
Abbreviations to Annex 11	271
Executive summary	271
1. Introduction	273
2. Purpose	273
3. Scope	273
4. Glossary	274
5. Objectives	276
6. Key considerations	276
7. Overview of a regulatory system for medical products	277
7.1 Components of the regulatory framework	277
7.2 Components of a regulatory system	279
8. Principles of good regulatory practices	282
8.1 Legality	283
8.2 Consistency	284
8.3 Independence	286
8.4 Impartiality	287
8.5 Proportionality	288
8.6 Flexibility	290
8.7 Clarity	292
8.8 Efficiency	294
8.9 Transparency	297
9. Enablers of good regulatory practices	299
9.1 Political and government-wide support	299
9.2 Effective organization and good governance supported by leadership	300
9.3 Inter- and intra-organizational communication, collaboration and coordination	300
9.4 A robust, well-functioning quality management system	300
9.5 Sufficient, sustainable financial resources	300
9.6 Competent human resources	301
9.7 Organizational ethics and values	301
9.8 Science- and data-driven decision-making process	301
10. Implementing good regulatory practices	301
References	302

Acknowledgements

WHO acknowledges all the authors, stakeholders and organizations who contributed to the preparation of this document.

Abbreviations to Annex 11

APEC	Asia–Pacific Economic Cooperation
ASEAN	Association of Southeast Asian Nations
GRP	Good regulatory practices
OECD	Organisation for Economic Co-operation and Development

Executive summary

A fundamental role of government is to protect and promote the health and safety of the public, including providing health care. A well-functioning health care system requires available, affordable medical products that are safe, effective and of consistently assured quality.

The medical products sector is one of the most regulated of all industries, because of the impact of the diverse range of medical products on health, the difficulty in assessing their quality, safety and efficacy or performance¹ and the complexity of 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 facilitating innovation and access to safe, effective and good-quality medical products. The framework should also have the necessary flexibility and responsiveness, particularly for managing public health emergencies, addressing new technologies and practices and promoting international regulatory cooperation.

Governments incur costs by establishing and maintaining regulatory systems to protect and promote the health of their citizens. Regulated parties incur costs in complying with regulations. Inefficient regulatory systems, however,

¹ Medicines and vaccines: efficacy; medical devices including in-vitro diagnostics: performance

have impacts on the health system, with potentially significant implications for morbidity and mortality, health care costs and the economy.

A sound legal framework, adoption of international norms and standards and 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 in organizations entrusted with regulating medical products in formulating decisions that are clear, transparent, consistent, impartial, proportionate, timely and based on sound science and legislation.

GRP can be defined as a set of principles and practices applied to the development, implementation and review of regulatory instruments – laws, regulations and guidelines – to achieve public health policy objectives in the most efficient way. Successful application of GRP is the hallmark of a modern, science-based, responsive regulatory system in which regulations are translated into desired outcomes. GRP provide a means of establishing and implementing sound, affordable, efficient regulation 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 derived from an extensive review of public documents issued by governments and multilateral organizations as well as many consultative workshops, benchmarking exercises and interactions with Member States. The nine principles presented in this document – legality, consistency, independence, impartiality, proportionality, flexibility, clarity, efficiency and transparency – are relevant to all authorities responsible for the regulation of medical products, irrespective of their resources, sophistication or regulatory model. Regulated parties and other stakeholders also have important roles to play in achieving an efficient regulatory environment.

GRP serve as a basis for guidance documents on best regulatory practices. The body of WHO guidance documents is intended to provide regulatory authorities with comprehensive guidance for improving their performance. This document will be supplemented by practical guides and tools designed to facilitate implementation of GRP.

1. Introduction

This document responds to requests from national authorities responsible for regulation of medical products (see 4. Glossary) for guidance in addressing common gaps in regulatory practices identified during benchmarking exercises. The document draws on documents published by multilateral bodies such as the Asia-Pacific Economic Cooperation (APEC) (10), the Organisation for Economic Co-operation and Development (OECD) (11, 12), the World Bank (13) and the Association of Southeast Asian Nations (ASEAN) (14), as well as guides published by a number of governments. The document also takes account of earlier WHO documents that touch on aspects of GRP (15–22) and of WHO experience in applying the WHO Global Benchmarking Tool (GBT) and promoting the principles of good regulatory practices (GRP). Proper implementation of GRP through GRP enablers across the regulatory system (see 4. Glossary) can result in desired regulatory outcomes and impact.

2. Purpose

This document presents the high-level principles of GRP. They are intended to serve as benchmarks and thereby guide Member States in applying good practices in regulation of medical products. This document is also meant to guide Member States in prioritizing the functions of their regulatory system according to their resources, national goals, public health policies, medical products policies and the medical product environment. This “principles-based” document will be supplemented by practical guides and tools to facilitate implementation of GRP by organizations responsible for the regulation of medical products. This basic document is complemented by related guidance on best regulatory practices, including good governance practices (24), good reliance practices (25), good review practices (26) and quality management systems (see 4. Glossary) for national regulatory authorities (NRAs) (27). The group of documents is intended to provide regulatory authorities with comprehensive guidance on improving performance.

3. Scope

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

The document is relevant to all regulatory authorities, irrespective of their resources, maturity or regulatory model. High-level GRP principles are

equally applicable to supranational (e.g. regional), national and subnational regulatory systems, and systems in which several institutions are charged with regulating certain products or activities in a country or jurisdiction. The document is also intended for a number of related audiences: institutions and policy-makers responsible for formulating health policies, laws, regulations and guidelines; institutions that, together, form national or supranational systems for regulation of medical products; and regulatory networks and parties affected by or otherwise interested in regulatory frameworks, such as industry or other developers of medical products.

4. 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 guidance for more complete definitions relevant to best regulatory practices (see References).

Co-regulation. A system of shared regulatory responsibilities in which an industry association or professional group assumes some regulatory functions, such as surveillance and enforcement or setting regulatory standards.

International standards and guidelines. For the purpose of this document, the term includes relevant WHO standards and guidelines and any other relevant, internationally recognized standards (e.g. International Organization for Standardization or pharmacopoeial standards) and guidelines (e.g. the International Council on Harmonisation of Technical Requirements for Pharmaceuticals for Human Use or guidelines of the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme).

Medical product. For the purpose of this document, the term includes medicines, vaccines, blood and blood products and medical devices, including in-vitro diagnostics.

Public health emergency. The condition that requires a governor to declare a state of public health emergency, 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 fatalities or incidents or permanent or long-term disability.

The declaration of a state of public health emergency permits a governor to suspend state regulations and change the functions of state agencies (1).

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

Recognition. Acceptance of the regulatory decision of another regulator or other trusted institution. Recognition should be based on evidence that the regulatory requirements of the reference regulatory authority are sufficient to meet the regulatory requirements of the relying authority. Recognition may be unilateral or mutual and may, in the latter case, be the subject of a mutual recognition agreement.

Regulatory convergence. A voluntary process whereby the regulatory requirements in different countries or regions become more similar or “aligned” over time. Convergence results from 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 (2).

Regulatory cooperation. A practice among regulatory authorities for efficient and effective regulation of medical products. May be practised by an agency, an institution or a government. The formal mechanisms include creation of joint institutions, treaties and conventions such as mutual recognition agreements, while less formal mechanisms include sharing information, scientific collaboration, common risk assessment, joint reviews and inspections and joint development of standards. May also include work with international counterparts to build regulatory capacity or provide technical assistance, thus contributing to improvement of international regulatory governance practices (3–6).

