



**WHO GLOBAL MODEL REGULATORY FRAMEWORK FOR  
MEDICAL DEVICES  
INCLUDING IVDS  
(May 2016)**

***DRAFT FOR COMMENT***

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1 SCHEDULE FOR THE PROPOSED ADOPTION PROCESS OF DOCUMENT QAS/15.664:  
 2 WHO GLOBAL MODEL REGULATORY FRAMEWORK FOR MEDICAL DEVICES  
 3 INCLUDING IVDS

World Health Assembly 2014 adopted Resolution 67.20 on regulatory system strengthening for medical products. The Resolution emphasizes the need for regulating medical devices: REQUESTS the Director-General: ... (4) to prioritize support for establishing and strengthening regional and subregional areas of regulation of health products that are the least developed, such as regulation of medical devices including diagnostics.	24 May 2014
WHO decided to develop a model for regulating medical devices	April 2015
Formation of the Working Group for the development of a model regulation for medical devices (Working Group), consisting of professionals in regulating medical devices	June 2015
Telephone conference with the Working Group. The Working Group approved the project plan for the development of the model regulation for medical devices including IVDs	July 2015
First face-to-face meeting of the Working Group. The Working Group agreed on: the table of contents of the Model Regulatory Framework (Model), the definition of a medical device, definition of an in vitro medical device (IVD); risk classes of medical devices; life cycle; stepwise approach of three steps; good regulatory practices for effective implementation; and a number of specific topics, e.g. donations of medical devices.	29–30 September 2015
Expert Committee for the Specifications of Pharmaceutical Preparations (ECSP) meeting. A discussion on the Model was added to the agenda of the 50th ECSP meeting.	12 October 2015
Expert Committee for Biological Standardization (ECBS) meeting. ECBS agreed to receive the Model for information.	12 October 2015
Development of the first draft of the Model, by a drafting group consisting of three	5–10 December 2015

Working Group members, with input from the full Working Group	
Circulation of the Draft of the Model to the Working Group and WHO staff members for comments and feedback	December 2015–January 2016
Compilation of feedback	January 2016
Second face-to-face meeting of the Working Group. The Working Group concluded the draft needed to be simplified and made easier to read. The scope of the draft needed to be refined, the title changed and chapters merged. The stepwise approach was changed to a two-steps model.	9–10 February 2016
Compilation of the comments from the face-to-face meeting of the Working Group	February–March 2016
Development of a revised version of the Model, with input from Working Group members	21–26 March 2016
Circulation of the revised version of the Model to the Working Group and WHO staff members for comments and feedback	Mid-April 2016
Compilation of the comments of the Working Group to the Model	End-April 2016
Public consultation	May–mid-June 2016
Compilation of all comments received	Mid-June–end-June 2016
Teleconference with the Working Group on the comments received	Early July 2016
Second public consultation	July–mid-August 2016
Compilation of all comments received	End-August 2016
Teleconference with the Working Group on the comments received	End-August 2016
Submitting the draft of the WHO Global Regulatory Model for medical devices including IVDs to ECSP and ECBS	September 2016
Presentation to the 51st ECSP meeting, with a view to its endorsement	17–21 October 2016
Any follow-up action, as needed	

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DRAFT FOR COMMENT

## 1 Acronyms

- 2 **CAB:** Conformity Assessment Body
- 3 **CLSI:** Clinical and Laboratory Standards Institute
- 4 **FSCA:** Field Safety Corrective Action
- 5 **GHTF:** Global Harmonization Task Force
- 6 **GMDN:** Global Medical Device Nomenclature
- 7 **IEC:** International Electrotechnical Commission
- 8 **IFU:** instructions for use
- 9 **IMDRF:** International Medical Device Regulators Forum
- 10 **ISO:** International Organization for Standardization
- 11 **IVD:** in vitro diagnostic medical device
- 12 **NRA:** national regulatory authority
- 13 **QMS:** quality management system
- 14 **SSFFC:** substandard/spurious/falsely-labelled/falsified/counterfeit products
- 15 **SUMD:** single-use medical device
- 16 **UN:** United Nations
- 17 **WHA:** World Health Assembly

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## Chapter 1. Introduction

### Introduction

Medical devices contribute to the attainment of the highest standards of health of individuals.

Without medical devices, routine medical procedures – from bandaging a sprained ankle, to diagnosing HIV/AIDS, implanting an artificial hip or any surgical intervention – would not be possible. Medical devices are used in many diverse settings: by lay persons at home; by paramedical staff and clinicians in remote clinics; by opticians and dentists; or by highly trained health-care professionals in advanced medical facilities. Such health technologies are used to diagnose illness, to monitor treatments, to assist disabled persons, or to intervene and treat illnesses, both acute and chronic. Today there are an estimated 500 000 different kinds of medical devices on the world market, separated into more than 10 000 generic devices groups.<sup>1</sup>

What can governments do to give citizens justified confidence in the medical devices used in their countries?

In May 2007, the first resolution on health technologies was adopted by the World Health Organization (WHO) World Health Assembly (WHA) (WHA 60.29) setting the framework for an unprecedented focus on health technologies, more specifically medical devices. In 2014, the WHA adopted a resolution regarding regulatory system strengthening for medical products (WHA 67.20).

In the context of Resolution 67.20, the growing interest in medical devices in the global health community and lack of regulatory systems for medical devices in many countries, WHO decided to develop this publication. It is intended to provide guidance and support to WHO Member States that have yet to develop and implement regulatory controls relating to medical devices, as they take steps to ensure the quality and safety of medical devices available in their jurisdictions. This WHO Global Model Regulatory Framework for Medical Devices (hereafter referred to as the Model) will provide a basis for such work.

Many countries have neither the financial resource nor technical expertise to transition successfully from an unregulated market to a comprehensive medical devices law in a single programme. Instead, the Model recommends a progressive, or stepwise, approach to regulating the quality, safety and performance of medical devices. It provides guidance for a staged development from developing law with basic regulatory requirements, registration of establishments that put medical devices on the market, to listing of medical devices and post-market controls.

The resources – people, funds, technology and facilities – available in any country for regulatory control of medical devices are, and likely always will be, limited. Generally, such resources will be allocated to support overall government policy objectives and priorities but will also reflect the characteristics of the national market for medical devices: public health needs and burden of disease; demographic trends; economic development; size of the country; form of government (e.g. unitary or decentralized); industry structure (if any); sources of supply (e.g. primarily imported vs domestic sources); and nature of devices on the market.

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<sup>1</sup> GMDN issued over 500000 codes [http://www.who.int/medical\\_devices/innovation/GMDN\\_Agency\\_User\\_Guide\\_v120810.pdf](http://www.who.int/medical_devices/innovation/GMDN_Agency_User_Guide_v120810.pdf).

More broadly, it should be understood that regulation of medical devices does not take place in isolation, but should be coordinated with regulation of other medical products (medicines, vaccines, etc.) and other government policy objectives

#### **The WHO Global Model Regulatory Framework for Medical Devices including IVDs**

The Model recommends guiding principles, harmonized definitions and the essential elements required for effective and efficient regulation, to be embodied within binding and enforceable law. Its main elements refer to international harmonization guidance documents developed by the Global Harmonization Task Force (GHTF) and its successor, the International Medical Device Regulators Forum (IMDRF).

The Model is particularly relevant for WHO Member States with no or limited regulation for medical devices in place, yet it foresees that countries will progress from basic controls towards an expanded level as their resources allow. It will also describe circumstances in which a regulatory authority may rely upon, or recognize, the work products from trusted regulatory systems (scientific assessments, audit and inspection reports) or WHO prequalification.

Chapter 2 of this document recommends definitions of the terms “medical devices” and “in vitro diagnostic devices” (IVDs). It describes how they may be grouped into risk classes according to their potential for harm to the patient or user. The chapter specifies essential principles that the device manufacturer must demonstrate to a regulator that its medical device has been designed and manufactured to be safe and perform as intended during its lifetime.

Chapter 3 presents the principles of good regulatory practice and enabling conditions for effectively regulating medical devices. It then introduces essential tools for regulation, including the function of the regulatory entity and the resources required.

Chapter 4 describes a stepwise approach to implementing and enforcing regulatory controls for medical devices, from basic to expanded level. It describes elements from which a country may choose according to national priorities and challenges. It also describes the option of “reliance” or “recognition” of regulatory decisions made in other jurisdictions, and the importance of international convergence of regulatory practice.

Chapter 5 provides a list of specific topics to be considered when developing and implementing regulations for medical devices. It describes the relevance of these topics and provides guidance for regulators to ensure these topics are appropriately addressed.

#### **Limitations of the WHO Global Model Regulatory Framework for Medical Devices including IVDs**

The Model provides a general approach and cannot provide country-specific guidance on implementation. While it does not offer detailed guidance on regulatory topics, it provides references to relevant documents. The Model is written for the legislative and executive branches of government and mainly describes the role and responsibilities of a country’s regulatory authority. It does not detail responsibilities of other stakeholders such as manufacturers, distributors and health-care professionals, all of whom have roles in assuring the quality, safety and performance of medical devices.

## Chapter 2. What is a medical device? Definition, classification and essential principles

### Definition of medical device and IVD medical device

The GHTF developed a definition of the terms medical device and IVD medical device. Major jurisdictions have accepted the principles of this definition and it is recommended to preserve it. WHO endorses this definition.

**“Medical device”** means any instrument, apparatus, implement, machine, appliance, implant, reagent for in vitro use, software, material or other similar or related article, intended by the manufacturer to be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s) of:

- diagnosis, prevention, monitoring, treatment or alleviation of disease;
- diagnosis, monitoring, treatment, alleviation of or compensation for an injury;
- investigation, replacement, modification or support of the anatomy or of a physiological process;
- supporting or sustaining life;
- control of conception;
- disinfection of medical devices;
- providing information by means of in vitro examination of specimens derived from the human body;

and which does not achieve its primary intended action by pharmacological, immunological or metabolic means, in or on the human body, but which may be assisted in its intended function by such means.<sup>2</sup>

**“IVD medical device”** means a medical device, whether used alone or in combination, intended by the manufacturer for the in vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes.<sup>3</sup> [1]

There may be products on the market that, according to these definitions, are not a medical device but, for reasons of protecting public health, are regulated as if they were so. Examples are: impregnated bednets to protect against malaria mosquitos; personal protective devices to avoid cross-infection;

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<sup>2</sup> Note from GHTF definition (<http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n071-2012-definition-of-terms-120516.pdf#search>): Products which may be considered to be medical devices in some jurisdictions but not in others include disinfection substances, aids for persons with disabilities, devices incorporating animal and/or human tissues, devices for in vitro fertilization or assisted reproduction technologies.

<sup>3</sup> Note 1 from GHTF definition (<http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n071-2012-definition-of-terms-120516.pdf#search>): IVD medical devices include reagents, calibrators, control materials, specimen receptacles, software and related instruments or apparatus or other articles and are used, for example, for the following test purposes: diagnosis; aid to diagnosis; screening; monitoring; predisposition; prognosis; prediction; determination of physiological status.

Note 2: In some jurisdictions, certain IVD medical devices may be covered by other regulations.

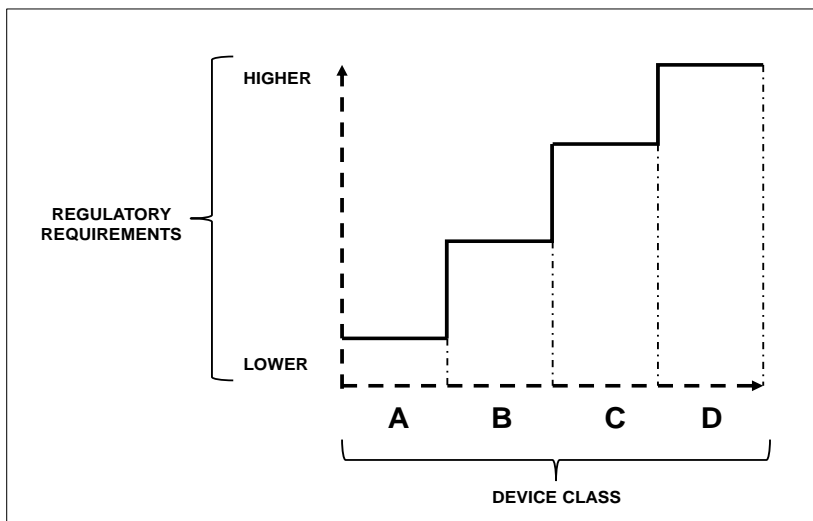
lead aprons to protect against radiation; medical gases; and implantable or other invasive products for cosmetic rather than a medical purpose.

### Medical devices classification and classification rules

The universe of medical devices is diverse with widely varying potential for harm to the patient or user. This Model recommends the regulator allocates its resources and imposes controls, proportional to the potential for harm associated with the medical device. The establishment in the law of a definition of a medical device and an IVD medical device, a classification system for medical devices and IVDs guides the regulatory controls to be implemented for each device class. [2]

It is widely accepted that different types of medical devices are separated into groups or classes, typically four.

Figure 1. Principles of medical devices classification



Source: Global Harmonization Task Force.

The risk class of a medical device depends primarily on its intended use and the technology it utilizes, for example, whether the device:

- is life supporting or sustaining;
- is invasive and if so, to what extent and for how long;
- incorporates medicinal products;
- incorporates human or animal tissues or cells;
- is electrically or pneumatically powered;
- delivers medicinal products, energy or radiation;
- could modify blood or other body fluids;
- the technical/scientific/medical expertise of the intended user (lay person or health-care professional);
- or is used in combination with another medical device;

or, for IVDs:

- the importance of the information to the diagnosis (sole determinant or one of several), taking into consideration the natural history of the disease or disorder including presenting signs and symptoms which may guide a physician;
- the impact of the result (true or false) to the individual and/or to public health.

