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**Good regulatory practices:
guidelines for national regulatory authorities for medical
products**

NOTE:

This document has been prepared for the purpose of inviting comments and suggestions on the proposals contained therein, which will then be considered by the Expert Committee on Biological Standardization (ECBS) and the Expert Committee on Specifications for Pharmaceutical Preparations (ECSPP).

This guideline was developed based on the outcomes and consensus of the WHO workshops convened in July 2014 and October 2015, and a consultation in May 2016, with participants from national regulatory authorities, national control laboratories, manufacturers, academia researchers and stakeholder organizations.

The text in its present form does not necessarily represent an agreed formulation of the ECBS or the ECSPP. Written comments proposing modifications to this text MUST be received by 15 December 2016 in the Comment Form available separately and should be addressed to the World Health Organization, 1211 Geneva 27, Switzerland, attention: Department of Essential Medicines and Health Products (EMP). Comments may also be submitted electronically to the Responsible Officer: Ms Daniela Decina at email: decinad@who.int.

The outcome of the deliberations of the Expert Committees will be published in the WHO Technical Report Series. The final agreed formulation of the document will be edited to be in conformity with the "WHO style guide" (WHO/IMD/PUB/04.1).

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2	Acronyms	
3	APEC	Asia-Pacific Economic Cooperation
4	ASEAN	Association of Southeast Asian Nations
5	GHTF	Global Harmonization Task Force
6	GRP	Good Regulatory Practices
7	GMP	Good Manufacturing Practices
8	ICH	International Council for Harmonisation of Technical Requirements
9		for Pharmaceuticals for Human Use
10	IMDRF	International Medical Device Regulators Forum
11	MOU	Memorandum of understanding
12	MRA	Mutual recognition agreement
13	NRA	National regulatory authority
14	OECD	Organisation for Economic Co-operation and Development
15	PIC/S	Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation
16		Scheme
17	RIA	Regulatory impact analysis
18	WHO	World Health Organization

19 **Background**

20 In resolution WHA67.20, the Sixty-seventh World Health Assembly in 2014 recognized “that
21 effective regulatory systems are an essential component of health system strengthening and contribute
22 to better public health outcomes, that regulators are an essential part of the health workforce, and that
23 inefficient regulatory systems themselves can be a barrier to access to safe, effective and quality
24 medical products” (1). Good regulatory practices (GRP) provide a means for establishing sound,
25 affordable and effective regulation of medical products as an important part of health system
26 strengthening. In 2013, a guideline for GRP was listed among the normative work to be developed
27 within the WHO Department of Essential Medicines and Health Products (EMP). A concept paper
28 was drafted in October 2013 and guideline development was advanced in two subsequent workshops
29 with the participation of WHO Member States and public health stakeholder organizations. The
30 outcome was an outline of a high-level guideline for GRP for medical products. This guideline draws
31 upon documents from multilateral bodies such as the Asia-Pacific Economic Cooperation (APEC), the
32 Organisation for Economic Co-operation and Development (OECD), the World Bank and the
33 Association of Southeast Asian Nations (ASEAN) (2) (3) (4) (5) (6) as well as guides published by
34 some national regulatory authorities (NRAs). The guideline adapts general GRP principles to the
35 regulation of medical products.

36

1 Introduction

2 The Constitution of the World Health Organization states (7): “The enjoyment of the highest
3 attainable standard of health is one of the fundamental rights of every human being.” A fundamental
4 role of government is to protect and promote the health and safety of the public in its jurisdiction,
5 including in the delivery of health care. That objective is achieved, in part, through systems of laws
6 and regulatory controls. Application of those laws and regulations,¹ compliance with which is
7 mandatory, may be supported by the use of instruments such as pharmacopoeial monographs,
8 international standards, and regulatory guidelines.

9 In national systems for the regulation of medical products, there is no single correct approach. Each
10 approach will reflect national health policies and priorities, the level of socioeconomic development,
11 the availability of resources and infrastructure, the health system, the disease burden and the legal
12 system. Nonetheless, as in other regulated sectors, there is growing international consensus on the best
13 practices that may be applied widely.

14 In general, GRP may be described as a set of practices that are to be applied to the development,
15 implementation and maintenance of controls – including laws, regulations and guidelines – in order to
16 achieve a public policy objective. GRP can be applied to the preparation and management of
17 regulations for the control of health products. A review of public documents (2) (5) (6) (8) on the
18 subject reveals common themes for the principles of good regulation. Creation and implementation of
19 regulations should be a transparent, non-discriminatory and predictable process that involves robust
20 stakeholder engagement. The development of regulations should be preceded by rigorous assessment
21 of the need for a regulatory instrument, its legal basis, and an evaluation of potential alternatives and
22 impacts, such as benefits, burdens and cost-effectiveness. Once regulations are implemented, there
23 should be processes for monitoring their effectiveness and for improving them whenever appropriate.

24 There is a strong internationally recognized need to share experiences and build upon the best
25 regulatory practices. Several WHO guidelines, notes, communications and other information on
26 specific regulatory topics already exist (9) (10) (11) (12) (13) (14) (15) (16) (17) (18). They have been
27 used, or are under development, to assist Member States in developing elements of their regulatory
28 systems.

29 GRP are built on a foundation of transparency, good governance (18) and sound government policy-
30 making. Public confidence in health products depends on confidence in the integrity of regulatory
31 oversight. GRP help to ensure that national regulatory systems, and international regulatory
32 cooperation programmes, remain relevant, current and flexible as technology evolves and unforeseen
33 needs and emergencies occur. GRP take into account compliance with international treaty obligations
34 and regional agreements. They contribute to efforts to promote convergence of international
35 regulatory requirements and practices, as well as harmonization efforts where they are undertaken.
36 GRP, widely adopted, also facilitate formal and informal cooperation and work-sharing among NRAs.

37 In itself, adoption of GRP is not a sufficient condition for improvement; sustained support at the
38 highest levels, along with adequate resourcing, is essential.

¹ Throughout this document, the term “regulation” is used in a general sense to include laws, regulations, decrees or other similar terms used in national legal systems and having mandatory effect on affected parties.

1 One of the main audiences for this guideline is the “national regulatory authority” or NRA which
2 exists in many countries. The term is taken to include not only national authorities but also sub-
3 national, supra-national and multi-agency regulatory systems.

4 **Scope**

5 This guideline outlines internationally accepted principles of GRP and shows how they may be
6 applied to the regulation of medical products for human use. The guideline is intended for a number
7 of related audiences: institutions and senior policy-makers responsible for the formulation of health
8 policies, laws, regulations and guidelines; staff in institutions that, together, form national systems for
9 regulatory oversight of medical products; and parties affected by or otherwise interested in regulatory
10 frameworks, such as civil society and the regulated industry. This document is intended to assist
11 Member States in the implementation of GRP, both in establishing new regulatory systems for
12 medical products and in updating existing ones.

13 **Part 1. Principles of good regulatory practices**

14 This guideline presents the desirable attributes and practices of regulatory systems for medical
15 products. Part 1 presents nine principles on which regulatory systems may be established and by
16 which they may be evaluated. These principles are:

- 17 • **Legality:** Regulation should have a sound legal basis and should be consistent with existing
18 legislation, including international norms or agreements.
- 19 • **Impartiality:** Regulation and regulatory decisions should be impartial in order to be fair and
20 to avoid conflicts of interest, unfounded bias or improper influence from stakeholders.
- 21 • **Consistency:** Regulations should be clear and predictable; both the regulator and the
22 regulated party should understand the behaviour and the conduct that are expected and the
23 consequences of noncompliance.
- 24 • **Proportionality:** Regulations and regulatory decisions should be proportional to the risk and
25 should not exceed what is necessary to achieve the objectives.
- 26 • **Flexibility:** Regulations should not be prescriptive; they should allow flexibility in
27 responding to a changing regulated environment and different or unforeseen circumstances.
- 28 • **Effectiveness:** Regulations should produce the intended result.
- 29 • **Efficiency:** Regulations should achieve their goals within the required time, effort and cost.
- 30 • **Clarity:** Regulations should be accessible to, and understood by, the users;
- 31 • **Transparency:** Regulatory systems should be transparent; requirements and decisions should
32 be made known to affected parties and, where appropriate, to the public in general.

34 **1.1 Legality**

- 35 • All regulatory decisions must be founded on valid legal authorities, respecting the rule of law.
- 36 • Delegation of powers and responsibilities to different levels of the regulatory system should
37 be as clear as possible.
- 38 • If multiple levels of government are involved, the system should ensure consultation,
39 cooperation and coordination.
- 40 • The NRA must have the resources and powers to accomplish duties and take timely action.

- 1 • The NRA should be empowered to benefit from international cooperation, exchanges of
2 information and regulatory forums.

3 According to the principle of legality, regulatory processes should be structured so that all regulatory
4 decisions are founded on valid legal authority, thus respecting the “rule of law”. Delegation of power
5 should be explicit, ensuring that all regulations are authorized by the relevant constitutional authority
6 and are supported by the pertinent laws and higher-level regulations.

7 The mechanisms by which powers are delegated to the different levels of the regulatory system should
8 be as clear as possible regarding the nature, responsibilities and boundaries of the authority that is
9 being delegated. NRAs should be competent to issue regulations that impose or prohibit certain
10 conduct, as well as other non-prescriptive rules that aim to guide actions, provide recommendations
11 and induce appropriate behaviours.

12 On the basis of the principles of effectiveness and efficiency, regulators should choose the level of
13 government that is most appropriate to take action. Under the principle of subsidiarity, the lowest
14 level of government that can competently execute the required control – i.e., the one “closest to the
15 citizen” – should have primary responsibility for implementing regulatory controls. If multiple levels
16 of government are involved, effective systems of mutual consultation, cooperation and coordination
17 between the different levels should be in place.

18 In decentralized models of administration that involve a central regulatory authority, states/provinces
19 and municipalities, the regulatory system should clearly establish the constitutional authorities of each
20 level of government and should promote cooperation and coordination between them. It is important
21 to identify which level of government should deal with which problem and stakeholder, and
22 responsibilities should be clearly assigned. In decentralized models, an adequate balance should be
23 reached between promoting national uniformity of regulatory requirements and accommodating local
24 responsibilities. For instance, in some jurisdictions the marketing authorization of a product may be
25 performed at the federal level but additional controls on access to the product may apply at a local
26 level.

27 In its dealings with other national government bodies, the NRA should be appropriately empowered to
28 maintain the public health perspective of actions and measures taken. For instance, there should be
29 mechanisms for coordination between the NRA, trade promotion officials and customs authorities.

30 In order that that regulations can be implemented successfully, regulators should ensure that
31 administrative capacities to accomplish tasks and duties are fully in place at each level of
32 administration. Training programmes designed for government authorities and, when applicable, for
33 other stakeholders, should be carried out.

34 Systems should be in place to ensure that decisions made by bodies empowered to issue regulatory
35 sanctions can be reviewed. The systems should include ombudsman roles, internal appeal mechanisms
36 and the right to appeal decisions of regulators on legal grounds – including on the grounds of
37 procedural fairness and due process – in addition to scientific and administrative grounds.

38 Regulatory bodies are meant to exercise their authority only within the scope permitted by law,
39 observing the principles of accountability, impartiality and equality. Administrative and judicial
40 review may also discourage the abuse of authority.

1 Regulatory convergence and harmonization are desirable at both national and international levels. The
2 legal framework for regulation of medical products should include a means for the NRA to participate
3 in or benefit from international cooperation, exchanges of information and regulatory forums on
4 convergence, harmonization and cooperation. The development or modification of regulations should
5 take into account any legal obligations from treaties, mutual recognition agreements, and
6 harmonization or other initiatives. For instance, where an NRA has mutual recognition agreements in
7 place with other countries, a change in that authority's testing standards, whether higher or lower,
8 could have an impact on the agreements with its mutual recognition partners and should therefore be
9 evaluated.

10 The regulatory authority should have the resources and powers necessary to take timely and effective
11 action – by itself and/or in concert with other government bodies – to enforce regulatory requirements.
12 For instance, if the customs authority suspects that an imported medical product is nonconforming,
13 the responsible NRA should have the power and resources to perform the necessary investigations and
14 launch appropriate actions. Similarly, an NRA should be resourced and empowered to investigate, and
15 take appropriate actions against, physicians responsible for noncompliant clinical trials.

16 Where there is no regulatory system in place, or the system is not enforceable for the regulation of
17 some or all categories of medical products, or in some emergency situations pertaining to medical
18 products, short-term measures based on a country's existing legal framework should be taken in order
19 to address the immediate necessity of protecting public health. This could include looking at existing
20 legislation – such as that on consumer protection or imports – and the mandate that it may give to act
21 in the interim. For instance, if an authority becomes aware that a medicine is being promoted in a
22 false, misleading or unsupported manner, the authority may consider recall and prosecution under the
23 provisions of general consumer protection law, even in the absence of specific regulations regarding
24 the labelling of medical products. Other measures may involve adaptation of other national authorities'
25 decisions, adoption of decisions taken in other jurisdictions or by multilateral bodies, or reliance on
26 another national authority's evaluations. For instance, it may be possible for the authority to rely on
27 evaluations conducted by other competent authorities in determining whether to allow an urgently
28 needed vaccine to be placed on the national market to address a pressing public health need. Medium-
29 and long-term strategies should then be developed in order to fill the gap permanently.