Regulatory harmonization. A process whereby the technical guidelines of participating authorities in several countries are made uniform (7).

Regulatory impact analysis. Process of examining the probable impacts of a proposed regulation and of alternative policies to assist the policy development process (8).

Regulatory stock. Collection or inventory of accumulated regulations.

Regulatory system. The combination of institutions, processes and the regulatory framework with which a government controls particular aspects of an activity (9).

Reliance. The act whereby a regulatory authority in one jurisdiction takes into account and gives significant weight to assessments by another regulatory

authority or trusted institution or to any other authoritative information in reaching its own decision. The relying authority remains independent, responsible and accountable for the decisions taken, even when it relies on the decisions, assessments and information of others.

5. Objectives

GRP ensure sound, effective regulation of medical products as an important part of health system performance and sustainability. If they are implemented consistently and effectively, they can result in higher-quality regulation, better regulatory decision-making and compliance, more efficient regulatory systems and better public health outcomes. They help to ensure that regulatory systems remain up to date as the technologies and systems in which they are used continue to evolve. In an increasingly complex, interconnected regulatory environment, GRP also promote trust among regulatory authorities and other stakeholders, such as industry, academia, research centres and health care professionals and thereby facilitate international cooperation and the adoption of more effective and efficient approaches to ensuring the quality, safety and efficacy or performance of medical products in the global regulatory community. The ultimate aim of GRP is to serve and protect public health and patients' interests, with respect for all applicable ethical principles.

6. Key considerations

The medical products sector is one of the most regulated of all industries because of the impact that the diverse range of medical products can have on health and society, the difficulty in assessing their quality, efficacy or performance and safety, lessons learnt from public health tragedies and the complexity of developing, producing, supplying and monitoring medical products to ensure that they consistently perform as intended. Many countries therefore have increasingly sophisticated sets of laws, regulations and guidelines to control all aspects of the life cycle of medical products.

In providing the necessary regulations and tools for fulfilling publicly entrusted mandates, regulatory authorities have a duty to ensure that they regulate in a manner that achieves public policy objectives. They must therefore establish and implement a coherent regulatory framework to provide the required level of oversight and control while facilitating innovation and access to safe, effective and high-quality medical products. They must also build the necessary flexibility and responsiveness into the regulatory framework, particularly for managing public health emergencies (see 4. Glossary), addressing new technologies and best practices and promoting international regulatory cooperation (see 4. Glossary).

Increasingly, policy-makers and regulatory authorities are adopting modern models of regulation that are responsive to resource constraints while meeting the challenges posed by scientific development, globalization, rising public expectations and public health emergencies. Weak or inefficient regulatory systems can limit access to safe, effective and, high quality medical products and pose a threat to public health. As countries strengthen their regulatory capacity, they must ensure that their regulatory systems are science-based, that they adhere to international standards and guidelines and that their approach leverages the work of other, trusted regulatory authorities and institutions when possible. To this end, countries are encouraged to formulate and implement policies and strategies that promote international collaboration (23), convergence, harmonization, information- and work-sharing and reliance (see 4. Glossary) as part of GRP (25). WHO is establishing a framework for evaluating NRAs and regional regulatory systems and for designating those that meet the requirements of WHO listed authorities (28).

Regulatory control of medical products to protect public health is fully acknowledged, as noted above. The issue is how to regulate effectively, efficiently and transparently, such that the interests of the health care system are served. Consistent application of GRP in all aspects of oversight is essential in ensuring that those interests are served and in providing the foundation for a well-performing, respected regulatory system. GRP are principles and practices applied to the development, implementation and review of regulatory instruments – laws, regulations and guidelines – in order to achieve public health policy objectives in the most efficient way. GRP instil a culture of best practices among institutions responsible for regulatory oversight to ensure that regulation is fairly, consistently and effectively applied.

7. Overview of a regulatory system for medical products

Definitions are essential for a common understanding of concepts. While more terms are defined in the Glossary, the terms “regulatory framework”, “legal framework”, “regulatory authority”, “regulatory system” and “regulatory outputs” are explained below to ensure proper understanding of their use in this document.

7.1 Components of the regulatory framework

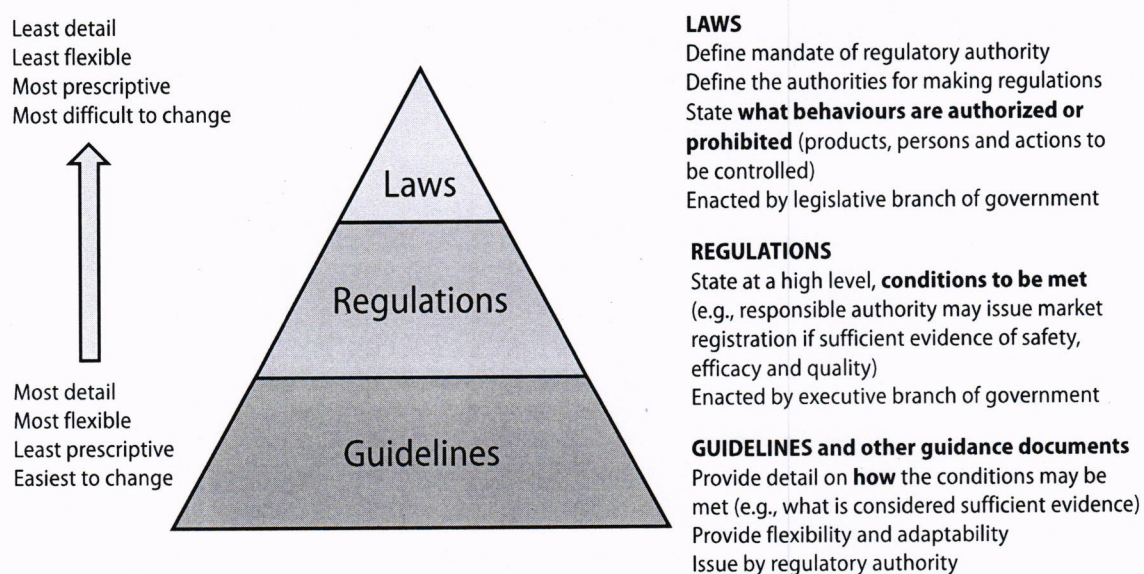
In this document, the terms “law” and “regulation” are used to describe the components of the legal framework (binding legislation). Other terms may be used in some jurisdictions, such as “act” instead of “law” or “ordinance” instead of “regulation”.

Laws generally define the roles and responsibilities of institutions, in this case, a regulatory authority, ministry of health or 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 an institution to make lower-level (or subordinate) regulations.

Regulations are a diverse set of instruments by which governments place requirements on enterprises and citizens. Regulations usually state at high level the conditions to be met and the requirements defined in laws. For instance, a law may prohibit the manufacture, importation or sale of a medical product in the absence of specific authorization, while regulations would set out the conditions for obtaining authorization, such as the provision of certain types of information (the results of non clinical testing and clinical trials, data on manufacturing and control) that allow the regulatory authority to establish the quality, safety and efficacy or performance of a medical product.

Guidelines (and other guidance documents) provide further detail on how the regulated stakeholders can comply with laws and regulations. Guidelines may also provide details of the processes of enforcement of the respective legislation (laws and regulations). Within a regulatory framework for medical products, such documents are usually non-binding and are generally more detailed and scientific in nature. They are thus appropriate for describing the approaches that are generally considered suitable for satisfying regulatory requirements but unsuitable for inclusion in legislation.