The GHTF has published separate documents on the classification of medical devices and IVDs that use these principles to establish sets of “classification rules” [2] [3]. Both are widely accepted. Based on these *principles* of risk classification, a Member State may develop detailed classification *rules* to guide manufacturers. [4] The manufacturer has the primary obligation to classify its medical device but its decision may be subject to verification and acceptance by the regulatory authority.

Public health considerations in a particular jurisdiction may justify assigning a risk class to a type of medical devices different to that determined by the general classification rules.

## Essential Principles of safety and performance

Regulations should specify that a medical device be safe and effective when placed on the market. Those requirements, known as Essential Principles, have been widely adopted. [5] Manufacturers must be able to demonstrate to the regulatory authority that their product complies with the Essential Principles and has been designed and manufactured to be safe and perform as intended during its lifetime, when used according to the manufacturer’s stated intended purpose. The general Essential Principles are supplemented by those principles specific to particular medical device types (e.g. IVDs, implants, electrically powered, etc.). The Essential Principles should be referenced in the law and detailed in regulations, but may be included in full in a schedule or annex to the law.

The GHTF established a list of Essential Principles, one for medical devices and one specifically for IVDs. [5]

The general Essential Principles of safety and performance for medical devices include:

- the design and production of a medical device, if used according to the intended purpose and meeting the conditions of technical knowledge and training of the user, should be safe and not compromise the clinical condition of the patient or the health of the user;
- the manufacturer should perform a risk assessment of known and foreseeable risks and mitigate these risks in the design and production of the medical device;
- medical devices should meet the requirements of performance when used under normal conditions;
- performance and safety should not be affected during the life time of a medical device in such a way that it affects the safety of the patient or the user;
- performance and safety should not be affected by transport or packaging and storage, provided the instructions for packaging, transport and storage are met;
- known and foreseeable risks should be minimized and weighed against the benefits of the intended purpose.

Assuring that a medical device consistently conforms to the requirements for safety, efficacy and quality, including clinical evidence, [6] is primarily the responsibility of the manufacturer. The evidence of conformity to the Essential Principles is subject to review by the regulatory authority, before or after market introduction. The degree of involvement of the regulatory authority or the

Conformity Assessment Body (CAB)<sup>4</sup> (see chapter 4) in the routine assessment of a medical device is dependent on the risk class: the higher the risk class, the more is the involvement of the regulatory authority or CAB. [7]

#### Assessing conformity to the medical devices regulation

To a large extent, the quality, safety and performance of a medical device are determined by the systematic controls applied by the manufacturer to its design, development, testing, manufacture and distribution over the device life cycle. In general, this is done through implementation of a quality management system (QMS). The assessment of the QMS by the regulator or CAB depends on the risk class. [7] (See chapter 4.)

For class A medical devices, the manufacturer states himself that he meets the Essential Principles. Class A medical devices do not require submission of a design dossier, but do require that the manufacturer maintains a technical file demonstrating conformity with the Essential Principles. Class A medical devices are usually notified by the manufacturer to the regulatory authority before being placed on the market and are not subject to pre-market on-site audits. The regulatory authority may, at its discretion, require submission of the technical file and/or other evidence of conformity with the regulatory requirements.

Examples of class A medical devices are syringes and needles, examination gloves, patient hoists, glucose test strips, stethoscopes, wheel chairs, hearing aids.

For classes B, C and D medical devices the regulatory authority or CAB may audit on site the QMS of the manufacturer.

For classes C and D medical devices, the pre-market audit includes the evaluation of the design and product development of the medical devices. For class D medical devices, summary technical documents are individually assessed by the regulatory authority or CAB before marketing authorization.

Examples of class B medical devices are surgical gloves, infusion sets, impregnated gauze dressings, sterilizers for medical devices.

Examples of class C medical devices are condoms, intrauterine devices (IUDs), infusion pumps, incubators, therapeutic X-ray, lung ventilators, haemodialysers, anaesthesia equipment.

Examples of class D medical devices are implantable cardioverter defibrillators (ICDs), pacemakers, hip implants, dental implants, angioplasty balloon catheters.

For all classes of device, the manufacturer should prepare, hold and be prepared to submit as required, a declaration of conformity with the relevant Essential Principles.

#### Figure 2. Conformity assessment processes by device class

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<sup>4</sup> Certain technical elements of the regulatory framework may be delegated to designated or recognized CABs. They may perform initial certification and surveillance audits of device manufacturer QMS and/or pre-marketing evaluation of device conformity to the Essential Principles. Satisfactory compliance with requirements is typically documented with a CAB certificate. Based on the CAB's evaluation the regulatory authority may make final decisions on compliance. The CAB performs its evaluation under the oversight of the regulatory authority and may be subject to periodic assessments by that authority.

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

## Regulation of IVDs

The WHO Global Model Regulatory Framework includes IVDs as medical devices, with the same basic regulatory requirements. However, there are some points of difference which require consideration in developing a regulatory system. This section discusses those differences and advises on steps to address them.

## Classification of IVDs

As for other medical devices, risk-based classification of IVDs provides a basis for allocating and prioritizing resources in assessment of the IVDs supplied in a particular market. There are a large number and variety of IVDs available, with varying impact on the diagnosis and treatment of patients. The higher the risk of an IVD, the more stringent the assessment should be. Unlike other medical devices, the risk associated with an IVD is indirect and is related to the risk of an incorrect diagnosis, to both the patient being examined and the population in general, for instance, if a patient with a serious infectious disease remains undiagnosed and other community members are exposed.

Because of the different risk profile, the classification rules developed for other medical devices on the basis of interaction with the body are not suitable for IVDs. The GHTF has published a document which provides a classification scheme for IVDs, based on risk to the individual and to public health. [3] The highest risk IVDs are those which may impact on public health, in terms of detection of infectious disease, or in determining the safety of blood or blood products for transfusion or tissue for transplantation. The IVD classes, in descending order of risk are as follows:

- highest risk;
- moderate public health risk, but high individual risk;
- low public health risk and/or moderate individual risk; and
- low individual risk.

The importance of the result of the IVD in making a diagnosis is also a factor; a higher risk class is assigned where the IVD is the sole determinant in making a diagnosis.

The classification rules for IVDs should be referenced in the law and detailed in regulations, but may be included in full in a schedule or annex to the law.

#### **Essential Principles of safety and performance for IVDs**

The GHTF has identified and described six general Essential Principles of safety and performance which apply to all medical devices, [5] but has developed a separate set of additional Essential Principles which apply to IVDs. While the Essential Principles are similar in nature for each product type, the different use conditions of IVDs require more specific wording in some cases and more detailed explanation in others.

The main differences are that the IVD Essential Principles:

- do not cover incorporation of substances considered to be a medicinal product/drug, as even if these substances are present, there is no effect on the human body;
- place less emphasis on the need for veterinary controls on animals used as the source of biological material, as the risk of transmissible spongiform encephalopathy (TSE) infection is reduced due to the mode of use of IVDs;
- include a requirement for the design to ensure that performance characteristics support the intended use;
- do not include requirements in relation to protection against ionizing radiation, since this is not a function of IVDs;
- have more limited requirements in relation to electrical safety and supplied energy, since IVDs do not connect to, or supply energy to the patient;
- include requirements for IVDs for self-testing; and
- include requirements for performance evaluation, rather than clinical evaluation.

In developing and implementing a regulatory system, jurisdictions are advised to adopt the GHTF Essential Principles specific to IVDs, as separate from those for other medical devices.

#### **Clinical evidence for IVDs**

In relation to collection of clinical data for IVDs, a considerable amount of information on the performance of an IVD is gained from analytical performance studies carried out using human specimens. The purpose of the clinical performance study is to generate data. To replicate normal use,

a typical user performs the test with unselected specimens. The information that the test collects from the specimen during a study is typically not provided to patients or used in patient management decisions, removing direct consequences of the performance study. This changes the risk profile of a clinical study as compared to clinical investigations for medical devices to be used on human patients. The application of ISO 14155 – *Clinical investigation of medical devices for human subjects – Good clinical practice* [8] is therefore not suited to IVDs. A standard specific to IVDs is being developed by ISO Technical Committee 212 and will be published as ISO 20916:20XX *Clinical performance studies for in vitro diagnostic medical devices (IVDs) using specimens from human subjects – Good study practice* (under development). [9]

#### Lot verification testing of IVDs

WHO recommends that where the regulatory system is not fully developed, a system of batch testing, or lot verification, be implemented for imported high risk (class D) IVDs. The objective of lot verification testing is to verify that each lot supplied meets its safety, quality and performance requirements, and that transport and/or storage conditions have been well controlled so as not to affect the performance of the IVD.

Lot verification testing should be organized under the oversight of the regulatory authority of the receiving country or of the procurement agent. Testing of distributed lots may lead to a change from systematic sampling of each lot towards random sampling of lots in accordance with their quality assurance policies. The testing should be done by an accredited laboratory (see chapter 4).

The testing is conducted after shipment to the buyer (country), but before distribution to the end user. The need for this depends upon the other controls in place in the importing country and the extent of pre-market evaluation conducted. In many countries, tests for diagnosis for HIV and malaria, for instance, are performed outside of the traditional laboratory setting and often by unsupported users with minimal training. Then, lot verification testing may be indicated. Where there are stringent controls on transport and storage, and the receiving laboratory has in place a strong quality control programme that will detect problems in a new batch on arrival, lot verification testing may not be needed.

Continued compliant results in predistribution lot verification testing may lead to a change from systematic sampling of each lot towards random sampling of lots.

## Chapter 3. What are the enabling conditions for effective regulation of medical devices?

Public confidence in medical devices requires effective and efficient regulation built upon a sound legal and policy foundation, as well as good regulatory practices. It also requires that the regulatory authority have the resources necessary to fulfil its duties. WHO is developing *Good Regulatory Practices: Guideline for National Medical Products Regulatory Authorities (under development)*. [10] The general principles therein should be applied when establishing a new, or revising an existing, system of regulating medical devices and IVDs. They include:

- a foundation in law;
- consistency;
- effectiveness;
- efficiency;
- impartiality;
- clarity;
- transparency;
- flexibility.

### Legal requirements

There is no single approach to the legal foundation of the medical device regulatory framework. The approach will depend on the national constitution and existing general national legal and administrative systems. Nonetheless, medical device regulation must have a sound basis in law.

Amongst other elements, that law should define the products within its scope and identify the organizations subject to regulation. It should create a general requirement that only medical devices that are safe, perform as intended and are of appropriate quality may be marketed or made available for use in the jurisdiction. The law should delineate the responsibilities of the regulatory authority and establish its enforcement powers to include removing products from the market as well as consequences for bad practices, along with its accountability to the executive, judicial and legislative branches of government. It would address coordination with other bodies such as the justice ministry, police and customs authorities. In countries with decentralized systems, the respective powers and coordinating roles of the central regulatory authority and authorities in the political subunits will have to be defined.

The law should establish the responsibilities of manufacturers, importers, distributors and authorized representatives. Where a regulatory authority is delegated to an independent administrative agency or placed at arm's length, there should be clear lines of political oversight and accountability, e.g. through the ministry of health. The legal framework should also provide scope for administrative and enforcement discretion that allows the regulatory authority to apply the principles of "reliance" and "recognition" (see also chapter 4), taking into account output or decisions by authorities in other jurisdictions when taking regulatory actions. The law should accommodate a transition from basic to expanded regulatory controls as resources allow and experience is gained. It should also provide sufficient administrative flexibility to allow the regulatory authority to respond to public health emergencies in an appropriate and timely manner.

The authority should be required to adhere to good regulatory practices such as creating opportunities to obtain and review meaningful public comment on proposals, assessing regulatory impacts, allowing reasonable transition periods and adopting requirements that are the least burdensome ways of achieving policy goals. The provisions of laws, regulations and guidelines should be as transparent, predictable and internally consistent as possible. Measures should be non-discriminatory, so that all similarly situated parties are treated in the same ways and that decisions are taken without regard to national origin of a medical device.

## Gap analysis of existing controls

It is important at an early stage to evaluate any existing regulatory controls over medical devices. This will allow the policy maker to understand the steps needed to achieve national public health goals and to develop regulatory capacity, as well as the resources required. A gap analysis may be helpful in assessing the degree to which national regulations are aligned with international guidance and best practices.

Non-exhaustive list of elements to be considered for the medical device regulation gap analysis	
• Are medical devices regulated at all?	
• Are they currently regulated as medicines or some other product category?	
• Is there a specific and sound legal foundation for regulation of medical devices?	
• What is the public health risk in the country associated with medical devices?	
• Is there a clear definition of the term “medical device” and does it match that recommended by this Model?	
• Is there a national regulatory authority with clear powers and responsibilities for medical devices?	
• Do the regulators have the proper competencies required for effective implementation and enforcement?	
• Where there is a published regulation, is it enforced and does the regulatory authority have sufficient resources, expertise and funding to perform its duties?	
• What proportion of medical devices are imported and from where?	
• Are there local manufacturers of medical devices? If so, are their activities regulated and how?	
• Are distributors and importers subject to appropriate controls?	
• Is there evidence that substandard/spurious/false-labelled, falsified/counterfeit medical devices have been placed on the market?	
• Do existing laws and regulations comply with international good practices and treaty obligations?	

## Implementation plan

Once national medical device legislation has been adopted, the appointed regulatory authority should adopt and publish a plan for its implementation. The plan will be driven by public health priorities and needs and by the availability of resources. As a first step, the authority should conduct a gap analysis as outlined above and seek the views of interested parties. The results of that assessment will aid setting priorities for implementation. For example, in a country with little or no domestic production, at an early stage it may be appropriate to first focus on import, rather than manufacturing controls. As another example, in a country with a high prevalence of sexually transmitted diseases, it may be prudent to give priority to regulatory controls for medical devices used in the prevention, diagnosis and treatment of those diseases.

