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ASIAN HARMONIZATION WORKING PARTY

PLAYBOOK

FOR IMPLEMENTATION OF MEDICAL DEVICE REGULATORY FRAMEWORKS

Asian Harmonization Working Party

WORKING TOWARDS MEDICAL DEVICE HARMONIZATION IN ASIA

Playbook
for
Implementation of a Medical Device Regulatory Framework

Asian Harmonization Working Party
Technical Committee (TC)

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Message from AHWP Chairman

Asian Harmonization Working Party (AHWP) has come a long way. With the foresights, planning and tremendous determinations of its leaderships and member economies, has overcome numerous obstacles and challenges, paving the way for more countries to join its endeavor to Harmonization.

AHWP has captured the interests of many countries beyond Eastern Asia and extended into Middle East, Africa, and even Latin America. This is obvious from its expansion to 23 member economies including countries in the Middle East (Saudi Arabia, Kingdom of Jordan, Kuwait and United Arab Emirates), South Africa from Africa, and Chile from the Latin America region.

The growth of AHWP is in pace with the rising public expectations and demands in the respective member economies for the medical devices marketed in their member economies to be safe, effective, high quality, and perform according to the intended purposes.

Many countries around the world, particularly, emerging markets are beginning to realize the importance and needs for a robust and harmonized medical devices regulatory system to appropriately regulate the medical devices placed in their market. As regulators strive to develop their medical devices regulations in their countries, I would like to encourage them to join AHWP, to share and benefit from each other's experience and the established strength of common knowledge pool and expertise built over more than a decade. Joining the AHWP will allow member countries to benefit from the work and documents developed by AHWP working groups over the years and engage in information sharing and capacity building of its regulatory and healthcare professionals.

The AHWP Technical Committee worked very closely with its advisors to develop this playbook. The information provided in this playbook is primarily based on the Global Harmonization Task Force (GHTF) guidance documents and approach. The playbook is intended to guide regulators in the understanding and implementation of an efficient and cost-effective medical devices regulatory system.

I would like to express my thanks and appreciation to those who contributed to this playbook and urge regulators to benefit from it.

Saleh S. ALtayyar, Ph.D
Chair
Asian Harmonization Working Party

Foreword

Taken together, the member economies of the Asian Harmonization Working Party represent a large and growing share of the world's population. Although very diverse, these economies all show demographic and socioeconomic trends that pose important challenges for policymakers and public health officials. Among them are ageing populations (in some cases, rapidly ageing); a shift in the burden of disease from acute, mostly infectious, diseases to chronic conditions; rising economic prosperity; and global information flows. These trends have driven, and will continue to drive, growing demand for timely and equitable access to appropriate and affordable diagnostic and therapeutic medical device technologies as important elements of health care systems.

Implicit in that demand is the public expectation that those medical devices will be reasonably safe, of high and consistent quality, and perform as intended throughout their life cycle. Medical devices are increasingly used in the home or settings outside hospitals and by users other than trained health care professionals. They must be accompanied by instructions for use appropriate to the intended users. Information accompanying medical devices must also allow the clinician and patient or user to evaluate the risks and benefits of a particular diagnostic or therapeutic device. To fulfill those expectations, and as in other health product domains, countries round the world have established, or are in the process of establishing, regulatory systems for medical devices.

As their modes of action on or in the human body differ, it is important that those regulatory systems be appropriate and specific to medical devices, and not simply those for medicines, foods, biologics, or cosmetics. The laws and regulations should take into account the differences in industry structures, distribution channels, and technologies. A medical device regulatory system must also recognise the diversity of medical devices – from lower to higher risk – and accommodate the rapid iterative advances in device technologies.

The medical device regulatory model outlined in this Playbook is built on the foundation of guidance documents framed over twenty years by the Global Harmonization Task Force (GHTF). It represents a consensus view of experts, developed through a public consultative process, from regulators and the regulated industry in countries and regions with established regulatory systems, on basic requirements and good regulatory practices for medical devices. It provides a graduated set of controls – from the most basic to the more advanced – proportionate to device risks and across the medical device life cycle.

This Playbook is intended to guide AHWP member economies and others in the implementation of such a system, taking into account national legal frameworks, resources, and policy priorities. However, rules alone are insufficient. Each economy must assure that it also devotes sufficient resources and appropriately qualified people to the establishment, running, and continuing evolution of the regulatory system – now and in the future.