Fig. 1
Architecture of a regulatory framework



7.2 Components of a regulatory system

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

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

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

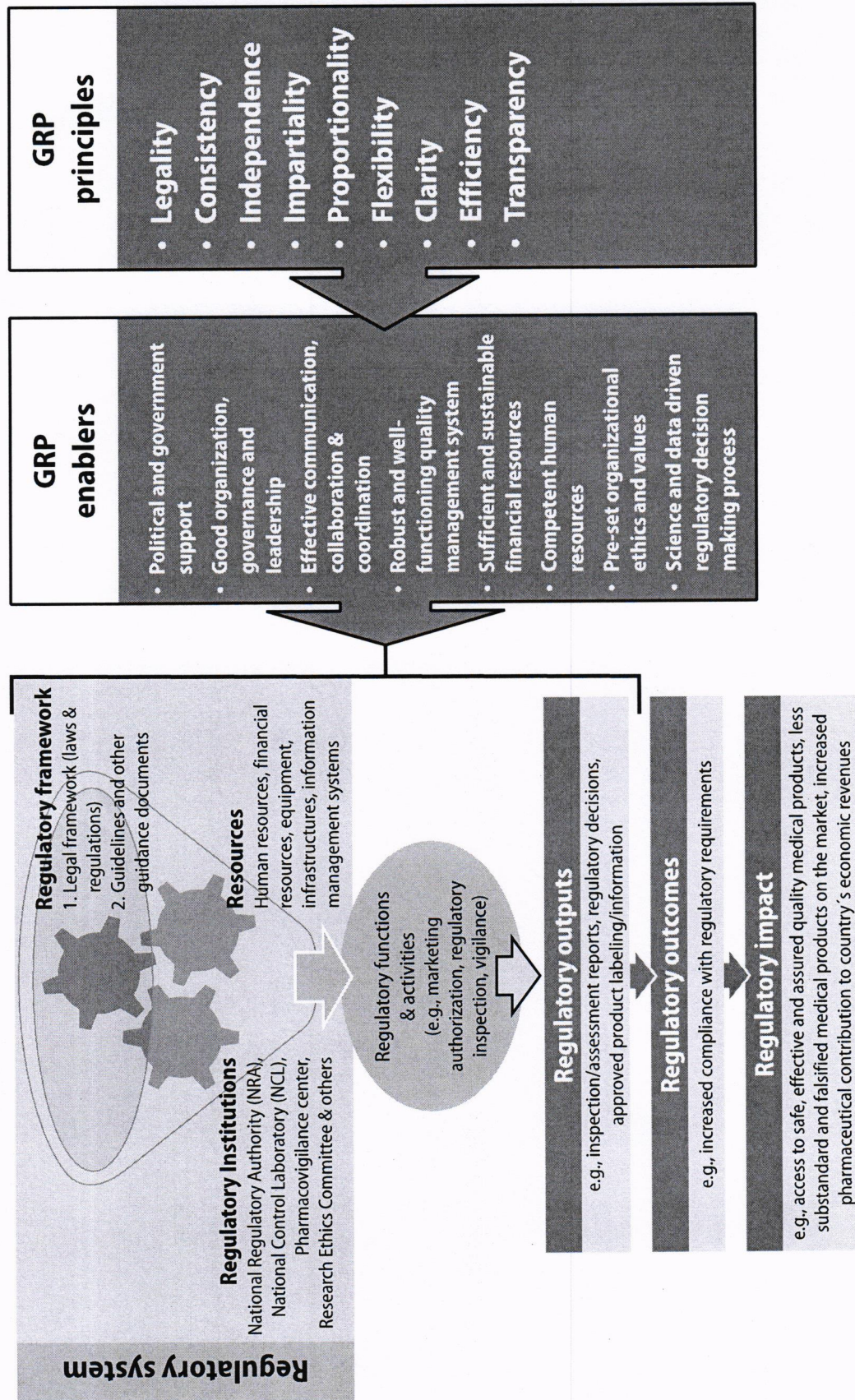
Regulatory outputs are the results or products of the regulatory authority, such as reports of inspections and assessments, decisions and product labels.

The term *regulatory system* is used to describe the combination of institutions, processes, regulatory framework and resources which, taken together, are integral to effective regulation of medical products in a country or multi country jurisdiction. GRP should be considered and applied to the whole regulatory system.

Fig. 2 illustrates the principles and enablers of GRP and the components of a regulatory system.

Fig. 2

Principles and enablers of good regulatory practices (GRP) and components of a regulatory system



In the overall regulatory system, three components (inputs) contribute most to regulatory functions and activities: (i) the regulatory framework, composed of the legal framework (laws and regulations), guidelines and other guidance documents; (ii) regulatory institutions, which may be represented by one or more entities, including the NRA, the national control laboratory, pharmacovigilance centres and research ethics committees; and (iii) all types of resources, including human and financial, infrastructure and equipment and information management systems. The regulatory outputs depend on the functions and activities concerned (e.g. regulatory and marketing authorization, inspection and assessment reports). The concepts and principles of GRP apply to the overall regulatory system, as explained above. For application and implementation of GRP, several enablers are essential (see section 9. Enablers for Good Regulatory Practices). When the principles of GRP are properly implemented through the enablers, the desired regulatory outcome and impact can be achieved.

WHO classifies the spectrum of regulatory activities for medical products into seven common regulatory functions, which are applicable to all medical products: clinical trials oversight, marketing authorization, vigilance, market surveillance and control, licensing of establishments, regulatory inspection and laboratory testing (29). In addition, a number of non common functions apply to certain medical products, such as official lot release of vaccines and other biologicals.

The term *regulatory authority* implies that a single organization is mandated to perform all regulatory functions. This is not always the case. For example, different organizations may be legally responsible for regulating medicines and vaccines and for medical devices. Even when one body is responsible for all regulatory functions, aspects critical to certain functions may lie outside its authority, such as those performed by surveillance or vigilance centres that have formal relations with the authority; these include activities such as collecting reports on adverse events, surveillance for substandard and falsified medical products and monitoring advertising. Certain regulatory functions may be undertaken by third parties, as in the case of auditing organizations for medical devices. In order to ensure a comprehensive and efficient regulatory system, clear roles, responsibilities, processes and communication channels must be established among the different organizations responsible for performing regulatory functions.

Regulatory activities may also be undertaken at supranational (e.g. regional), national or subnational level. Examples include supranational evaluation of certain products for the purpose of granting marketing authorization that is valid for several countries or inspections of certain manufacturing sites for medical products for good manufacturing practices at national level.

8. Principles of good regulatory practices

There is no universal model for regulation of medical products. Each approach reflects national health policies and priorities, national socioeconomic development, the availability of resources and infrastructure, the health system, the national legal system, research and development capacity and local production capacity. Nonetheless, as in other regulated sectors, there is growing international consensus on best practices to be applied in regulation of medical products.

A review of public documents on GRP (10, 13, 14, 30) reveals common practices that should be adopted by all institutions responsible for or involved in regulation 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. Nine principles are listed in Table 1 and described below, with considerations relevant to regulation of medical products. The principles, practices and examples will be further elaborated in supplementary guidance that will complement this document.