The plan should include time for promoting awareness, drafting proposals for implementing regulations and seeking public comments. The plan should include appropriate transition periods to allow industry to come comply with new requirements. It should also address how medical devices already in the market, in the distribution chain, or in use will be handled, e.g. allowing well-defined exemptions and transitions provisions. The regulatory authority should hold meetings and publish guidance to ensure that medical device manufacturers, importers, distributors and purchasers are aware of the requirements so as to avoid shortages of devices when the transition period ends.

### **Monitoring effective implementation**

At the time of development of the regulatory implementation plan, goals and performance indicators should be established to allow periodic assessment. Progress towards those goals should be reported to the public and to the legislature or parliament. Such reports will contribute to transparency and political accountability. They may also be used to evaluate adequacy and use of resources. Progress made may be used to help determine the timing of future steps in implementing the regulatory framework. If expanded level controls are established, it may be appropriate to include performance measures such as timely response by the authority or CAB in case of quality defects and serious injury associated with the use of a medical device. Other, more general, performance assessments may include periodic consultations with interested parties such as medical device users, patient representative groups and industry. Ultimately, the public and parliament or legislature will want to see that their confidence in the regulatory authority and its use of resources is justified.

### **Regulatory authority**

Implementation of the medical device law will require the appointment of an independent national regulatory authority, either within an existing structure such as the ministry of health, or an independent administrative agency accountable to a ministry. The governance of the authority should be defined, along with appropriate checks and balances and periodic public reports on performance. The law should create a means for the regulatory authority to implement the various provisions of the law by, for example, issuing regulations and guidelines. It should also provide the necessary enforcement powers.

While retaining in full the responsibilities placed upon the regulatory authority by the law, it should be permitted to designate CABs to assist the regulatory authority to carry out its duties. In this situation the legislation will include requirements for appointing a CAB, setting the scope of its responsibilities and monitoring performance (see also chapter 2). Although the CAB may perform some such evaluation functions, the final decisions and enforcement powers would remain with the regulatory authority.

### **Funding the regulatory system**

Implementation of the regulatory system will require staff, infrastructure, facilities and information technology. Resources allocated should be consistent with the activities mandated in the law, with a provision to be increased over time as the regulatory system moves from the basic level to expanded level controls. One element of the pre-implementation gap analysis should be assessment of the financial resources required. Consistent with a country's financial and legislative intent, a country may choose to fund all regulatory activities from public funds, or from a mixture of public funds and fees collected from the regulated industry. If user fees are imposed, they should be predictable, transparent, non-discriminatory, reasonable in relation to the services rendered and subject to periodic

review. Permission for the regulatory authority to impose fees for selected activities should be established through the medical devices law.

It should be borne in mind that costs of doing business, both direct (e.g. through user fees) and indirect (e.g. the regulatory burden of compliance with local requirements), may be factors that influence whether medical devices are introduced to a particular market. If the costs of compliance are disproportionately high with reference to the potential of a market, or if regulatory requirements are not harmonized with those of other countries, manufacturers and importers may be discouraged from offering their products and that may impede achievement of national public health goals. One way to increase efficiency and avoid unnecessary burdens will be for the authority to take into account the outputs (e.g. reports) and decisions of regulatory authorities in other jurisdictions in reaching its own decisions, i.e. reliance or recognition, where appropriate.

### **Conflict of interest and impartiality**

Public confidence in the integrity of the regulatory authority and its actions is essential. The authority and its staff should be seen to act consistently, impartially and transparently. Actual or perceived lack of impartiality of regulatory decisions can lead to unfair and unjust competitive advantages for parties in the medical device sector as well as a lack of confidence in medical devices supplied to the market. This can be prevented by the adoption and consistent adherence to a code of conduct by all members of staff. It should provide a framework for decisions and actions, and allow for public and legislative scrutiny of the authority. Staff must avoid situations where there may be a conflict, real or perceived, between their private interests and the public good. Leaders in the organization must set the tone by good example in their own conduct.

### **Regulatory competencies and resources**

The practice of regulating medical devices effectively and efficiently may be considered a profession that requires appropriate individual expertise, reinforced by the institutional capacity of the regulatory authority, to act according to good regulatory practices. General competencies for regulatory professionals include an understanding of public health principles, analytical and communication skills, information handling and skills in effective intervention and crisis management. [11] Additional specific competencies include essential knowledge of the regulatory system for medical devices, the responsibilities of the regulator, the concepts of international standards and harmonization, and an understanding of device technologies. [12]

At each stage of implementing the regulatory system a transition period would be allowed. This allows the regulatory authority to ensure it has sufficient qualified and trained staff, appropriate resources and adequate information systems for the increased responsibilities and functions. The regulatory authority requires legal support to interpret its responsibilities under the law, particularly in respect of monitoring, enforcement and safeguarding activities. In addition information technology (IT) and administrative resources are required.

The basic level regulatory controls would require general technical expertise on medical devices, whereas the expanded level controls would require some regulatory staff to have more specific technical expertise. As the regulatory system and its implementation become more comprehensive, additional resources will be required.

In view of the importance of quality management systems in the regulating medical devices, the authority should recruit staff members with experience in that field. Such staff may inspect or audit manufacturers, authorized representatives, importers and distributors. Taken together, these skills

1 should allow the regulator to provide appropriate oversight and control throughout the medical device  
2 life cycle. [13]

3 Given the diverse nature of medical devices, the regulatory authority should, according to the  
4 priorities in regulating specific medical devices, over time, recruit and retain technical staff members  
5 with appropriate expertise. [14] To retain staff a competitive package may be offered as well as  
6 valuing regulating medical devices as a profession.

7 As it may be impractical for a regulatory authority to have all these experts “in house” the creation of  
8 an advisory committee, consisting of independent experts in a variety of fields, is an alternative. It  
9 can be invited to advise the regulator in specific technical areas. The regulator remains responsible for  
10 the regulatory decision based on the advice. Periodically performing a basic level assessment of the  
11 regulator’s current competencies gives insight into the gaps in competencies. Guidance can be sought  
12 from the Global Competency Self-Assessment of RAPS [15] (under development) and the WHO  
13 Global NRA benchmarking tool (under development). According to the gap assessments, initial and  
14 continuing training of medical devices regulators according to a training plan would be implemented.

15

## **Chapter 4. How can a stepwise approach to regulating medical devices be established?**

### **Stepwise approach**

This Model recommends a regulatory system for medical devices in a staged or stepwise approach – from basic to expanded controls. The basic controls will form the foundation for the expanded controls. Without effective implementation of basic controls, the elements of expanded controls will be of limited value.

The regulatory framework must be sustainable, expandable and must accommodate advances in clinical practices, public health needs and evolving technologies. The stepwise approach will allow the regulator to respond to national public health priorities and to progressively develop the capacity, knowledge and experience required. This approach helps the regulator determine the resources needed for further implementation.

This Model recommends that in order to promote international regulatory convergence and harmonization, Member States are encouraged to adopt in their legislation internationally harmonized principles and technical guidance. [16]

Basic regulatory controls fall into three broad groups:

- those applied before a medical device is placed on the market;
- those applied once the device has been authorized for market placement; and
- those applied after the device has been put on the market.

The regulator has an opportunity to reduce the demands on its own staff by either relying upon or recognizing the work or decisions made by another regulatory authority. Resources can be targeted to post-market controls, which are the responsibility of the national regulatory authority. The regulatory authority will indirectly gain knowledge of the regulatory status in other jurisdictions of devices placed on the national market. As a regulatory authority subsequently moves to implement expanded level controls, emphasis will shift to controls on the placing of devices on the market, while continuing to rely upon or recognize the work of other jurisdictions (see below).

### **Basic level controls and their enforcement**

The Model recommends basic controls are incorporated into a medical devices law that determines the scope of regulation, stipulates the responsibilities of the regulatory authority, describes conditions for a medical device to be placed on the market, requires certain organizations to be registered, establishes port of entry controls and requires post-market surveillance activities. The latter would typically include a system to act upon reports of quality defects and serious adverse events associated with medical devices.

1    Figure 3. Basic level controls and enforcement for medical devices

# LEGAL FRAMEWORK

Basic level controls and enforcement		
Pre-market	On the market	Post-market
<ul style="list-style-type: none"><li>• Publish law and regulation(s) with transition period</li><li>• Define medical device, IVD and the parties in the scope of the law</li><li>• Establish medical device risk classification</li><li>• Establish essential principles of safety and performance</li><li>• Identify regulatory status using reliance and recognition</li><li>• Establish requirements for Declaration of Conformity</li><li>• Establish requirements for QMS</li><li>• Establish requirements for labels and labelling</li><li>• Prohibit deceptive, misleading, false advertising</li><li>• Establish controls for import of donated medical devices</li></ul>	<ul style="list-style-type: none"><li>• Register establishments: manufacturer, authorized representative, importer, distributor</li><li>• List all medical devices placed on the market under the law</li><li>• Establish port of entry controls</li></ul>	<ul style="list-style-type: none"><li>• Establish a reporting system of adverse events involving death or serious injury</li><li>• Require mandatory notification by the manufacturer of FSCA including recall</li><li>• Establish procedure to withdraw unsafe medical devices from the market</li><li>• Establish procedure to issue safety alerts to users</li><li>• Undertake market surveillance</li></ul>

## Legal foundation and principles

The national law for medical devices will consist of statutes that set out broad outlines and principles, delegating authority to the regulatory authority. In particular it will:

- define the products and parties within its scope, in particular the terms medical device [1] and IVD, using harmonized definitions;
- designate the national regulatory authority and its powers, including enforcement powers, oversight mechanisms, the power to issue implementing regulations and the responsibility for publishing guidance documents to aid understanding of legal requirements;
- provide the regulatory authority with administrative and enforcement discretion for reliance and recognition upon work or decisions of regulatory authorities in other jurisdictions (see below);
- require that only safe medical devices, that perform as the manufacturer describes in its labelling, may be placed on the market;
- specify market entry conditions;
- establish recordkeeping and reporting requirements for all parties within the scope of the law, including the regulatory authority;
- specify a transition period sufficient to allow parties affected by the law to comply with its requirements and ensure minimal disruption to the continuing supply of medical devices to health facilities and other users.

To allow progressive adoption and implementation of the stepwise approach recommended in the Model, the law should foresee and include provisions covering the more advanced levels of control, even though those provisions would likely not be implemented in the early stages.

Experience in many jurisdictions with established regulatory systems suggests that affected parties are allowed time to adapt to the law, i.e. a transition period. A reasonable transition period is 2 to 5 years. In part, the length of the period will reflect the number of potentially affected parties and the number of devices in the national market. It may be helpful to first establish new requirements on a voluntary basis, gain experience and then move to mandatory compliance. An important element of the regulatory authority in such transition periods is the development and dissemination of voluntary guidance documents to affected parties.

## Medical device classification

The law, defining medical device and IVD, should include a medical devices classification to enable an efficient way of regulating the medical devices according to their risk class. [2] It should include provisions for the regulatory authority to issue regulations and guidance on the classification of medical devices, including IVDs. The manufacturer is responsible for determining the class of its devices but its decision may be reviewed and approved by the regulatory authority (see chapter 2).

## Essential Principles of safety and performance

The law would also establish the requirement that all medical devices be shown to be safe, perform as intended and be of good quality for their intended purpose before they are placed on the market. It would require the manufacturer or its authorized representative or importer to declare and be prepared to provide timely evidence that their device fulfils the Essential Principles (see chapter 2). [5] Failure to make such a declaration of conformity, [7] or making a false declaration, would be grounds for enforcement action by the regulatory authority.

### 1 *Reliance and recognition*

2 The law should establish to what extent the regulatory authority may reasonably rely upon or  
3 recognize the work of regulatory authorities in other jurisdictions in assessing evidence that a device  
4 conforms to national requirements. Examples of these techniques are:

- 5 • reliance. Is the process whereby a regulatory authority may take into account and give  
6 significant weight to (i.e. rely upon) evaluations performed by another regulatory authority or  
7 other trusted institution for reaching its own decision. For example, another regulator  
8 authorizes a medical device to be placed on its own market but the national regulatory  
9 authority requires the manufacturer to provide it with a copy of all the relevant labelling as it  
10 reaches its own decision.;
- 11 • recognition. Is routine acceptance by the regulatory authority of an importing country of the  
12 regulatory *decision* of another regulatory authority or other trusted institution that evidence of  
13 conformity with the regulatory requirements of that country is sufficient evidence of  
14 conformity with the regulatory requirements of the importing country. For example, a  
15 regulator or CAB audits a manufacturer and issues it with a QMS certificate. The national  
16 regulatory authority of the importing country has sufficient confidence in the issuing authority  
17 to accept certificates as a regulatory decision without repeating the audit.

18 In order for the regulator to decide whether to use the reliance technique or recognition, it must have a  
19 clear understanding of the regulatory system that applies within the country where the medical device  
20 is manufactured. For example, some medical device regulations permit a manufacturer to follow  
21 minimal controls by restricting the marketing of the device to export only, with the outcome that the  
22 regulatory authority of that exporting country may not have performed any evaluation of the  
23 conformity of that medical device with its own regulatory requirements. This places responsibility on  
24 the regulatory authority of the importing country making recognition an inappropriate technique.

