WHO GLOBAL MODEL REGULATORY FRAMEWORK FOR MEDICAL DEVICES INCLUDING IVDS
(21 July 2016)

REVISED DRAFT FOR COMMENT

Please address any comments on this proposal by 1 September 2016 to Ms Josée Hansen, Senior Adviser, Department of Essential Medicines and Health Products, World Health Organization, 1211 Geneva 27, Switzerland, fax: (+41 22) 791 4730 or email: hansenj@who.int.

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Please send any request for permission to:
Dr Sabine Kopp, Group Lead, Medicines Quality Assurance, Technologies, Standards and Norms, Regulation of Medicines and other Health Technologies, Department of Essential Medicines and Health Products, World Health Organization, CH-1211 Geneva 27, Switzerland, Fax: (41-22) 791 4730; email: kopps@who.int.

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<table>
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<td>24 May 2014</td>
<td>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.</td>
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<tr>
<td>April 2015</td>
<td>WHO decided to develop a model for regulating medical devices</td>
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<tr>
<td>June 2015</td>
<td>Formation of the Working Group for the development of a model regulation for medical devices (Working Group), consisting of professionals in regulating medical devices</td>
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<tr>
<td>July 2015</td>
<td>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</td>
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<td>29–30 September 2015</td>
<td>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.</td>
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<tr>
<td>12 October 2015</td>
<td>Expert Committee for the Specifications of Pharmaceutical Preparations (ECSPP) meeting. A discussion on the Model was added to the agenda of the 50th ECSPP meeting.</td>
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<tr>
<td>12 October 2015</td>
<td>Expert Committee for Biological Standardization (ECBS) meeting. ECBS agreed to receive the Model for information.</td>
</tr>
<tr>
<td>5–10 December 2015</td>
<td>Development of the first draft of the Model, by a drafting group consisting of three Working Group members, with input from the full Working Group</td>
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<tr>
<td>Activity</td>
<td>Date</td>
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<tr>
<td>Circulation of the Draft of the Model to the Working Group and WHO staff members for comments and feedback</td>
<td>December 2015–January 2016</td>
</tr>
<tr>
<td>Compilation of feedback</td>
<td>January 2016</td>
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<tr>
<td>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.</td>
<td>9–10 February 2016</td>
</tr>
<tr>
<td>Compilation of the comments from the face-to-face meeting of the Working Group</td>
<td>February–March 2016</td>
</tr>
<tr>
<td>Development of a revised version of the Model, with input from Working Group members</td>
<td>21–26 March 2016</td>
</tr>
<tr>
<td>Circulation of the revised version of the Model to the Working Group and WHO staff members for comments and feedback</td>
<td>Mid-April 2016</td>
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<tr>
<td>Compilation of the comments of the Working Group to the Model</td>
<td>End-April 2016</td>
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<td>Public consultation</td>
<td>May–mid-June 2016</td>
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<tr>
<td>Compilation of all comments received</td>
<td>Mid-June–end-June 2016</td>
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<td>Teleconference with the Working Group on the comments received</td>
<td>Early July 2016</td>
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<tr>
<td>Second public consultation</td>
<td>July–1 September 2016</td>
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<tr>
<td>Compilation of all comments received</td>
<td>September 2016</td>
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<tr>
<td>Teleconference with the Working Group on the comments received</td>
<td>September 2016</td>
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<tr>
<td>Submitting the draft of the WHO Global Regulatory Model for medical devices including IVDs to ECSPP and ECBS</td>
<td>Mid-September 2016</td>
</tr>
<tr>
<td>Presentation to the 51st ECSPP meeting, with a view to its endorsement</td>
<td>17–21 October 2016</td>
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<td>Any follow-up action, as needed</td>
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Acronyms

CAB: conformity assessment body
CLSI: Clinical and Laboratory Standards Institute
FSCA: Field Safety Corrective Action
GHTF: Global Harmonization Task Force
GMDN: Global Medical Device Nomenclature
IEC: International Electro Technical Commission
IFU: instructions for use
IMDRF: International Medical Device Regulators Forum
ISO: International Organization for Standardization
IVD: in vitro diagnostic medical device
NRA: national regulatory authority
QMS: quality management system
SSFFC: substandard/spurious/falsely-labelled/falsified/counterfeit products
SUMD: single-use medical device
UN: United Nations
UNFPA: United Nations Population Fund
WHA: World Health Assembly
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REFERENCES

FURTHER READING

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Acknowledgements

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This document has been developed by the Department of Essential Medicine and Health Products under the direction of Josée Hansen, WHO headquarters, Switzerland.

Secretary General, CIOMS, Geneva, Switzerland from 18 April 2016.
Chapter 1. Introduction

Medical devices contribute to the attainment of the highest standards of health of individuals. Without medical devices, common 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: for example 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 5 million different kinds of medical devices on the world market, separated into more than 22,000 generic devices groups.²

In May 2007, the first resolution on health technologies was adopted by the World Health Organization (WHO) World Health Assembly (WHA) (WHA 60.29), which set the framework for an unprecedented focus on health technologies, but more specifically on medical devices. In 2014, the WHA adopted a resolution regarding regulatory system strengthening for medical products (WHA 67.20). The Resolution states “effective regulatory systems are an essential component of health system strengthening and contribute to better health outcomes”.

In the context of Resolution 67.20, because there was growing interest in medical devices in the global health community and a 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 well as jurisdictions that are continuing to improve their regulatory frameworks as they take steps to ensure the quality and safety of medical devices available in their countries. 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 resources nor the 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 of the regulatory system 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.

² The GMDN Agency has published over 22,000 generic device groups for medical devices (Source: GMDN Agency).
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 attributes of 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 regulatory controls towards an expanded level as their resources allow. The Model is written for the legislative, the executive branches and regulatory authorities of government when developing and establishing the regulations.

It describes the role and responsibilities of a country’s regulatory authority for implementing the regulations. It also describes circumstances in which a regulatory authority may either rely on, 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 medical 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 of safety and performance that the device manufacturer must fulfill. It explains how the manufacturer must demonstrate to a regulatory authority 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. Also it provides information on when the techniques of reliance and recognition may be considered, and on 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 regulatory authorities 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 but cannot provide country-specific guidance on implementation. While it does not offer detailed guidance on regulatory topics, it provides references to relevant documents. It does not detail responsibilities of other stakeholders such as manufacturers, distributors, procurement agencies and health-care professionals, all of whom have roles in assuring the quality, safety and performance of medical devices.
Chapter 2. Definition, classification, Essential Principles and conformity assessment of medical devices

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. In the interest of international convergence it is recommended to promote its widespread use.