Table 1
Principles of good regulatory practices

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 that execute regulation of medical products should be independent.
Impartiality	All regulated parties should be treated equitably, fairly and without bias.
Proportionality	Regulation and regulatory decisions should be proportional to risk and to the regulator's capacity to implement and enforce them.
Flexibility	Regulatory oversight should not be prescriptive but rather be flexible in responding to a changing environment and unforeseen circumstances. Timely responsiveness to a specific need and in particular to public health emergencies should be built into the regulatory system.
Clarity	Regulatory requirements should be accessible to and understood by users.

Table 1 *continued*

Efficiency	Regulatory systems should achieve their goals within the required time and at reasonable effort and cost. International collaboration promotes efficiency by ensuring the best use of resources.
Transparency	Regulatory systems should be transparent; requirements and decisions should be made known, and input should be 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 authority, scope and flexibility to safeguard and promote health.
- Delegation of power and responsibilities to various 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.
- The regulatory framework should clearly define the scope and lines of authority of the institutions that form the regulatory system to ensure its integrity.
- The regulatory authority must be held accountable for its actions and decisions to the public, those regulated and the government within a legal framework.

The principle of legality requires that a regulatory system be structured such 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 with the powers conferred by the legal framework (31). The law or act that establishes the regulatory authority should clearly state the objectives of the enabling legislation, the powers of the authority, the scope of the products and general activities that the authority is mandated to regulate and the provisions for making regulations.

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 regulating medical products, the functions and responsibilities of each should be clear and complementary, and the processes for communication and coordination among them should be defined (see section 8.2 Consistency).

As cooperation among regulatory authorities is essential to manage increasingly complex and cross jurisdictional issues, a modern legal framework for medical products must support and encourage all forms of cooperation, including convergence, harmonization, information- and work-sharing, reliance and recognition (see 4. Glossary). Ideally, this is stated explicitly in provisions of laws and/or regulations, with operational detail provided in policies and procedural guidance. A legal framework should at least not prohibit all forms of regulatory cooperation, such as the use of assessments and decisions of other trusted regulatory authorities and institutions in conducting 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 the exchange of good practices and may save resources and avoid duplication.

Legislation must be in place to control and perform all the 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 ensure the integrity of the regulatory system by providing clear authority, scope, power, roles and responsibilities to the institutions that form the system. Conflict in organizational authority or responsibilities should be avoided.

All regulatory authorities must be accountable to the public, the bodies they regulate and the government for their actions and decisions as part of good governance and accountability. In the context of GRP, regulatory authorities are accountable when they 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 the authority and controls provided for by the legal framework. Processes should therefore be in place for review of regulatory decisions, including internal appeals and judicial appeal of the decisions of regulators, such as on the grounds of procedural fairness and due process, in addition to scientific and administrative grounds.

8.2 Consistency

Regulation of medical products should be consistent with government policies and legislation and be applied consistently and predictably.

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 implemented and enforced consistently for all medical product sectors and stakeholders.

Regulation 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. It should also be coherent with any treaties, conventions and regional or international agreements to which the country is a party as well as any supranational legislation that affects constituent member states.

Any overlap or conflict with existing laws and regulations should be avoided, as this causes confusion, duplication of mandates and unnecessary regulatory work and increases the likelihood of noncompliance. Manufacturers (for the purpose of this document, manufacturers also means marketing authorization holders), importers, distributors and other stakeholders should be able consistently to identify the responsible authority in laws and regulations. Consistency is particularly important when regulation of medical products is decentralized, for instance, with central and state or provincial authorities. Effective systems should be in place for consultation, cooperation and coordination among the different levels of government to promote national uniformity of regulatory requirements while respecting local responsibilities. All regulatory functions and activities should be efficiently integrated to ensure the uniformity of the regulatory system. Similar considerations apply when more than one institution or department at the same level of government is responsible for different, or the same, regulatory functions and products – a situation that is not uncommon. Unclear or conflicting mandates and requirements create complex regulatory systems and challenge effective communication and coordination. In all instances, formal mechanisms for proper coordination should be established during the drafting and execution of regulatory instruments and the operations of bodies charged with the regulation of medical products.

Consistency in regulatory actions and decisions is ensured when the same or similar circumstances lead to the same or a similar outcome. It is therefore important that the regulatory system build an institutional memory, by recording decisions, to ensure similar, fair treatment in future situations.

Regardless of differences in technology, the level of regulatory oversight in relation to the risk posed by different types of medical products and regulated entities (manufacturers, importers and distributors) must be consistent. Consistency is upheld when the regulatory framework provides for impartial appeal of regulatory decisions. The enforcement of such appeals and corrective measures should also be consistent among sectors.

Consistency is also ensured by sufficient, clear regulatory guidance, based, when possible, on international guidelines; orientation and training programmes for staff; and regular, transparent interactions with regulated parties and other stakeholders (e.g. industry associations, patients, health care professionals associations and other relevant government institutions). These are mechanisms for improving process and for the identification and resolution of issues.

Application of a well-functioning quality management system that covers all regulatory activities (33) is critical for regulatory consistency. This includes adoption of a process approach, involving systematic definition and management of regulatory processes and their interactions 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 may also be important in ensuring consistency in the application of regulations and regulatory operations.

8.3 Independence

Institutions responsible for regulation 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.
- Regulatory activities and decisions should be free of improper and undue influence of stakeholders.
- Appropriate funding and clear funding processes are essential.
- The independence of the leadership should be established to ensure independent behaviour during and after employment.

According to an OECD publication entitled *Creating a culture of independence* (32):

Regulatory agencies (authorities) often find themselves under various pressures from different stakeholders and interest groups which can subject them to different forms of influence. To ensure they conduct their activities correctly and achieve the right policy outcomes they must take on board legitimate interests and protect themselves from inappropriate or undue influence.

Good governance and anti-corruption measures (24) should be built into the regulatory framework to obviate actual or perceived conflicts of interest, unfounded bias or improper influence by stakeholders (also known as “regulatory capture”). To maintain public confidence, the regulatory authority must operate, and be seen to operate, independently, authoritatively and impartially and to discharge its duties independently of the regulated entities (e.g. researchers and industries).

When regulators are funded by fees, an appropriate cost-recovery mechanism is essential to set the “right” fee and to avoid a regulator that is under-funded, captured by industry or undermined by the executive. It may be easy to influence a regulator that is funded from general government revenues by reducing its resources. Annual appropriations make it easier to influence a regulator than multi annual appropriations, which are less susceptible to short-term shocks, such as political or electoral imperatives. Adequate safeguards can protect the budget from being used to unduly direct the regulator.

The nomination and appointment of the regulator’s leadership should be based on transparent and accountable processes. Clear rules to avoid conflicts of interest should be in place to ensure independent behaviour during and after employment.

8.4 Impartiality

All regulated parties should be treated equitably, fairly and without bias.

Key elements:

- Regulatory activities and decisions should be free of conflicts of interest or unfounded bias.
- The regulatory system must operate impartially.
- The regulatory authority should not be engaged in the activities it regulates nor be hierarchically subordinate to the institutions that perform the regulated activities.
- Regulatory decisions should be based on science and evidence, and the decision-making process should be robust, according to defined criteria.

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

The regulatory authority must operate impartially, discharging its duties independently of the regulated entities (see section 8.3 Independence). This principle extends to researchers and other experts sitting on scientific and advisory committees that make recommendations to the regulatory authority on regulatory policy or the authorization of medical products. Declarations of interest must be completed and reviewed, and rules for withdrawal should be defined before discussions in order to maintain the integrity and impartiality of the committee and its recommendations.