To the extent that it promotes international regulatory convergence, it is hoped this Playbook will guide member economies in implementing medical device regulatory systems that are efficient, predictable, transparent, and cost-effective in protecting and promoting public health, and in fostering continued innovation and international trade.

Michael B. Gropp
Advisor
Asian Harmonization Working Party Technical Committee

Preface

In line with the goal of the Asian Harmonization Working Party (AHWP) to study and recommend ways to harmonize medical device regulations in the Asian and other regions, the AHWP Technical Committee (AHWP TC) as the executive arm of the Party has worked over the years to develop technical documents and policy papers in recommendation of regulatory best practices to member economies.

It is important to recognize the necessity of a regulatory framework for medical devices and the benefits international convergence of controls may have to facilitate market access and reduce regulatory burden. However, while member economies are familiar with "why" regulatory controls are necessary, the question of "how"– how such recommended controls may be implemented - has been less frequently addressed. Given the cultural and socio-economic variations across member economies, implementation processes will inevitably vary and no single set of implementation plans prescribed can effectively address the needs of each country.

Nevertheless, a general set of guidelines for consideration can be provided to member economies to facilitate this process, along with the collation of existing tools, developed by the collective experience and expertise of various other international organizations, for the member economy's reference.

With the efforts of the AHWP TC in line with the goal of the AHWP, this playbook was developed to provide the guidelines and referenced tools needed to bridge this gap, to guide member economies in development of their medical device regulatory framework.

Joanna Koh
Chair
Asian Harmonization Working Party Technical Committee

Table of Contents

Acknowledgements i
Foreword ii
Preface iv
Convention for this Playbook 2
Introduction 3
Chapter 1: Objective of this Playbook 5
Chapter 2: Introduction to Regulatory Controls 7
2.1 Basic Regulatory Controls 8
2.2 More Advanced Controls 12
Chapter 3: Legislation and Policy Framework 16
Chapter 4: Phased Implementation Considerations 20
Chapter 5: Manpower Considerations 26
Chapter 6: Registration Databases 28
Chapter 7: Essential Principles of Safety and Performance and Recognition of Standards 30
Conclusion 36
References 38

Convention for this Playbook

Field Safety Corrective Action: any remedial action, including preventive and corrective, taken by a manufacturer for reducing the risk of death or serious deterioration in the state of health associated with the use of the medical device. The action includes product recalls, device modification, implant alert, device precaution and user warming.

Medical device: for the purpose of this playbook, refers to the definition developed by the Global Harmonization Task Force (GHTF) and adopted by the AHWP [1], and generally 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 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.

Note: The definition of a device for in vitro examination (note: in the text referred to as **IVD medical device**) includes, for example, reagents, calibrators, sample collection devices, control materials, and related instruments or apparatus. The information provided by such an in vitro diagnostic device may be for diagnostic, monitoring or compatibility purposes. In some jurisdictions, reagents and the like may be covered by separate regulations.

A member economy may develop their own guidance document for any detailed descriptions to define or clarify the medical device definition they may require.

Medical or IVD medical device dealer (in the text referred to as **device dealer**): is the manufacturer and/or the distributor and/or the importer unless specifically specified otherwise.

Introduction

Increased economic development, greater interest in healthcare and the globalization of the medical device industry has led to the pressing need for countries to develop regulatory frameworks for these devices in order to safeguard the public health and safety of their populations. Medical devices, which include IVD medical devices, are an essential part of healthcare and refer to a huge variety of reagents, equipment, appliances and software. With the quality of healthcare being highly dependent on the safety and performance of these medical devices that patients have access to, it inessential that member economies have an effective regulatory framework in place for oversight of the medical devices that enter their markets. The regulatory framework should be consistent with national health care and regulatory policies, and take into account available resources.

Particular to IVD medical devices, there has been rapid emergence of promising new technologies and products in responding to an increasing demand for personalized diagnosis and therapy.IVD tests results often influence therapeutic treatment decisions which significantly impact patient safety. As such, it is important to also consider the controls through which this group of devices may be effectively regulated. Although IVD medical devices are medical devices, two key aspects of how IVD medical devices are used make them different from other devices and will drive the need for separate aspects in the regulatory framework for IVD medical devices:

- IVDs never come into contact with patients; they always interact exclusively with specimens taken from patients to obtain information relevant for the patient. Once tested, the specimens are not reintroduced nor do they ever come back in contact with the patient.
- The risks posed by IVDs to patients are based on the information which they provide; therefore all risks to patients are indirect. Controls carried out at the time of testing, and the confirmatory tests which follow most IVDs help to mitigate these indirect risks.