25 The use of reliance or recognition as mechanisms for marketing authorization specifically of IVDs is  
26 complex. This is due to the wide variance in classification of IVDs in existing regulatory systems  
27 (which determines the level of regulatory intervention). For instance, the current European system  
28 requires independent evaluation for a limited group of IVDs, the so-called high risk IVDs (Annex II  
29 of the EU Directive 98/79/EC on in vitro diagnostic medical devices, lists A and B). [18] This means  
30 that most IVDs bearing a CE Mark are self-assessed by the manufacturer and have not been subject to  
31 scrutiny by a European CAB known as a Notified Body. This is another example where knowledge of  
32 the regulatory system on which reliance or recognition is based upon is important.

### 33 *International collaboration*

34 Where resources permit, the regulatory authority should participate in formal and informal  
35 information sharing networks with other regulatory authorities. This will often allow earlier detection  
36 of a potential problem than would be possible within a single jurisdiction. It also allows reliance upon  
37 and confidence building with other regulatory authorities.

38 In general, a regulatory authority would seek to rely upon information from the authority of another  
39 jurisdiction, provided there is sufficient confidence between the authorities and agreement on the  
40 exchange of confidential information. [46]

## National responsibilities

There are certain regulatory activities that, by their nature, are inherently only within the competence of the national authority. Examples include port of entry controls, registration of domestic manufacturers, importers, distributors and authorized representatives; handling reports of adverse events, market surveillance activities and communication and monitoring of field safety corrective actions (FSCA).

## Basic level controls – pre-market

The law should require that only medical devices that are safe and effective may be placed on the market. The safe and effective use of most medical devices requires that the user be given information on how to properly use them and, as appropriate, to install and maintain them.

## Declaration of conformity

The medical devices law should require an organization seeking to place a medical device on the market draw up a written “Declaration of conformity” to attest that its device complies fully with the law and all regulatory requirements incorporated within it.

As a minimum, this declaration should contain the following information:

- an attestation that each device that is subject to the declaration is safe and perform as intended during its lifetime when used according to the manufacturer’s stated intended purpose;
- information sufficient to identify the device/s to which the Declaration of conformity applies;
- the classification of the device;
- the name and address of the natural or legal person with responsibility for design and/or manufacture of a medical device with the intention of making the medical device available for use, under his name;
- the date on which the declaration is issued; and
- the name, position and signature of the responsible person who has completed the declaration upon the manufacturer’s behalf.

The requirements are dependent on the classification of the medical device, becoming more robust and demanding as the classification increases from class A to class D.

The preferred, but non-exclusive, way by which the manufacturer may demonstrate conformity with the Essential Principles is to apply appropriate relevant voluntary international standards. The law should include provisions allowing the regulatory authority to formally recognize such standards for that purpose (see below).

## Quality management systems

To ensure devices are designed and manufactured meet safety and performance requirements during their lifetime, the law should require manufacturers of all classes of medical devices to establish and maintain a QMS. The QMS should be appropriate to the specific characteristics of their processes and products, and to maintain the associated records. This Model recommends the QMS aligns with the principles found in ISO 13485:2016 *Medical devices* (WHA 60.29) *Quality management systems – Requirements for regulatory purposes* [19] and ISO 14971:2007: *Medical devices – Application of risk management to medical devices*. [20]

The QMS is important not only for assuring the quality, safety and performance of a device, but also for controlling the collection of technical evidence used by the manufacturer in declaring the device conforms with the principles of safety and performance.

#### *Labels and labelling<sup>5</sup>*

The safe and effective use of most medical devices requires that the user be given information on how to properly use them and, as appropriate, to install and maintain them. Labels, instructions for use and other labelling (e.g. displays, service manuals and information for patients) serve that purpose and help to reduce risks associated with the use of medical devices. The law should include a requirement that labels and labelling are appropriate to the intended user of a device, especially for lay persons, and an element on the language requirement. To begin establishing regulatory controls, regulatory authorities must provide specific guidance on the labelling and language requirement for medical devices and fully describe any exceptions to these requirements by means of decree. Regulatory authorities should ensure that labelling is in an official language or in a language acceptable for the jurisdiction. The authority should consider whether instructions for use may be provided in alternative media such as via the Internet or on CD-ROMs. [22]

#### *Advertising*

In addition to requirements for safety and performance and labelling of medical devices, consideration should be given to the inclusion in the law of provisions and prohibitions with respect to advertising and promotion for medical devices, including explicit enforcement measures. The regulatory authority should issue clear guidance to make these requirements explicit.

Those basic regulatory controls should ensure that promotion:

- does not target inappropriate audiences;
- makes only claims that are supported by credible evidence;
- covers only medical devices that have been authorized for marketing; and
- does not make false or misleading claims.

As a basic level control the regulatory authority should investigate any suspected violations that are brought to its attention. If the regulatory authority discovers the requirement is breached, it shall take appropriate enforcement action which could include preventing the medical device from being placed on the market.

#### *Provisions for exemptions from regulatory requirements, e.g. donations and humanitarian use*

From time to time there will be unusual situations that may require limited exemptions from regulatory requirements. Such exemptions should, however, be done in such a way as to allow the regulatory authority to evaluate the risks and benefits of the specific situation and authorize the proposed deviation.

The law would establish, and provide enforcement discretion for, defined exemptions from compliance with certain requirements, for example, for charitable donations of imported medical

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<sup>5</sup> Label: written, printed or graphic information provided upon the medical device itself. Where physical constraints prevent this happening, this term includes information provided on the packaging of each unit or on the packaging of multiple devices. Labelling/information supplied by the manufacturer: written, printed or graphic matter (1) affixed to a medical device or any of its containers or wrappers, or (2) accompanying a medical device, related to identification, technical description and use of the medical device, but excluding shipping documents.

Note: Some regional and national regulations refer to "Labelling" as "Information supplied by the manufacturer" (Source – ISO 13485) <http://www.imdrf.org/docs/ghrf/final/sg1/technical-docs/ghrf-sg1-n43-2005-labelling-medical-devices-050603.pdf>.

devices, humanitarian use, public health emergencies or for clinical investigations. Regulators should issue clear guidance on such exemptions (see chapter 5).

### Basic level controls – on the market

Key element for basic level controls for on market is to have oversight of the medical devices placed on the domestic market and the parties responsible for bringing medical devices to the market. Countries worldwide import medical devices and many depend almost entirely on imported medical devices. It is not feasible or economical for a medical device manufacturer to have a physical and legal presence in every country. The law should require that a manufacturer outside the jurisdiction to appoint an authorized representative within the country. [21]

### Registration of establishments

The law should require local manufacturers, authorized representatives, importers and distributors, who place medical devices on the market or make medical devices available for use in the jurisdiction, to be registered by the regulatory authority. [23] That registration should be subject to periodic updates by the manufacturer, importer, distributor, and/or authorized representative to ensure that it is timely and correct. Amongst other purposes, the registration process allows the regulatory authority to determine who is responsible for a product's conformity to the regulatory requirements and for taking corrective actions in the event of a device problem. It may also be useful in facilitating regulatory actions such as compliance inspections (e.g. of warehouses or manufacturing plants), notifying and monitoring of field safety corrective actions (FSCA), and for law enforcement purposes. When registration and listing information is publicly accessible, it allows device purchasers or users of medical devices to identify products available to them and determine the identity and location of their manufacturers and/or distributors and/or importers.

**Authorised representatives** - the minimum requirements for registration should be that the authorized representative provides the regulatory authority with information on its place of business, the name and position of a responsible person and the manufacturer it represents. [21] Over and above this, implementing regulation may require the applicant authorized representative to attest that it will act on behalf of the manufacturer in its dealings with the regulatory authority by, in general:

- submitting a regularly updated listing of the medical devices placed on the domestic market;
- representing the manufacturer in its dealings with the regulatory authority;
- providing the regulatory authority with the information it requires when the manufacturer seeks authorization to market its devices;
- informing the regulatory authority of any reportable adverse events involving death or serious injury that have occurred either within the local market (or outside it, if there are any consequences for the local market) and providing information on the corrective action the manufacturer has taken or intends to take;
- informing the regulatory authority of any FSCA to be taken within the local market;
- cooperating with the manufacturer's importers and distributors; and
- cooperating with the regulatory authority and providing it with any information it requires during market surveillance activities.

**Importers and distributors** - the minimum requirements for registration should be that the importer or distributor provides the regulatory authority with information on its place of business, the name and position of a responsible person and the manufacturer it is acting for. Over and above this, an implementing regulation may require the applicant importer or distributor to attest that it will, for example:

- ensure the medical devices it imports or distributes comply with the medical devices law and are accompanied by the proper documentation and labelling;
- trace individual medical devices through that part of the supply chain with which it is directly involved;
- comply with the manufacturer's requirements for the storage, handling and transport of medical devices;
- submit a regularly updated listing of the medical devices placed on the domestic market.

If the device manufacturer appoints its distributor to also act as its authorized representative, there should be separate registration and, where appropriate, licensing procedures for each activity.

#### *Listing of medical devices*

The regulatory authority should establish a requirement and information system for registered manufacturers and their authorized representatives, importers and distributors to submit a listing of medical devices they place on the national market and update the listing periodically. Amongst other elements, the listing should provide the standardized generic descriptive names of those medical devices, for example, those of the Global Medical Device Nomenclature (GMDN) (see below: expanded level controls). Listing of medical devices will allow the regulatory authority to determine which products are introduced and by whom. In the event of a suspected problem with a medical device, listing also allows the regulatory authority to contact the parties responsible for that product.

It should be understood that registration and listing are not equivalent to, or evidence of, a marketing authorization.

#### *Port of entry controls*

Beyond the basic controls of registration and listing, additional controls may be appropriate at the port of entry. They include registration of importers, listing of imported medical devices, approval of importation documents *before* shipment and verification of imported products either at the port of entry or at the importer's premises. Knowing in advance what medical devices are to be imported gives an opportunity for regulators to verify whether the medical device has previously been listed and marketed in the country. It also allows a review of evidence of conformity with regulatory requirements. To promote compliance by importers, the regulatory authority should publish guidance documents. Where possible, collection of samples may be required for suspicious products or for routine analysis (e.g. batch testing for selected products).

There should be mechanisms for cooperation between the regulatory authority and customs service so that medical devices will not be released from the port of entry unless there is proof of authorization for import from the regulatory authority for medical devices. It may be helpful to designate official ports of entry for medical devices so that the regulatory authority may better focus its enforcement activities.

#### *Basic level controls – post-market*

In clinical use medical devices may not always perform as expected. This may reflect improper device selection, installation, use or maintenance; or it may indicate problems in the design, manufacture, labelling, storage or distribution of devices.

#### *Reporting of experience with medical devices once placed on the market*

At the basic level, the regulatory authority should establish a system whereby users and manufacturer directly or through its authorized representative of medical devices may report voluntarily problems,

complaints or adverse events involving medical devices, and in particular those resulting in death or serious injury. [24] Such reports may trigger investigation, trend analysis and/or possible FSCA or enforcement actions. [25] They may also prompt the regulatory authority to exchange information with regulatory authorities in other jurisdictions on similar occurrences elsewhere. [26]

#### *Mandatory notification of field safety corrective actions*

The law should require a manufacturer, either directly or through its authorized representative, to report to the regulatory authority any FSCAs it is undertaking within the country. As a regulatory authority learns, either through its own work or from communications with other authorities or manufacturers, of a potential hazard associated with a device, it should have an established system for the timely issuance of alerts or advisories on FSCAs. Such a system should allow the targeting of specific parties, usually in consultation with health-care professionals, so that they may act appropriately to protect public health and to prevent unnecessary concern or confusion on the part of medical device users or patients who are not affected. It should use communications technologies appropriate and accessible to the intended recipients as well as to the urgency of the action. The regulatory authority should establish means by which the effectiveness of corrective or remedial actions may be monitored. It prepares the regulator to respond to questions from the public, clinicians, media or government, and to exchange information with authorities in other jurisdictions.

#### *Issue safety alerts to users*

Although the manufacturer, directly or through the authorized representative, would typically have primary responsibility for notifying users of problems with a medical device, this Model recommends the regulatory authority establish a procedure to directly notify medical device health-care facilities and other users of serious adverse incidents and FSCAs by issuing safety alerts and advisories. The text of any such alert should be discussed with the manufacturer or his authorized representative but the final decision lies with the regulator.

#### *Market surveillance*

Market surveillance is the activity of the regulatory authority related to oversight of the medical devices on the domestic market. The regulatory authority may perform targeted activities based on a risk assessment of the distribution chain, evaluation of complaints and adverse event reporting and information that may come from the post-market surveillance systems of the manufacturers and authorized representatives. [27]

#### *Enforcement of regulations*

Regulatory authorities have an obligation to enforce laws and regulations on medical devices to ensure that the public is protected from unsafe products. Regulators are required to monitor compliance with requirements by registered entities and others, and to take appropriate action when the regulatory authority believes that public health has been put at risk.