"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.5

3 Note from GHTF definition (http://www.imdrf.org/docs/ghtf/final/sg1/technical-docs/ghtf-sg1-n071-2012-definition-of-terms-120516.pdf#search): Some jurisdictions include ‘accessories to a medical device’ and ‘accessories to an IVD medical device’ within their definitions of ‘medical device’ or ‘IVD medical device’, respectively. Other jurisdictions do not adopt this approach but still subject an accessory to the regulatory controls (e.g. classification, conformity assessment, quality management system requirements etc.) that apply to medical devices or IVD medical devices.

4 Spare parts, supplied for the replacement of existing components of a medical device that has already been registered are not usually considered to be medical devices unless they are likely to significantly change the characteristics or performance of the finished device. If this is the case then such spare parts are likely to be considered to be medical devices in their own right and therefore may require regulatory control.

5 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.
“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.\(^6\) [1]

There may also be products on the market that are similar to medical devices in function and risk that do not fit within these definitions. For reasons of protecting public health they are regulated as if they were. Examples include: impregnated bed nets to protect against malaria bearing mosquitos; personal protective devices to avoid cross-infection; lead aprons to protect against radiation; some 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 that the regulatory authority allocates its resources and imposes controls proportional to the potential for harm associated with medical devices.

The regulation specifies the manner in which a manufacturer should demonstrate conformity to safety, performance and quality requirements. The regulatory oversight by the authority should increase in line with the potential of a medical device to cause harm to a patient or user (i.e. the hazard it presents). The risk class of a medical device is primarily determined by the level of invasiveness and the duration of use in the body. A classification system for medical devices and IVDs guides the regulatory controls to be implemented for each device class.

It is widely accepted that medical devices are separated into groups or classes, typically four, A, B, C and D, by applying a set of classification rules [2], and specify separately the different conformity assessment procedures that should apply to each group of devices.

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\(^6\) 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.
Figure 1. Impact of device classification on regulatory scrutiny. As the regulatory requirements increase, so does the scrutiny by the regulatory authority.

The classification rules for non-IVD medical devices depend on the features of the device, such as whether it:

- 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 an active medical device;
- 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.

For IVDs, the risk classification depends both on the risk for the individual and for public health, such as:

- the intended use (including what is detected, the IVD function, the specific disorder, condition or risk factor of interest that the IVD is intended to detect, define or differentiate, and the testing population);
- the intended user;
- the importance of the information to the diagnosis, screening, monitoring or staging of disease (sole determinant or one of several);
- the impact of the test result to the individual and/or to public health.

The GHTF has published documents on the classification of medical devices and IVDs that use the principles above to establish classification rules [2] [3]. These rules have been widely accepted. Additionally, the regulatory authority may develop explanatory guidance to help a manufacturer apply the rules. [4] While the manufacturer has the primary obligation to classify its medical device, its decision may be challenged by the regulatory authority.

The figure below shows examples of medical devices according to their risk class.
Figure 2. Examples of medical devices by risk class

<table>
<thead>
<tr>
<th>Class</th>
<th>Risk</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Low</td>
<td>syringes, examination gloves, patient hoists, stethoscopes, wheelchair, hearing aids, IVD instruments, microbiological culture media.</td>
</tr>
<tr>
<td>B</td>
<td>Low-moderate</td>
<td>surgical gloves, infusion sets, pregnancy tests</td>
</tr>
<tr>
<td>C</td>
<td>Moderate-high</td>
<td>condoms (unless with spermicide (class D)), infusion pumps, neonatal incubators, therapeutic and diagnostic X-ray, lung ventilators, haemodialysers, anaesthesia equipment, self-test glucose strips</td>
</tr>
<tr>
<td>D</td>
<td>High</td>
<td>implantable cardioverter defibrillators (ICDs), pacemakers, breast implants, angioplasty balloon catheters, spinal needle, hepatitis C enzyme immunoassay.</td>
</tr>
</tbody>
</table>

**Essential Principles of safety and performance**

Regulations should specify that a medical device be safe and perform as intended when placed on the market. GHTF has established a list of Essential Principles of safety and performance for medical devices including IVDs. [5] These requirements have been widely adopted. 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. implants, electrically powered, etc.).

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

- the processes for the design and production should ensure that a medical device when used according to the intended purpose and meeting the conditions of technical knowledge and training of the user is safe and does not compromise the clinical condition of the patient or the health of the user;
- the manufacturer should perform a risk assessment to identify known and foreseeable risks and to mitigate these risks in the design, production and use of the medical device;
- medical devices should perform as the manufacturer intended 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 weighed against the benefits of the intended purpose.
Ensuring that a medical device consistently conforms to the Essential Principles [5] is primarily the responsibility of the manufacturer. The documented evidence of conformity to the Essential Principles may be subject to review by the regulatory authority, before or after market introduction. The degree of involvement of the regulatory authority or conformity assessment body (CAB) [6] (see Chapter 4) in the assessment of a medical device is dependent on the risk class: the higher the risk class, the greater is the involvement of the regulatory authority or CAB. [6]

Clinical evidence

Amongst other requirements, the Essential Principles require that “…. the device will perform as intended by the manufacturer and not compromise the clinical condition or the safety of patients …” Clinical evidence is important to demonstrate these requirements. It is a component of the technical documentation of a medical device, which along with other design verification and validation documentation, device description, labelling, risk analysis and manufacturing information, is needed to allow a manufacturer to demonstrate conformity with the Essential Principles.

Some technologies have been available for many years and their clinical safety and performance have been well characterized. On the other hand, many devices utilize new technology that has had little prior application in the diagnosis or treatment of humans and for which safety and clinical performance have not yet been established.

For long established technologies, clinical investigation data that might be required for novel technologies, may not be necessary. The available clinical data in the form of literature, reports of clinical experience, post-market reports and adverse event data for previous versions of the device may, in principle, be adequate to establish the safety and performance of the device, provided that new risks have not been identified, and that the intended use(s)/purpose(s) has/have not changed. The manufacturer should perform a documented comprehensive evaluation of all the available clinical evidence under the control of its quality management system. That clinical evaluation report becomes part of the technical documentation for the device and may serve as the basis for determining whether a new clinical investigation is appropriate. [7] A widely used international standard for the practice of clinical investigation is: ISO 14155 – Clinical investigation of medical devices for human subjects – Good clinical practice. [8]

Assessing conformity to the Essential Principles

To a large extent, the quality, safety and performance of a medical device are determined by systematic controls applied by the manufacturer to its design, development, testing, manufacture and distribution over the device life cycle. In general, the manufacturer does this through implementation of a quality management system (QMS). The degree of assessment of the QMS by the regulatory authority or CAB depends on the medical device risk class. [6] (See Chapter 4.)