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

Regulatory activities and decisions should be based on science and evidence and be predictable. While good regulatory judgement and discretion are necessary in enforcement, actions and decisions should be based on regulatory requirements and on the evidence for or the circumstances of the situation (see also sections 8.2 Consistency and 8.6 Flexibility).

Regulators should avoid actual or perceived influence and be open and transparent about their decisions and decision-making process. The scientific and technical basis for regulatory oversight should be objective and accessible. Public consultation and transparency throughout decision making should ensure impartiality, better regulatory outcomes and greater public confidence in the use of regulated products.

8.5 Proportionality

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

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.

Box continued

- Regulations should not exceed the national capacity to implement and enforce them.
- Assessment of medical products should be based on a benefit–risk evaluation and continuous monitoring of the benefit–risk profile in a robust vigilance system.

The principle of proportionality demands that an action not exceed what is necessary to achieve the 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 for the aim and not 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 necessary to ensure the safety and efficacy of a new medicine for marketing authorization, whereas studies such as of in-vivo bioequivalence or, when appropriate, in-vitro studies are sufficient for generic medicines.

Regulatory enforcement and inspection regimes should also be proportionate to the risk and severity of an infraction in order 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 a regulation is proportionate to the nature of the risk. For instance, the frequency of inspections could be determined in part by a manufacturer's history of compliance.

The principle of proportionality also applies to the policies and processes by which regulations are made. Regulation-making should be flexible and proportionate to the complexity and/or impact of the problem that it is to address. For instance, a rigorous cost–impact analysis may be required for a new, complex regulatory framework, whereas a more pragmatic approach could be used for simple regulations or when the policy alternatives are limited.

Regulation should not exceed national capacity to implement and enforce it.

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 (21).

Furthermore, lack of resources or ability to implement and enforce represent a liability for governments.

Assessment of medical products should be based on a benefit–risk evaluation based on the evidence submitted on the quality, safety and efficacy

or performance of the product. All the demonstrated benefits of the medical products should be weighed against the identified risks. Regulatory systems should include appropriate surveillance or vigilance to monitor the benefit–risk profile and to take any actions required.

8.6 Flexibility

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

Key elements:

- The regulatory system, including its frameworks, should provide sufficient flexibility to reflect or respond to changes in the regulated environment, such as evolving science and technology.
- The regulatory system should be prepared to provide timely responses to urgent situations such as public health emergencies and shortages of medical products.
- The language of regulation should reflect performance when possible, allowing for alternative approaches to achieve the same result.
- The regulatory system should provide the flexibility for applying good judgement.

Flexibility is essential to ensure that regulatory frameworks and regulatory systems remain “fit for purpose”. The design and use of regulatory instruments must therefore be appropriate. A meaningful, understandable, enforceable regulatory framework should contain sufficient detail to ensure clarity. It should also allow flexibility to respond to new technologies and innovation and to changes in the regulated environment and to ensure a timely response to unforeseen public health threats. Flexibility in regulatory oversight should be risk-based and should not compromise the quality, safety, efficacy or performance of a product (28).

Responsiveness is an extended principle of flexibility. It represents the possibility of responding more rapidly than usual in certain circumstances. For example, an expedited response or review might be necessary in a public health emergency.

Responsiveness is time-bound and temporary, as it is necessary in urgent situations such as a public health emergency, serious shortages of a medical product with no alternative, an unmet medical need or rare disorder and medical products for compassionate use or donation. Regulatory systems should be well prepared and have the necessary regulatory instruments to respond to and manage such situations. The NRA should have flexible and

expedited development programmes or review processes to accelerate the access to patients by approval of innovative products for serious, life threatening and rare diseases and to address unmet medical needs. Flexible and responsive provisions are critical for ensuring that the authority can make decisions based on the best available science and on benefit–risk considerations, often in the face of less than complete information (e.g. compassionate use, emergency use authorization or listing). Lack of the necessary regulatory tools and flexibility can be a real, significant impediment to ensuring public safety, particularly during public health emergencies.

When regulatory responsiveness is essential, a regulatory authority should consider prioritizing its activities through a risk-based approach. The involvement of policy- and decision makers and regulatory collaboration and coordination within the international regulatory community significantly contribute to regulatory responsiveness.

The aim of flexibility and responsiveness in regulatory frameworks should be to accommodate the evolution of science and technology. The language of the regulations that support laws is usually based on performance rather than being prescriptive (15), thus allowing regulated parties to use alternative approaches to achieve the same outcome.

Guidelines and other guidance documents are the most detailed, most flexible and most amendable regulatory instruments. These attributes ensure that the regulatory framework can respond to new risks in a timely manner and allow for possible use of advances in regulatory science and technology for 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 in the regulation and used to describe how compliance with the regulation may be achieved. They should also allow for other, justified approaches to compliance. Alternative approaches to the principles and practices described in guidance may be acceptable, provided they are adequately justified. The flexibility and amendable attributes of guidelines are lost if such detailed texts become part of regulation.

For science that is evolving rapidly but not sufficiently mature to justify regulatory guidelines, lists of “points to consider” can provide useful principles-based guidance and definitions for promoting best practices, a common regulatory understanding and international convergence and prepare the ground for eventual guidelines. International guidelines and standards should always be considered in developing new guidance documents, and regulators should support international harmonization and convergence. National requirements beyond international standards should be well justified.

The regulation of medical products is complex and evolving. New technologies and practices will continue to pose challenges to regulatory systems and redefine the boundaries of what can and should be regulated. Before

developing regulations to address new technologies or address certain practices, regulators should have the necessary regulatory flexibility to interpret existing legislation and regulations appropriately. It should be possible to revise or withdraw a regulation or guideline when it is no longer required.

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.
- The terminology should be defined and consistent with international norms when possible.
- Consultation, education and training in new requirements contribute to clarification 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.

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 the intended users. This will require collaboration with legal personnel in considering the objectives of the legal instrument, the intended audience, other stakeholders who may be impacted and feedback from internal and external consultations, including subject matter experts. Drafting of instruments in clear, unambiguous, precise language in a form consistent with other laws and regulations reduces possible disputes or misinterpretation and promotes compliance. Meetings between NRAs and regulated entities can be helpful in clarifying the application of guidance and cases in which there is no guidance.

As an initial step, an authority that is drafting medical product regulations should conduct a review to identify unclear areas and resolve any inconsistencies in the regulation itself or with other regulations. This step also provides an opportunity to review the “regulatory stock” – the accumulated body of applicable regulations (see 4. Glossary) – to identify whether updating

and better integration of regulatory requirements are necessary to eliminate inconsistencies, redundancy and complexity or to adapt to new requirements.

Interested parties, including the public, should be informed of and contribute to regulatory development and regulatory impact analysis (see 4. Glossary) in order to improve the quality and language of a regulatory instrument, ensuring 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 valuable for systematic assessment of the expected effects of regulatory proposals. It is usually undertaken by policy analysts in the regulatory departments, agencies or ministries that are sponsoring the proposal, primarily to assist decision-makers in considering a proposal. The product of a regulatory impact analysis is a document that summarizes the regulatory proposal, possible alternatives and the aspects and impacts of implementing the proposal.

Terms should be defined in order to avoid ambiguity or misinterpretation. When possible, they should be consistent with established international norms, standards and harmonized guidelines. As noted previously, international standards and guidelines (see 4. Glossary) are particularly important vehicles for promoting common regulatory language, convergence and international cooperation.