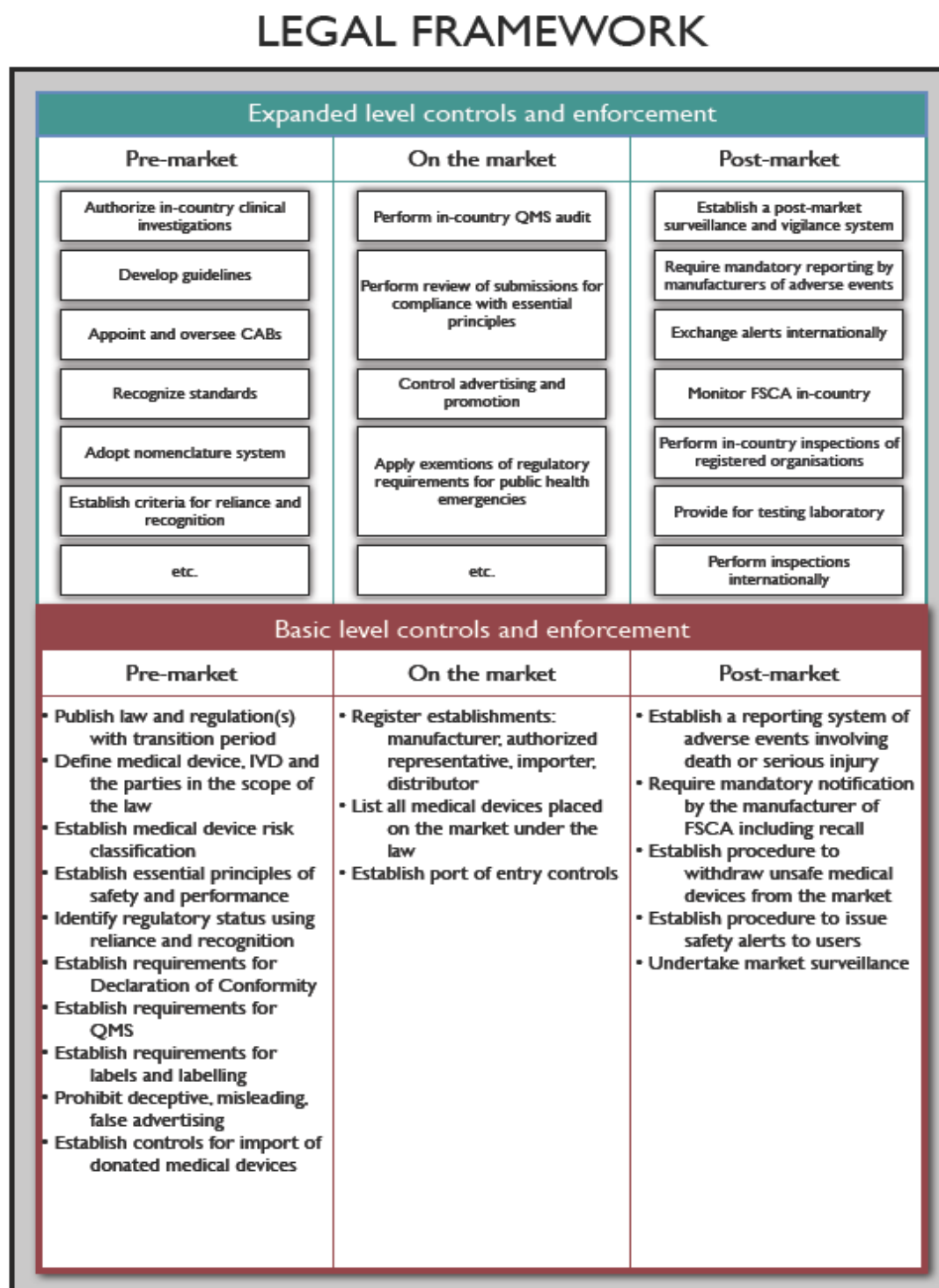
In enforcing regulations, various approaches may be used, for example: deregistration of local manufacturers, importers or distributors; withdrawal of marketing authorization for particular medical devices; recall, quarantine and disposal of medical devices. Manufacturers may be required to review and revise labelling information (including precautions and warnings), especially for products that have been found to be associated with adverse events or those where labelling has been shown to be inadequate. Enforcement may also include issuance of public alerts, warning letters, prosecution and financial penalties.

Regulators are also advised to collaborate and work closely with other bodies to ensure that regulations are adhered to. They include regulatory authorities from other jurisdictions, customs officials, judiciary, manufacturers and users or patients.

#### Expanded level controls

Once the basic level controls have been implemented effectively and efficiently, the regulator should consider implementing more advanced controls. To do so, the law should provide the legal basis for expanded controls, the regulatory authority must have developed an understanding of the system, and additional resources (financial and technical expertise) must be available to the regulatory characteristics of the national medical device market and how devices are used in its health-care authority. Building on the basic level controls, expanded level controls are intended to address other stages in the medical device life cycle and to exert more comprehensive controls. In adopting expanded level controls, the regulatory authority may choose to implement one or more of the following controls in a stepwise and a la carte manner.

Figure 4. Expanded level controls and enforcement for medical devices



## Expanded level controls – pre-market

### *Clinical investigations*

Under the law, the national regulatory authority should have to regulate and oversee clinical investigations of – approved or unapproved – medical devices. There should be a requirement that a sponsor (i.e. local manufacturer, importer or local academic institution or investigator who initiates the clinical investigation) wishing to conduct a new clinical investigation, seek prior authorization from the regulatory authority. [28] To assure adequate consideration of the design of studies and protection of the interests of participating subjects, such investigations should also be conducted under the oversight of a local ethics committee or institutional review board. Medical device clinical investigations should be designed and conducted in accordance with international standard ISO 14155:2011: *Clinical investigation of medical devices for human subjects – Good clinical practice*.<sup>6</sup> [8] The national regulatory authority should also establish a mechanism for periodic update reports and for the reporting of serious adverse events that occur during clinical investigations. [29] In-country clinical investigations should generally not be required, unless there is a compelling and sound scientific reason.

### *Appointment and oversight of conformity assessment bodies (CAB)*

Certain technical elements of the regulatory framework may be delegated to designated or recognized third-party organizations, often private, mostly indicated as CABs. [30] [31] These bodies may perform initial certification and surveillance audits of device manufacturer QMS and/or pre-marketing reviews of device conformity to the Essential Principles. The CAB may be designated by the regulatory authority to undertake conformity assessment of specific medical devices where it is judged to have the necessary skills (e.g. active implantable and/or IVDs and/or electromedical, etc.). Satisfactory compliance with requirements is typically documented with a CAB certificate. Based on the CAB evaluation, the regulatory authority may make final decisions on compliance. The CAB performs its evaluation under the oversight of the regulatory authority. [32] The regulatory authority should consider adopting mechanisms to rely upon, or recognize, certificates issued by a CAB, even those outside its jurisdiction or direct oversight. [33]

### *Recognition of standards*

Conformity with voluntary standards, especially those that have been recognized by the national regulatory authority, is an important means by which the manufacturer may demonstrate that a medical device conforms to the mandatory Essential Principles of safety, performance and quality, consistently throughout its life cycle. [34]

Medical device standards can be largely grouped into three categories:

- basic standards (also known as horizontal standards), which cover fundamental concepts, principles and requirements applicable to a wide range of products and/or processes, e.g. QMS, risk management system, clinical investigation;
- group standards (also known as semi-horizontal standards), which cover aspects applicable to families of similar products or processes with reference to basic standards, e.g. sterility, electrical safety, biocompatibility;

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<sup>6</sup> This standard excludes IVDs from its scope.

- product standards (also known as vertical standards), which cover safety and performance aspects of specific products or processes, e.g. standards for infusion pumps, X-ray machines, blood glucose meters for self- testing, for IVDs. [35]

Preference should be given to international standards, e.g. those of the International Organization for Standardization (ISO) [36] and the International Electrotechnical Commission (IEC), regional standards, and the national versions of international standards. It is also important that national standards correspond to the current version of international standards. As international standards are periodically revised, national standards will have to be revised accordingly, and the authority should establish a transition period for manufacturers to adopt the new versions. To maintain the necessary flexibility in utilizing standards, it is better to adopt a system of recognizing standards through guidance documents or guidelines versus placing the standards into legislation; they can be updated to stay current with practice and can be revised much faster typically than legislation can be updated.

#### *Adopt medical device nomenclature system*

The regulatory authority may require the manufacturer, either directly or through its authorized representative, of the device to be identified using a medical device nomenclature system as a “descriptive language” for use in the listing of medical devices, and other requirements such as adverse event reporting. The use of an internationally standardized nomenclature system is intended to allow for a common understanding of, and exchange of information regarding, a group of related medical devices, including IVDs. Without national deviations from the standard, it also facilitates the exchange of information amongst national regulatory authorities. To that purpose the regulatory authority should adopt a medical device nomenclature system.

The GMDN (Global Medical Device Nomenclature) [37] was endorsed by the GHTF as the global nomenclature system to be used by regulators for the classification, registration of and exchange of information regarding medical devices for regulatory purposes. [38] There are other established nomenclature systems such as the Universal Medical Device Nomenclature System (UMDNS) [39] and ISO 9999:2011 *Assistive products for persons with disability—Classification and terminology*. [40]

To implement the selected nomenclature system, the regulatory authority should publish a regulation and guidance specifying that that system shall be used in medical device labelling and in any required submissions, e.g. registration, listing, applications for marketing authorization and post-marketing surveillance adverse event reports. The authority’s administrative and information systems will have to be adapted accordingly and will have to be updated as new generic descriptive terms are adopted.

#### *Expanded level controls – on the market*

##### *Quality management systems*

The QMS is important not only for assuring the quality, safety and performance of a device, but also as the source of much of the evidence in the technical file used by the manufacturer in demonstrating device conformity with the Essential Principles and the associated declaration of conformity. Good recordkeeping practices and record retention policies should be observed in the QMS.

The legal requirement for manufacturers of all classes of medical devices to *implement* a QMS should be supplemented by regulation, ministerial decree and/or guidance as the regulator moves to enact expanded level controls.

## QMS audit

The regulatory authority should establish means to verify that the manufacturer conforms to the relevant requirements, especially for higher-class devices. The law should include provisions for the regulatory authority or to designate or recognize [32] [33] CABs (see chapter 2) to perform QMS audits or otherwise gather and assess evidence of the manufacturer's effective implementation of the QMS requirements. [41]

For countries in which most medical devices are imported, it will not usually be necessary or appropriate for the regulatory authority to travel to the manufacturer's site to perform a QMS audit. Rather, it will often be sufficient for the regulatory authority to rely upon evidence, including audit reports, of the manufacturer's compliance with internationally recognized QMS requirements in other jurisdictions. [42] The receiving country thereby relies upon the information of the QMS audit or recognizes the decision of the other jurisdiction regarding the QMS audit. The regulatory authority may also review and recognize the manufacturer's own declaration of conformity and current certificates of conformity with ISO 13485:2016, issued by a recognized CAB. The regulatory authority should verify that such certificates remain valid (typically 3 to 5 years) and cover the scope of medical devices and activities appropriate for the devices being imported.

In the event of suspected noncompliance or product problems, the regulatory authority may perform a "for cause" inspection, regardless of whether a CAB has performed a QMS audit.

## Conformity assessment reviews [7]

For higher-class medical devices, the regulatory authority would establish a requirement for the pre-marketing review of a manufacturer's submission. This will usually be in the manner of a prescribed form or Internet portal. Guidance on the process for application and approval should be provided.

IMDRF has established a comprehensive internationally harmonized modular structure and format for such submissions: the table of contents (ToC). Separate ToC have been established for medical devices [43] and IVDs. [44] This format provides guidance for the presentation of evidence that a medical device conforms to the regulatory requirements of the Essential Principles of safety and performance.

Sometimes there are situations that trigger a more extensive review. For example, when:

- the device incorporates innovative technology;
- an existing compliant device is being used for a new intended use;
- the device type is new to the manufacturer;
- the device type tends to be associated with an excessive number of adverse events, including use errors;
- the device incorporates innovative or potentially hazardous materials;
- the device type raises specific public health concerns (particularly for IVDs).

The decision on approval may be based on the regulatory authority's own pre-market assessment, a report from a CAB, or the reliance or recognition process. In pre-market assessment non-discriminatory country-specific requirements can be considered, e.g. local language labelling, electrical supply, public health policies and genetic characteristics of the population. Despite the pre-market assessment having been done by another body, the regulatory authority is ultimately responsible for determining whether a medical device may be supplied in its jurisdiction. It may

conduct a post-market conformity assessment review in response to adverse events or uncertainty about the compliance of the manufacturer with the regulatory requirements.

The regulatory authority may be assisted in reaching its decision on pre-market assessment (or any other regulatory decision) by advice from an expert medical device committee, which may include experts from outside the regulatory authority. Where advice from external experts is sought, the final decision rests with the regulatory authority.

The regulatory authority makes a decision on marketing authorization based on transparent criteria established in the law, regulation and guidance. The law should also prescribe the form in which approval is given (such as a certificate or entry in a database) and make provision for post-market commitments, where appropriate.

#### *Advertising and promotion*

As part of their market development efforts, manufacturers, importers and distributors generally seek to promote medical devices to health-care professionals, users and/or patients. Advertising and promotion at a minimum should not be false, misleading or deceptive. Building upon basic level controls, expanded level controls may include review of advertising and promotional material at the pre-market stage. Regulatory authorities may also contemplate a role for preclearance agencies, which act as independent entities to review advertising materials to ensure compliance with the regulatory requirements. The regulatory authority should consider whether existing rules for general advertising to consumers (e.g. under fair competition rules) are sufficient for application to medical devices. If not, they should consider whether specific guidance is required.

#### **Expanded level controls – post-market**

##### *Post-market surveillance and vigilance*

Post-market surveillance and vigilance ensures that problems or risks associated with the use of devices, once marketed, are identified and reported to the regulatory authorities so that corrective actions may be taken to reduce the likelihood of recurrence. A properly structured post-marketing surveillance system can identify serious problems in the safety, quality or performance of a medical device that may not have been foreseen or detected during pre-market evaluation. This may include exchange of information in a standardized manner with other regulatory authorities in other jurisdictions. [26]

Regulators should establish a system for post-market surveillance and vigilance encompassing:

- adverse events reporting and complaint handling systems with clear responsibilities for the regulator, manufacturer, authorized representative, importer and distributors;
- analysis and investigation of reported adverse events by the manufacturer and regulatory authority;
- maintenance of appropriate records by parties in the distribution chain; and
- implementation of corrective actions and preventive actions, including FSCA, when appropriate.