30 **1.2 Impartiality**

- 31 • Regulatory decisions should be impartial and must avoid conflicts of interest.
- 32 • Regulatory decisions should be legitimate, evidence-based and ethical.
- 33 • All stakeholders should be treated equitably.
- 34 • Governmental and nongovernmental bodies should be regulated according to the same
35 framework to ensure neutrality.
- 36 • Systems should be in place to manage potential conflicts of interest.

37 Regulations and regulatory decisions should be impartial in order to be fair and to avoid conflicts of
38 interest, unfounded bias or improper influence by stakeholders. The objectives of regulations and
39 regulatory decisions must be legitimate, evidence-based and ethical. The objectivity, effectiveness,
40 certainty, integrity and impartiality of regulatory texts and measures, adopted in the public interest,
41 increase confidence in the regulatory system and in the products it regulates.

1 All stakeholders, objectively considered, should be treated equitably, which means that no stakeholder
2 should be discriminated against. Governmental and nongovernmental bodies should be regulated
3 according to the same framework so that competitive neutrality is achieved. For instance, the
4 regulatory pre-marketing evaluations of two competing *in vitro* diagnostic tests – one based on a test
5 method developed in-country and the other developed in another country – should be based on the
6 same scientific criteria.

7 Regulators should be independent of influence and potential sources of bias; boundaries of their
8 powers and competences should be established to prevent undue influence and maintain trust in the
9 regulatory system. Systems should be in place to manage potential conflicts of interest.

10 Regulators should avoid actual or perceived influence by being open and transparent about their
11 decisions. Decisions that are based on clear objectives, empirical evidence or research, post-
12 implementation evaluation and stakeholder input can help build confidence and trust. The scientific
13 and technical basis of regulation should be objective and accessible. The adoption of tools of public
14 consultation and transparency throughout the decision-making process should ensure impartiality,
15 better regulatory outcomes and increased public confidence in the use of the regulated products.

16 Impartiality contributes to the consistency of the regulatory decisions regarding the quality, safety,
17 efficacy and accessibility of medical products, despite the specificities of each product and regulatory
18 processes.

19 **1.3 Consistency**

- 20 • New regulations should support and complement, and not conflict with, existing regulations.
- 21 • Overlaps or conflicts in responsibility should be avoided.
- 22 • The rules need to be consistently implemented and enforced across medical product sectors
23 and stakeholders.
- 24 • Regulatory decisions and enforcement actions should not be seen as arbitrary or capricious.
- 25 • The regulations should include provisions for appeals against regulatory decisions and
26 enforcement actions.

27 Regulation of medical products does not take place in isolation. It must be done in the context of, and
28 in ways consistent with, the national legal framework, general government policies, and specific
29 public health protection policies. New regulations should support and complement, and not conflict
30 with, existing regulations.

31 When drafting or revising regulatory instruments, efforts should be made to ensure they are consistent
32 and coherent with the competence and jurisdiction of the regulatory authority that will be responsible.
33 Overlaps or conflicts in responsibility should be avoided. Manufacturers, importers and distributors
34 should be able to identify consistently which authority is responsible for what. This is especially
35 important where the regulation of medical products is decentralized – when, for instance, there may
36 be central and state/provincial-level authorities. Formal mechanisms should be established to ensure
37 proper coordination during the drafting and execution of the regulations.

38 Regardless of differences in their technologies, there must be consistency between the regulatory
39 requirements for medicines, medical devices, vaccines and biologicals. Enforcement should also be
40 consistent across sectors; the rules applied to manufacturers, importers and distributors need to be
41 consistent and also compatible with the rules applied to medical product users.

1 Legislators and policy-makers should ensure that laws and regulations are consistently implemented,
2 applied and enforced throughout the country and for all stakeholders. For instance, medicine
3 manufacturers in one area of a country should meet the same requirements as similar manufacturers in
4 another area, and all advertisers of similar medical products should be treated in similar ways. The
5 regulatory requirements and human subject protections for clinical trials should be uniformly enforced,
6 no matter where in the country a trial is conducted. Similarly, domestic producers of medical products
7 should be held to the same regulatory requirements as those that apply to importers and foreign
8 manufacturers.

9 Although there will always be a need for good regulatory judgement and discretion in enforcement,
10 inconsistency within and between regulations may create opportunities for unfair treatment or
11 corruption. If public confidence in medical products and the regulatory system is to be maintained,
12 enforcement should not be seen as arbitrary or capricious. The regulatory framework should include
13 provisions for appealing regulatory decisions, and there should be an impartial ombudsman to whom
14 concerns can be raised. Recruitment, retention and promotion of medical product regulators and
15 enforcement staff should be carried out consistently in adherence with a publicly available code of
16 conduct. Thus the NRA's resources must be appropriate to its responsibilities and powers of
17 enforcement.

18 Medical product regulations must continue to evolve to reflect advances in science, standards of care
19 and technology. Nevertheless, regulatory requirements and their application and implementation must
20 be consistent and predictable over time in order to allow all parties to make reasonably informed
21 decisions on investments, resources and steps to ensure continued compliance. When changes are
22 necessary, clearly stipulated measures and transition periods should be established.

23 Wherever possible, national regulatory measures to protect public health should be consistent with the
24 provisions of treaties and regional or international agreements and norms.

25 **1.4 Proportionality**

- 26 • Regulation should be adequate to the aim being pursued without being excessive.
- 27 • Regulatory compliance measures should be proportionate to the risk and severity of
28 infractions.

29 The principle of proportionality means that an action does not go beyond what is needed to achieve an
30 intended objective. This principle should be applied to all elements of a regulatory system. Regulation
31 should be created only when necessary and should be adequate to the aim being pursued without
32 being excessive. The content and form of regulation should be appropriate to both the problem and the
33 risk² posed by the problem. Thus detailed evidence of safety and efficacy may be needed for the
34 marketing authorization of a vaccine, whereas adherence to a prespecified monograph may be
35 sufficient for an over-the-counter medicine that contains well-characterized medicinal ingredients.

36 Regulatory enforcement and inspection regimes should also be proportionate to the risk and severity
37 of infractions. For example, a consistently compliant manufacturer may be inspected less frequently
38 than one with a history of noncompliance. This allows the regulator to allocate resources where the

² Health risk is understood to combine the likelihood that a negative event (hazard, harm) will occur and the potential magnitude of the damage caused (number of persons affected and the severity of damage to each).

1 need is greater. The cost of complying with regulation should also be proportionate to the nature of
2 the risk.

3 The principle of proportionality also applies to the policies and processes by which regulation is made.
4 Regulation-making process should be flexible and proportionate so that the length and structure of an
5 impact analysis reflects the complexity and/or impact of the problem that it addresses. For instance, a
6 rigorous cost analysis would be appropriate for a new complex regulatory framework but not for
7 simple regulations where the policy alternatives are limited.

8 **1.5 Flexibility**

- 9 • Regulation should be sufficiently flexible to allow for a rational response to changes in the
10 regulated environment.
- 11 • The language of regulation should be descriptive and not prescriptive and should allow for
12 alternative approaches that achieve the same result.
- 13 • There should be flexibility to respond to emergencies, shortages of medicines, and use for
14 humanitarian purposes.
- 15 • The regulatory system should provide the flexibility to apply good judgement within the
16 regulatory framework.

17 In the creation of meaningful, understandable and enforceable regulation there is a need to provide
18 sufficient detail to ensure clarity. At the same time the regulation should allow flexibility to respond
19 rationally to changes in the regulated environment. Thus the regulatory system should include
20 mechanisms to address unforeseen public health threats as well as to take new technologies and
21 innovations into account. However, flexibility should be risk-based and must not compromise the
22 ability to ensure the quality, safety and efficacy of the product (19).

23 The language of regulation should be descriptive and not prescriptive (6), thus allowing for alternative
24 approaches that achieve the same result. For instance, if a product is intended to be offered in a sterile
25 state, the regulation should establish requirements for the acceptable sterility level and process
26 validation but should not specify the specific sterilization method to be used. Regulations should aim
27 to accommodate continuing evolution in technology and the scientific state of the art. Regulations
28 should also reflect inherent differences between regulated product types; what may be appropriate for
29 medicines is not necessarily appropriate for medical devices, in vitro diagnostic devices, biologicals
30 or vaccines.

31 While regulation should be adaptable to scientific and technological change and should encourage
32 innovation, it should not cause unintended negative consequences. New risks must be addressed in a
33 timely manner, so regulation should allow for the possibility that an unforeseen technology may be
34 used in a future medical product. There should be a hierarchy of regulatory instruments in which the
35 highest level of detail on requirements for compliance is provided in the instrument that is most
36 readily amendable. Hence, the text of guidelines on requirements for compliance should be the most
37 specific. The regulations should include sufficient administrative flexibility to allow for participation
38 in international cooperation frameworks, such as for information-sharing, convergence, harmonization,
39 work-sharing, reliance and recognition. Examples include reliance on pre-marketing assessment
40 reports for quality, safety, efficacy and performance or good manufacturing practices (GMP)
41 compliance inspections conducted by other authorities.

1 Additionally, sufficient flexibility should be provided to allow the NRA to respond to such situations
2 as emergencies, shortages of medicines, rare disorders, and use for compassionate and humanitarian
3 purposes.

4 The regulatory system should, on the basis of a legal framework, provide for the regulator's
5 administrative and enforcement discretion – i.e., the flexibility to apply good judgement within the
6 regulatory framework. This discretion must be subject to appropriate controls and oversight.

7 **1.6 Effectiveness**

- 8 • Effective regulations are those that achieve the intended public health goals.
- 9 • An effective regulatory system allows investigation without delay and leads to the necessary
10 corrective and preventative actions.
- 11 • The effectiveness of a regulation should be periodically assessed using performance-based
12 indicators.

13 Demographic trends, changes in the global burden of disease, and economic development drive the
14 demand for medical products of assured quality that result in improved health outcomes. Ultimately,
15 the measure of an effective medical products regulatory system is how well it achieves the policy
16 goals of protecting and promoting public health in both the near and long term. At the same time,
17 regulatory policies should neither inhibit continued innovation and investment in new health
18 technologies nor be unjustified barriers to international trade and regulatory cooperation.

19 Regulatory tools that the public (in both private and public sectors) sees as proportionate and
20 legitimate are the most likely to be effective. Such tools will have a sound legal basis and will be
21 consistently enforceable. Effective medical product regulations and practices prevent or reduce the
22 likelihood of adverse health outcomes that are associated with products (whether imported or
23 domestic) that are unsafe, substandard and not effective or efficacious. When noncompliance is
24 detected, an effective regulatory system allows investigation without delay and leads to the necessary
25 corrective and preventive actions. Effective regulations prevent false or misleading advertising and
26 promotion, and provide protection to subjects who participate in clinical investigations of medical
27 products both before and after marketing authorization. An effective regulatory system will also have
28 complementary control points at different stages in the medical product lifecycle in order to avoid
29 placing too much emphasis on a single control.

30 The effective regulatory system should recognize and take account of differences between different
31 types of regulated products. Controls should be proportionate to the level of potential harm and risks
32 associated with medical products. For instance, measures appropriate to vaccines may not be
33 appropriate to a product intended for over-the-counter sales in a local pharmacy.

34 Successful establishment of regulatory controls on medical products depends on comprehensive early-
35 stage planning for implementation. Application and enforcement should not be after-thoughts. When
36 new rules are being developed and subjected to regulatory impact analysis, the regulatory authority
37 should develop “strategies for education, assistance, persuasion, promotion, economic incentives,
38 monitoring, enforcement, and sanctions”.³ For instance, the NRA should consider what measures
39 should be taken to ensure that those affected by regulations are properly informed. The authority must

³ 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 (OECD); 1995.

1 decide which incentives for compliance will be established and whether consumer awareness and
2 market forces can reasonably be used in addition to the threat of penalties. The role of civil society in
3 monitoring adherence to regulation should also be considered, if appropriate.

4 Planning should include arrangements for publishing periodic assessments of the performance of the
5 NRA and government. Quantitative measurement tools should be established to monitor, for example,
6 review times for marketing authorization applications, response times to requests for information, or
7 numbers of enforcement actions. In addition, more qualitative measures – such as readiness to take
8 action against emerging public health threats or ability to assess new technologies – should be
9 considered. It may also be helpful for an authority to use “benchmarking” to compare itself to
10 authorities in other, similar, jurisdictions. Such (self-) assessments should lead to effective adaptation
11 and corrective actions.

12 In assessing the effectiveness of regulation, the difficulty of measuring potential harms that have been
13 avoided must be recognized. Policy-makers and regulators may have to rely on information about
14 narrowly-avoided harms or experience in other jurisdictions. Systematic, periodic or ad hoc risk
15 assessments, including assessments of newly-identified public health threats, are important for
16 maintaining a system’s effectiveness.