The principle of clarity is also applicable to regulatory and administrative guidelines, which are instrumental for interpreting and providing operational clarity to regulations. Guidelines should be developed according to good guidance practice to ensure that they are written clearly and concisely and are consistent with other guidelines and the underlying regulations. Standard templates and formats, style guides, editors, experts in the regulatory framework and users' feedback obtained with established tools (e.g. forms, webinars, institutional polls) should be used.

Draft guidelines, like regulations, should be submitted for internal and external consultation to confirm that the language is clear or requires revision to improve comprehension. Plain language and simple sentence structure should be the goals, with illustrative examples when possible. Education, awareness sessions and training, with clear timelines for adoption of new regulations and guidelines, should be considered for ensuring clarity and compliance when introducing or amending regulations and guidelines, particularly when they are complex.

Regulations and supporting guidelines should be reviewed periodically to ensure that they reflect the authority's current practices and expectations, are adapted to scientific and technological developments and are aligned with current international standards and guidelines, when applicable. Review and revision of a guideline should include consideration of the consequential changes in other guidelines, which should be revised simultaneously.

The process and basis for taking regulatory decisions and enforcing them should be clear and accessible to those directly impacted or otherwise affected (see section 8.9 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.

8.8 Efficiency

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

Key elements:

- Efficient regulatory systems achieve the intended public health goals.
- A sound regulatory framework, competent staff and 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, least burdensome means of achieving their regulatory purposes and confirm effectiveness after implementation.
- The total burden and resources required for cumulative regulation should be evaluated.
- Regulatory authorities should continually explore ways of improving efficiency in fulfilling their mandate.
- Alignment of regulatory requirements with those of other countries and international collaboration promote efficiency.
- Regulated entities contribute critically to the efficiency of regulatory systems.
- The efficiency of regulatory instruments and regulatory operations should be assessed with performance-based indicators.

An efficient regulatory system must be based on science and evidence and the principles of risk assessment and management and embed a strategy of international regulatory cooperation into daily business. A regulatory system in which sound decisions cannot be made in a timely, consistent fashion is not effective. Its efficiency depends not only on sufficient resources but also on the type of resources and their effective use, irrespective of size. In this context, lack of integrity in the overall regulatory system is a barrier to regulatory efficiency.

Regulatory systems with fewer resources can be as effective as those with more resources if they use a risk-based approach, take advantage of the

work and decisions of other regulatory authorities and focus their resources on essential, value-added activities that can be provided only by the regulatory authority (26).

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

- analysis of options, including the results of consultations with stakeholders, as regulations are more likely to be effective if those who are impacted have provided input;
- regulations that are proportional to the perceived risk, encourage innovation and pose no unnecessary barriers to trade (e.g. sample testing at import); and
- early planning for implementation and for the practicalities of future enforcement. Application and enforcement should not be after-thoughts.

In developing new regulatory instruments and analysing their impact, the regulatory authority should develop “strategies for education, assistance, persuasion, promotion, economic incentives, monitoring, enforcement, and sanctions” (34). The authority should decide which compliance strategies to establish and whether 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. Co-regulation (see 4. Glossary) may be considered in certain circumstances. In such situations, a government issues regulations and enters into a non-statutory agreement with a body (e.g. industry or professional health care association) to develop and administer a compliance programme. When a government works with and through such a body in regulating the activity, it does not delegate its oversight of the activity.

Regulatory authorities may also consider use of third parties to conduct their activities. This model is prevalent in the regulation of medical devices, such as use of recognized auditing organizations to audit manufacturers’ quality management systems to ensure that they are of an international standard and respect applicable regulatory requirements. Regulatory resources are used to establish and maintain oversight of audit organizations, resulting in more effective use of limited resources (35).

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

costs accrue in inefficient regulatory systems. If the cost of complying with a regulation is disproportionately high, companies may decide not to develop a product and/or commercialize it in a particular market. For instance, a mandatory requirement to conduct local clinical trials as a condition for marketing authorization could be a disincentive to entering that market, particularly if trials conducted elsewhere reflect the patient profiles of the intended market and demonstrate the safety and efficacy of the product. Similarly, long and/or unpredictable times for product review result in lost revenue and unnecessary delays in the availability of products for patients, with potentially significant negative implications for morbidity, mortality, health care costs and the economy. Healthy economies require healthy people.

Inefficiency also results in a negative impact on a regulatory authority's resources, reputation and job satisfaction and increases the time spent addressing complaints about performance. Regulatory frameworks that reflect the principles of proportionality, flexibility and consistency are more likely to be efficient, as they allow resources to be allocated to the regulatory activities that most need them.

International collaboration. Regulatory frameworks that are consistent and aligned with those of other countries and regions encourage the necessary investment to bring appropriate, 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 inefficient duplication of regulatory evaluations of medical products and inspection or audit of facilities. International collaboration thus facilitates access to medical products for all.

Regulatory authorities should continually explore means of improving their efficiency while maintaining standards for evaluating the quality, safety and efficacy or performance of medical products. This could include introduction or refinement of good review practices (28) and a quality management system (28); greater, more effective use of information technology; consultations with industry, health care professionals and patients 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 noted above – regulatory cooperation and reliance (26).

Industry also contributes critically to the efficiency of regulatory systems. For example, high-quality applications for marketing authorization

reduce the overall review time by reducing the number of review cycles. Similarly, a manufacturer with a good compliance record should not require the same frequency or depth of inspection as a poorly performing manufacturer. Consultations and training can effectively complement enforcement in achieving the desired level of compliance.

In a regulatory impact analysis, policy-makers should seek the most efficient, least burdensome means of achieving their regulatory purposes at a minimum reasonable cost. A regulatory approach should include consideration of the total burden and resources required for cumulative regulation.

Periodic performance assessments should be conducted to evaluate the actual efficiency of regulatory instruments to ensure that the foreseen benefits are realized and, if so, the direct and indirect costs.

8.9 Transparency

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

Key elements:

- Transparency requires investment and a culture of openness, supported by government policy, commitment and action.
- Stakeholders should be consulted in the development of new or revised regulatory instruments.
- Regulatory requirements, processes, fees, assessments, decisions and actions should be as accessible as possible.
- The policies of the regulatory authority with respect to disclosure should be consistent with national laws on access to information.

The WHO Constitution states “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.” Transparency is in the interests of patients, consumers, governments, health care workers and manufacturers, as it increases public trust and confidence in the regulation of medical products. Transparency in regulatory requirements and actions results in better informed decisions about investment in the public and private sectors and discourages discriminatory, corrupt or abusive practices.

With transparency, all affected and potentially interested parties – domestic, foreign, public and private – have a meaningful opportunity to be informed of new or amended regulations and guidelines and to make their

views known before they are enacted. With transparency, once medical product regulations and guidelines are adopted, they 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 often work with regulatory authorities to disseminate new regulatory texts or to provide opportunities for exchanges of relevant information.

The assessments (positive and, when possible, negative), decisions and actions of the regulatory authority should be documented and made publicly available, with the rationale for the decisions, ideally by issuing a public assessment report. This information is important to a range of stakeholders, including industry, researchers, health professionals, patients and consumers, who use the information for various purposes. It is also essential for building trust and confidence in the regulatory system.

Regulated parties should be able to access the full reports of a product assessment or site inspection that pertains to them. This not only provides insight into the basis for comments and decisions but is also educational, helping to 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 operational and management levels. Furthermore, it can lead to higher-quality reports by ensuring that they clearly explain how such assessments led to decisions. The manufacturer should be given the opportunity to redact any trade secret or confidential personal or commercial information before publication.