The lack of regulatory controls eventually leads to a serious compromise in patient safety. For example:

- Lack of quality management systems (QMS) would lead to sub-standard manufacturing of medical devices and IVD medical devices.
- Inadequate documentation by dealers would result in loss of traceability of medical devices on the field.
- lack of post-market oversight to monitor imports and domestic supply of medical devices would allow defective or counterfeit devices to enter the local market.

Such situations potentially lead to a common outcome - that the very same medical equipment intended to treat a patient would potentially lead to his harm or death.

There is clear merit in encouraging countries to learn from the experience of others and to adopt best practices from more mature regulatory frameworks. A key advantage is that the path to implementing medical device regulatory controls from an existing framework is a well-trodden one, and information in the form of published guidance documents from international organizations and regulatory agencies is readily available on the internet for reference. The second advantageous that stakeholders that are well-versed in an existing set of regulatory controls in one jurisdiction can simply transpose their know-how to another jurisdiction, hence saving time and cost in extensive training that would otherwise need to be done by the regulator in order to help stakeholders to

adapt to different controls. Ultimately, the use of harmonized, coordinated controls enables cross-border leveraging of regulatory resources, reduces regulatory burden to the industry and expands public health benefits.

The importance of having a regulatory framework for medical devices is a widely held understanding that has been emphasized and iterated on multiple international platforms for decades. However, the way in which member economies may go about developing such controls has been less frequently addressed, given the complexity and variation across jurisdictions of processes for regulatory control implementation.

This playbook was developed in view of this need, to guide member economies in development of their medical device regulatory framework. It does not address other elements of health care delivery, insurance, payment or reimbursement, or health technology assessment.

Chapter 1: Objective of this Playbook

This playbook intends to provide considerations and guidance for member economies looking to develop their country's medical device regulation framework. This playbook also aims to guide member economies in leveraging existing country resources to improve their regulatory framework and strategically work towards internationally harmonized regulatory approach.

Through this playbook, member economies are guided to:

- Identify best practices and adapt them to their system
- Identify key considerations and potential limitations inherent in their system
- Ensure resources and priorities are aligned to elements of the regulatory framework
- Accelerate implementation of the regulatory framework, quickly and effectively
- Most effectively use their limited regulatory resources
- Provide a policy framework in support of domestic and international trade

Each member economy is noted to present distinct socio-economic backgrounds and hence different medical device market profiles. For instance, certain jurisdictions may have higher proportions of reprocessing activities or import-export activities. As such, each member economy may differ in their regulatory policies, depending on the controls needed for specific medical device activities in each jurisdiction. With this consideration, this playbook does not set out to prescribe regulatory controls to a granularity that would render it impractical to implement across the various member economies.

The rationale and risks in including or excluding certain regulatory elements such as good manufacturing and distribution practices, post-market surveillance and device registration, will also be provided for member economies to consider whether there is practical need to mandate such controls. Regulatory elements will be presented in tiers to illustrate possible implementation milestones.

Practical consideration for the implementation of each tier of regulatory control needs to be balanced against the member economy's financial resources, manpower and existing legal framework. Much like specifying the blueprint of a house, the guidelines in this playbook aim to guide member economies in planning for a basic implementation/harmonization framework, with the flexibility to permit further developments and enhancements to be done at subsequent stages.

Many of these guidelines are drawn from global experiences, international organizations and best practices of countries that have been through the process of establishing medical device guidelines. Drawing from such vicarious experiences will allow member economies to avoid known pitfalls during the implementation process and align their controls to global practices, in support of global efforts of convergence and harmonization of regulatory controls.