Where the manufacturer is located outside the jurisdiction of the regulatory authority, there should be an agreement between that manufacturer and their authorized representative, defining who fulfils the national regulatory requirements and maintains records of the distribution of the device. The agreement should require the authorized representative to report serious adverse events, quality problems and complaints to the manufacturer for investigation and corrective action.

### *Mandatory reporting by manufacturer of adverse events*

As investigation and information management resources allow, the regulatory authority should establish a mandatory requirement for the timely reporting by the manufacturer or authorized representative of adverse events associated with medical devices. It should define the threshold for reporting (i.e. what kinds of events should be reported), reporting time limits, required information and which party/ies shall report. In general, those criteria should be consistent with GHTF guidance on adverse event reporting. [45]

### *In-country inspection*

As the regulatory system advances to expanded controls and enforcement, the regulatory authority may choose to determine a manufacturer's compliance with the regulatory requirements by undertaking the QMS evaluation itself, either through a desk-top review of documents or on-site inspection.

### *In-country inspection of registered organizations and their establishments*

The regulatory authority may inspect all registered organizations to confirm they have the facilities, procedures and records in place that will allow them to comply with the attestations made when they were registered. The regulatory authority may issue licenses to the registered organization, renewable on an annual basis. In this situation, the license may be withdrawn or suspended if shortcomings are found during inspection.

### *Local production*

Most countries import most of the medical devices into their domestic market. However, there may be a number of local manufacturers. Manufacturers who produce medical devices within the jurisdiction of the regulatory authority should be subject to the same regulatory controls as manufacturers of imported medical devices. However, because the local manufacturer is physically located in the jurisdiction of the authority, that regulatory authority would generally conduct its own QMS inspections of the manufacturer's plant(s) and warehouse(s), or a designated or recognized CAB may perform a QMS audit. In the case of for-cause inspections – e.g. suspected noncompliance or product problems – the regulatory authority would perform the inspection.

### *Testing laboratories*

The work of the regulatory authority may benefit from having access to an independent, accredited test laboratory to supplement its own resources. Tasks that may be undertaken by an appropriately qualified and equipped testing laboratory include:

- examination and testing of medical devices that are suspected as substandard/spurious/falsely labelled/falsified/counterfeit (SSFFC) (see chapter 5);
- institute a programme of post-market testing of specific imported devices according to specific national public health risks;
- investigation of devices allegedly involved in serious adverse event;
- investigation of devices sent to the regulatory authority by lay persons.

Given the diversity of medical devices, it is unlikely that a national regulatory authority will have all the necessary resources internally to establish and maintain its own laboratory. This Model does not recommend a regulatory authority sets up its own testing laboratory since, if it is to be effective, it requires a significant budget and expert staff. Although in many jurisdictions such organizations do not exist in-country, they may exist regionally.

When relying upon a testing laboratory, inside or outside the national jurisdiction, the authority should consider whether a laboratory has:

- accreditations;
- technical competence;
- access to external experts, as needed;
- adequate resources, such as specialized equipment;
- internal QMS and instrument calibration facilities; and
- conformity with standards.

Figure 5. The elements indicated in red are those for which international regulatory harmonization guidance documents have been developed. The elements that may be subject to reliance and recognition are indicated in blue.

1 Stepwise approach, convergence, harmonization, reliance, recognition

## LEGAL FRAMEWORK

Expanded level controls and enforcement		
Pre-market	On the market	Post-market
<div>Authorize in-country clinical investigations</div> <div>Develop guidelines</div> <div>Appoint and oversee CABs</div> <div>Recognize standards</div> <div>Adopt nomenclature system</div> <div>Establish criteria for reliance and recognition</div> <div>etc.</div>	<div>Perform in-country QMS audit</div> <div>Perform review of submissions for compliance with essential principles</div> <div>Control advertising and promotion</div> <div>Apply exemptions of regulatory requirements for public health emergencies</div> <div>etc.</div>	<div>Establish a post-market surveillance and vigilance system</div> <div>Require mandatory reporting by manufacturers of adverse events</div> <div>Exchange alerts internationally</div> <div>Monitor FSCA in-country</div> <div>Perform in-country inspections of registered organisations</div> <div>Provide for testing laboratory</div> <div>Perform inspections internationally</div>
Basic level controls and enforcement		
Pre-market	On the market	Post-market
<ul style="list-style-type: none"> <li>Publish law and regulation(s) with transition period</li> <li>Define medical device, IVD and the parties in the scope of the law</li> <li>Establish medical device risk classification</li> <li>Establish essential principles of safety and performance</li> <li>Identify regulatory status using reliance and recognition</li> <li>Establish requirements for Declaration of Conformity</li> <li>Establish requirements for QMS</li> <li>Establish requirements for labels and labelling</li> <li>Prohibit deceptive, misleading, false advertising</li> <li>Establish controls for import of donated medical devices</li> </ul>	<ul style="list-style-type: none"> <li>Register establishments: manufacturer, authorized representative, importer, distributor</li> <li>List all medical devices placed on the market under the law</li> <li>Establish port of entry controls</li> </ul>	<ul style="list-style-type: none"> <li>Establish a reporting system of adverse events involving death or serious injury</li> <li>Require mandatory notification by the manufacturer of FSCA including recall</li> <li>Establish procedure to withdraw unsafe medical devices from the market</li> <li>Establish procedure to issue safety alerts to users</li> <li>Undertake market surveillance</li> </ul>

2

3 Regulating medical devices is taking place in an ever more globalizing world. Regulatory  
4 convergence and harmonization enable countries to align their regulatory system and legal

1 requirements, reflected in their law, regulations, decrees and guidance documents. Once harmonized,  
2 a country may rely upon or recognize a decision of another jurisdiction (see above).

3 Countries that start regulating medical devices will, at the early stages of regulating medical devices,  
4 not have a harmonized regulatory system with countries that are exporting to their jurisdiction. Even  
5 without having harmonized their regulatory systems, countries may rely upon or recognize decisions  
6 of jurisdictions, provided they have knowledge of and confidence in the regulatory framework and  
7 decisions of the regulatory authority of the originating country.

8

DRAFT FOR COMMENT

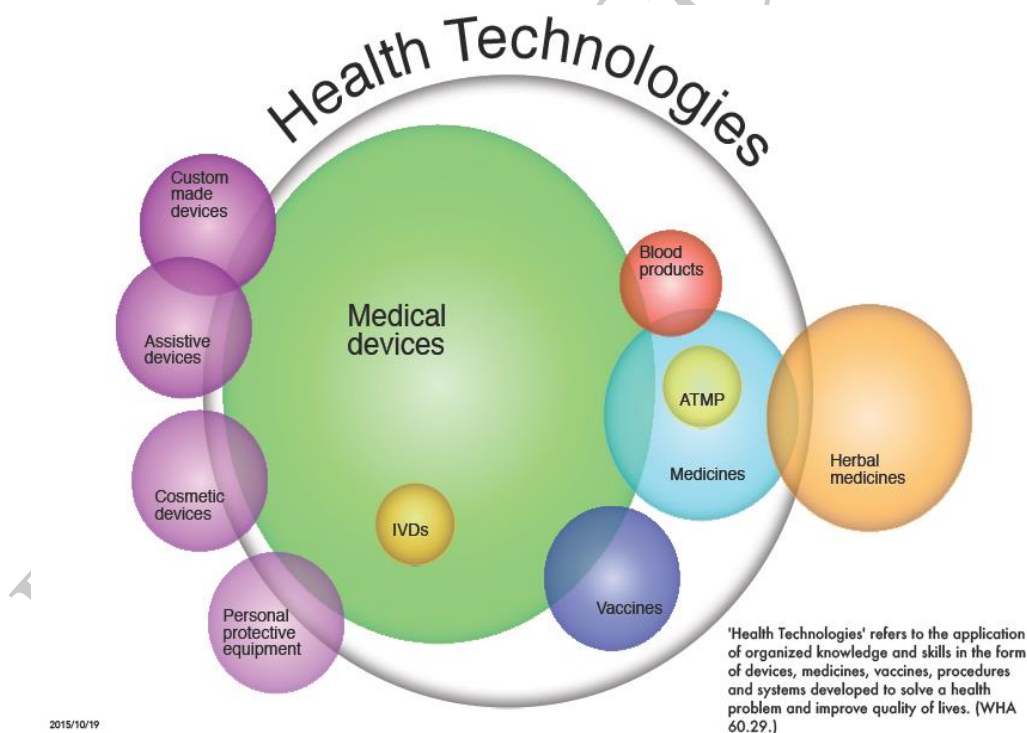
## Chapter 5. Specific topics

Beyond the general elements described in earlier chapters, this chapter covers specific topics to be considered when developing and implementing regulations for medical devices. It describes the relevance of these topics and provides guidance for regulators to ensure they are appropriately addressed.

### Determination to establish whether a medical product is a medical device

Many products are used in the delivery of health care, yet not all fit comfortably within an existing definition for a medical product, more specifically the term “medical device”. Examples include medical gases, some laxatives, cosmetic articles, clinical laboratory reagents and articles of protective clothing worn by medical personnel during procedures. A lack of clarity in such cases may lead to overlapping or conflicting regulatory requirements for a product, or (worse), to no effective regulation being applied. It is in the public interest to ensure the safety, quality and performance of all such “borderline”<sup>7</sup> products through appropriate regulatory controls; either those for medical devices or for other regulated product sectors (e.g. medicines including advanced therapy medicinal products (ATMP), cosmetics, food supplements or personal protective equipment). [47] [48]

Figure 6. Interrelation of (medical) products inside and outside health care



<sup>7</sup> Borderline products are generally medical products for which it is unclear which legislation applies. Although they may have some of the attributes of two or more categories of regulated products, they are not combination products. A combination product is a product comprised of two or more components which are regulated as medical products, i.e. medicine/medical device, or vaccine/medical device, that are physically, chemically or otherwise combined or mixed and produced as a single entity (modified from US FDA definition <http://www.fda.gov/CombinationProducts/AboutCombinationProducts/ucm118332.htm>). Combination products are beyond the scope of this Model.

To be predictable and transparent, the regulator should develop criteria and mechanisms for determining the appropriate regulatory regime for such products through a guideline. It should describe considerations and the process whereby an applicant may obtain an advisory opinion from the regulatory authority. As necessary, that process should allow for consultation with subject matter experts as well as with regulatory authorities from other product sectors like medicines or food. It may also take into account determinations made by regulatory authorities of other jurisdictions. A decision by the regulatory authority on the regulatory status of a product should provide the option of appeal in case the applicant does not agree with the decision.

## Disposal

A medical device that reaches the end of its intended life cycle must be disposed of safely. In some cases it may be necessary to dispose of a device even before the end of device life if it is confirmed that the device can no longer perform its function properly and may cause a hazard to users or patients.

Disposal of a medical device should follow safety procedures to ensure that it does not cause harm to people or the environment, especially contaminated devices such as syringes or hypodermic needles, and devices that contain infectious, toxic or radiological materials. Medical device labelling and instructions for use should include information on proper disposal at end of device life.

Due to their diversity and complexity, there are many ways that medical devices may be disposed of. For durable equipment, mechanisms may include replacement and decommissioning. For disposable devices, decontamination and proper waste management practices according to the manufacturer's instructions should be required. The responsible regulatory authority, whether or not the regulatory authority for medical devices, should establish criteria for replacement and decommissioning criteria based on the manufacturer's recommendations. Consultation between the user and manufacturer is critical especially for high technology and complicated products in order to decide the best way to dispose of the product. [49] [50] [51] [52]

## Donations

Charitable donations of medical devices and IVDs can be very helpful, may improve the efficiency of health facilities, may save costs of purchasing new equipment, and may make some diagnoses or therapies accessible to patients, especially in resource-limited settings. Donations may be beneficial but they can also cause health risks if their safety and performance are not verified. Another source of difficulty is the lack of clear documentation on the donated medical device, its state, its origin and history and the responsibilities of donors. Quality problems associated with donated medical devices have been reported in many countries. They include short expiry dates, defective equipment, and gifts of unnecessary items not requested by the recipient. These factors often result in receiving countries incurring unwanted costs for maintenance and disposal and may also create the impression that the medical devices are "substandard" and have been "dumped" on a receiving country. [53] [54]

Medical devices imported as donations should at all times comply with all regulatory safety and quality requirements and their quality should not differ to those that are imported through a regular supply chain (see chapter 4).

Regulatory authorities should therefore establish a mechanism to verify and authorize the importation of donated medical devices. [55] Institutions that intend to donate devices should communicate with the recipient to determine their needs before the products are shipped. To avoid delay and additional expense, importation documents must be submitted to the regulator of the recipient's country for approval *before* shipment of the consignment. Supporting documents will typically include: a list of

products to be donated; manufacturer(s) of the products, expiry dates (if applicable), donation certificate<sup>8</sup> and a commitment letter that confirms the safety and performance of the devices to be donated. Each donor is required to familiarize themselves with the donation requirements before they decide to donate medical devices. Donations that do not comply with the requirements should be rejected and sent back to the recipient's country at the donor's expense.

## WHO Prequalification programme for IVDs

Lack of access to quality health technologies, in particular IVDs, reduces the opportunity for progress towards addressing high-burden diseases in countries with limited access to quality health products. The WHO Prequalification programme provides countries with the appropriate technical support, tools and guidance on the provision of IVDs and laboratory services. In addition to relying upon the work of other authorities, for some medical devices (mostly IVDs), the regulatory authority may choose to rely upon evaluations conducted by the WHO Prequalification Programme for IVDs. The WHO Prequalification Programme for IVDs is a United Nations (UN) quality assurance programme that aims at promoting and facilitating access to safe, appropriate and affordable IVDs of good quality. Focus of this programme is placed on IVDs for priority diseases such as HIV/AIDS, malaria, hepatitis C and others, and their suitability for use in resource-limited settings. [17]

The WHO Prequalification Programme for IVDs undertakes an assessment of individual IVDs through a standardized procedure aimed at determining if the product meets WHO prequalification requirements. The process includes three components:

- review of a product dossier;
- independent performance evaluation; and
- manufacturing site(s) inspection.