Transparency requires investment and a culture of openness, which, in turn, should be supported by government policy, commitment and action. While not all regulatory authorities may be able to implement the full range of measures for an optimally transparent regulatory system, a step wise approach can be adopted. Given the prevalence of smart devices and the Internet, an up-to-date, searchable public website could be established and maintained that contains basic information such as:

- the roles, responsibilities, organization and contact information of the regulatory authority;
- access to the laws, regulations, guidelines and procedures necessary to satisfy regulatory requirements and improve the efficacy, safety and quality of medical products;
- a searchable registry of approved, suspended and withdrawn products;
- product information for health care professionals and patients;
- the licensing status of manufacturing sites;

- health advisories, safety information, alerts on quality or on substandard or falsified medical products, advisory notices, recalls and other time-sensitive information of public health interest;
- performance targets and results and annual reports;
- proposed new regulatory instruments, including periods for comment and how to provide input; and
- public assessment reports and reports of facility audits or inspections.

The findings of all audits or oversight reviews of the performance and functioning of the regulatory authority should be made public. Such reviews are important elements of public accountability, as are reports of performance against targets and annual reports.

In fulfilling their responsibilities, regulatory authorities will create or access proprietary or confidential information. Examples include identifiable personal information from clinical trials or reports of adverse events, trade secrets or confidential commercial information such as specifications of medical product compounds or materials or manufacturing processes. Measures should be established to prevent the disclosure of such information, with a mechanism to address disputes about the proprietary nature or confidentiality of information.

In general, national laws and regulations should favour transparency and public access to both the process and the criteria of regulatory decision-making. The disclosure policies of a regulatory authority should be consistent with national laws on public access to government information or “freedom of information”. Procedures and contact points for obtaining information held by a regulatory authority should be accessible and clear.

Transparency enables adoption of new, more efficient ways of conducting regulatory operations. It is incumbent upon regulators to practise transparency in regulatory operations and decisions, not only as a fundamental principle of GRP but also to build trust and maximize opportunities for cooperation and reliance as part of the shared responsibility of the regulatory community.

9. Enablers of good regulatory practices

An enabling environment facilitates successful implementation of GRP. Some elements are described below.

9.1 Political and government-wide support

Sustained support at the highest political and government levels, including policy-makers, is essential for proper implementation of the concept and principles of GRP. GRP should form an integral part of all government policies on regulatory systems and be backed by strong political support.

9.2 **Effective organization and good governance supported by leadership**

The structure and line of authority among and within all institutions in the regulatory system should be well defined. The integrity of the overall regulatory system is critical to the efficient performance of each of its constituent institutions. If more than one institution is involved in the regulatory system, the legislation or institutional regulation should provide for clear coordination and no overlap of regulatory activities. Leadership is critical for setting and realizing 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, effective communication plays a fundamental role in the exchange of information within and outside the institutions that form the regulatory system. When regulatory authorities communicate regularly, both internally and externally, they remain more transparent and accountable. Communication of correct information prevents potential misunderstandings and dissemination of misleading information to patients and the public. Communication is a powerful tool for collaboration and coordination with relevant national and international stakeholders, which leads in turn to efficient use of resources and better regulatory outcomes.

In view of their responsibilities, regulatory authorities should have the personnel, infrastructure and technical tools adequate for the performance of their tasks. Coordination may be facilitated by communication technologies and efficient, rapid information-sharing, which will result in fewer gaps and less duplication of effort.

9.4 **A robust, well-functioning quality management system**

A quality management system (28), which includes application of quality risk management principles, makes the decisions of regulatory authorities more credible and their operations more stable and consistent. A quality management system contributes to systematic planning, control and improved quality in all processes in regulatory functions and ensures a comprehensive approach.

9.5 **Sufficient, sustainable financial resources**

Investment in a regulatory system is critical to a well-functioning health care system. Adequate financial resources to fulfil its regulatory mandate effectively and to improve the performance of regulatory activities continuously are essential

for the independence, impartiality, consistency and efficiency of a regulatory system. The financial resources of all institutions of the regulatory system should be sustainable, apart from donations from donors or philanthropic entities.

9.6 **Competent human resources**

An array of technical and scientific knowledge and skills of regulatory staff contribute to the development, implementation and maintenance of an effective regulatory system for medical products. Policies and measures for personal and career development (e.g. training programmes, competitive remuneration schemes) are critical for regulatory authorities to attract competent staff and retain them in the service.

9.7 **Organizational ethics and values**

Regulatory personnel should abide by organizational ethical principles and values and show professionalism. All regulatory staff should be made aware of and be trained in the ethical principles and values of the regulatory authority (e.g. a code of conduct). A system should be established, within or outside the regulatory system, for managing departures from organizational ethics and values.

9.8 **Science- and data-driven decision-making process**

Regulatory decisions and decision-making should be based on scientific foundations and accurate data rather than intuition or arbitrariness. Science-based decisions provide for consistent, predictable regulatory outcomes. Adherence to international standards and guidelines is a key enabler of science based regulatory decision-making.

The enablers listed above are not effective when present individually. Rather, they work in harmony in the application and implementation of GRP. For example, sufficient, sustainable financial resources contribute to the recruitment, development and maintenance of competent human resources. Similarly, financial resources should be managed according to good governance practices.

10. Implementing good regulatory practices

WHO Member States are encouraged to implement GRP in their regulatory systems with due consideration of the realities of their legal and regulatory systems. Transparent, predictable processes should be used to ensure high-quality regulatory oversight that achieves the intended objectives while minimizing negative impacts and costs. At the same time, regulatory systems should be sufficiently flexible for the processes to be applied proportionately

to the scope, magnitude and complexity of the issue. Sustained support at the highest levels, with adequate resources, is essential.

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

References

1. WHO definitions: emergencies. Geneva: World Health Organization; 2020 (<https://www.who.int/hac/about/definitions/en/>, accessed 29 January 2021).
2. Regulatory harmonization. Geneva: World Health Organization; 2014. WHO Drug Inf. 2014;28(1):3–10. (http://www.who.int/medicines/publications/druginformation/issues/DrugInformation2014_Vol28-1/en/, accessed 29 January 2021).
3. International regulatory co-operation: addressing global challenges. Paris: Organisation for Economic Co-operation and Development; 2013 (<http://dx.doi.org/10.1787/9789264200463-en>, accessed 29 January 2021).
4. Guidelines on international regulatory obligations and cooperation. Ottawa: Treasury Board of Canada Secretariat; 2007 (<http://www.tbs-sct.gc.ca/hgw-cgf/priorities-priorites/rtrap-parfa/guides/iroc-cori/iroc-cori-eng.pdf>, accessed 29 January 2021).
5. International regulatory cooperation – better rules for globalization. Paris: Organisation for Economic Co-operation and Development; 2013 (<http://www.oecd.org/gov/regulatory-policy/irc.htm>, accessed 29 January 2021).
6. Recommendation of the Council on Regulatory Policy and Governance. Paris: Organisation for Economic Co-operation and Development; 2012 (<http://www.oecd.org/gov/regulatory-policy/2012-recommendation.htm>, accessed 29 January 2021).
7. Regulatory harmonization and convergence. Silver Spring (MD): US Food and Drug Administration; 2015. (<http://www.fda.gov/BiologicsBloodVaccines/InternationalActivities/ucm271079.htm>, accessed 29 January 2021).
8. Best practice regulation handbook. Canberra: Australian Government; 2007 (http://regulationbodyofknowledge.org/wp-content/uploads/2013/03/AustralianGovernment_Best_Practice_Regulation.pdf, accessed 29 January 2021).
9. Evaluating the effectiveness of infrastructure regulatory systems. Washington DC: The World Bank; 2006:17 (https://ppp.worldbank.org/public-private-partnership/sites/ppp.worldbank.org/files/documents/world_bank-ppi-af-handbook_for_evaluating_infrastructure_regulatory_systems_2006_english.pdf, accessed 29 January 2021).
10. APEC–OECD Co-operative Initiative on Regulatory Reform. APEC–OECD integrated checklist on regulatory reform. Paris: Organisation for Economic Co-operation and Development; 2005 (<http://www.oecd.org/regreform/34989455.pdf>, accessed 29 January 2021).
11. The OECD report on regulatory reform. Paris: Organisation for Economic Co-operation and Development; 1997 (<http://www.oecd.org/gov/regulatory-policy/2391768.pdf>, accessed 29 January 2021).
12. OECD guiding principles for regulatory quality and performance. Paris: Organisation for Economic Co-operation and Development; 2005 (www.oecd.org/fr/reformereg/34976533.pdf, accessed 29 January 2021).