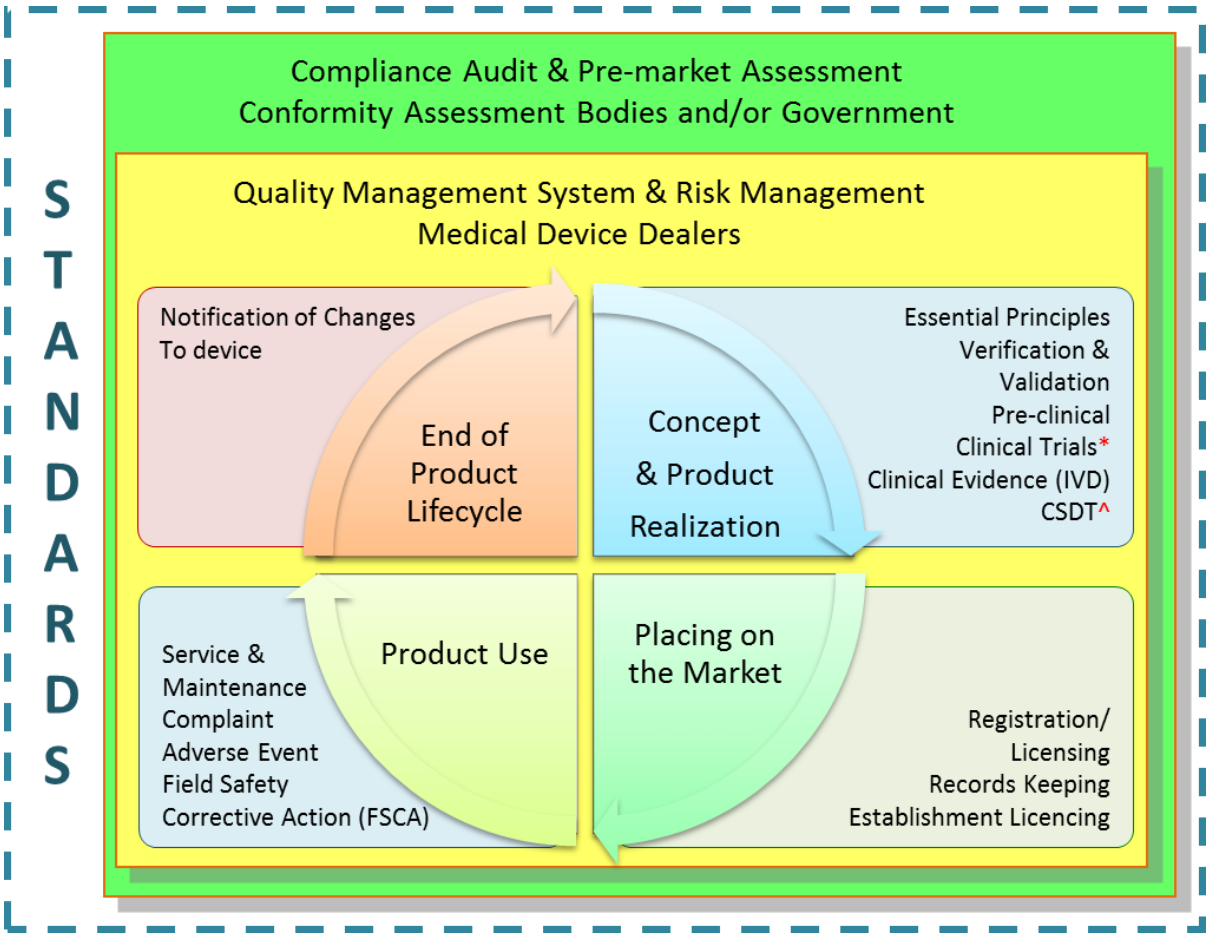
As many AHWP member economies import most of the medical devices used in health care in their territories, the focus of this playbook is on regulatory controls on importers and distributors, rather than on those who develop and manufacture devices. Nonetheless, each economy should ensure

that appropriate regulatory controls are effectively established, implemented, and maintained in a non-discriminatory manner for all medical devices, regardless of their country of origin.

Chapter 2: Introduction to Regulatory Controls

Regulatory controls globally have been developed with basic guiding principles in mind. The structuring of a regulatory framework should be done with the fundamental goal of the protection of public health and safety. However, this must also be balanced against the need for timely access to innovative medical technology and the facilitation of trade. Over-regulation can become counter-productive as medical professionals are delayed or deprived of new and effective treatment options for their patients. In achieving this balance, member economies will need to determine the appropriate regulatory controls by assessing the risks against the benefits.