[7] 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.
Figure 3. Conformity assessment processes as determined by device class

<table>
<thead>
<tr>
<th>Conformity assessment element</th>
<th>Class A</th>
<th>Class B</th>
<th>Class C</th>
<th>Class D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality management system</td>
<td>Regulatory audit normally not required, except where assurance of sterility or accuracy of the measuring function is required.</td>
<td>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.</td>
<td>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.</td>
<td>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.</td>
</tr>
<tr>
<td>Technical documentation</td>
<td>Pre-market submission normally not requested.</td>
<td>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.</td>
<td>The regulatory authority will undertake a review sufficient to determine conformity to Essential Principles prior to the device being placed on the market.</td>
<td>The regulatory authority will undertake an in-depth review to determine conformity to Essential Principles, prior to the device being placed on the market.</td>
</tr>
<tr>
<td>Declaration of conformity</td>
<td>Submission normally not requested.</td>
<td>Review and verify compliance with requirements by the regulatory authority (see footnote 7).</td>
<td>Review and verify compliance with requirements by the regulatory authority (see footnote 7).</td>
<td>Review and verify compliance with requirements by the regulatory authority (see footnote 7).</td>
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</table>

For all medical devices, the manufacturer prepares and holds a declaration of conformity to regulatory requirements. [6] Depending on the class of the medical device, the evidence of conformity may be subject to regulatory assessment by the regulatory authority or CAB. Class A medical devices do not require pre-market submission of technical documentation8, but the manufacturer is required to maintain technical documentation demonstrating conformity with the Essential Principles.

Class A medical devices, except those that are sterile or have a measuring function, 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 a summary of the technical documentation and/or other evidence of conformity, with the regulatory requirements.

For classes B, C and D medical devices a regulatory authority or CAB would usually audit the manufacturing site to ascertain compliance with the QMS requirements.

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8 There are many terms used to describe a product’s technical documentation. The terms include technical file, standard technical documentation, design dossier, product design dossier, product summary file, product master file.
For class C and D medical devices, the pre-market assessment usually includes a review of the summary technical documentation. This would typically include a device description, the Essential Principles checklist, the risk analysis, information on design and manufacturing, product verification and validation, and labelling. The regulatory authority should specify whether summarized or detailed information should be submitted; typically for class D devices detailed information would be needed, while class C devices may require only summary information.

For all classes of devices, the manufacturer should prepare, hold and be prepared to submit as required, a declaration of conformity that the device complies fully with all regulatory requirements.

**Special considerations for regulation of IVDs**

In the Model, IVDs must comply with regulatory requirements similar to those for other medical devices. However, there are some points of difference which require consideration. 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, an undiagnosed patient with a serious infectious disease can put a whole community at risk.

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, A, B, C and D, in ascending order of risk are:

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

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

The GHTF has developed additional Essential Principles which apply to IVDs. [5] While the Essential Principles are similar in nature for each product type, the different conditions of use 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, in addition to those for other medical devices.

Clinical evidence for IVDs
Clinical evidence for an IVD is all the information that supports the scientific validity and performance for its use as intended by the manufacturer. It is an important component of the technical documentation of an IVD, which along with other design verification and validation documentation, device description, labelling, risk analysis and manufacturing information, is needed to allow a manufacturer to demonstrate conformity with the Essential Principles. Clinical evidence includes analytical performance, clinical performance and clinical validity data.

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. 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. [9]

Lot verification testing of IVDs
Some countries that have yet to implement an effective regulation for medical devices but need to import high risk (class D) IVDs, may implement a system of batch testing, or lot verification of such IVDs before they are put into service. 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.

The need for lot verification testing depends upon the other controls in place in the importing country and the extent of pre-market evaluation conducted. 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.
Chapter 3. 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. 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; and
- flexibility.

Legal requirements

Medical device regulation must have a sound basis in law. There is no single approach to the legal foundation of such a regulatory framework since it depends on the national constitution and existing general national legal and administrative systems within the country.

The law should define the products within its scope and identify the entities 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 penalties. It should establish mechanisms for the accountability of the executive, judicial and legislative branches of government. It would address coordination with other bodies such as the justice ministry and the 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 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 assessments and decisions by authorities in other jurisdictions when taking its own 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 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 proportionate and 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 or to the source of financing or the sector of the health care system
where it is used (e.g. whether primary, secondary or emergency healthcare; whether delivered through
public, private or military facility).

**Gap analysis of existing controls**

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

The authority should conduct a gap analysis and seek the views of interested parties, including patient
representatives. The results of that assessment will aid in setting priorities for implementation. For
example, in a country with little or no domestic production, it may be appropriate to focus first on
import controls, rather than on manufacturing controls; 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.

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

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 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 transition provisions. The regulatory authority should hold meetings and publish guidance to ensure that medical device manufacturers, importers, distributors, and purchasers are aware of their responsibilities, thereby avoiding disruption in the supply of medical devices during the transition period.

Monitoring implementation

At the time of development of the regulatory implementation plan, goals and performance indicators should be established to allow progress of implementation to be assessed against a baseline that represents the current status of medical devices regulation. Progress towards those goals should be reported to the legislature/parliament and the public. 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 medical devices. 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 a national regulatory authority, with the ability to exercise independent decision making within the regulatory framework. That body may be either within an existing government department 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 a requirement to publish periodic public reports on performance. In countries where the law (or decree) consist of statutes setting out broad outlines and principles only, it must delegate power to the regulatory authority to issue secondary legislation (also known as statutory instruments or implementing acts), specifying substantive requirements, and procedural regulations for implementing them. It should also provide the necessary enforcement powers.

While retaining in full the responsibilities placed upon it by the law, the regulatory authority should be permitted to designate CABs to assist in carrying out its duties. In this situation the legislation will include requirements for appointing a CAB, setting the scope of its responsibilities and monitoring performance. Although the CAB may perform some evaluation functions, the final decisions and enforcement powers 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 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 policies 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 then be established through the medical devices law.