17 Policy-makers and the NRA should also consider the extent to which the system encourages
18 international regulatory harmonization, convergence, cooperation, work-sharing and reliance on the
19 decisions of others.

20 **1.7 Efficiency**

- 21 • Efficient regulations are those that achieve the intended goals within reasonable time, effort
22 and cost.
- 23 • In considering a regulatory approach there should be a consideration of the total burden and
24 resource needs of cumulative regulation.
- 25 • The efficiency of rules that are implemented should be evaluated by periodical performance
26 assessments to ensure that the benefits foreseen have been achieved.
- 27 • A country’s regulatory requirements may be aligned with those of other countries to be more
28 efficient.

29 The regulatory system should be not only effective but also efficient, achieving its objectives in an
30 optimal way. Regulations will have financial implications. Direct costs include those resulting from
31 establishing and maintaining an NRA and from compliance and record-keeping by industry. Indirect
32 and hidden costs may include costs due to market and trade distortions, discouragement of investment
33 in innovation, and the lost opportunity costs of diverting public funds away from other, potentially
34 more productive, purposes. Inefficient regulations may create perverse incentives for evasion,
35 unforeseen effects and “externalizing” of costs to consumers and others. Legislators and policy-
36 makers should ensure that new laws and regulations will reasonably and equitably produce benefits
37 that justify the costs, taking economic, environmental and social effects into account. Similarly, when
38 existing rules are reviewed, they should be critically assessed for both demonstrable health-care
39 benefits and cost implications. As part of the regulatory impact analysis, policy-makers should seek
40 the most efficient and least burdensome means of achieving their regulatory purposes at minimum
41 reasonable cost.

42 Health care is paid for, directly or indirectly, by taxpayers, employees and consumers, as well as by
43 the patient. These stakeholders will naturally wish to see the most efficient use of their funds. To the

1 extent that medical product regulation contributes to the costs of goods and services used in health
2 care, inefficient regulation represents a hidden financial burden on patients, consumers and the
3 national health-care system.

4 Efficient regulatory requirements and practices will be seen by the public to produce benefits that
5 justify their costs. The distribution of the economic, environmental and social effects across society
6 will be considered throughout the health-care system by patients, health-care professionals, consumers
7 and manufacturers. Negative effects disproportionately affecting specific groups, individuals or
8 product classes should be minimized. Regulatory requirements should be performance-based rather
9 than prescriptive, and should avoid unnecessary trade restrictions.

10 Regulations should not hinder patients' access to necessary, appropriate and affordable health
11 technologies that address public health needs. Because of the nature of medical products and their
12 intended uses, medical product regulations are necessarily rigorous. If, however, the resulting costs
13 incurred by the regulation are disproportionately large or administration is inefficient in a particular
14 market, suppliers may be discouraged from placing products in that market. For instance, a
15 requirement to conduct local clinical trials in a small country as a condition for marketing
16 authorization could be discouraging, especially if trials conducted elsewhere reflect the patient
17 profiles of the intended market. Inefficiencies may also create an opening for unscrupulous suppliers –
18 domestic or foreign – who do not fulfil all the requirements, or for corrupt enforcement practices.

19 For many medical products, the costs and risks of development are high. If a country's regulatory
20 requirements are not aligned with those of other countries, inefficiencies and the local costs of
21 compliance will rise – perhaps out of proportion to the potential returns in that market. Such
22 conditions may discourage the investment needed to bring appropriate and affordable products to that
23 market. At international level, duplication of regulatory evaluations of medical products and audits of
24 suppliers create inefficiencies and additional costs. While respecting national sovereignty and political
25 accountability for regulatory decision-making, the policy-maker and regulator should evaluate
26 opportunities for convergence and, where possible, should adopt internationally harmonized
27 regulatory guidelines. Regulators should also participate in regional or international collaboration,
28 joint reviews and work-sharing networks of competence. "Reliance" on the work of other authorities
29 may also contribute to efficiency and reduce the burden on existing resources. International
30 collaboration is further discussed in Appendix 3.

31 Regulation of medical products includes explicit or implicit assessment and management of risks.
32 Regulatory impact analyses should include evaluation of the probability and severity of potential harm
33 from exposure to a product – both harm to the health of individuals and harm to public health in
34 general – and should consider how a proposed regulation will reduce those risks, and at what costs.
35 The health risk assessment may also direct regulatory priorities for implementation. For instance, if
36 infectious diseases are leading contributors to the national burden of disease, the NRA may prioritize
37 the allocation of limited resources to the evaluation of products used in national vaccination
38 programmes.

39 In evaluating the potential costs and benefits of a proposed new regulation, policy-makers and
40 regulators should consider not only the costs of that proposal but also the burden and total resource
41 needs of cumulative regulation. They should take into account how the costs and benefits of a new
42 regulation would add to those of the existing body of related regulations, and whether there are
43 conflicts or inconsistencies between rules. It should be clear whether existing rules can be revised or

1 withdrawn, and whether there are effective and more efficient alternatives. Similarly, periodical
2 performance assessments should evaluate the actual efficiency and effectiveness of rules that are
3 implemented in order to ensure that the benefits foreseen have been achieved and, if so, what the
4 direct and indirect costs are.

5 Just as the national regulation of medical products requires qualified staff and appropriate systems, so
6 too it requires the tools and administrative capacity for assessment of regulatory efficiency and
7 effectiveness.

8 **1.8 Clarity**

- 9 • Proposed rules should be accessible to and understood by the users and others to whom they
10 will apply.
- 11 • In the making of regulations the means by which stakeholders can contribute should be made
12 clear.
- 13 • Rules should be drafted in a language and form consistent with other laws and regulations to
14 promote compliance.
- 15 • The process and basis for taking regulatory decisions and enforcement actions should be clear.
- 16 • Terminology should be consistent with established international norms whenever possible.

17 Lawmakers and regulators should ensure that proposed rules are both accessible to and understood by
18 the users and those to whom they are intended to apply. Clear, unambiguous and precise rules that are
19 drafted in a language and form consistent with other laws and regulations reduce the potential for
20 disputes or misinterpretation and also promote compliance. Regulators should consider whether
21 manufacturers, importers and distributors of medical products can clearly understand which rules
22 apply to them and what is expected of them.

23 The process by which the need for a new regulation is identified, and by which it is developed, should
24 be publicly accessible and should be clear to the affected parties. Interested parties should have
25 reasonable opportunity to be informed of, and to contribute to, the processes of regulatory impact
26 analysis and development of regulations. The means by which they can contribute should be made
27 clear.

28 The authority drafting medical product regulations should assess whether requirements will
29 reasonably be understood and can be acted upon, both by those affected and by those who assess
30 conformity. A critical review should be conducted to reveal ambiguities and identify areas that lack
31 clarity. The review should also resolve any inconsistencies – whether within the regulation itself or
32 between the regulation and other requirements such as taxation, customs, general consumer
33 protections, and treaties or international agreements.

34 Terminology should be defined whenever possible to avoid ambiguity or misinterpretation. Terms
35 used should be clear, precise and readily understood. Where possible, terminology should be
36 consistent with established international norms, standards and regulatory harmonization guideline
37 documents, such as those from WHO. The latter are particularly important as they form the basis for
38 international exchange of information among NRAs, work-sharing, reliance, referencing and mutual
39 recognition agreements. Consistent and wider use of those terms promotes international convergence
40 of regulatory requirements and practices, harmonization and information-sharing.

Care should be taken to ensure the clarity and adequacy of definitions and the logical sequence of drafting. The use of technical jargon should be minimized. Other regulations cited or included by reference should be readily available and accessible.

The process and basis for taking regulatory decisions and enforcement actions should be clearly specified in the rules. The titles of those responsible, along with their chains of administrative and political accountability, should be clear.

For greater clarity and understanding of regulatory requirements, supporting guidance documents may be issued. Guidelines should be reviewed periodically to ensure that they still reflect the authority's current practices and expectations, are in keeping with scientific and technological developments, and are aligned with current international standards, where applicable.

1.9 Transparency

- The process of developing new medical product regulations should include public consultation.
- Efforts should be made to seek the feedback of affected and interested parties
- Medical product regulations and guideline documents should be available and accessible to stakeholders and the general public.
- Consideration should be given to make the decisions and actions of the NRA publicly available.
- The NRA's disclosure policies should be consistent with national laws on access to information.

As noted in the World Health Organization Constitution (7):

"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."

It is in the general interests of patients, consumers, governments, health-care workers and manufacturers that there should be a high level of public trust and confidence in the regulation of medical products. Trust depends, in part, on regulations that are seen to be proportionate to policy objectives, that are developed openly and transparently, that are effective in achieving their goals and are enforced appropriately, fairly and in a timely manner. 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.

The process of developing new medical product regulations, or revising existing ones, should include public consultation mechanisms appropriate to the national context (e.g., public meetings, written comments, and/or engagement via an online platform). Public consultation should be timely and should take place as early as possible in the process. It should be of reasonable length – generally at least 60 days (20) – and the scope of the consultation should be clearly understood. All affected and potentially interested parties – domestic, foreign, public and private – should have meaningful opportunities to be informed and to make their views known. Particular efforts should be made to seek the views of groups that may be disadvantaged by a regulatory proposal or that may not be sufficiently well organized to make their views known (e.g., small and medium-sized enterprises). It should also be clear how public input is analysed and acted upon (incorporated or rejected), both in the regulatory impact analysis and in the regulation that is adopted. The decisions of the NRA and

1 feedback on the disposition of the comments received should be communicated. These steps provide
2 clarity and accountability, and create a public record of the rationale for regulatory policies and future
3 decisions. The means by which treaties and trade agreements are taken into account in regulations
4 should be outlined, especially where they promote international regulatory harmonization,
5 convergence, mutual recognition, work-sharing and reliance.

6 Once adopted, medical product regulations and guideline documents should be readily available and
7 accessible to stakeholders and the general public. These documents and their sources should be
8 regularly reviewed and updated as necessary so that the information may reasonably be relied upon to
9 reflect current regulatory requirements and practices.

10 The NRA should develop and implement a plan to disseminate adopted regulations to those affected –
11 by mailing, for instance – and should provide easy and continuing access to them. Regulations should
12 be made available in official publications of the government. Posting regulations and guideline
13 documents on the authority’s Internet website is particularly useful. Additionally, national industry
14 and professional associations will often work with NRAs to provide educational seminars and training.
15 In countries where several languages are widely used, it may be appropriate to prepare rules and
16 guideline documents in several language versions.

17 The decisions and actions of the NRA should be documented and made publicly available. For
18 example, publication of marketing authorizations granted or withdrawn, public assessment reports,
19 advisory notices and recalls, and facility audits or inspections are of public interest. Such information
20 may be important for other manufacturers, importers, distributors, health professionals and consumers.
21 The findings of all audits or oversight reviews of the NRA should be made public. Such reviews are
22 an important element of public accountability.

23 As it fulfils its responsibilities, the NRA will necessarily create or come to possess proprietary or
24 confidential information. Examples include personal identifiable information from clinical trials or
25 reports of adverse events, specifications of medical product compounds or materials, and key
26 manufacturing processes. Measures should be established to prevent the inappropriate disclosure of
27 such specific information. There should be an appeal mechanism to address instances when the
28 proprietary nature or confidentiality of the information is in dispute. Similar measures should be
29 established to provide for limited non-disclosure of information that may be necessary for legal
30 reasons – as, for instance, when disclosure may prejudice a pending investigation or legal proceedings.

31 In general, however, national law and regulation should favour transparency and public access in both
32 the process and the criteria of regulatory decision-making. The NRA’s disclosure policies should be
33 consistent with the national laws on public access to government information or “freedom of
34 information”.

35 **Part 2. Implementing good regulatory practices**

36 This part of the guideline presents GRP for developing, maintaining and evaluating a regulatory
37 framework for the control of medical products. Laws, regulations and guidelines are the most
38 common components of such a framework but alternatives such as standards and self-regulation may
39 be used effectively to achieve a public policy objective. Appendix 2 describes various regulatory and
40 non-regulatory instruments. Governments develop policies and processes on how regulation is
41 developed, adopted, implemented, monitored and reviewed. They are typically issued and overseen at
42 the highest levels of government, possibly by the office of the President or Prime Minister, and

1 applied government-wide. Countries may develop different policies and processes for legislation and
2 for regulation that reflect the differences in their respective decision-making processes.

3 World Health Assembly resolution WHA67.20 (1) recognizes that an effective regulatory system
4 contributes to better public health. WHO Member States are encouraged to implement GRP through
5 their regulatory policies and processes to the extent that the maturity of their legal and regulatory
6 systems make this possible. Transparent and predictable processes should aim to develop high-quality
7 regulation that achieves the intended objectives while also minimizing negative impact and costs. At
8 the same time, there should be sufficient administrative flexibility to allow the processes to be applied
9 proportionately to the scope, magnitude and complexity of the problem.