In developing a regulatory model, consideration should be given to a framework that provides comprehensive oversight of the medical device (including IVD medical device) lifecycle activities. Policy makers should also consider where in the medical device life cycle regulatory controls are likely to be most effective and efficient.



** Medical device only*

^Common Submission Dossier Template – developed by the AHWP for pre-market submissions [1, 2]

Figure 1: Overview of the medical device lifecycle and the associated regulatory activities

In reference to the first quadrant of figure 1, it should be noted that importers and distributors do not typically carry out conceptualization and product realization activities and hence are not directly involved in developing the evidence to meet regulatory requirements in this lifecycle phase. Such

activities are usually carried out by the manufacturer. However, for AHWP member economies that import majority of their medical devices, they would not have jurisdiction over foreign manufacturers from which the devices are sourced. Such member economies may need to consider mandating local device dealers assume the responsibility of ensuring the requisite regulatory evidence from the foreign manufacturer is available, documented and meets local regulatory requirements prior to introducing the device on the local market.

It is recommended that regulatory authorities consider the GHTF regulatory model [3]. It illustrates a common framework implemented by regulatory agencies, globally. While the full model might be implemented over time there are a few key elements (Basic Regulatory Controls) that member economies might want to start with:

- registration or licensing of medical device dealers and products,
- pre-market controls -definitions and qualification of 'medical device'
- QMS and risk management process
- post-market vigilance and surveillance.

More advanced controls may be considered later in the implementation process, such as the classification and conformity assessment of medical devices.

2.1 Basic Regulatory Controls

2.1.1Registration / licensing of medical device dealers and products

Device dealer information facilitates governments in tracking medical device distributors, importers, and manufacturers. The licensing or registration process also imposes obligations on the parties for post-market surveillance; promotion; and appropriate storage and handling; and/or other duties. It is also used to identify the device dealers and identities of those involved in manufacturing, handling, and promoting or selling medical devices and, thereby establishing jurisdiction for enforcement of laws and regulations. This is particularly important in the case of follow-up for adverse events or field safety corrective actions. It is important to establish corresponding QMS standards, described in more detail in section 2.1.4, for identified medical device activities. Those duties should be linked to the corresponding systems of the medical device dealers.

Once the identity of manufacturers, importers, and distributors has been established by registration or licensing, member economies should seek to establish and maintain a registration database of medical devices being placed on the national or regional market. It should include the contact information for the manufacturer (including regulatory contact) and authorized importers and distributors. The main objective of the database is to capture information on medical devices distributed in the member economy's jurisdiction and the responsible parties, and to provide a level of identification and traceability in support of post-market surveillance and vigilance. More information on registration databases can be found in chapter 6.

The process of device registration need not always be tied to an obligatory process of conformity assessment, especially at the member economy's initial stages of framework implementation. Until the member economy develops the capacity to perform assessments of medical devices, it is recommended the registration process start with a focus on first capturing key device information.

2.1.2 Pre-market controls– definitions and qualification of 'medical device'

Across all elements of the regulatory framework, member economies need to identify and establish definitions for commonly used terms such as "medical device", "IVD medical device", "adverse event" and "device dealer". Definitions are the cornerstones of the framework as they are used to determine "who" and "what" are subject to regulatory controls and when. They are essential in ensuring that scopes of controls are consistently and clearly interpreted across all parties involved in the implementation and maintenance of the national regulatory framework. It is strongly encouraged to adopt harmonized definitions for medical device terms that have been established by international organizations and widely adopted, globally.

Defining what qualifies as a medical devices one of the first steps in establishing a device regulatory framework. Medical devices vary widely in form and function - for example, the range of devices that may be used for wound treatment alone may include plasters, liquid wound sealants, surgical staples, sutures, and negative pressure wound therapy equipment. A definition thus distinguishes the types of products the regulatory authority intends to have oversight on as medical devices. In addition, the definition for "medical device" is especially important in distinguishing medical devices from pharmaceuticals, which may already have a separately established set of controls in the member economy.

The GHTF has developed a proposed harmonized definition for "medical device" that is also adopted by the AHWP, which takes into account the variations in device form, defines a list of intended uses and excludes products (i.e. pharmaceuticals) that achieve their primary intended action by pharmacological, immunological or metabolic means. Member economies are strongly encouraged to consider this definition, which is widely adopted across jurisdictions.