Costs of doing business, both direct (e.g. through paying 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 appear disproportionately high compared with 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, as 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, advisory committees and third parties 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 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] These competencies are needed even where the regulatory authority relies on or recognizes regulatory decisions of other jurisdictions. 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 sufficient transition period should be established: 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 the manufacturer’s QMS, the authority should recruit and train staff members with experience in that field. Such staff may inspect or audit manufacturers, authorized representatives, importers and distributors. These skills should allow the regulatory authority to provide appropriate oversight and control throughout the medical device life cycle. [13]

Given the diverse nature of medical devices, the regulatory authority should, according to the priorities in regulating specific medical devices, over time, recruit technical staff members with a variety of appropriate expertise. [14] A career path, professional development and recognition of the value of regulating medical devices as a profession, may be important in recruiting and retaining staff.

Even advanced or well-resourced regulatory authorities find it impractical to have all these experts “in house”. Instead they create advisory committee(s), consisting of independent experts in a variety of fields to advise in specific technical areas. The regulatory authority remains responsible for the decision based on the advice. Performing a basic level assessment of the authority’s current regulatory competencies gives insight into the identified gaps in competencies. Guidance can be sought from WHO NRA Global benchmarking tool (under development), the Global Competency Self-Assessment of RAPS [15] (unpublished), the and IMDRF Good Regulatory Review Practices-Competence and Training Requirements for Pre-Market Reviewers (under development). According to the gap analysis, initial and continuing training of medical devices regulators according to a training plan should be implemented.
Chapter 4. Establishing a stepwise approach in regulating medical devices.

Stepwise approach
This Model recommends establishing a regulatory system for medical devices in a staged or stepwise approach – from basic to expanded controls. The regulatory framework must be sustainable, expandable and accommodate advances in clinical practices, public health needs and evolving technologies. The basic controls will form the foundation for the expanded controls. In order to promote international regulatory convergence and harmonization, this Model encourages countries to adopt the principles from internationally harmonized technical guidance into their legislation. [16]

Basic regulatory controls fall into three broad groups:

- those applied before a medical device is placed on the market;
- those applied when placing the device on the market; and
- those applied after the device has been placed on the market.

The stepwise approach will allow the regulatory authority to respond to national public health priorities and to progressively develop the capacity, knowledge and experience required. This approach helps the regulatory authority determine the resources needed for further implementation. Without effective implementation of basic controls, the elements of expanded controls will be of limited value and difficult to manage effectively.

The regulatory authority has an opportunity to reduce the demands on its own staff by either relying upon or recognizing the work or decisions made by another medical devices regulatory authority. Resources may then 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.

Reliance and recognition
The law should establish to what extent the regulatory authority may reasonably use the work of regulatory authorities in other jurisdictions in assessing evidence that a device conforms to national requirements. Examples of these techniques are:

- Reliance. This is the process whereby a regulatory authority may take into account and give significant weight to (i.e. rely upon) assessments performed by another regulatory authority or other trusted institution for reaching its own decision. For example, another regulatory authority authorizes a medical device to be placed on its own market and the national regulatory authority uses this information, possibly supplemented with information from the manufacturer, to reach its own decision.

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9 In this document “assessment” is used in relation to medical devices, in the same sense as “evaluation” is used for some other medical products.
• Recognition. This is the 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. For
example, a regulatory authority or CAB audits a manufacturer and issues it with a QMS
certificate. The national regulatory authority of the importing country accepts certificates
issued by another authority as proof of compliance with its own QMS requirements.

In order for the regulatory authority to decide whether to use either the reliance or recognition
technique, it must have a clear understanding of the regulatory system that applies within the country
where the medical device is manufactured. For example, medical device regulations in some
jurisdictions permit a manufacturer to follow minimal controls by restricting the marketing of the
device to export only, with the outcome that the regulatory authority of that exporting country may
not have performed any evaluation of the conformity of that medical device with its own regulatory
requirements. This places responsibility on the regulatory authority of the importing country and may
make reliance and recognition inappropriate. Reliance and recognition are not appropriate for the
assessment of specific requirements, such as language of labelling and electrical supply that do not
apply in the exporting country.

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 entities in other
jurisdictions, the regulatory version is not substantially different from the product version that is
proposed for placing on the market. Specifically for IVDs, the use of reliance or recognition as
mechanisms for marketing authorization is complex. This is due to the wide variance in classification
of IVDs in existing regulatory systems (which determines the level of regulatory scrutiny). For
instance, the current European system requires independent assessment for the high risk IVDs (Annex
means that most IVDs bearing a CE Mark are self-assessed by the manufacturer and have not been
subject to scrutiny by a European CAB (known as a Notified Body). This is another example where
knowledge of the regulatory system upon which reliance or recognition is based upon is important.

National responsibilities
There are certain regulatory activities that, by their nature, are inherently only within the competence
of the national authority. Examples include import 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).
Reliance and recognition are not appropriate to these activities.

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

In general, where a regulatory authority seeks to rely upon information from a counterpart in another
jurisdiction, it must first establish confidence with the counterpart authority, and agreement on the
exchange of confidential information. [18]
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 import controls and, requires post-market surveillance activities. The latter would typically include a system to act proportionately to reports of quality defects and serious adverse events associated with medical devices.
Figure 4. Basic level controls and enforcement for medical devices

## LEGAL FRAMEWORK

### Basic level controls and enforcement

<table>
<thead>
<tr>
<th>Pre-market</th>
<th>Placing on the market</th>
<th>Post-market</th>
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<tbody>
<tr>
<td>- Publish law, including definition, and regulations with transition period&lt;br&gt;- Establish medical device classification for regulatory purposes&lt;br&gt;- Establish Essential Principles of safety and performance&lt;br&gt;- Establish basis for reliance and recognition&lt;br&gt;- Establish requirements for Declaration of Conformity&lt;br&gt;- Establish requirement for manufacturers for a Quality Management System&lt;br&gt;- Establish requirements for labels and labelling&lt;br&gt;- Prohibit deceptive, misleading and false advertising&lt;br&gt;- Establish provisions for exceptional pre-market situations</td>
<td>- Registration of establishments&lt;br&gt;- Listing of medical devices&lt;br&gt;- Import controls</td>
<td>- Establish a system for vigilance reporting&lt;br&gt;- Require mandatory notification by the manufacturer of field safety corrective actions&lt;br&gt;- Establish a procedure to withdraw unsafe medical devices from the market&lt;br&gt;- Establish procedure to issue safety alerts to users&lt;br&gt;- Undertake market surveillance</td>
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Publish law, including definition, and regulations with transition period

The national law for medical devices will set out principles and broad requirements and delegate 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 must be allowed time to adapt to the law, i.e. a transition period. Where the necessary prerequisites are in place, a reasonable transition period is 3 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 role of the regulatory authority during the transition period is the development and dissemination of voluntary guidance documents to affected parties.