10 **2.1 Policy-making process and regulatory impact analysis (RIA)**

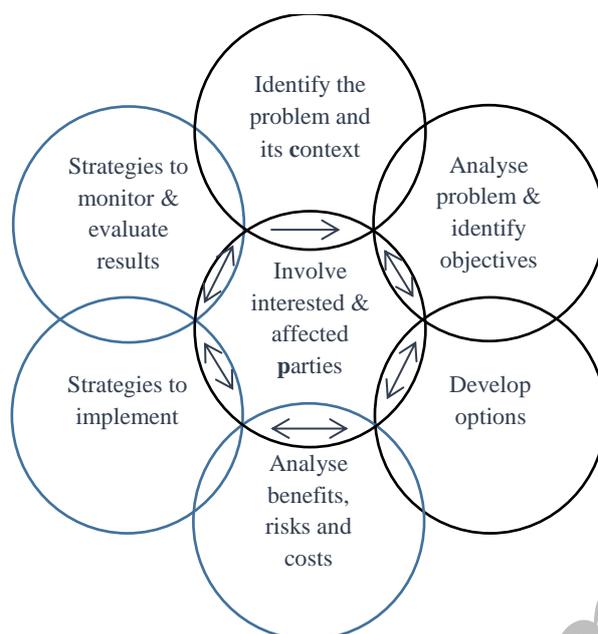
11 Policy analysts follow similar policy-making processes in responding to a concern or problem. While
12 the steps may vary, the process is usually described as a full life-cycle from identification of the
13 problem to development and analysis of options, implementation of the preferred option, and then
14 monitoring and evaluation of its effectiveness.

15 A policy-making process within a health context should also involve an examination of health
16 benefits and risks so that the severity of the health problem is clear. Policy-making is an iterative
17 process, so a step may need to be revisited in light of information arising in a subsequent step. In line
18 with the GRP principle of transparency, good policy-making is consultative and broadly seeks the
19 input of interested and affected parties at any step in the process (21) (22).

20 When a solution to a concern or problem proposes regulation, the policy-making process is adapted to
21 include a formal regulatory impact analysis (RIA). The RIA is a valuable tool for systematic
22 assessment of the expected effects of regulatory proposals. The RIA is undertaken by the policy
23 analysts of the regulatory departments, agencies or ministries that sponsor the proposal and is aimed
24 mainly at assisting decision-makers⁴ in their consideration of a recommended proposal. As such,
25 processes that include the RIA are generally within a government's policies for regulation-making.

⁴ Decision-makers: subordinate regulations can be approved by the head of government, by an individual minister or by the cabinet according to authorities delegated through primary legislation passed by the legislature/parliament.

Figure 1. Regulatory impact analysis process



1 Through the RIA process described in Figure 1, the policy analyst describes the problem and
2 identifies underlying causes. The RIA process should demonstrate that government action is needed
3 and then analyse the advantages and disadvantages of options to resolve the problem. The analysis
4 should look at the benefits and risks related to the options, including whether an option increases or
5 decreases any risk to health posed by the problem that the proposed regulation is trying to resolve. For
6 instance, an option may be judged to be risky if compliance with it is expected to be low. If the option
7 drives noncompliant behaviour underground, it could actually increase the risk to human health.

8 The impact of regulation is often viewed in terms of costs to the regulated industry. However, the
9 analysis should not overlook costs and other impacts on the regulator, the public health sector or the
10 public. For regulatory proposals involving health and safety, a traditional cost–benefit analysis may
11 be difficult or inappropriate. This is discussed in Appendix 1.

12 The RIA process includes consideration of any concerns about implementation and how the
13 effectiveness of the proposed regulation will be monitored and evaluated following implementation.
14 These steps help to avoid unexpected delays in implementation and assure decision-makers that all
15 costs have been properly taken into account, especially in the case of complex regulatory proposals.

16 Contributions to the RIA should be sought within the NRA – e.g., policy analysts, science experts,
17 and operational and administrative staff who can help to ensure that the analysis reflects the health
18 risks correctly and that options are feasible and implementable. Other government departments or
19 agencies may need to be consulted because of intersecting regulatory mandates.

20 The RIA process described in Figure 1 has six steps (21). As in the policy-making process, the steps
21 are iterative; thus an earlier step can be revisited should the context for the problem change or if more
22 information become available. A more detailed description of each step is found in Appendix 1.

23 The product of the RIA process is a document that summarizes the regulatory proposal, the potential
24 alternatives, and the impacts and implementation aspects of the proposal.

1 Consultation may take place throughout the RIA process to inform the individual steps. Additionally,
2 there should be a formal public consultation for the proposal as a whole. When the RIA document,
3 including the summary of public consultations, is presented to decision-makers it demonstrates the
4 consistency and rigour of regulatory decision-making. In some countries, decision-makers approve the
5 dissemination of draft regulations with an RIA-like document⁵ for the formal public consultation on
6 the proposal. The RIA thus increases transparency and, in effect, becomes a public accounting of the
7 need for each regulation (5) (23) (24).

8 **2.2 Compliance and enforcement**

9 A well-functioning regulatory system for medical products is designed and implemented to ensure the
10 highest probability of compliance. Consequently, NRAs need to assess whether the regulated sector is
11 complying with the regulations.

12 Regulations should be performance-based rather than prescriptive. They should not describe a specific
13 manner of compliance but rather feasible outcomes to be achieved. As an example, the electrical
14 safety of a medical device, as required by regulation, may be demonstrated by testing in-house or by
15 testing at an accredited external laboratory according to an international standard. As another example,
16 required records may be equally acceptable on paper or in computer-based media so long as they fulfil
17 the regulatory requirements.

18 Regulations should be clear, accessible, proportionate and achievable. Effective compliance can be
19 achieved only if the affected parties understand the message delivered by the regulator and the
20 regulations are both realistic and adequate for the country and business.

21 Performance-based regulations support an inspection and enforcement strategy that provides
22 compliance incentives for regulated parties and guidelines for enforcement agencies. The balance
23 between compliance verification, through inspections, and the burden of control can be achieved by
24 combining compliance-promotion initiatives with well-targeted controls and deterrent sanctions for
25 serious violations. In order to achieve optimal outcomes, the characteristics of the market affected by
26 regulation should be well-known and the incentives for compliance correctly identified.

27 The regulatory cost to affected parties can be reduced by efficient inspections which can also guide
28 regulators regarding adaptations or changes in the regulations that could increase compliance. For
29 example, an analysis of inspection findings from several medical product manufacturing sites may
30 indicate areas where the requirements are not well understood and there is a high degree of
31 noncompliance. Additional regulatory guidance may be appropriate. Similarly, frequent reports of
32 adverse events associated with a category of medical products may indicate the need for more
33 education of users or closer scrutiny by the regulator of a specific product feature.

34 NRAs should develop inspection and enforcement strategies that ensure the highest possible level of
35 compliance while keeping the costs and burdens for affected parties as low as possible (25). For
36 instance, the frequency of inspections could be determined in part by a manufacturer's history of
37 compliance: more frequent inspections would be required for persistent violations, whereas less
38 frequent inspections would be conducted where the manufacturer has a consistent history of
39 compliance and well-implemented controls. Inspection and enforcement strategies should be

⁵ This document would not include policy advice that may be considered confidential under legislation on access to information.

1 proportional, with resources proportional to the level of risk and the stringency of control measures
2 proportional to the seriousness of violations. A product recall may not be the most appropriate
3 regulatory response for a case of technical noncompliance where there is no significant risk to public
4 health. A warning letter or report of an inspection finding may be more appropriate in such a case.

5 Risk-based strategic planning should ensure that sufficient resources are available to address key risks.
6 Given the scarcity of financial, personnel and infrastructure resources, prioritization strategies are
7 essential. It is impossible to inspect and enforce all cases, so inspection and enforcement resources
8 should be based on risk analysis and a more targeted approach. A well-designed prioritization strategy,
9 considering all levels of decision-making on regulatory enforcement, can enhance efficiency.

10 The NRA should have in place the necessary tools and powers of inspection and enforcement. In
11 decentralized models, all levels of the NRA should, in accordance with its regulatory powers and
12 attributions, contribute to the monitoring, evaluation and enforcement of compliance. Besides the
13 required powers, all levels of the NRA should, in view of its responsibilities, have adequate
14 infrastructure, technical tools and trained personnel for the performance of these tasks. In line with the
15 principle of efficiency, inspection and enforcement activities should, as far as possible, be coordinated
16 and consolidated across all levels of the regulatory system in order to reduce the burden on regulated
17 parties and make efficient use of resources. Coordination may be facilitated by communication
18 technologies and effective, efficient and rapid information-sharing, which will result in fewer gaps
19 and less duplication of efforts.

20 Three main elements of compliance verification for medical products are inspections against good
21 practices guidelines, adverse event (vigilance) reports and post-marketing monitoring information.
22 Vigilance reports may occasionally trigger an investigation that concludes there may have been a
23 failure to comply with a regulatory requirement (e.g., labelling, design and manufacturing controls)
24 and consequently lead to enforcement action. However, most investigations of vigilance reports do
25 not result in enforcement action. As a matter of regulatory policy and public health protection,
26 regulation should not discourage manufacturers or others from reporting adverse events because of the
27 threat, or perceived threat, that a report will lead to enforcement action against them, since this may
28 result in problems going unrecognized. In general, reporting time limits are too short to allow a
29 complete investigation of an incident, so early reports are often incomplete and may be misleading.
30 The reporting an adverse event – as required in many regulatory systems – must not be seen as
31 incriminating or as a conclusion by the reporting party that the health product has actually caused or
32 contributed to a death or serious injury and/or that there was a failure to comply with regulatory
33 requirements. Adverse event reports must be investigated and assessed for causality (i.e., whether or
34 not there is causal relationship with the medical product), and the outcome of the assessment will
35 determine if regulatory action is needed.

36 Appropriate guidelines, instructions and codes of conduct should be issued to guide officials in charge
37 of inspections and enforcement. Training of inspectors and auditors should emphasize fairness,
38 impartiality and objectivity. Governance and human resources policies for inspections and other
39 enforcement measures should encourage transparency, professionalism and integrity, and should
40 focus on outcomes. Inspections and other enforcement outcomes should be independent of political
41 influence and should be carried out by well-trained personnel who have a full understanding of the
42 aims of the regulations and have the authority to enforce those regulations. Compliance promotion
43 efforts should also be rewarded. Objective, clear mandates should be given to personnel in charge of
44 inspections and enforcement actions. Different interpretations of requirements lead to a lack of
45 predictability as to what is expected by a regulation and must be avoided. Rights and obligations of

1 affected parties should be clear and should be established objectively. Moreover, inspections and
2 enforcement initiatives should be evidence-based, with their effectiveness regularly evaluated against
3 well-defined indicators and reliable data.

4 Regulations and inspection and enforcement strategies should have clear objectives (and roadmaps for
5 reaching them) as well as clear guidelines, toolkits and checklists that help affected parties to
6 understand the requirements and how to comply with them. Inspections and other enforcement
7 measures should also be flexible enough to allow room for adaptation when this is proved to be
8 necessary. However, the ultimate decision lies with the NRA.

9 The use of a variety of regulatory and non-regulatory instruments has the potential to reduce the
10 regulatory burden and make efficient use of the NRA's inspection and enforcement resources. The
11 manner in which the private sector and civil society can support a compliance and enforcement
12 strategy should also be explored wherever possible. For example, the NRA could encourage the
13 development and adoption of a new voluntary standard to address widespread incompatibility of
14 connectors used on different devices; compliance could be verified by the standard-setting
15 organization or another third party. As another example, an industry code of good practice in labelling,
16 advertising and promotion of over-the-counter medicines may be helpful in discouraging misleading
17 advertisements. The fear of damage to reputation in the eyes of customers may encourage
18 manufacturers to comply with regulatory requirements.

19 **2.3 Regulatory consultation**

20 Appropriate consultation is a key tool when developing new regulations or reviewing existing ones
21 since it ensures transparency and improves the efficiency and effectiveness of regulation. The
22 likelihood of compliance with regulations is increased when affected parties understand the
23 underlying policy considerations and feel that their input has been seriously considered.

24 As Figure 1 illustrates, both affected and interested parties may be engaged at any stage in the policy
25 development process. This ensures that both the regulator and affected parties have a common
26 understanding of the problem, options to address it, potential administrative and compliance
27 mechanisms, and associated benefits, risks and costs (13).

28 Regulatory consultation is most effective when it is built on a culture of open, meaningful and
29 balanced dialogue. Openness ensures that those directly and indirectly affected have an opportunity to
30 contribute their views, while a meaningful consultation means that these views will be considered
31 seriously. If some elements of the proposal are not open to change, this should be clearly
32 communicated so that participants can focus their efforts appropriately. Balanced consultations seek
33 broad or opposing views.

34 The nature of the consultation should be appropriate to the stage of policy development of the
35 regulatory lifecycle. For instance, an NRA may meet a number of different groups to discuss an issue
36 raised by a particular patients' group. The objective would be to understand the issue from various
37 perspectives so that subsequent analysis and options will target the problem accurately. If new aspects
38 of the issue arise at subsequent stages in policy development, these can be discussed either in
39 additional targeted consultations or, preferably, during the public consultation that is a mandatory part
40 of the RIA process.