A legalized medical device definition ensures prescribed controls over the identified range of products are enforceable. As this definition is typically general in scope, it may be necessary to define, through guidelines or policies, any detailed clarifications on what will - or will not - be regulated as a medical device to reduce ambiguity in interpretation. An example of such a guideline is the *Manual on Borderline and Classification in the Community Regulatory Framework for Medical Devices* published by the European Commission, which is updated periodically on the outcomes of the discussions of the working party on borderline and classification [4].

2.1.4 Quality management systems (QMS)

A QMS is defined as the organizational structure, policies, procedures, processes and resources needed to implement quality management, which aims to ensure predictable and consistent

outputs as well as continuous improvement, through corrective and preventive plans and actions, of the system.

In relation to medical devices, having an appropriate QMS ensures dealers can provide products and services that consistently meet customer and regulatory requirements. AQMS, combined with a risk management process, would cover the regulatory compliance of a dealer's methods, facilities and controls employed across the activities of the product lifecycle - design, manufacture, packaging, labelling, storage, installation, servicing and post-market handling of medical devices.

For medical devices manufacturers, this provides the requisite quality assurance across medical device batches, especially in vast majority of regulatory frameworks where conformity of medical devices to performance and safety requirements are reliant on declarations and paper-based conformity assessments. For importers and distributors, having a QMS assures continued conformity of the safety and performance of finished medical devices during storage, transportation and maintenance. Customer feedback and corrective actions of medical devices may also be conducted effectively by the importers and distributors in cooperation with the device manufacturers.

In specifying the QMS requirements or standards that dealers are to conform, member economies are encouraged to recognize harmonized standards in order to minimize regulatory barriers, facilitate trade and reduces the cost of implementing the QMS. Such standards include the widely-adopted ISO 13485, a QMS standard covering design and manufacture of medical devices [5], and the AHWP document "Guidance on the Quality Management System for Medical Device Distributor" [6], prepared by the AHWP Work Group 3. For more details on standards recognition, please refer to Chapter 7.

Elements of the quality system are periodically subject to internal audits, management review, and corrective or preventive actions that will maintain product quality. It also is necessary to ensure compliance and consistency through external audits performed on the device dealer. The AHWP Work Group 4 and GHTF Study Group 4 have developed technical guidelines on the regulatory audit of QMS, which member economies may reference [7, 8].

2.1.3 Post-market surveillance and vigilance

Member economies need to have a regulatory mechanism for continual oversight of the safety and performance of medical devices when used in the field. While pre-market review and registration pays attention to the design of the device to assure its quality, safety and performance, it is only at the post-market level that there can be oversight on the actual use of devices. Medical devices will inevitably be subject to various operating conditions upon placement in the market, and no amount of rigor in the pre-marketing clinical evaluation and review process can fully identify all possible device failures or incidents arising from device misuse or failure. Such problems may arise from batch manufacturing error, unfamiliarity of the end-user with the technology, or use of the device out of its intended scope of clinical

indications. It is through actual use that unforeseen problems related to safety and performance can be detected.

A comprehensive post-market surveillance framework ensures that medical device dealers monitor the safety and performance of the device in the field, which in turn facilitates identification of safety signals that may result in a decision to implement post-market corrective actions for devices already on the field. In this manner, timely and effective minimization of risk from device defects and misuse can be accomplished. Through such systems, it is hoped that the likelihood of recurrence of an adverse event will be minimized.

Post-market vigilance is a subset of surveillance activities that involve the submission of regulatory reports to regulatory authorities, usually as a result of identifying surveillance data that suggests an adverse event or potential adverse event has occurred. Member economies should establish and communicate clear definitions, timelines and criteria for post-market reporting to the regulatory authority, to reduce ambiguity and arbitrary determinations for the actions to be taken. Terms, requirements and criteria for post-market vigilance reporting can be adopted from the AHWP Work Group 2 and GHTF Study Group 2 guidance documents [9, 10].

For all stakeholders, the roles in post-market surveillance should be clearly defined.

- Regulatory authorities of member economies should maintain oversight on post-market activities, which include reviewing adverse event reports and monitoring investigation and field safety corrective actions from local device dealers.