Establish medical device classification for regulatory purposes

The law should include a medical devices classification scheme to provide an efficient way of regulating each medical device according to its risk class. [2] It should include provisions for the regulatory authority to issue implementing acts and guidance on the classification of medical devices, including IVDs. The manufacturer is responsible for determining the class of its devices and its decision may be challenged by the regulatory authority (see chapter 2).

Establish Essential Principles of safety and performance

The law would also establish the fundamental 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 (see page 27), [6] or making a false declaration, would be grounds for enforcement action by the regulatory authority.
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 page 35).

Basic level controls and enforcement – pre-market
The law should require that only medical devices that are of good quality, safe and perform as intended may be placed on the market. The safe use and performance of most medical devices requires that the manufacturer, through its labelling, provides the user with information on how to properly install, use and maintain them.

Establish basis for reliance and recognition
The medical devices law should allow reliance and recognition techniques to be used by the regulatory authority to determine whether a medical device complies with the regulatory requirements of another jurisdiction and uses this information as the basis for allowing the medical devices to be placed on the domestic market. However, the national regulatory authority is ultimately responsible for determining whether a medical device may be supplied in its jurisdiction (see pages 22-23).

Establish requirements for Declaration of Conformity
The medical devices law should require an organization seeking to place a medical device on the market to draw up a written declaration of conformity to attest that its device complies fully with the law and all regulatory requirements.

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

- an attestation that each device that is subject to the declaration is of good quality, is safe and will perform as intended during its lifetime when used according to the manufacturer’s instructions and manufacturer’s stated intended purpose;
- information sufficient to identify the device/s to which the declaration of conformity applies;
- regulation under which the declaration is made
- 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 list of standards used in demonstrating compliance with Essential Principles

Establish requirement for manufacturers for a Quality Management System
To ensure devices are designed and manufactured to 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, and the associated records. The QMS should be appropriate to the specific characteristics of the manufacturer’s processes and products. This Model recommends the

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Standards indicated in this document are standards current at the time of publication. The reader should refer to the standards body to verify the current edition.

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 Essential Principles of safety and performance.

**Establish requirements for labels and labelling**

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 set language(s) 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. 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. [21]

Another function of labelling is to allow the identification of medical devices for example by batch or lot number, serial number etc. This allows traceability to facilitate FSCAs and helps in the reporting and investigation of adverse events. A recent development is the addition of an internationally harmonized Unique Device Identifier (UDI) to the label. [22]

**Prohibit deceptive, misleading and false advertising**

In addition to requirements for labelling of medical devices, consideration should be given to 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.

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Those basic regulatory controls should ensure that promotion, including online promotion:

- does not target inappropriate audiences;
- makes only claims that are supported by evidence;
- covers only medical devices that have been authorized for marketing;
- is consistent with indications for use and other information in the product labelling; 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.

Establish provisions for exceptional pre-market situations

In situations such as public health emergencies, exemptions from some regulatory requirements may be needed. 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 should establish defined exemptions from, and provide enforcement discretion for, compliance with certain requirements, for example, medical devices for humanitarian use, public health emergencies, clinical investigations, exhibition use, and medical devices donated to the country by charities or the manufacturer. Regulators should issue clear guidance on such exemptions. (See Chapter 5.)

Basic level controls and enforcement – placing on the market

Many countries depend almost entirely on imported medical devices. However, it is impractical for a medical device manufacturer to have a physical or legal presence in every country. Therefore, the law should require a manufacturer outside the jurisdiction to appoint an authorized representative within the country. [23]

Registration of establishments

A key element for basic level controls is to have oversight of medical devices placed on the domestic market and the parties responsible for bringing medical devices to the market. The law should require local manufacturers, authorized representatives, importers and distributors (in some cases the authorized representative may also be importer and/or distributor) who place medical devices on the market or make medical devices available for use in the jurisdiction, to be registered by the regulatory authority. [24] That registration should be subject to periodic updates by the manufacturer, importer, distributor, and/or authorized representative to ensure that it is current 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 is also 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.
Authorized 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. [23] Over and above this the 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;
- providing the regulatory authority with the information it requires when the manufacturer seeks authorization to market its devices;
- informing the manufacturer and 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 and distributor provides the regulatory authority with information on its place of business, the name and position of a responsible person and the manufacturer(s) it is acting for. Over and above this the 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 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, transport and, as appropriate, maintenance of medical devices;
- submit a regularly updated listing of medical devices placed on the domestic market.

If the device manufacturer appoints its importer or distributor to also act as its authorized representative, there should be a separate registration for each activity.

Listing of medical devices

The regulatory authority should establish a requirement and information system for authorized representatives of manufacturers outside the jurisdiction, importers and distributors to submit a listing of medical devices they place on the national market and update the listing periodically [24]. 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 placed on the market 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. The regulatory authority should have a means by which to provide information to other parties, upon request, on medical devices legally placed on the market.
It should be understood that listing is not of itself equivalent to, or evidence of, a marketing authorization.

**Import controls**

Apart from the basic controls of registering establishments and listing marketed medical devices, additional import controls may be appropriate. These may include 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. Collection of samples may be required for suspicious products or for routine analysis (e.g. batch testing for selected products – see ‘Lot verification testing of IVDs’ in Chapter 2). Once the processes of registration of establishments and listing of devices become mature, the imposition of these controls may be unnecessary.

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 indicate potential problems in the design, manufacture, labelling, storage or distribution of devices. It could also reflect improper device selection, installation, use or maintenance.

**Establish a system for vigilance reporting**

At the basic level, the regulatory authority should establish a system whereby users, patients and the manufacturer directly or through its authorized representative of medical devices can report problems, complaints or adverse events involving medical devices, and in particular those resulting in death or serious injury. [25] For high risk IVDs severe events may include higher than expected false-negative results. Vigilance reports may trigger investigation, trend analysis and/or possible FSCA or enforcement actions. [26] They may also prompt the regulatory authority to exchange information with regulatory authorities in other jurisdictions on similar occurrences elsewhere. [27]

**Require mandatory notification by the manufacturer of field safety corrective actions**

The law should require a manufacturer, either directly or through its authorized representative, to report to the regulatory authority in a timely manner 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 regulatory authority to respond to questions from the public, clinicians, media or government, and to exchange information with authorities in other jurisdictions.
Establish a procedure to withdraw unsafe medical devices from the market

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 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: withdrawal of registration of local manufacturers, importers or distributors; withdrawal from the list of marketed medical devices for particular medical devices or recall, quarantine and disposal of medical devices. Manufacturers may be required to review and to 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.