1 Consultation should be commensurate with the size of the problem and the potential impact of the
2 proposal. A document-based consultation may be appropriate for minor or technical corrections in
3 existing regulations. For more complex issues, however, written submissions may need to be
4 supplemented with face-to-face meetings such as public hearings, community advisory forums and
5 symposia. There are, of course, practical limitations to the extent of consultation that can be
6 conducted by small or medium-sized NRAs. For instance, it may be difficult to identify the affected
7 parties, especially in countries with few domestic manufacturers, distributors or investigators. Seeking
8 input through industry associations, whenever possible, can broaden the perspective and ensure that
9 the NRA is not unduly influenced by the vested interests of a single manufacturer.

10 It is important to involve a wide range of interests. The views of patients, consumers and health-care
11 workers can provide important insights into an issue. In many cases these groups can be represented
12 by academia, professional associations, patients' groups, and other bodies.

13 In decentralized systems, state and municipality authorities should be engaged throughout to ensure
14 that regulatory policies are consistent, aligned and complementary across jurisdictions. NRAs that are
15 working in a harmonized community should consult their harmonization partners to ensure that the
16 initiative does not have a negative impact on existing agreements. International cooperation initiatives
17 can be a source of best practice information and can assist in building mutual capacity so that
18 meaningful consultation can occur. The views of regional or pan-regional specialists can complement
19 those of domestic specialists.

20 Consultation partners should be given sufficient time to receive and study the proposal and to prepare
21 a considered response. This can be facilitated by publishing a forward-looking agenda showing
22 upcoming or planned consultations on the NRA website, in a public gazette, or through emails or
23 newsletters. All available tools should be adopted to ensure access to the consultation and all relevant
24 information. Where a consistent and predictable approach is taken to integrate consultation into the
25 regulation development process, affected parties are able to plan more effectively for their own
26 contributions.

27 Small and medium-sized businesses and patients' groups which may lack the resources to respond
28 quickly should not be forgotten. The consultation period should match or exceed the minimum
29 requirements of international agreements to which the country is a party. There is usually sufficient
30 flexibility in these agreements to allow for the quick passage of a regulation in urgent situations.
31 Consultations are made more meaningful when the proposal is distributed (and accepted) in the most
32 common languages of the regional, pan-regional and, where necessary, international communities
33 whose views are being sought.

34 If consultations have been conducted throughout the development of the proposal, a summary should
35 be prepared of the comments received and how they were taken into consideration. This feedback
36 gives credibility to the consultation process and increases the likelihood of regulatory success.

37 Consultation is a vital regulatory tool. Failing to engage affected parties appropriately while
38 developing or implementing regulations can lead to regulations that are inadequate to the
39 circumstances, unpopular, unnecessarily costly to comply with and poorly adhered to.

40 **2.4 A forward-looking regulatory agenda**

41 Forward-looking regulatory planning helps an NRA to identify short-, medium- and long-term
42 priorities in the management and maintenance of regulations. It helps regulation-making and reform

1 to become more efficient by planning actions at the right time. Establishment of regulatory principles
2 helps the construction and management of a forward-looking regulatory agenda.

3 The creation of a regulatory agenda is aligned with the principles of transparency and consistency.
4 Those affected by the regulatory activity should be both consulted and involved in the identification
5 of regulations to be reviewed, modified, eliminated, simplified or issued by the NRA. By creating a
6 regulatory agenda, priorities and action plans can be published and regularly updated, and progress by
7 the authority can be reported. The agenda may include:

- 8 • a brief description of the problem to be addressed by the regulation, taking into account
9 the potential risks and consequences of the regulatory issue under debate;
- 10 • a schedule for the technical debate and planned consultations; and
- 11 • the technical team responsible for coordinating the regulatory process.

12
13 A regulatory agenda should cover a defined time period (e.g., 1–5 years) and should be regularly
14 reviewed (annually or semi-annually). In this way, regulatory action plans can be adjusted in
15 accordance with changing drivers and can provide updated information on the public participation
16 schedule. The review gives NRAs the opportunity, if appropriate, to withdraw some regulatory
17 proposals under development, to add new regulatory proposals which were not foreseen in the
18 previous version of the agenda, and to amend the schedule for a given proposal. However, the changes
19 should be kept to a minimum and must be based on sound reasoning in order to maintain the
20 predictability of the regulatory changes.

21 Even in the absence of an official institution responsible for overseeing regulatory planning, NRAs
22 can plan their activities by setting objectives to be addressed in terms of creating and revising
23 regulations, identifying priority regulatory areas, and preparing roadmaps and schedules.

24 **2.5 Monitoring and evaluation**

25 The RIA process can evaluate the potential impacts of a regulation before it is selected and
26 implemented. This is often referred to as *ex ante* evaluation, or evaluation “before the event”.
27 Regulatory quality can be further strengthened if impact analyses are also conducted following
28 implementation of a regulation (*ex post*), after the action has taken effect. In this way, direct and
29 indirect impacts and unintended consequences may be detected.

30 Since *ex post* analysis provides information for improvements, the monitoring and evaluation stage of
31 regulation-making creates a feedback loop in the regulatory lifecycle. The strategy to be used for
32 monitoring and evaluation of an implemented regulation should be defined during the RIA process
33 (see Appendix 1). In addition to a monitoring and evaluation plan, regulations may include clauses
34 that trigger periodic statutory review. Beyond the evaluation of a specific regulation, a broader
35 assessment of the regulatory framework can be periodically undertaken (see section 2.6).

36 ***Evaluation indicators and criteria***

37 An objective of the evaluation of a regulation, although difficult to achieve in some cases, is the
38 establishment of causal connections between the adopted regulation and observed changes in the
39 regulated environment. Such an evaluation should also take into consideration intentional and non-
40 intentional outcomes (including externalities) arising from the regulation.

1 The measures or indicators needed to monitor and evaluate regulations should be identified as soon as
2 possible in the RIA process and should reflect the objectives to be achieved by the regulation that is
3 being developed. This allows for continuous monitoring of the regulation as data are collected. If
4 regulations are shown to be ineffective or more costly than expected, or if there are unintended
5 consequences, changes can be initiated early.

6 When evaluating a broad regulatory framework or one of its components, preplanned indicators and
7 data may not be readily available. Therefore data would need to be collected retrospectively.

8 An indicator is a “measure that captures relevant information regarding distinct attributes and
9 dimensions” (26) of the expected performance of a given regulation. A good indicator should ensure
10 that data collected are able to disclose a situation that is not self-evident. Essential characteristics that
11 ensure the quality and utility of an indicator are (26):

- 12 • Validity – the indicator should effectively measure what is intended to be evaluated.
- 13 • Reliability – the indicator should be replicable when similar conditions are maintained.
- 14 • Specificity – the indicator should measure specifically the assessed phenomenon.
- 15 • Sensibility – the indicator should be able to capture changes in the assessed phenomenon.
- 16 • Measurability – the indicator should be based on data that are available and easy to access.
- 17 • Relevance – the indicator should be able to give clear answers to the most important issues
18 under assessment.
- 19 • Cost-effectiveness – the results should justify costs in terms of time and other resources.

20 Well-developed and well-implemented assessments help to improve current and future regulatory
21 interventions on the basis of lessons learned from practical experience. The disclosure of the
22 assessment results makes the NRA more transparent and accountable for its actions and decisions, and
23 informs affected parties of the effects and outcomes reached by the regulatory intervention to which
24 they are subjected.

25 The analysis of assessment data should reveal how well the regulation or regulatory framework is
26 performing. The use of “criteria” should assist in drawing conclusions from the assessment. The
27 criteria of a well-developed assessment should include (27):

- 28 • Relevance – whether the regulation addressed the original problem.
- 29 • Effectiveness – whether the intended goals of the regulation were achieved, why the
30 intervention was effective and how this might be further improved.
- 31 • Efficiency – whether the results achieved justified the costs and whether there is opportunity
32 to further streamline cost-effectiveness.
- 33 • Transparency – whether those affected by the intervention were adequately informed.
- 34 • Legitimacy – whether affected stakeholders accepted the change.
- 35 • Equity – whether the effects of the regulation are distributed fairly and there is equal access to
36 information on the process.
- 37 • Persistence – whether the intervention will have a sustained effect.

38 Broader considerations such as consistency with the national legal and regulatory framework and
39 convergence with international regulations can also be evaluated, as can regulatory simplification
40 which takes into consideration the assessment of costs of compliance.

2.6 Management of the regulatory stock

There is a tendency to add to the regulatory framework without evaluating existing regulations and their suitability for addressing a problem. Evaluation of what already exists in the regulations is noted in the second step of the RIA process (Appendix 1). There are valid reasons for not modifying, replacing or phasing out current regulations when introducing a new one. It may be more appropriate to note these issues and to address them during a broader framework review. For instance, decision-makers may be reluctant to increase the complexity of a new regulatory proposal with anything except the most simple and essential consequential changes to other regulations. The accumulation of regulations within the regulatory framework can result in inconsistencies, lack of clarity and redundancies. The regulatory framework itself can become too complex and difficult to maintain. Unintended consequences can result, as can increased costs for the regulator to enforce the regulations and for the regulated community to comply with them.

Regulations should be periodically reviewed in their entirety to eliminate those that are outdated or no longer needed, to correct contradictions between regulations, and to address other complications that may have arisen over time. This simplifies the framework while ensuring that it continues to regulate new medical products and technological changes effectively.

It is preferable to review the entire regulatory framework. However, if resources or competence are not available for a complete *ex post* analysis, a more targeted evaluation could proceed through planned phases, namely:

1. Identify the regulations for a particular regulatory theme – such as regulations for the marketing authorization of generic drugs or quality management systems for medical devices.
2. Review the identified regulations, searching for gaps, conflicts or other problems.
3. Identify regulations that can be reduced, simplified, improved, updated or eliminated.

The RIA process facilitates continuous monitoring (*ex ante* and *ex post*) of the existing framework and provides a basis for initiating either a broad or a targeted review of the regulatory framework. Planned management of the regulatory stock allows NRAs to take a measured approach to: filling regulatory gaps; eliminating inconsistencies, lack of clarity or redundancies; verifying the adequacy of existing regulations; and interrupting regulatory expansion and accumulation. A broad evaluation can also identify areas that should be prioritized via regulatory planning and the forward-looking regulatory agenda.

Glossary

The definitions given below apply to the terms as used in this guideline. They may have different meanings in other contexts.

Audit: an independent and systematic verification of records.

Best practices: exemplary approaches to problems, as used by certain NRAs and which could be adapted or adopted by other regulatory authorities.

Collaboration: working with others to achieve shared goals. Collaboration involves informal peer-to-peer information-sharing between experts. It may be supported by International Regulatory Cooperation agreements that provide for the sharing of confidential information between NRAs (28).

- 1 **Convergence:** (see Regulatory convergence)
- 2 **Cooperation:** (see Regulatory cooperation)
- 3 **Enforcement:** all activities of state structures (or structures delegated by the state) aimed at ensuring
4 compliance with regulations and achievement of the regulations' objectives (25).
- 5 **Good manufacturing practices (GMP):** the element of quality management which ensures that
6 products are consistently produced and controlled according to the quality standards appropriate to
7 their intended use and as required by the marketing authorization, clinical trial authorization or
8 product specification. GMP is concerned with both production and quality control. GMP is aimed
9 primarily at managing and minimizing the risks inherent in pharmaceutical manufacture in order to
10 ensure the quality, safety and efficacy of products (29).
- 11 **Harmonization:** (see Regulatory harmonization)
- 12 **Incorporation by reference:** a term used to describe a mechanism that allows a document or list that
13 is not in the text of the regulations to be made a part of the regulations. The incorporation may be
14 "static" – i.e., incorporating a specific version of a document at a defined date – or "dynamic" –
15 i.e., incorporating a document that will be amended from time to time (30).
- 16 **Information-sharing:** the exchange of non-confidential or confidential information between NRAs
17 with the aim of establishing confidence in other regulators' regulatory systems, thereby providing a
18 basis for reliance, work-sharing or recognition.
- 19 **Inspection:** an official examination, usually conducted on-site by a relevant authority, of the
20 compliance with practices set out in policy or regulation (e.g., Good manufacturing practices, Good
21 clinical practices) (31).
- 22 **Memorandum of understanding (MOU):** a formal agreement between two or more parties. MOUs
23 are often used to support international regulatory cooperation by setting out operational arrangements.
- 24 **Mutual recognition agreement (MRA):** a government-to-government arrangement whereby two or
25 more countries agree to recognize each other's conformity assessment results. MRAs specify the
26 conditions under which the conformity assessments performed by one party will be accepted as
27 showing compliance with the other party's requirements and vice versa (32,33).
- 28 **Post-implementation review:** a review of a rule or regulation after it has entered into force (34).
- 29 **Primary legislation:** regulations which must be approved by the parliament or congress. Primary
30 legislation may also be referred to as "principal legislation" or "primary law" (34). (See also
31 Regulation, Subordinate regulation)
- 32 **Recognition:** the routine acceptance by the NRA in one jurisdiction of the regulatory decision of
33 another NRA or other trusted institution. Recognition indicates that evidence of conformity with the
34 regulatory requirements of country A is sufficient to meet the regulatory requirements of country B.
35 Recognition may be unilateral or multilateral, and may be the subject of a mutual recognition
36 agreement.
- 37 **Regulatory consultation:** a two-way exchange in which stakeholders are given an opportunity to
38 provide input that is taken into consideration in the development of a regulatory proposal.