- Device dealers, including importers and distributors, shoulder responsibility for most of the obligations in the post-market framework. For robust post-market regulation, member economies should require device dealers to have a post-market surveillance system in place as part of their QMS. Key surveillance activities to include in the QMS are maintenance of distribution records, complaint handling, reporting of unexpected problems of safety or usage (adverse events) detected by the surveillance system and carrying out corrective actions and preventive actions, including field safety corrective actions. The earlier cited QMS standard and guidelines in section 2.1.2 cover surveillance requirements for the QMS of manufacturers and distributors respectively [5, 6] and can be recognized by member economies for this purpose.

- Patients and users should be encouraged to report adverse events as they are the parties directly affected by problems arising from device use. Such reports may be addressed either directly to the regulatory authority, or to the local device dealers, or to both depending on national practices. Where the user informs the regulatory body directly about an event, the regulatory body should adopt administrative measures to ensure that the pertinent manufacturer is informed without delay of such a notification.

Access to post-market experiences of a device on an international scale will maximize the effectiveness of post-market surveillance. Member economies may wish to consider participation in international programs that facilitate exchange or dissemination of device

safety information between and to regulatory agencies. Such programs include the AHWP Safety Alert Dissemination System (SADS) and the GHTF National Competent Authority Reporting System (now maintained under the International Medical Device Regulators Forum (IMDRF)) respectively.

2.2 More Advanced Controls

2.2.1 Pre-market controls - classification and conformity assessment of medical devices

A more in-depth pre-market conformity assessment of medical devices for quality, safety and efficacy prior to their inclusion on the medical device registration database and supply on the local market is a huge regulatory burden. Not all member economies may have the capacity to perform this assessment, especially in the early stages of establishing the regulatory framework. As such, the registration process may start with the simple approach of having a list of medical devices which are on the market in the member economy (see 2 above).

Member economies that mainly perform import of medical devices from other jurisdictions that already have an established device assessment process may choose to generally recognize the approval or clearance granted by that other jurisdiction. It is important, however, that the member economy is aware of the assessment criteria of the jurisdiction it chooses to recognize, and ensure there are no contradictions or gaps with those of its own local regulatory framework and health policies. In addition, for reasons of political accountability, the national regulatory authority of the member economy should always retain the authority and autonomy to reach its own decision regarding approval or clearance of the medical device.

Where resources and regulatory capacity permits, member economies may then proceed to prescribe requirements for detailed review of technical information supporting the essential principles of safety and performance.. The review may be performed by the individual authority, affiliation of country authorities, or organization for multiple jurisdictions through international agreement. Acceptance of international standards will facilitate this approach.

It may also be necessary to consider titration of conformity assessment requirements against different categories of medical devices, including identification of exceptions to the pre-market conformity assessment process. However, the identification and qualification of a category of devices for exemption from the conformity assessment must be accompanied by safeguards by the member economy to ensure the exemptions are not abused, which may be administered by additional requirements and limitations to the device dealer’s activities and licenses.

To this end, a recommended approach as basis for such consideration is the risk classification of medical devices. Risk classification forms a key element of medical device regulatory frameworks globally and allows the methodical and systematic titration of regulatory requirements for premarket conformity assessments, including the identification of low-risk device categories for exemption from conformity assessment. Having a transparent rule-based classification system provides clarity and predictability to manufacturer and regulator on the

applicable requirements. The GHTF study group 1 has developed a set of published guidance documents on medical device classification principles for both general and in vitro diagnostic medical devices. These guidelines are readily available for adoption and currently widely-implemented by various regulatory bodies. By these guiding principles, examples of such very low risk devices identified may include wooden tongue depressors and simple non-sterile plasters, specimen collection devices and microbiological culture media.

2.2.2. QMS– oversight of audit of the device dealers' QMS

Where external audits of QMS are outsourced to third-party auditing organizations (i.e. conformity assessment bodies (CABs)), member economies may eventually need to build the capacity for oversight on the QMS audits conducted by CABs.

The merit of outsourcing external audits of QMS to third-party auditing CABs is the greater coverage in the auditing of dealers to recognised standards, especially foreign manufacturers, as opposed to relying solely on the resources of individual countries. This system can especially be leveraged on when member economies adopt harmonized QMS standards. However, in such a system the regulatory authority is recommended to have oversight of the third party auditing organizations ensure uniform level of assessment practice and competence in CABs.