Establish procedure to 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. [26] Where possible, the text of any such alert should be discussed with the manufacturer or his authorized representative but the final decision lies with the regulator.

Undertake market surveillance

Market surveillance is the activity of the regulatory authority related to oversight of 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. [28]

Expanded level controls

Once the basic level controls have been implemented effectively and efficiently, the regulatory authority should consider implementing more advanced controls. To do so, the law should provide the legal basis for such expanded controls, the regulatory authority must have enforced effectively the basic controls, and additional resources (e.g. financial and technical expertise) must be available to it. Building on the basic level controls, expanded level controls are intended to be more comprehensive. In adopting expanded level controls, the regulatory authority may choose to implement one or more of those described below according to the priorities of the country.
Figure 5. Expanded level controls and enforcement for medical devices

### LEGAL FRAMEWORK

#### Expanded level controls and enforcement

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#### Basic level controls and enforcement

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Expanded level controls – pre-market

Create oversight of clinical investigations

The regulatory framework should provide the authority the power to regulate and oversee the conduct of clinical investigations. Manufacturers have various reasons for undertaking clinical investigations in a particular country. Primarily to collect and provide clinical evidence to a regulatory authority that a device for which it is seeking approval is safe and performs as intended.

The regulatory framework should clearly distinguish clinical investigations from market acceptability studies where a device is tested for factors such as ergonomics. These studies are not considered to be clinical investigations.

There should be a requirement that a sponsor (the individual or organization taking responsibility and liability for the initiation or implementation of a clinical investigation: such as: 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. [29] 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. A widely used international standard for the practice of clinical investigation is: ISO 14155 – Clinical investigation of medical devices for human subjects – Good clinical practice. [8]

The national regulatory authority should also establish a mechanism for periodic progress reports and for the reporting of serious adverse events that occur during clinical investigations. [30] In-country clinical investigations should generally not be required, unless there is a compelling and sound scientific reason.

Appoint and have 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, generally known as CABs. [31] Authorities may establish criteria for designation of CABs. 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 [33]. Based on the CAB evaluation, the regulatory authority makes final decisions on compliance. The CAB performs its evaluation under the oversight of the regulatory authority. [34] The regulatory authority may consider adopting mechanisms to rely upon, or recognize, certificates issued by a CAB, even those outside its jurisdiction or direct oversight. [35]

Recognize 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 and performance consistently throughout its life cycle. [36]

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12 Standards indicated in this document are standards current at the time of publication. The reader should refer to the standards body to verify the current edition.
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;
- **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. [37]

Preference should be given to international standards, e.g., those of the International Organization for Standardization (ISO) [38] and the International Electro technical 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 [39]; they can then be updated to stay current and can be revised much faster than legislation can be updated.

**Adopt a medical device nomenclature system**

The regulatory authority may require the manufacturer to identify a medical device using a generic 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 those purposes the regulatory authority should adopt an international medical device nomenclature system.

The GMDN (Global Medical Device Nomenclature) was endorsed by the GHTF as the global nomenclature system to be used by regulators for the classification, registration and exchange of information regarding medical devices for regulatory purposes. [40] [41] There are other established nomenclature systems such as the Universal Medical Device Nomenclature System (UMDNS) [42] and ISO 9999:2011 Assistive products for persons with disability—Classification and terminology. [43]

To implement the selected nomenclature system, the regulatory authority should publish a regulation and guidance specifying that that system shall be used 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 updated as new generic descriptive terms are adopted.

**Control 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, including on line promotion. If not, they should consider whether specific guidance is required.

### Expanded level controls – placing on the market

**Perform in-country quality management systems audits**

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 documentation used by the manufacturer in demonstrating device conformity with the Essential Principles and the associated declaration of conformity. Good record keeping practices and record retention policies should be observed in the QMS.

At the basic level the law requires manufacturers of all classes of medical devices to establish and maintain a QMS. As the regulatory authority moves to enact expanded level controls, the requirement in the law - should be supplemented by implementing acts, ministerial decree and/or guidance. At this expanded level, manufacturers are expected to have their QMS implemented. The regulatory authority or a CAB on its behalf will verify through inspection or audit the QMS of either a local manufacturer or the manufacturer in another jurisdiction.

**QMS audit**

The regulatory authority should establish means to verify that the manufacturer conforms to the relevant QMS requirements. The law should include provisions for the regulatory authority to designate or recognize [34] [35]CABs (see chapter 2) to perform QMS audits or otherwise gather and assess evidence of the manufacturer’s effective implementation of the QMS requirements. [6]

For countries in which most medical devices are imported, the option of reliance or recognition may be appropriate: 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. [35] [44] The receiving country thereby relies upon the information of the QMS audit or recognizes the decision of the other jurisdiction regarding the QMS audit. [45] 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.

**Perform review of submissions for compliance with Essential Principles.** [6]

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.

At the basic level, assessing the safety and performance of medical devices depends primarily on an assessment by another regulatory authority (see pages 22-23) reinforced by the manufacturer’s
declaration of conformity (see page 27). At the expanded level the national regulatory authority may establish a requirement for the pre-marketing review of a manufacturer’s submission. Guidance on the process for application and approval should be provided. This will usually be in the manner of a prescribed form or Internet portal.

Internationally harmonized formats for submission of technical documentation for conformity assessment purposes have been developed by various bodies, e.g. the GHTF Summary Technical Documentation (STED [46] [47]) and the ASEAN Common Submission Dossier Template (CSDT) [48]. These formats provide guidance for the presentation of evidence that a medical device conforms to the regulatory requirements for safety and performance.

The IMDRF Table of Content (ToC) is more recent. It describes a modular structure and format for such submissions in electronic form. Separate ToCs have been established for medical devices [48] and IVDs. [50]

National regulatory authorities are encouraged to adopt such harmonized formats if they require submission of technical documentation.

Sometimes there are situations that trigger a more extensive review of the manufacturer’s submitted technical documentation. 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).

Considerations (or “triggers”) for notification to the regulatory authority after initial approval could include change of specifications, change in mode of action on the human body or change in intended population for use of the device.

In pre-market assessment non-discriminatory country-specific requirements should be considered, e.g. local language labelling, electrical supply, public health policies and genetic characteristics of the population and health care delivery conditions. The regulatory authority may also 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.

Expanded level controls – post-market

Establish within the regulatory authority a post-market surveillance and vigilance reporting system

At the basic level, a system for vigilance reporting to the regulatory authority for adverse events involving medical devices in particular those resulting in death or serious injury, is established. At the expanded level, this may be extended to post-marketing surveillance and a capacity to monitor a manufacturer’s investigation of adverse events. 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 product development or pre-market evaluation and provide for corrective actions. This may include exchange of alerts internationally in a standardized manner. [27]

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 the manufacturer and its authorized representative, defining who fulfills 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.