1 Consultation may occur at any stage of regulatory development, from problem identification to the
2 evaluation of existing regulation (35) (36).

3 **Regulatory cooperation:** a practise between NRAs aimed at efficiently regulating medical products.
4 Regulatory cooperation can be practised by an agency or institution or on a government-wide basis.
5 The range of formal mechanisms include the creation of joint institutions and treaties and conventions
6 such as MRAs, while the less formal practices include sharing of information, scientific collaboration,
7 common risk assessment, joint reviews, and development of standards. Regulatory cooperation may
8 also include work with international counterparts to build regulatory capacity or provide technical
9 assistance, thus contributing to the improvement of international regulatory governance practices (28)
10 (37) (38) (39).

11 **Reliance:** the act whereby the NRA in one jurisdiction may take into account and give significant
12 weight to – i.e., totally or partially rely upon – evaluations performed by another NRA or trusted
13 institution in reaching its own decision. The relying authority remains responsible and accountable for
14 decisions taken, even when it relies on the decisions and information of others.

15 **Regulation:** the diverse set of instruments by which governments place requirements on enterprises
16 and citizens. Regulation includes all laws, formal and informal orders, subordinate rules,
17 administrative formalities and rules issued by nongovernmental or self-regulatory bodies to whom
18 governments have delegated regulatory powers (34). (See also Primary legislation, subordinate
19 Regulation)

20 **Regulatory authority:** the agency, institution or body authorized by law to exercise regulatory
21 powers concerning the registration of, and other regulatory activities related to, medical products.
22 Also referred to as the “regulator” (17).

23 **Regulatory convergence:** a voluntary process whereby the regulatory requirements in different
24 countries or regions become more similar or “aligned” over time. The process results from the gradual
25 adoption of internationally recognized technical guideline documents, standards and scientific
26 principles, common or similar practices and procedures, or the establishment of appropriate domestic
27 regulatory mechanisms that align with shared principles to achieve a common public health goal (40).

28 **Regulatory framework:** the collection of laws, regulations, guidelines and other regulatory
29 instruments through which a government controls particular aspects of an activity.

30 **Regulatory harmonization:** the process by which technical guidelines are developed in order to be
31 uniform across participating authorities in multiple countries (41).

32 **Regulatory impact analysis:** the process of examining the likely impacts of a proposed regulation
33 and alternative policy options to assist the policy development process (42).

34 **Regulatory system:** the combination of institutions, processes and the regulatory framework through
35 which government controls particular aspects of an activity (43).

36 **Standard operating procedure (SOP):** an authorized written procedure providing a documented
37 process to follow in a specific situation (17).

38 **Subordinate regulation:** a regulation that can be approved by the head of government, by an
39 individual minister or by the cabinet – that is, by an authority other than the parliament/congress.

1 Many subordinate regulations are subject to disallowance by the parliament/congress. Subordinate
2 regulations are also referred to as “secondary legislation”, “subordinate legislation” or “delegated
3 legislation” (34). (See also Primary legislation, Regulation)

4 **Technical regulation:** a document which lays down product characteristics or their related processes
5 and production methods, including the applicable administrative provisions, with which compliance is
6 mandatory. A technical regulation may also include or deal exclusively with terminology, symbols,
7 packaging, marking or labelling requirements as they apply to a product, process or production
8 method (20).

9 **Transparency:** ensuring that regulators and others involved in the regulatory process act and
10 communicate openly, defining policies and procedures in writing and publishing the written
11 documentation, and giving reasons for decisions to the public (17).

12 **Work-sharing:** a process by which NRAs of a number of jurisdictions share activities. Work-sharing
13 entails exchange of information consistent with the provisions of existing agreements and compliant
14 with each agency's or institution's legislative framework for sharing such information with other
15 NRAs. Other opportunities for work-sharing include: jointly assessing applications for marketing
16 authorizations or therapeutic product manufacturing sites, joint work in the post-marketing
17 surveillance of therapeutic product safety, joint development of technical guidelines or regulatory
18 standards, and collaboration on information technology (44).

19 **Vigilance:** the science and activities relating to the detection, assessment, understanding and
20 prevention of adverse reactions or any other medical product-related problem. Pharmacovigilance is
21 used for medicines and vaccines (45).

22 **Voluntary standard/Standard:** a documented agreement containing technical specifications or other
23 precise criteria to be used consistently as rules, guidelines or definitions of characteristics to ensure
24 that materials, products, processes and services are fit for their purpose (46).

25

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1 **Appendix 1. The process of regulatory impact analysis**

2 This appendix outlines a process for gathering and analysing evidence to support the development of a
3 regulatory proposal. The process describes the problem, identifies the underlying causes, assesses
4 whether government action is needed, and analyses the advantages and disadvantages of available
5 solutions. While not exhaustive, questions and considerations are provided at each step to assist in
6 gathering the information to support the identification and analysis of solutions.

7 In general, the process for developing/reviewing new or existing regulation is:

8 Step 1: Identify the problem and its context

9 Step 2: Analyse the problem and identify objectives

10 Step 3: Develop and analyse options

11 Step 4: Analyse the benefits, risks and costs

12 Step 5: Select/recommend an option

13 Step 6: Develop strategies for implementation

14 Step 7: Develop strategies for monitoring and evaluation.

15 The steps of the impact analysis process are not intended to be a step-by-step recipe but rather an aid
16 to policy development and decision-making.

17 **Step 1. Identify the problem and its context**

18 A clear description and analysis of the problem gives the best chance of arriving at an effective
19 solution that will target actions efficiently. In most cases, the problem would be described in terms of
20 risks to human health and safety in a population and whether the problem is likely to get better or
21 worse if left unaddressed. Whenever possible, the magnitude of the problem should be described in
22 terms that can be measured.

23 The problem should be described by use of objective facts that allow for analysis and an explanation
24 of why regulatory action may be needed. For example, a problem statement that there is an absence of
25 regulations for a certain medical product does not in itself suggest why this might pose a risk to
26 human health. On the other hand, the problem description would be more tangible if it included the
27 number of patients exposed to the medical product and the nature and number of adverse events
28 reported.

29 The root causes of the problem should be identified so that actions can be targeted where they will do
30 the most good. For example, a sudden increase in the rates of cross-infection following endoscopy
31 procedures may be the result of a defective medical device design, ineffective sterilization products or
32 procedures, staff training, or even a simple change in reporting protocols. The solution(s) to this
33 problem could range from new regulation to education to no action at all.

34 If there is a history to the problem, consider providing a timeline of events to provide context. If
35 regulations currently exist, the analysis should outline why they are no longer effective. If the problem
36 has been examined in the past, review the previous work. Consider the age of any previous analysis
37 and whether the underlying data are still sufficiently current. Describe how the situation has changed
38 since the problem was previously analysed.

1 **Step 2. Analyse the problem and identify objectives**

2 The problem analysis should consider all the parties directly and indirectly affected by the problem
3 and the nature of the impact on them. The problem should be approached from the perspectives of
4 patients and medical practitioners interested in effective, safe and affordable medical products.
5 Industry, academia and donors may also have some useful perspectives on the problem. For some
6 complex issues, early stakeholder consultation may be necessary to ensure that the problem is
7 accurately understood and that the eventual choice of regulatory instrument is appropriate. It may also
8 be necessary to obtain specialized technical or scientific advice from experts both within and outside
9 the NRA.

10 The jurisdictional context of the problem should be thoroughly described and analysed. Determine
11 whether the problem is within the legal jurisdiction/responsibilities of the government or NRA.
12 Identify whether the government has sole jurisdiction or if it is a shared responsibility. For example,
13 there may be different regulatory roles and responsibilities set out for the federal, state (provincial)
14 and local governments. Where appropriate, identify whether any responsibilities have been delegated,
15 through legislation, to nongovernmental parties such as colleges that oversee the practice of medicine
16 or pharmacy. Any other shared or possibly conflicting roles and responsibilities within the health
17 department, or between government departments, should also be identified. Further, any international
18 treaty obligations and regional economic and trade cooperation agreements should be reviewed since
19 they are part of the legal context and may have an impact on the range of options for the problem
20 being analysed.

21 National, regional and international cooperation and collaboration are means to achieve an effective,
22 efficient and consistent regulatory system. As outlined in Appendix 3, NRAs everywhere are under
23 pressure because of the significant number of applications they receive, their complexity and the
24 growing number of categories of medical products. As the production and distribution of medical
25 products have become globalized, NRAs can no longer work in isolation (40). Consequently, the
26 problem analysis should include an international review to determine how other NRAs may have dealt
27 with similar problems (i.e., best practices) and whether an existing solution could be adapted.
28 Government policy on, or any opportunities for, international cooperation, harmonization and
29 convergence should be noted and should be taken into account both in developing options and in the
30 cost–benefit analysis.

31 Once the problem is examined, the objectives that any proposed intervention is intended to achieve
32 should be identified. If there are constraints, such as funding government policy objectives or treaty
33 obligations, these should be stated clearly in the objectives. The stated objectives guide the
34 development of options and provide a challenge against which the options may be measured. For
35 complex problems, objectives can be used to develop an options selection grid which may also be
36 known as a multi-criteria analysis. Following implementation, the objectives provide a measure
37 against which performance may be evaluated.

38 A common error when starting an analysis is to confuse the desired “end” outcome with the “means”
39 of achieving it. For example, there may be a policy objective to reduce deaths due to a certain disease.
40 Vaccination may be one means of achieving the objective but it is not the objective itself. Other
41 means (that is options) could be to treat the disease itself or to improve sanitary conditions (47). For
42 medical devices, the policy objective of regulation may be to reduce the rate of in-hospital
43 cross-infection arising from endoscopy procedures. Banning the use of certain medical devices may

1 be one means of achieving this objective. A thorough analysis of the problem may also point to more
2 effective sanitizers and improved sterilization processes as alternative means to achieve the objective.

3 **Step 3. Develop and analyse options**

4 An effective regulatory system produces the intended results, facilitating access to high-quality, safe
5 and effective medical products. However, an efficient regulatory system delivers those results with
6 minimal cost and effort by employing various regulatory and non-regulatory instruments to achieve
7 policy objectives. A description of commonly-used instruments is provided in Appendix 2. Potential
8 options should be proportionate to the potential benefits and risks associated with the problem and/or
9 the medical product. While regulation may be necessary for one problem, a non-regulatory approach
10 such as public education may be an efficient and effective resolution for another.

11 Deregulation, or reducing regulation, should also be given thorough consideration. It challenges the
12 policy analyst to think broadly about the options available. For example, in a scenario where the
13 analysis of the endoscopy cross-infection rates described above reveals an existing regulatory
14 requirement to use a specific but outdated sterilizing product or method, an option to resolve the
15 problem could be to update the existing regulation to something more scientifically current. However,
16 another option could be to remove overly prescriptive requirements from the regulatory framework
17 entirely and, where appropriate, employ more flexible instruments such as guidelines or
18 industry/professional standards.

19 Options should be developed to leverage and facilitate cooperation, collaboration and harmonization
20 (see Appendix 3). Whenever possible, options should permit the use of harmonized requirements and
21 practices that reflect a consensus among experts from government, industry and interested parties.
22 Where appropriate, measures should be considered that permit reliance on the evaluations of other
23 NRAs since this increases not only efficiency but also opportunities for regulatory convergence.

24 The status quo (i.e., no change in the regulatory framework) should always be included as an option
25 since it is the baseline against which other options can be compared.

26 **Analyse the options**

27 The analysis of each option should include questions such as the following:

- 28 • How will the option achieve or contribute to the policy objective (i.e., the desired outcome)?
- 29 • How will the option fit within the current regulatory framework of laws, regulations, policies
30 and processes, and in the wider strategic priorities of the government?
- 31 • Will the option have an impact on other sectors or agencies, and will it affect national or
32 international commitments?
- 33 • What obligations will the option impose on affected parties?
- 34 • Will the option deviate from policies on international convergence or internationally
35 harmonized requirements? If so, what is the explanation for the variation and what would be
36 the resulting implications for the NRA and the affected parties?
- 37 • Who would be, or could be, involved in implementing the option, and what would be the
38 respective roles and accountabilities? For instance, with a proposal to amend a regulation to
39 require compliance to a third-party standard, would the NRA assess compliance or could this
40 be undertaken by the third party?

- 1 • What new guidelines or standard operating procedures are needed to implement this option?
2 The time and cost of creating these administrative instruments should be included in the
3 cost–benefit analysis.
- 4 • Would success be measured directly or through appropriate surrogates? What is the feasibility
5 of obtaining these measurements?