13. Better regulation for growth. Governance frameworks and tools for effective regulatory reform. Washington DC: The World Bank; 2007 (<http://documents1.worldbank.org/curated/en/955811468330978599/pdf/556350WP0Box0310Governance01PUBLIC1.pdf>, accessed 29 January 2021).
14. ASEAN good regulatory practice (GRP) guide. Bangkok: Association of Southeast Asian Nations; 2009 (<http://regulatoryreform.com/wp-content/uploads/2015/08/ASEAN-Good-Regulatory-Practice-GRP-Guide-2009.pdf>, accessed 29 January 2021).
15. The "blue book". Marketing authorization of pharmaceutical products with special reference to multisource (generic) products, a manual for national medicines regulatory authorities (NMRAs). Second edition. Geneva: World Health Organization; 2011 (https://apps.who.int/iris/bitstream/handle/10665/44576/9789241501453_eng.pdf;jsessionid=52D37F5BD27B9BB5055CF9DA79453B5B?sequence=1, accessed 29 January 2021).
16. National drug regulatory legislation: guiding principles for small drug regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: thirty-fifth report (WHO Technical Report Series, No. 885). Geneva: World Health Organization; 1999: Annex 8 (https://www.who.int/medicines/technical_briefing/tbs/National_drug_regulatory_legislation_Annex8TRS885_en.pdf), accessed 29 January 2021).
17. Regulation of vaccines: building on existing drug regulatory authorities. Geneva: World Health Organization; 1999 (document WHO/V&B/99.10) (http://apps.who.int/iris/bitstream/10665/65968/1/WHO_V-B_99.10_eng.pdf, accessed 29 January 2021).
18. Effective drug regulation: a multi-country study. Geneva: World Health Organization; 2002 (<https://apps.who.int/iris/bitstream/handle/10665/42470/9241562064.pdf?sequence=1&isAllowed=y>, accessed 29 January 2021).
19. Medical device regulations: global overview and guiding principles. Geneva: World Health Organization; 2003 (http://www.who.int/medical_devices/publications/en/MD_Regulations.pdf, accessed 29 January 2021).
20. A model regulatory programme for medical devices: an international guide. Washington DC: Pan American Health Organization; 2001 (http://new.paho.org/hq/dmdocuments/2009/AmodelRegulatoryProgramforMedicalDevices_AnInternalGuide.pdf?ua=1, accessed 29 January 2021).
21. How to develop and implement a national drug policy, second edition. Geneva: World Health Organization; 2001 (http://www.who.int/medicines/areas/policy/emp_ndp2nd/en/, accessed 29 January 2021).
22. Global model regulatory framework for medical devices including IVDs. Geneva: World Health Organization; 2017 (<https://apps.who.int/iris/bitstream/handle/10665/255177/9789241512350-eng.pdf?sequence=1>, accessed 29 January 2021).
23. Resolution WHA67.20. Regulatory system strengthening for medical products. In: Sixty-seventh World Health Assembly, Geneva, 19–24 May 2014. Resolutions and decisions: resolutions. Geneva: World Health Organization; 2014 (http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R20-en.pdf, accessed 29 January 2021).
24. Good Governance for Medicines: Model Framework, Geneva: World Health Organization; 2014 (http://www.who.int/medicines/areas/governance/ggm_modelframe_updated/en/, accessed 29 January 2021).
25. Good Reliance Practices: Good reliance practices in regulatory decision-making: 6 high-level principles and recommendations 8 Draft. Geneva: World Health Organization; 2020 (working document QAS/20.851 (https://www.who.int/medicines/areas/quality_safety/quality_assurance/QAS20_851_good_reliance_practices.pdf?ua=1, accessed 29 January 2021)).

26. Good review practices: guidelines for national and regional regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: forty-ninth report. Geneva: World Health Organization; 2015: Annex 9 (WHO Technical Report Series, No. 992; http://www.who.int/medicines/areas/quality_safety/quality_assurance/Annex9-TRS992.pdf?ua=1, accessed 29 January 2021).
27. WHO guideline on the implementation of quality management systems for national regulatory authorities. In: WHO Expert Committee on Specifications for Pharmaceutical Preparations: fifty fourth report. Geneva: World Health Organization; 2020: Annex 13 (WHO Technical Report Series, No. 1025, <https://www.who.int/publications/i/item/978-92-4-000182-4>, accessed 29 January 2021).
28. Policy evaluating and publicly designating regulatory authorities as WHO-listed authorities. Draft. Geneva: World Health Organization; 2019 (working document QAS/19.828; https://www.who.int/medicines/areas/quality_safety/quality_assurance/QAS19_828_Policy_on_WHO_Listed_Authorities.pdf?ua=1, accessed 29 January 2021).
29. WHO Global Benchmarking Tool (GBT) for evaluation of national regulatory systems (https://www.who.int/medicines/regulation/benchmarking_tool/en/, accessed 29 January 2021).
30. APEC Sub-committee on Standards and Conformance. Information notes on good practice for technical regulation. Singapore: Asia-Pacific Economic Cooperation; 2000 (<http://www.inmetro.gov.br/qualidade/comites/pdf/docAPEC.pdf>, accessed 29 January 2021).
31. Improving regulation and regulatory review. Executive Order 13563. Executive Office of the President. Federal Register: the Daily Journal of the United States Government, 21 January 2011 (<https://federalregister.gov/a/2011-1385>, accessed 29 January 2021).
32. The governance of regulators. Creating a culture of independence. Practical guidance against undue influence. Paris: Organisation for Economic Co-operation and Development; 2017 (<https://www.oecd.org/gov/creating-a-culture-of-independence-9789264274198-en.htm>, accessed 29 January 2021).
33. Recommendation of the Council of the OECD on improving the quality of government regulation, including the OECD reference checklist for regulatory decision-making and background note. Paris: Organisation for Economic Co-operation and Development; 1995 (<https://legalinstruments.oecd.org/public/doc/128/128.en.pdf>, accessed 29 January 2021).
34. Medical device single audit program (MDSAP). Silver Spring (MD): Food and Drug Administration; 2020 (<https://www.fda.gov/medical-devices/cdrh-international-programs/medical-device-single-audit-program-mdsap>, accessed 29 January 2021).