Require 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 authorized representative or manufacturer 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. [51]

Inspections of registered establishments

The regulatory authority may inspect periodically 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 periodic basis. The registration may be withdrawn or suspended if non-conformities [52] are found during inspection.

Distribution of medical devices

The manufacturer of a medical device is required to implement a QMS covering activities of design and development, production, distribution, installation and servicing. However, quality, safety and performance of finished medical devices may be affected after release from the manufacturer by various conditions such as warehouse environment and practices, transportation, installation, servicing, duration of storage, and user training. The distributor shares responsibility for many of these activities. The manufacturer has the responsibility to:

- select appropriately qualified distributors (appropriate and adequate facilities, information systems, and qualified staff);
- specify the requirements for medical device storage, handling, transport, installation, servicing and record keeping;
- periodically verify the conformity of distributors with the contract requirements.
Collection of customer feedback and implementation of correction and corrective actions, post-market surveillance activities, implementation of field safety corrective actions for medical devices may be conducted by the manufacturer through cooperation with its distributor. A documented quality management system for a distributor ensures the conformity of medical devices through its life cycle.

With the exponential increase in internet connectivity those engaged in the manufacture, distribution and supply of SSFFC medical products have gained access to a global market place\textsuperscript{13}. Operators of the distribution chain should comply with a good practice guideline, such as a code of good distribution practice (GDP), as part of the global effort to combat SSFFC medical products. The requirements of GDP may be enabled by the implementation of a QMS in accordance with ISO 13485\textsuperscript{[19]}. The AHWP has published guidance on the application of ISO 13485 in an organization which distributes or imports medical devices.\textsuperscript{[53]}

\textbf{Local production}

Many countries import most of the medical devices used in 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 and have a procedure for authorizing devices to be placed on the market. In the case of for-cause inspections – e.g. suspected noncompliance or product problems – the regulatory authority would perform the inspection.

The regulatory authority should provide guidance specifically for local manufacturers.

\textbf{Provide for 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 SSFFC (see Chapter 5);
- institution of 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 as, if it is to be effective, it requires a significant budget and expert staff. In many jurisdictions such organizations do not exist in-country, but may exist regionally.

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

\textsuperscript{13} http://www.who.int/entity/mediacentre/factsheets/fs275/en/ (accessed 5 July 2016).
accreditations;
2 technical competence;
3 access to external experts, as needed;
4 adequate resources, such as specialized equipment;
5 internal QMS and instrument calibration facilities; and
6 conformity with standards.

Stepwise approach, harmonization, reliance, recognition

WHA resolution 67.20 emphasizes the importance of collaboration and harmonization. It requests the Director-General “to prioritize support for establishing and strengthening regional and subregional networks of regulatory authorities, as appropriate, including strengthening areas of regulation of health products that are the least developed, such as regulation of medical devices including diagnostics” and “to promote the greater participation of Member States in existing international and regional initiatives for collaboration and cooperation in accordance with WHO principles and guidelines”.

Regulation of medical devices is taking place in an increasingly globalized world creating a need for convergence. Accordingly, countries which align their medical device regulations with existing harmonized documents will promote this necessary regulatory convergence.

WHA resolution 67.20 also urges Member States to “engage in global, regional and subregional networks of national regulatory authorities, as appropriate, recognizing the importance of collaboration to pool regulatory capacities to promote greater access to quality, safe, efficacious and affordable medical products” and “promote international cooperation, as appropriate, for collaboration and information sharing, including through electronic platforms”.

Harmonization, recognition and reliance thereby contribute to more effective regulatory systems. They are an essential component of health system strengthening and contribute to better public health outcomes.
Figure 6. The elements indicated in red are those for which international regulatory harmonization guidance documents have been developed. The elements that may be implemented through reliance or recognition are indicated in blue.

### LEGAL FRAMEWORK

#### Expanded level controls and enforcement

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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. The topics are listed in alphabetical order.

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” 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), biologics and regenerative medicine products; cosmetics, food supplements or personal protective equipment).[54] [55] [56]

\[^{14}ностей продукты являются общей медицинской продукцией, для которой неясно, под какой закон она подпадает. Хотя могут быть сходство с несколькими регулируемыми продуктами. Комбинированные продукты - это продукт, состоящий из двух или более компонентов, которые регулируются как медицинские продукты, т.е. лекарство/медицинское устройство, или вакцина/медицинское устройство, что физически, химически или в другом виде скомбинировано или смешано и изготовлено в единую целостность (смоделировано из определения FDA http://www.fda.gov/CombinationProducts/AboutCombinationProducts/ucm118332.htm). Комбинированные продукты выходят за рамки этого Модели.

Herbal medicines according to WHO include herbs, herbal materials, herbal preparations and finished herbal products, that contain as active ingredients parts of plants, or other plant materials, or combinations. http://www.who.int/medicines/areas/traditional/definitions/en/
To be predictable and transparent, the regulatory authority 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, as appropriate for the type of device.

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. [60] [61] [62] [63]
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 or labelling 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. [58] [59] [60]

To safeguard public health, medical devices imported as donations should comply with all regulatory safety, quality and performance requirements and should not differ to those that are imported through a regular supply chain.

Regulatory authorities should therefore establish a mechanism to verify and authorize the importation of donated medical devices. 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 regulatory authority 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 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 donor at the donor’s expense.

Reprocessing of single use medical devices

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

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15 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.

16 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.
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 exist. These considerations include 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. 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 regulatory authority should consider the following: 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. [64][65] [66] [67] This applies equally to a health-care facility fully reprocessing single-use medical devices for reuse within its own facility.

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 electro medical devices**

Some medical devices, typically durable electro medical devices, are meant to be reused many times over a long design life. They may be subject to refurbishing by an organisation other than the original manufacturer to extend their service life, often for economic reasons.

Refurbishing can be described as a restoration of a device to a condition of safety and performance that is comparable to when new. This includes reconditioning, repair, installation of certain software/hardware updates that do not change the intended use of the original device, and replacements of worn parts.

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. [68] [69] [70] [71]

**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. [17]

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.

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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. 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. Falsified condoms, contact lenses, catheters, syringes and needles have been reported from Africa, Asia and Europe. 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. 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 sale of medical devices will assist in the prevention of SSFFC devices reaching users and patients. Balanced awareness raising amongst consumers, health-care providers and distributors can help to minimize the threat posed by SSFFC medical products whilst retaining confidence in health technologies. It is important to educate the general public to buy from reliable sources particularly on the Internet.