6 It is important that the policy options are developed and analysed in conjunction with internal
7 operations and with any external bodies that might be expected to implement them. If the solution is
8 not operationally feasible, or if there is no capacity for implementation, then the option has no benefit.
9 The implementation plan should be started at this point. For complex problems, stakeholder
10 consultation at the options development and analysis stages may be warranted.

11 **Step 4. Analyse the benefits, risks and costs**

12 Good regulatory practices require the analysis of the impact or consequences of the options, especially
13 when regulation is being proposed. An analysis of the benefits, risks and costs should be prepared and
14 compared for all options. These are often especially challenging for health-related problems for which
15 benefits and costs may be difficult to quantify and monetize. However, the analysis should be
16 undertaken to the extent that is possible. Any opinions on the relative importance of the benefits, risks
17 and costs that are identified should be communicated so that the basis for decision-making is clear.

18 The length and structure of the analysis should reflect the complexity and/or impact of the issue. For
19 example, a proposal to create a regulatory framework for a new category of medical products would
20 warrant a more rigorous analysis than a proposal to add a compliance measure to an existing
21 regulatory framework. An abbreviated analysis or a descriptive outline may be appropriate for
22 problems that are simple, clear-cut or where policy alternatives are limited, as may be the case for
23 national security issues (24).

24 There may be concern that an analysis of costs might lead an NRA to compromise health and safety.
25 However, it is understood that regulatory systems are essential for the protection of human health and
26 contribute to better public health outcomes. Therefore risks to human health should be evaluated for
27 every option. At the same time, several options may be equally effective in achieving public health
28 goals but at significantly different costs.

29 A number of analytical techniques and approaches exist for the examination of benefits and costs;
30 some are considered more suitable to the public health environment than others (42) (48). This
31 appendix does not attempt to provide instruction for a formal cost–benefit analysis or a cost-
32 effectiveness analysis or any other technique. Rather, it describes some aspects of a systematic
33 comparison of options with the aim of ensuring that the option to be recommended is both effective
34 and imposes the least cost burden on all who are affected, including the NRA itself.

35 A policy analyst may tend to view the benefits of an option primarily in terms of patient or consumer
36 safety. However, benefits could accrue to others as well. For instance, the regulated community could
37 benefit from a proposal that adopts internationally-harmonized product labelling requirements that
38 make the labels easier for patients to understand. Academia could see increased research opportunities
39 as a result of a regulatory proposal that increases the evidence threshold for safety. Budgetary savings
40 for an NRA may result in a case where regulation is reduced or is eliminated entirely.

1 Risk associated with a regulatory option can be viewed in two ways: the health risks associated with
2 the problem and the regulatory risk associated with the option itself. The health risks are described
3 and analysed at the problem identification stage (step 1) of the RIA process. They are also described
4 in the objectives that the regulatory proposal is intended to achieve. In this fourth step of the RIA
5 process, every option should be examined to determine if it can be implemented successfully, if it can
6 achieve the objectives, and if risk to health is increased or decreased by the success or failure of the
7 option. For example, a proposal to allow market access to medical products based only on notification
8 may be a feasible option to meet an objective aimed at faster market access. There would be a low
9 regulatory risk of it not being operationally successfully. From a health risk perspective, a notification
10 scheme may be reasonable for low-risk self-selection products, but it may present unacceptably high
11 risks to health for vaccines.

12 Regulatory risk relates to factors that could jeopardize the success or feasibility of the policy option.
13 Regulatory risk could emerge from internal sources, such as the impact of other policies or regulations,
14 timelines for obtaining approval for the recommended option or issues associated with operational
15 implementation (e.g., high costs of enforcement). It is important that both the authority and the
16 resources are provided so that an option can be implemented and enforced. Regulatory risks from
17 external sources could include potential conflicts with treaty obligations or international agreements.
18 These risks should be documented for each option along with the impact of that risk, its significance
19 and likelihood. Additionally, the analysis should consider whether the option can be amended to
20 minimize the risk or its impact.

21 Costs and/or savings should be considered for government and all other affected parties. The costs of
22 a policy option for government include such things as the costs for additional staff, staff training if
23 needed, information technology, guidance development, compliance and enforcement, and
24 communications. While most options would be delivered only by the NRA, some may involve other
25 departments, ministries, agencies or organizations. Their costs/savings should be counted along with
26 those of government. Both one-time and ongoing costs/savings should be included.

27 The costs/savings for all affected parties and, where appropriate, the costs/savings of the option for
28 the wider economy should also be included. While an NRA should be able reasonably to estimate
29 government costs/savings, it may be necessary to consult other affected parties to ensure a realistic
30 analysis of theirs. Affected parties are those identified early in the RIA (in step 1), but it is helpful to
31 review them at this step. Not only the regulated industry may be affected by a policy option. For
32 example, if a regulatory proposal affects the need for, or the nature of, scientific research, this could
33 have an impact on both industry and academia. A proposal that increases import restrictions could
34 inadvertently increase the regulatory burden and costs of humanitarian organizations and could
35 negatively affect their programmes. A proposal could increase the cost of a medical product and put it
36 out of reach for consumers, governments or funding agencies. Again, both one-time and ongoing
37 costs/savings should be included.

38 **Step 5. Select/recommend an option**

39 The option selected and recommended to decision-makers⁶ should be consistent with the objectives
40 stated earlier in the impact analysis. The rationale for the selection should be clear and easy to
41 understand and there should be no unexplained conflicts with the analysis supporting the
42 recommendation. In other words, there should be a logical flow from analysis to recommendation.

⁶ Decision-makers for subordinate regulations can be the head of government, an individual minister or the cabinet pursuant to authorities delegated through primary legislation passed by the legislature/parliament.

1 The recommended option should be consistent with other regulations/policies and should serve the
2 stated objectives with maximum benefit and minimum cost to both the government and other affected
3 parties. For complex issues with many viable options, the selection may be facilitated by an options
4 selection grid (multi-criteria analysis) that assigns a score to each viable option on the basis of how
5 well it achieves the stated objectives. Justification should also be provided for options that were
6 considered but not recommended.

7 An illustrative example of a multi-criteria selection grid is taken from an OECD handbook on
8 RIA (47) and relates to an objective of improving dental health. Criteria were established during the
9 analysis of the problem (step 2) and were assigned a weight reflecting the importance of each criterion.
10 In the example, effectiveness and cost were judged to be most important and given the highest
11 weights. The policy options were then assigned a score using some predetermined scoring system.
12 The total weighted score points to the recommended option.

Sample presentation of a multi-criteria analysis				
Criterion	Weight	Fluoride regulation	Advertising campaign	Free dentist visits
Effectiveness in improving dental health	4	5 (20)	3 (12)	3 (12)
Ability to address existing dental problems	2	0 (0)	1 (2)	5 (10)
Ability to improve dental health of the poorest groups	2	4 (8)	2 (4)	5 (10)
Ability to improve health in all regions	1	5 (5)	5 (5)	3 (3)
Cost (lowest cost assigned highest score)	4	5 (20)	4 (16)	2 (8)
Total weighted score		53	39	43

13

14 **Step 6. Develop strategies for Implementation**

15 Implementing an option can be challenging if it is not well considered during the development and
16 analysis of options (step 3). As the RIA process moves closer to recommending an option,
17 implementation planning should become more mature and more detailed.

18 Internal (e.g., operational units) and external parties should be involved during the policy
19 development since they have valuable experience that can inform the process and guide
20 implementation planning. The implementation plan should identify any information technology
21 systems, standard operating procedures or guideline documents that need to be created, amended or
22 withdrawn. The plan should also include the need for additional staff and staff training. Most of this
23 will have been costed in the analysis of benefits, risks and costs in step 4. However, previous work on
24 the recommended option should be reviewed to ensure it is as detailed as possible.

25 If the recommended option is expected to involve the cooperation of and/or coordination with partner
26 institutions such as a health care professional association, an academic institution, an industry
27 association, or other levels of government, then these should be identified. It is important to engage

1 these parties early and to ensure that any dependencies between the NRA and partner institutions are
2 well understood and well timed. For example, the implementation of a new regulation could be
3 compromised if the NRA is unaware that its partner requires several years to make it fully functional.

4 The implementation strategy should identify how compliance with the proposed regulation will be
5 determined and what enforcement actions will be considered. If the existing compliance and
6 enforcement system can accommodate the new regulation, the implementation plan should refer to
7 the existing relevant provisions. Otherwise the plan should identify any new measures that need to be
8 developed. Compliance and enforcement are discussed in more detail in the guideline document (23).

9 For some regulatory options, a transition period may be required to allow affected parties the time
10 they need to comply with the new measures. If such a delay is anticipated, the implementation plan
11 should address what measures, if any, will be taken during the transition period. For instance, if a new
12 regulation requires a change in the information allowed or required on the label of an over-the-counter
13 medicine, the industry may require time to deplete medicines currently on the shelf so as not to create
14 an unnecessary shortage. During the transition period, the NRA could undertake an educational
15 campaign to inform consumers of the issues that led to the new labelling.

16 Effective communication of an approved regulation is important for its success. While
17 communications may have been identified and costed earlier in the RIA process, the details of those
18 communications become more critical as a specific option is recommended.

19 A costed implementation plan should exist for any viable option recommended to decision-makers.
20 This ensures, as far as possible, that the solution is feasible, appropriately costed and deliverable.

21 **Step 7. Develop strategies for monitoring and evaluation**

22 At the time that an option is recommended, the NRA should have a solid understanding of how that
23 option will be monitored and evaluated. It is also important that monitoring and evaluation costs have
24 been incorporated into the analysis and that budgets will be provided.

25 Once approved, the implementation of a regulation should be monitored to ensure that every stage is
26 working as expected. This is especially important when many internal and/or external parties are
27 involved.

28 Once implemented, the regulation should be evaluated on the basis of indicators established during its
29 development. The evaluation is conducted to test whether the regulation is performing as intended and
30 is meeting the policy objective. If the objective is not being achieved, the evaluation should examine
31 the scope of the impact and assess whether unforeseen obstacles have arisen.

32 As discussed in Part 2 of the guideline, continued monitoring and evaluation after implementation will
33 allow for changes to the regulation to be made faster, especially if the impact puts public health and
34 safety at risk. As a result, the regulatory system becomes more responsive to these changes.

35

1 **Appendix 2. Legal Instruments and alternatives**

2 A broad range of options is available to government for influencing behaviour and advancing public
3 policy. These options range from laws and regulations to public education and even economic, public
4 and peer pressure. An appropriate choice of option, or mixture of options, can lead to an effective
5 public policy intervention at an acceptable cost (49).

6 This appendix describes some of the options that may be considered for the regulation of medical
7 products.

8 **Laws and regulations**

9 In its broadest sense, the term “regulation” is used to include the full range of legal instruments (also
10 called statutory instruments) by which institutions at all levels of government impose obligations or
11 constraints on behaviour. Constitutions, parliamentary laws, subordinate legislation, decrees, orders,
12 norms, licences, plans, codes and even some forms of administrative guidance can all be considered
13 as regulation. Governments may pass legislation to outline clearly the nature of its legal instruments
14 and the processes for approving them.

15 Laws, often referred to as primary legislation, are passed by the parliament or congress – i.e., the
16 legislative branch of government. Laws define in general terms the role, rights and obligations of all
17 parties involved (31).

18 NRAs are created by legislation that delegates responsibilities and powers, including the authority to
19 make and enforce rules, regulations or other statutory instruments regarding the medical products
20 needed to protect health and safety. Regulations proposed by the NRA are passed by the executive
21 branch of government and are specifically designed to achieve the administrative and technical goals
22 of the legislation. As a result, regulations are more detailed than the delegating legislation.

23 Other regulation-like instruments may be available to an NRA but the circumstances for which they
24 are used, the process and notification requirements may differ. For example, an order generally has
25 the same weight as a regulation but may be used for repetitive administrative actions such as adding a
26 new active substance to an already established prescription-only list.

27 When considering a legal instrument that could be applied to a problem, it is vital that there be clear
28 legal authority for its use. This may be a challenge for emerging NRAs for which the legislation and
29 subordinate regulations are still in development. Should a timely response be needed for a risk posed
30 by a medical product, higher-level laws, or those of other government departments, may provide the
31 authority for immediate action until a permanent solution is developed to close the gap (see the
32 guideline section on Legality). For instance, laws dealing with fraud or deceptive promotion could be
33 sufficient to remove urgently a dangerous medical product from the market.

34 **Guidelines**

35 Guidelines are administrative instruments that interpret regulatory requirements and assist regulated
36 parties to understand how to comply with them. Guidelines are also used by the NRA to assist in the
37 fair and consistent application of the regulations. As administrative instruments, guidelines do not
38 have the force of law. However, they are sometimes referred to as “quasi-regulation”, especially if
39 applied rigorously so that noncompliance poses an enforcement risk for the affected party (42).