Prequalification requirements are based on best international practice and are designed around the Essential Principles of safety and performance. As such, prequalification requirements reflect standards, guidance and other internationally recognized documents such as those of ISO, European Norm (EN), Clinical & Laboratory Standard Institute (CLSI) and IMDRF/GHTF, to ensure compliance with Essential Principles. Like other stringent regulatory reviews, prequalification assessments embrace quality, safety and performance aspects.

Although prequalification requirements are aligned with the approach adopted by regulators performing stringent reviews, they have been designed in such a way as to best serve resource-limited settings. Therefore, the aspects below are reflected in prequalification assessments:

- the regulatory version marketed on the global market is assessed;
- the scrutiny level reflects individual and public health risks in resource-limited settings;
- data submitted by the manufacturer is assessed from the resource-limited setting perspective in order to reflect the resource-limited settings environment and user.

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<sup>8</sup> Donation certificate confirms that the donation complies with the "Criteria for evaluating equipment donation offers" as stated in the WHO publication: Medical device donations: considerations for solicitation and provision. [http://apps.who.int/iris/bitstream/10665/44568/1/9789241501408\\_eng.pdf](http://apps.who.int/iris/bitstream/10665/44568/1/9789241501408_eng.pdf).

Countries may benefit from the programme by relying on prequalification assessment outcomes. The list of prequalified IVDs, along with the public report summarizing the assessment findings, is made publicly available by WHO. [56]

The findings of the WHO Prequalification Programme for IVDs, in conjunction with other procurement criteria, are typically used by UN agencies, WHO Member States and other interested organizations to guide their procurement of IVDs.

Note that sometimes devices may have different regulatory versions for different markets; these may vary in many aspects such as the intended use, site of manufacture, applied quality control, etc. It is therefore important to ensure that when relying on assessment outcomes by other entities, whether the WHO Prequalification Programme or assessments performed by other jurisdictions, the regulatory version is not substantially different from the product version that is proposed for placing on the market.

### Reprocessing of single use medical devices<sup>9</sup>

Single-use medical devices (SUMD) are designed and labelled for single use. They do not come with appropriate instructions for cleaning, disinfecting or sterilization procedures after use. This may pose a danger to the patient when SUMDs are used more than once, because conformity to their original standards for safety, quality and performance cannot be assured.

The claimed advantages to health-care practices of cost-effectiveness and waste reduction must be weighed against the potential risks associated with reprocessed SUMDs. These risks include possible cross-infection due to the inability to assure the complete removal of viable microorganisms, inadequate cleaning, decontamination and removal of pyrogens and material alteration. Exposure to chemical cleaning agents may cause corrosion or changes in the materials of the device, and exposure to repeated sterilization processes may also change the properties or degrade the device material.

In addition to the potential health risks associated with the use of reprocessed SUMDs. Ethical considerations whether it is justified to treat a patient with a reprocessed SUMD which may be of lower quality, performance or cleanliness than it was when used for the first time, even with informed consent, may be discussed. Other considerations include liability: the entity that reprocesses a medical device becomes the manufacturer with the associated responsibilities; and economic: to reprocess a SUMD in a validated process raises the costs; the perceived savings may not be realized.

In adopting a policy on the reprocessing of SUMDs, the following points should be considered by the regulatory authority: reprocessing of a SUMD as labelled by its manufacturer is not permitted unless the reprocessed SUMD meets the same initial standards as those of the original manufacturer. In order to allow their reuse, a party that reprocesses and distributes medical devices labelled by their original manufacturer for single-use only will be held to the same requirements of safety, quality and performance as manufacturers of new devices. [57] [58] [59] [60] [61] This applies equally to a health-care facility fully reprocessing single-use medical devices for reuse within its own facility.

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<sup>9</sup> Single-use device: means the medical device is intended to be used on an individual patient during a single procedure and then disposed of. It is not intended to be reprocessed and used again.  
<http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n43-2005-labelling-medical-devices-050603.pdf>.

When investigating complaints and adverse events, the regulatory authority should consider the possibility that reprocessing of SUMDs may have contributed to the complaint or adverse event.

### Refurbishing electromedical devices

Some medical devices, typically durable electromedical devices, are meant to be reused many times over a long design life. They may be subject to refurbishing to extend their service life, often for economic reasons.

Refurbishing can be described as a systematic renewal process that ensures the safety and effectiveness of medical equipment without significantly changing the equipment's or system's performance safety specifications and/or changing the intended use from that in its original marketing authorization.

In adopting a policy on refurbishing, the regulatory authority should clearly state that the original manufacturer or third party must meet the same regulatory requirements as applied to the original medical device. A party that refurbishes medical devices will be held to the same requirements of safety, quality and performance as manufacturers of new devices. [62] [63] [64] [65]

### Substandard/spurious/falsely-labelled/falsified/counterfeit products

SSFFC medical products are harmful to the health of patients, damage confidence in medical products and health-care providers and increase the burden on health systems.<sup>10</sup>

SSFFC medical devices can result from genuine manufacturing errors or deliberate falsification of a product. The latter is usually a clandestine activity, is often difficult to detect and is designed to deceive a health-care provider or patient into believing that the device is the genuine article and has been carefully assessed in terms of quality, safety and effectiveness.

Reports of SSFFC medical devices have emerged from all over the world. The United States Food and Drug Administration (USFDA) has issued warnings concerning contaminated surgical hernia mesh and glucose test strips that produced inaccurate blood glucose level measurements.<sup>11</sup> The United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) raided a business upon a complaint of a portable dental X-ray unit available on eBay. The portable dental X-ray was found to lack sufficient shielding of the X-ray tube which means that it could emit harmful radiation levels to operator and patients.<sup>12</sup> Falsified condoms, contact lenses, catheters, syringes and needles have been reported from Africa, Asia and Europe. [66] The trade in SSFFC medical devices is driven and motivated by profit. Where a demand exists those engaged in their manufacture and distribution will respond. They will utilize on-line distribution channels as well as the regulated supply chain to market their products, often accompanied by false safety and quality certification logos. Visual identification can be extremely difficult and laboratory analysis (see chapter 4) may be required to distinguish the SSFFC product from the genuine version.

The established approach is one of prevention, detection and response. [67] The existence of a legal framework providing for proportionate regulatory requirements and powers, including dissuasive sanctions, is critical. A regulatory system, with effective oversight of importation, distribution and

<sup>10</sup> <http://www.who.int/medicines/regulation/ssffc/en/>.

<sup>11</sup> <http://www.fiercemedicaldevices.com/tags/counterfeit-medical-devices>.

<sup>12</sup> <https://www.gov.uk/drug-device-alerts/medical-device-alert-counterfeit-or-non-ce-marked-dental-medical-devices>.

1 sale of medical devices will assist in the prevention of SSFFC devices reaching users and patients.  
2 Balanced awareness raising amongst consumers, health-care providers and distributors can help to  
3 minimize the threat posed by SSFFC medical products whilst retaining confidence in health  
4 technologies. It is important to educate the general public to buy from reliable sources particularly on  
5 the Internet.

6 Effective post-market surveillance and vigilance systems are both methods of detecting SSFFC  
7 medical devices early. Regulatory authorities should establish mechanisms that enable and encourage  
8 reporting of suspicious medical devices and regulatory authorities should be responsive to those  
9 reports. Regulator engagement with relevant stakeholders, including both public and private sector  
10 organizations, law enforcement, civil society, consumer groups and patients leads to increased  
11 reporting and earlier detection of SSFFC products. [68] [69] [70] [71] [72] [73]

12 New technologies, including unique identifiers and track and trace technology, currently being used in  
13 the field of medicines, also provides increased assurance of the supply chain and can lead to the early  
14 detection of SSFFC products.

15 Strengthening capacity amongst regulatory authorities to respond, transparently, consistently and  
16 proportionately will help to maintain confidence in health systems. Working in partnership with other  
17 stakeholders, including, where necessary, law enforcement and the judiciary, will help to ensure that  
18 serious cases of falsification are dealt with in a manner commensurate with the risk to public health.

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## Annex 1. Glossary

For the purpose of this document, the following definitions and descriptions apply.

**adverse event.** Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons, whether or not related to the investigational medical device (*GHTF/SG5/N5:2012 Reportable Events During Pre-Market Clinical Investigations*).

**analytical performance.** The ability of an IVD medical device to detect or measure a particular analyte (*GHTF/SG5/N6:2012 Clinical Evidence for IVD medical devices – Key Definitions and Concepts*).

**assessment.** A systematic, independent and documented process for obtaining assessment evidence and evaluating it objectively to determine the extent to which assessment criteria are fulfilled.

**audit.** A systematic, independent and documented process for obtaining audit evidence and evaluating it objectively to determine the extent to which the audit criteria are fulfilled (*ISO 19011:2002 Guidelines for quality and/or environmental management systems auditing*).

**authorized representative.** Any natural or legal person established within a country or jurisdiction who has received a written mandate from the manufacturer to act on his behalf for specified tasks, with regard to the latter's obligations under that country or jurisdiction's legislation (*GHTF/SG1/N055:2009 Definition of the Terms "Manufacturer", "Authorised Representative", "Distributor" and "Importer"*).

**clinical evaluation.** The assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance of the device when used as intended by the manufacturer (*GHTF/SG5/N3:2010 Clinical Investigations*).

**clinical investigation.** Any systematic investigation or study in or on one or more human subjects, undertaken to assess the safety and/or performance of a medical device (*GHTF/SG5/N3:2010 Clinical Investigations*).

**clinical performance.** The ability of an IVD medical device to yield results that are correlated with a particular clinical condition/physiological state in accordance with target population and intended user (*GHTF/SG5/N6:2012 Clinical Evidence for IVD medical devices – Key Definitions and Concepts*).

**conformity assessment.** The systematic examination of evidence generated, and procedures undertaken, by the manufacturer, under requirements established by the regulatory authority, to determine that a medical device is safe and performs as intended by the manufacturer and, therefore conforms to the *Essential Principles of Safety and Performance for Medical Devices* (*GHTF/SG1/N78:2012 Principles of Conformity Assessment for Medical Devices*).

**Conformity Assessment Body (CAB).** A body, other than a regulatory authority, engaged in determining whether the relevant requirements in technical regulations or standards are fulfilled (*GHTF/SG1/N78:2012 Principles of Conformity Assessment for Medical Devices*).

**convergence (regulatory).** Represents a process whereby the regulatory requirements across countries or regions become more similar or “aligned” over time as a result of the gradual adoption of internationally-recognized technical guidance documents, standards and scientific principles, common or similar practices and procedures, or adaptation of regulatory mechanisms, that might be specific to a local legal context but that align with shared principles to achieve a common public health goal. It does not necessarily represent the harmonization of laws and regulations, which is not a prerequisite for allowing the alignment of technical requirements and greater regulatory cooperation (*USFDA Regulatory Harmonization and Convergence* <http://www.fda.gov/BiologicsBloodVaccines/InternationalActivities/ucm271079.htm>).

**corrective action.** Action to eliminate the cause of a detected nonconformity or other undesirable situation (GHFT/SG3/N18:2010 *Quality management system – Medical Devices – Guidance on corrective action and preventive action and related QMS processes*).

**declaration of conformity.** The manufacturer’s written attestation that it has correctly applied the conformity assessment elements relevant to the classification of the device (GHFT/SG1/N78:2012 *Principles of conformity assessment for medical devices*).

**distribution chain.** A collective term for local manufacturers, authorized representatives, importers and distributors established within the jurisdiction.

**distributor.** Any natural or legal person in the supply chain who, on his own behalf, furthers the availability of a medical device to the end-user (GHFT/SG1/N055:2009 *Definition of the Terms “Manufacturer”, “Authorised Representative”, “Distributor” and “Importer”*).

**enforcement.** Action taken by an authority to protect the public from products of suspect quality, safety and effectiveness or to assure that products are manufactured in compliance with appropriate laws, regulations, standards and commitments made as part of the approval to market a product (*USFDA/21CFR26.1, Code of Federal Regulations Title 21* <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=26.1>).

**field safety corrective action (FSCA).** An action taken by a manufacturer to reduce or remove a risk of death or serious deterioration in the state of health associated with the use of a medical device that is already placed on the market (GHFT/SG2/N57:2006 *Medical Devices Post-Market Surveillance: Content of Field Safety Notices*).

**generic device group.** A set of devices having the same or similar intended purposes or commonality of technology allowing them to be classified in a generic manner not reflecting specific characteristics (Global Medical Devices Nomenclature System (GMDN) @ <https://www.gmdnagency>).

**governance.** Refers to the different ways that organizations, institutions, businesses and governments manage their affairs. Governance is the act of governing and thus involves the application of laws and regulations, but also of customs, ethical standards and norms. Good governance means that affairs are managed well, not that the laws, regulations or norms are themselves necessarily “good” (WHO, *Global Governance* <http://www.who.int/trade/glossary/story038/en/>).

**guidelines/guidance documents.** Non-statutory advisory publications intended to assist those parties affected by legislation to interpret requirements.

**harm.** A physical injury or damage to the health of people or damage to property or the environment (ISO/IEC Guide 51:1999 *Safety aspects - Guidelines for their inclusion in standards*).

**harmonization (regulatory).** The process by which technical guidelines are developed to be uniform across participating authorities (*USFDA Regulatory Harmonization and Convergence* <http://www.fda.gov/BiologicsBloodVaccines/InternationalActivities/ucm271079.htm>).