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

New technologies, including unique identifiers and track and trace technology, also provide increased assurance of the supply chain and can lead to the early detection of SSFFC products.

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

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

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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. [79]

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 the technical documentation (product dossier); [80]
- 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.

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. [81]

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.

**UNFPA Prequalification programme for IUDs and condoms**

A similar Prequalification Programme exists for the management of male latex condoms, female
condoms and intrauterine devices (IUDs). [82] The management of this programme was delegated
from WHO to UNFPA in 2005 for male condoms, and 2006 for the female condoms. WHO still
maintains the normative role in setting guidelines and requirements for the prequalification
programmes.

As for the IVDs, the prequalification programme for male and female condoms follows a systematic
process consisting of a detailed technical review of required documentation, on site factory
inspections, and product testing. This process determines whether the quality of products is in
accordance with international standards and WHO/UNFPA specifications and guidelines. UNFPA
maintains a list of prequalified manufacturers and sites that have successfully completed the
WHO/UNFPA prequalification process and have been approved by the WHO/RHR Technical Review
Committee for male and female condoms.

The findings are used to provide independent technical information on safety, quality and
performance of the products assessed to other UN agencies, WHO Member States and other interested
organizations. The UNFPA/WHO prequalification status, in conjunction with other procurement
criteria, is used by these entities to guide their procurement of the products covered by the WHO
prequalification programmes.
References


[22] UDI Guidance Unique Device Identification (UDI) of Medical Devices, IMDRF/UDI/WG/N7FINAL:2013 http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-


[49] Assembly and Technical Guide for IMDRF Table of Contents (ToC) Submissions (ToC-based submissions) International Medical Device Regulators Forum;2015(IMDRF/RPS WG (PD1)/N27R1).


[64] Therapeutic Goods Administration. ARGMD Single use devices (SUMDs) and the reuse of SUMDs; 2008.


[71] Placing on the market of fully refurbished medical devices. European Co-ordination of Notified Bodies Medical Devices; 2000, ; (NB-MED/2.1/Rec5; https://www.mdc-ce.de/fileadmin/user_upload/Downloads/Leitlinien/NB-Med/Recommendation-NB-MED-2_1-5_rev5_Pla}


[76] Buckley GJ, Gostin LO, editors. Countering the problem of falsified and substandard drugs. Institute of Medicine of the national academies; 2013, (https://books.google.ch/books?id=oBB1AgAAQBAJ&pg=PA59&lpg=PA59&dq=glucose+strips+falsified&source=bl&ots=VRKAFPmseN&sig=UffmUTamBwYU6DNLeun0ccCQQsBo&hl=en&sa=X&ved=0CB4Q6AEwAGoVChMlqpywppKcyQIVyesUCh0inAqZ#v=onepage&q=glucose%20strips%20falsified&f=false).


Further reading

Annex 1. Glossary

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

**accessory to an IVD medical device.** An article intended specifically by its manufacturer to be used together with a particular IVD medical device to enable or assist that device to be used in accordance with its intended use. *(GHTF/SG1/N071:2012) Definition of the Terms ‘Medical Devices’ and ‘In vitro Diagnostic (IVD) Medical Device)*

**accessory to a medical device.** An article intended specifically by its manufacturer to be used together with a particular medical device to enable or assist that device to be used in accordance with its intended use. *(GHTF/SG1/N071:2012) Definition of the Terms ‘Medical Devices’ and ‘In vitro Diagnostic (IVD) Medical Device)*

**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).

certainty 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).

certainty (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 (GHTF/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 (GHTF/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 their 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 (GHTF/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.org).
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 51:2014 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).


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 requirements 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 (GHTF/SI/G1/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 (GHTF/SI/G1/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 vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes (GHTF/SI/G1/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 (GHTF/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 (GHTF/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 (GHTF/SG1/N70:2011 Label and Instructions for Use for Medical Devices).

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

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

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

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

manufacturer. Any 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 its name; whether or not such a medical device is designed and/or manufactured by that person himself or on his behalf by another person(s) (GHTF/SG1/N055:2009 Definition of the Terms “Manufacturer”, “Authorised Representative”, “Distributor” and “Importer”).

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

market surveillance. Means the activities carried out and measures taken by public authorities to ensure that products comply with the requirements set out in legislation and do not endanger health, safety or any other aspect of public interest protection (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).

medical device. 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 (GHTF/SG1/N71:2012 Definition of the Terms “Medical Device” and “In Vitro Diagnostic
(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

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
thesystem (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

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).


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
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.

single-use medical device. A medical device intended by the manufacturer to be used on an individual patient during a single procedure and then disposed of.

standard. A document, established by consensus and approved by a recognized body, that provides, for common and repeated use, rules, guidelines or characteristics for activities or their results, aimed at the achievement of the optimum degree of order in a given context.

substandard/spurious/falsely-labelled/falsified/counterfeit medical products. There is currently no universally agreed definition of what used to be widely known as “counterfeit medicine”. Pending negotiation amongst Member States, WHO will continue to use the term substandard/spurious/falsely-labelled/falsified/counterfeit medical products.

technical documentation. The documented evidence, normally an output of the quality management system that demonstrates the medical device complies with the relevant principles of safety, performance and labelling specified through legislation.

user. The person, either professional or lay, who uses a medical device. The patient may be the user.

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

World Health Assembly. The forum through which the World Health Organization is governed by its 194 Member States.
## Annex 2. Hierarchy of regulation

<table>
<thead>
<tr>
<th>Level</th>
<th>Brief description</th>
<th>Examples</th>
<th>Examples of subject-matter regulated in the field of medical devices</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary legislation</strong></td>
<td>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 legislatives and/or executives.</td>
<td>Act of parliament; bill; statutory law; EU directive, ordinance; decree; executive order.</td>
<td>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 Principles of safety and performance; requirement for a quality management system; incident reporting; clinical trials; listing of medical devices; registration of establishments; process to recognize standards.</td>
</tr>
<tr>
<td><strong>Secondary legislation</strong></td>
<td>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.</td>
<td>Regulations, schedule.</td>
<td>Requirements for reliance; conduct of QMS audits; vigilance reporting; criteria for recalls and FSCAs; classification rules; responsibilities of an authorized representative.</td>
</tr>
<tr>
<td><strong>Guidelines</strong></td>
<td>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.</td>
<td>Technical standards, recommendations.</td>
<td>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.</td>
</tr>
</tbody>
</table>

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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.