1 Guidelines allow for flexibility. Alternate approaches may be acceptable provided that they are
2 supported by adequate evidence that they meet the policy objectives, principles and practices set out
3 in the regulation. For instance, a regulation may simply require sufficient information for the NRA to
4 assess the quality of a medicine, including details of tests to control purity. A guideline could then
5 outline the information that would be considered sufficient and any recognized methods to generate it
6 (e.g., pharmacopoeial standards). The guideline could further outline how the regulatory requirements
7 could be met using alternative, non-pharmacopoeial methods. The technical nature of many guidelines
8 supporting the marketing authorization of medical products, and the flexibility they are meant to
9 provide, makes guidelines unsuitable for incorporation into regulation.

10 Internationally harmonized guidelines – such as those from International Council for Harmonisation
11 of Technical Requirements for Pharmaceuticals for Human Use (ICH), the International Medical
12 Device Regulators Forum (IMDRF) and the Global Harmonization Task Force (GHTF) – aim to
13 ensure the consistency of requirements, information and format in a globalized environment for the
14 production and distribution of medical products. The use of harmonized guidelines and those of WHO
15 also facilitates the reliance on the decisions of other NRAs and increases opportunities for regulatory
16 convergence.

17 **Standards/voluntary standards**

18 Voluntary standards are developed by consensus by a recognized standard-setting body. They reflect
19 the consolidated results from science, technology and experience and are widely accepted by
20 governments and other parties. Standards reassure consumers of a product's safety. The use of
21 national and international standards as a basis for technical regulation facilitates trade and access to
22 medical products, and is supportive of international agreements such as the WTO's *Technical barriers
23 to trade agreement* (20).

24 A standard, or parts thereof, can be incorporated into a regulation by reference, thereby giving it the
25 same weight in law as the regulation. Incorporation by reference may be “static” whereby the
26 regulations refer to a specific version of the standard. If the standard is updated, the referencing
27 regulation would need to be updated to identify the new version properly. Incorporation by reference
28 may also be “dynamic” whereby the standard may be amended from time to time and the regulations
29 would always refer to the most recent version (30).

30 An example of a standard incorporated into regulation by reference in some jurisdictions is the
31 requirement for certification by an accredited body – i.e., that the quality management system, under
32 which a medical device is manufactured, satisfies *ISO 13485:03, Medical devices – Quality
33 management systems – Requirements for regulatory purposes* (50). Another example is found in
34 regulations for quality of medicines which may sometimes list acceptable pharmacopoeial standards
35 from which industry can choose to establish the identity, strength, quality and purity of drug
36 substances.

37 **Self-regulation and co-regulation** (42) (51)

38 Self-regulation is a voluntary arrangement whereby an organized group regulates the behaviour of its
39 members through rules and codes of conduct. The group is responsible for writing the rules and for
40 monitoring and enforcing compliance. A co-regulation arrangement may be similar except that there
41 would be direct government involvement to provide the legislative backing for the arrangement to be

1 enforced. Self-regulation and co-regulation approaches are suitable for health-care professions or
2 industry associations where detailed technical knowledge is involved.

3 For example, in many countries pharmacy and medicine are self-regulated professions. Colleges or
4 similar bodies are empowered through government legislation to set registration and licensing
5 requirements, as well as standards of conduct and operation. Government oversight is retained
6 through the colleges to ensure that the public interest is protected.

7 Where permitted, the advertising of medical products may be controlled through a co-regulation
8 arrangement. Government would issue the basic regulation which industry would then expand into a
9 code of conduct. The industry body would authorize use of its logo with any advertisements
10 compliant with code. Competition within the industry often helps make such codes of conduct
11 effective. The government would act on complaints only if the industry body could not resolve
12 disputes.

13 **Information, education and health promotion**

14 Faced with a problem, government seeks ways to influence behaviour effectively. Most instruments
15 work directly with the regulated industry. However, for some health-related problems, information
16 and education can be more effective and efficient than regulation. For instance, because of patient
17 noncompliance with a medicine dosing regimen, adverse events could be addressed with information
18 sent to prescribing practitioners or through a public education campaign. Education on the proper
19 prescribing and use of antibiotics is an approach to addressing the public health problem of
20 antimicrobial resistance, while public education on how to read product labels can reduce drug-drug
21 or drug-food interactions.

22 Information, education and health promotion campaigns can be combined with other regulatory
23 actions; they should not be viewed as solely the government's responsibility. Well-planned campaigns
24 can enlist industry, health professions and civil society – all of which have specific expertise and
25 influence.

1 **Appendix 3. International regulatory cooperation**

2 All NRAs for medical products have come under pressure because of a growing workload with new
3 and complex product categories. At the same time, institutional, technical and human resources have
4 become more limited and their capacities and expertise are challenged to keep up with the diversity of
5 products. In a globalizing world where production and distribution of medical products take place
6 outside the national jurisdiction, regulatory oversight is not limited to the NRA. The need for
7 international cooperation, in all its forms, has long been recognized.

8 Academic research has a long history of collaboration that leverages expertise, knowledge and
9 capacity to advance shared goals. At its most basic, experts informally share information and work
10 with peers with whom they have developed trust, confidence and respect. In spite of its benefits,
11 informal collaboration presents a number of challenges for an NRA, including aligning its expert
12 resources with the agency's workload priorities or in meeting legal obligations to safeguard
13 proprietary information. International regulatory cooperation agreements provide for formal and
14 legally-based collaboration to address, where appropriate, common challenges and to provide a
15 platform from which the relationship between NRAs may further develop.

16 The nature and content of formal cooperation agreements depend on the realities and needs of the
17 parties involved. Such agreements may be developed at the level of an agency or institution, or on a
18 government-wide basis, and they typically follow a period of confidence-building during which the
19 parties identify their common goals and assess to what extent their respective regulatory systems are
20 similar or perhaps equivalent. A memorandum of understanding (MOU) is a commonly used
21 agreement in which two or more parties set out operational arrangements and address the matters of
22 confidentiality relevant to the cooperation initiative. An MOU would support confidence-building
23 exercises, information-sharing and work-sharing arrangements.

24 Opportunities for international cooperation are greatly enhanced when NRAs strategically adopt
25 policies that promote regulatory convergence and harmonization. Regulatory convergence is a
26 voluntary progression whereby the regulatory requirements of countries or regions become more
27 similar or "aligned" through the gradual adoption of internationally-recognized technical guideline
28 documents, standards and scientific principles. Domestic regulatory mechanisms become aligned with
29 shared principles to achieve common public health goals (40). Regulatory harmonization is the
30 process by which technical guidelines are developed so that they are uniform across participating
31 authorities (41).

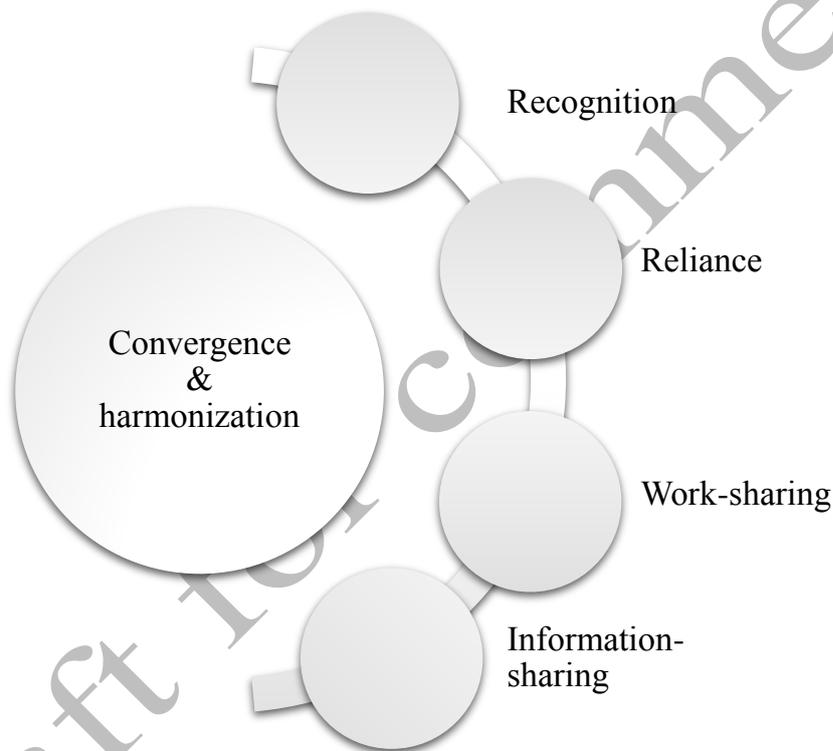
32 Regulatory convergence facilitates initiatives that aim at international harmonization by providing a
33 common ground. A large body of guidance on the harmonization of medical product regulatory
34 requirements and practices has been developed over the past two decades.⁷ That work reflects a
35 consensus among experts from government and industry, along with other interested parties, on good
36 practice guidelines. As far as is possible, as national regulatory requirements are adopted, or existing
37 ones revised, they should be made consistent with harmonized international guidelines, norms and
38 standards. It follows that the NRA should have a process to monitor and adopt changes in
39 international guidelines. Over time, these policies will promote international convergence of
40 regulatory requirements and the adoption of best practices for medical products, forming the basis for
41 formal and informal cooperation and exchange of information between authorities.

⁷ See, for instance, the websites of ICH (<http://www.ich.org>), IMDRF (formerly GHTF, <http://www.imdrf.org/>), APEC Regulatory Harmonization Steering Committee (<http://www.apec.org/>) and the Pharmaceutical Inspection Co-operation Scheme (<http://www.picscheme.org/>).

1 Regulatory convergence and harmonization provide common, or very similar, regulatory standards for
2 evaluation and inspection that facilitate not only regulatory communication but also other
3 international cooperation initiatives such as information-sharing, work-sharing, reliance and
4 recognition (Figure A1). The regulator’s time and cost for developing regulatory guidelines is reduced
5 and regulated parties have significant savings when developing regulatory documents for submission.
6 When regulatory requirements are the same or very similar, the amount of human and animal
7 experimentation is reduced and local products become more likely to be acceptable for export to other
8 countries.

9

10 **Figure A1. International regulatory cooperation typology**



11

12 There is a broad range of international cooperation initiatives. Some, such as information-sharing and
13 work-sharing, may be supported by the signature of an MOU. More complex and advanced
14 commitments – such as mutual recognition and the exchange of, for instance, inspections reports,
15 evaluation reports and lot release certificates – may require a mutual recognition agreement (MRA).

16 Work-sharing entails exchange of information consistent within the provisions of cooperation
17 agreements and compliant with each agency's or institution's legislative framework for sharing such
18 information with other NRAs. Opportunities for work-sharing include: jointly assessing applications
19 for marketing authorizations or medical product manufacturing sites, joint work in post-marketing
20 surveillance of medical product safety, the development of technical guidelines and regulatory
21 standards, and collaboration on information technology (44).

1 “Reliance” is the act whereby the NRA in one jurisdiction may take into account and give significant
2 weight to (i.e., totally or partially rely upon) evaluations performed by another NRA in reaching its
3 own decision. Work-sharing involving joint assessments of marketing applications could be
4 considered a form of reliance where the assessment of the components assigned to each party are
5 combined into a single assessment report. A reliance arrangement could be either unilateral or
6 bilateral, and it could be used as a stepping stone to greater reliance on, or recognition of, the other
7 NRA.

8 Recognition of another NRA’s decisions is the most complex and advanced cooperative arrangement.
9 It indicates that the evidence of conformity with the other country’s regulatory requirements is
10 sufficient to meet its own regulatory requirements. Recognition may be unilateral or multilateral, and
11 may be the subject of an MRA. Recognition examples include inspections reports, evaluation reports
12 and lot release certificates. At its most advanced, an NRA may recognize the marketing authorization
13 of another NRA without additional assessment other than to confirm, for example, that the medical
14 product in question is the same as that in the reference country.

15 As with any other regulatory intervention with great potential impacts, measures aimed at recognizing
16 another regulator’s decisions require an understanding of the other’s system and requirements, an
17 analysis of the impact of these decisions before they are applied, and the design of the best strategy
18 and regulatory option to be followed. The adoption of international cooperation arrangements depends
19 on the specific case and the potential impacts of such a decision.

20 Where an NRA chooses to rely on or recognize the regulatory decisions of another country it should
21 seek an agreement to obtain timely access to the technical and confidential information necessary for
22 this type of international cooperation.

23 It is also essential to develop and maintain the national capacities necessary to assess the technical and
24 confidential information received from other regulatory authorities, given the necessity of checking
25 their conformity and, when applicable, adapting them to national necessities and idiosyncrasies.

26 In all cases of cooperation, reliance and recognition, however, the sovereign responsibility and
27 accountability of each NRA to protect the health and safety of its citizens is not transferred or
28 delegated to another NRA. Some regulatory functions (e.g., assessment of clinical evidence or
29 auditing of a manufacturer’s compliance with GMP requirements) may be done on the basis of
30 evaluations performed by other authorities. Other functions (e.g., local market surveillance, protection
31 of human subjects participating in clinical trials, or investigation of adverse event reports) can be done
32 only by the NRA in whose jurisdiction they occur.

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