**hazard:** means potential source of harm (ISO/IEC Guide 51:1999 Safety aspects - Guidelines for their inclusion in standards).

**health-care facility.** Is any party within the country providing health-care services.

**health technologies.** Refers to the application of organized knowledge and skills in the form of devices, medicines, vaccines, procedures and systems developed to solve a health problem and improve quality of lives (*WHA60.29 Health technologies*).

**importer.** Any natural or legal person in the supply chain who is the first in a supply chain to make a medical device, manufactured in another country or jurisdiction, available in the country or jurisdiction where it is to be marketed (GHFT/ SG1/N055:2009 *Definition of the Terms "Manufacturer", "Authorised Representative", "Distributor" and "Importer"*).

**inspection.** An on-site evaluation by a regulatory authority of a manufacturing facility to determine whether such manufacturing facility is operating in compliance with regulatory acquirements and or commitments made as part of the approval to market a product (*USFDA/21CFR26.1, Code of Federal Regulations Title 21* <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=26.1>).

**instructions for use.** Information provided by the manufacturer to inform the device user of the medical device's intended purpose and proper use and of any precautions to be taken (GHTE/SG1/N70:2011 *Label and Instructions for Use for Medical Devices*).

**intended use/purpose.** The objective intent of the manufacturer regarding the use of a product, process or service as reflected in the specifications, instructions and information provided by the manufacturer (GHTE/SG1/N77:2012 *Principles of Medical Devices Classification*) .

**in vitro diagnostic (IVD) medical device.** A medical device, whether used alone or in combination, intended by the manufacturer for the in- tro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes (GHTE/SG1/N71:2012 *Definition of the Terms 'Medical Device' and 'In Vitro Diagnostic (IVD) Medical Device'*).

**IVD for self-testing.** Any IVD medical device intended by the manufacturer for use by lay persons (GHTE/SG1/N045:2008 *Principles of In Vitro Diagnostic (IVD) Medical Devices Classification*).

**label.** Written, printed or graphic information either appearing on the medical device itself, or on the packaging of each unit, or on the packaging of multiple devices (GHTE/SG1/N70:2011 *Label and Instructions for Use for Medical Devices*).

**labelling.** The label, instructions for use and any other information that is related to identification, technical description, intended purpose and proper use of the medical device, but excluding shipping documents (GHTE/SG1/N70:2011 *Label and Instructions for Use for Medical Devices*).

**law.** Is binding and enforceable legislation passed by a legislative body.

1           **lay person.** Individual that does not have formal training in a specific field or discipline  
2           (GHTF/SG1/N70:2011 *Label and Instructions for Use for Medical Devices*).

3           **licensing.** The process whereby the regulatory authority issues a license to an authorized  
4           representative, importer, distributor or local manufacturer which permits the party to undertake  
5           activities specified through legislation.

6           **life cycle.** All phases in the life of a medical device, from the initial conception to final  
7           decommissioning and disposal.

8           **listing.** The process whereby a party submits information to the regulatory authority in a  
9           jurisdiction, regarding the identification of a medical device(s) that is or will be supplied to the market  
10          in that jurisdiction (GHTF/SG1/N065:2010 *Registration of Manufacturers and other Parties and*  
11          *Listing of Medical Devices*).

12          **manufacturer.** Any natural or legal person with responsibility for design and/or manufacture  
13          of a medical device with the intention of making the medical device available for use, under his name;  
14          whether or not such a medical device is designed and/or manufactured by that person himself or on  
15          his behalf by another person(s) (GHFT/SG1 /N055:2009 *Definition of the Terms “Manufacturer”,*  
16          *“Authorised Representative”, “Distributor” and “Importer”*).

17          NOTE: This “natural or legal person” has ultimate legal responsibility for ensuring compliance with  
18          all applicable regulatory requirements for the medical devices in the countries or jurisdictions where it  
19          is intended to be made available or sold, unless this responsibility is specifically imposed on another  
20          person by the regulatory authority within that jurisdiction.

21          **market surveillance.** Shall mean the activities carried out and measures taken by public  
22          authorities to ensure that products comply with the requirements set out in legislation and do not  
23          endanger health, safety or any other aspect of public interest protection (*based on EU Council*  
24          *Directive EC No 756/2008 of 9 JULY 2008 concerning the requirements for accreditation and market*  
25          *surveillance relating to the marketing of products and repealing Regulation (EEC) No 339/93*).

26          **medical device.** Any instrument, apparatus, implement, machine, appliance, implant, reagent  
27          for in vitro use, software, material or other similar or related article, intended by the manufacturer to  
28          be used, alone or in combination, for human beings, for one or more of the specific medical purpose(s)  
29          of:

- 30          • diagnosis, prevention, monitoring, treatment or alleviation of disease;
- 31          • diagnosis, monitoring, treatment, alleviation of or compensation for an injury;
- 32          • investigation, replacement, modification or support of the anatomy or of a physiological  
33          process;
- 34          • supporting or sustaining life;
- 35          • control of conception;
- 36          • disinfection of medical devices;
- 37          • providing information by means of in vitro examination of specimens derived from the  
38          human body;

39          and which does not achieve its primary intended action by pharmacological, immunological or  
40          metabolic means, in or on the human body, but which may be assisted in its intended function by such  
41          means (GHTF/SG1/N71:2012 *Definition of the Terms “Medical Device” and “In Vitro Diagnostic*  
42          *(IVD) Medical Device”*).

**medical products.** Is a term that includes medicines, vaccines, diagnostics and medical devices (*WHA67.20 Regulatory system strengthening for medical products*).

**placing on the market.** All controls applied by the regulatory authority to the manufacturer and/or authorized representative at the stage of, and as a condition of, making available an individual medical device with a view to its distribution and/or use within the jurisdiction.

**post-market.** All controls applied by the regulatory authority to the manufacturer and/or authorized representative after a manufacturer's medical device has been placed on the market or put into service.

**post-market surveillance.** The activities carried out and measures taken by a regulatory authority to ensure that medical devices placed on the market comply with regulations and do not endanger health, safety or any other aspect of public health (*based on EU Council Directive 93/42/EEC of 14 JUNE 1993 concerning medical devices*).

**pre-market.** All controls applied by the regulatory authority to the manufacturer and/or the authorized representative before the manufacturer's medical device may be placed on the market or put into service.

**primary legislation.** A form of law, created by a legislative branch of government, consisting of statutes that set out broad outlines and principles and may delegate authority to an executive branch of government to issue secondary legislation.

**quality management system.** The organizational structure, responsibilities, procedures, processes and resources for implementing quality management. For the purpose of these guidelines "implementing quality management" is taken to include both the establishment and maintenance of the system (*GHTF/SG4/N28R4:2008 Guidelines for Regulatory Auditing of Quality Systems of Medical Device Manufacturers – Part 1: General Requirements*).

**recall.** Shall mean any measure aimed at achieving the return of a product that has already been made available to the end user (*based on EU Council Directive EC No 756/2008 of 9 JULY 2008 concerning the requirements for accreditation and market surveillance relating to the marketing of products and repealing Regulation (EEC) No 339/93*).

**recognition.** Is routine acceptance by the regulatory authority of an importing country of the regulatory decision of another regulatory authority or other trusted institution that evidence of conformity with the regulatory requirements of that country is sufficient evidence of conformity with the regulatory requirements of the importing country (*WHO Good Regulatory Practices: Guideline for National Medical Products Regulatory Authorities under development*).

**refurbishing.** A systematic process of rebuilding or restoring that ensures safety and effectiveness of the medical equipment without significantly changing the equipment's or system's performance safety specifications and/or changing intended use as in its original registration (*APEC 2012 Regulatory framework for control of refurbished medical devices*).

**registration.** The process by which a party submits information to the regulatory authority in a jurisdiction, regarding the identification and establishment location(s) of the manufacturer and other parties, responsible for supplying a medical device(s) to the market in that jurisdiction

(GHTF/SG1/N065:2010 *Registration of Manufacturers and other Parties and Listing of Medical Devices*).

**regulation.** A written instrument containing rules having the force of law.

**regulatory authority.** A government body or other entity that exercises a legal right to control the use or sale of medical devices within its jurisdiction, and that may take enforcement action to ensure that medical products marketed within its jurisdiction comply with legal requirements (GHTF/SG1/N78:2012 *Principles of Conformity Assessment for Medical Devices*).

**reliance.** Is the process whereby a regulatory authority may take into account and give significant weight to (i.e. rely upon) evaluations performed by another regulatory authority or other trusted institution for reaching its own decision (*WHO Good Regulatory Practices: Guideline for National Medical Products Regulatory Authorities under development*).

**reprocessing.** The process carried out on a used medical device in order to allow its safe reuse including, where appropriate, cleaning, disinfection, sterilization and related procedures, repackaging, relabelling, as well as testing and restoration of the technical and functional safety of the used device (2012/0266 (COD) *based on proposal for amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 of 26 SEPTEMBER 2012 concerning medical devices*).

**risk.** The combination of the probability of occurrence of harm and the severity of that harm (*ISO/IEC Guide 51:1999 Safety aspects - Guidelines for their inclusion in standards*).

**Secondary legislation:** a form of law, issued by an executive branch of government, specifying substantive regulations, and procedures for implementing them. The power to pass delegated legislation is defined and limited by the primary legislation that delegated those powers.

**serious adverse event.** Adverse event that:

- a) led to a death;
  - b) led to a serious deterioration in the health of the subject that either
    - 1) resulted in a life-threatening illness or injury, or
    - 2) resulted in a permanent impairment of a body structure or a body function, or
    - 3) required in-patient hospitalization or prolongation of existing hospitalization, or
    - 4) resulted in medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function;
  - c) led to foetal distress, foetal death or a congenital abnormality or birth defect
- (GHTF/SG5/N5:2012 *Reportable Events During Pre-Market Clinical Investigations*).

**serious injury.** (Also known as serious deterioration in state of health.) Is either:

- life-threatening illness or injury;
- permanent impairment of a body function or permanent damage to a body;
- a condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure

(GHTF/SG2/N54R8:2006 *Medical Devices Post Market Surveillance: Global Guidance for Adverse Event Reporting for Medical Devices*).

1       **single-use medical device.** A medical device intended by the manufacturer to be used on an  
2 individual patient during a single procedure and then disposed of (*GHTF/SG1/N70:2011 Label and*  
3 *Instructions for Use for Medical Devices*).

4       **standard.** A document, established by consensus and approved by a recognized body, that  
5 provides, for common and repeated use, rules, guidelines or characteristics for activities or their  
6 results, aimed at the achievement of the optimum degree of order in a given context  
7 (*GHTF/SG1/N44:2008 Role of Standards in the Assessment of Medical Devices*).

8       **substandard/spurious/falsely-labelled/falsified/counterfeit medical products.** There is  
9 currently no universally agreed definition of what used to be widely known as “counterfeit medicine”.  
10 Pending negotiation amongst Member States, WHO will continue to use the term substandard/  
11 spurious/falsely-labelled/falsified/counterfeit medical products. (*WHO 2014 Substandard, spurious*  
12 *falsely labelled, falsified and counterfeit medical products*).

13       **technical documentation.** The documented evidence, normally an output of the quality  
14 management system that demonstrates the medical device complies with the relevant principles of  
15 safety, performance and labelling specified through legislation (*based on GHTF/SG1/N78:2012*  
16 *Principles of Conformity Assessment for Medical Devices*).

17       **user.** The person, either professional or lay, who uses a medical device. The patient  
18 may be the user (*GHTF/SG1/N70:2011 Label and Instructions for Use for Medical Devices*).

19       **vigilance.** A process whereby a manufacturer records and investigates any adverse event  
20 report it receives, taking field safety corrective action where necessary, and informing the regulatory  
21 authority of those that meet criteria specified through legislation. The regulatory authority may  
22 monitor the investigation.

23       **World Health Assembly.** The forum through which the World Health Organization is  
24 governed by its 194 Member States.

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## Annex 2. Hierarchy of regulation

Level	Brief description	Examples	Examples of subject-matter regulated in the field of medical devices
<b>Primary legislation</b>	Law, or executive law as used in this WHO Global Model regulatory framework, refers to binding and enforceable legislation, usually adopted at the level of individual countries by their respective legislatures and/or executives.	Act of parliament; bill; statutory law; EU directive, ordinance; decree; executive order.	Establishment of the regulatory authority including enforcement power; reliance and recognition; definition of a medical device; placing on the market; market withdrawal, classification of medical devices; essential requirements; requirement for a quality management system; incident reporting; clinical trials; listing of medical devices; registration of establishments; process to recognize standards.
<b>Secondary legislation</b>	A form of law as used in this Model regulatory framework for medical devices, refers to written instruments that are binding and enforceable and are issued by the regulatory (executive) authority.	Regulations, schedule.	Requirements for reliance; conduct of QMS audits; vigilance reporting; criteria for recalls and FSCAs; classification rules; responsibilities of an authorized representative.
<b>Guidelines<sup>13</sup></b>	Guidance documents, that refer generally to non-binding normative documents issued by the regulatory authority that offer guidance on recommended practices. They allow for scientifically-justified, alternated approaches and translation of a regulatory, generally acceptable approach. Guidelines offer the current thinking, practices, explanations and expectations of the regulatory authority, but compliance with such documents is not mandatory. The manufacturer (or other party) may choose not to apply or comply with such guidance, but must provide a rationale for, and justify, a deviation from that guidance.	Technical standards, recommendations.	Guidance on interpretation and application of the classification rules; interpretation of the meaning of “primary intended mode of action” (related to the definition of “medical device”); specific labelling requirements; good laboratory practices; good clinical practices.

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<sup>13</sup> Note that the term “guideline”, as used in this WHO Global Model Regulatory Framework, does not refer to guidelines within the sense of the WHO Handbook for Guideline Development.