2.2.3. Clinical investigation & clinical performance study controls

To demonstrate safety and performance of a device for its intended use, it may be necessary to provide clinical data from scientific literature and/or via clinical investigations or clinical performance studies. In the case of clinical investigations, the aim is to assess the safety and performance of the device and evaluate whether the device is suitable for the purpose(s) and the population(s) for which it is intended. Clinical performance studies for IVD medical devices are done to demonstrate that their performance specifications (e.g. sensitivity and specificity) are appropriate for clinical needs, and typically in comparison to established methods of diagnosis.

The need to protect human subjects from unnecessary or inappropriate experimentation must be balanced with the need to protect public health through the use of clinical investigations where they are indicated. Member economies thus need to consider the types of requirements and controls needed for the supply and use of investigational or performance study devices on humans for the purpose of their verifying safety and performance.
Such requirements or controls for consideration are:

- ethical oversight of clinical investigation
- prescribing good clinical practice guidelines
- licensing or registration of investigational device dealers
- establishing a clinical trial registration database
- review and approval of investigation protocol design and
- clinical investigation adverse event reporting procedure

A properly conducted clinical investigation should ensure the protection of human subjects and the integrity of the data obtained for the purpose of conforming to the essential principles of safety and performance. In addition, to prevent unnecessary or inappropriate experimentation, clinical investigations should only be carried out by a manufacturer following a risk management process to identify the clinical data needed to support safety and performance of the device, and a clinical evaluation of existing data to determine the need for a one in the first place.

In the case of IVD medical devices, which analyze specimens derived from the human body, the characteristics of clinical performance studies differ from the clinical investigation of non-IVD medical devices. During clinical performance studies, these devices largely do not require contact with patients and rarely require their results to be used for patient diagnosis. As such, it should be considered whether controls prescribed for the clinical investigation of non-IVD medical devices are appropriate for clinical performance studies of IVD medical devices. For example, the approval from an ethics committee may not be required for clinical performance tests for certain IVD medical devices.

Member economies may reference the technical guidelines developed by the GHTF Study Group 5 for clinical investigation and clinical performance studies [11] and the international standard (ISO 14155) for Clinical investigation of medical devices for human subjects, which addresses good clinical practice for clinical investigations (note: standard does not include IVD medical devices) [12].

Further principles and technical details of the other elements of the recommended regulatory controls of a model regulatory framework are covered and can be found in the guidance documents developed by the AHWP, the GHTF and its successor the IMDRF, as well as publications by the World Health Organization (WHO). The web links to these documents and publications are provided [9, 13], which member economies are recommended to reference in supplement to the Playbook.

It must be emphasized that elements of the regulatory framework need to first be supported by a robust policy and legal framework for effective implementation and enforcement. This is further discussed in chapter 3. Without a strong policy and legal basis for the prescribed controls, there would be a lower than desired level of compliance and the member economy. With lack of legal clout, member economies would face difficulty in enforcing the requisite regulatory controls.

In addition, as a technical foundation for the regulatory framework elements, recognition by the regulatory authority of standards, especially international standards, may be considered in order to minimize regulatory barriers and to facilitate trade across borders. Application of relevant recognized standards is one means, usually preferred, by which the manufacturer may demonstrate that a device conforms to the regulatory requirements for safety, performance, and quality. Such international standards also often reflect a consensus view of the current “state of the art” for a particular technology. The regulatory authority of the member economy, in defining standards and guidelines for QMS for manufacture, import and distribution, thus sets the regulatory requirements and audit criteria for these activities. To the extent that national standards are aligned with

international standards, domestic manufacturers will be better prepared to export their products to other countries in which those standards are recognized. Standards are further discussed in Chapter 7.

Member economies are strongly encouraged to implement components of regulatory frameworks in a progressive manner. Depending on policy priorities, manpower and financial resources, the elements incorporated in each phase of the implementation can be strategized, as covered in the next chapter.

Chapter 3: Legislation and Policy Framework

Member economies will need to put in place legislation and policies that address the various activities in the medical device lifecycle. Sectoral legislation will be drafted to be consistent with general constitutional and legal frameworks and administrative systems. In jurisdictions that have an implemented framework, there is a general hierarchy of regulatory controls to ensure effective implementation. The hierarchy may be as follows:

1. National Legislation (e.g., designation of regulatory authority, political accountability and oversight, funding, scope of regulation, enforcement provisions)
2. Regulations (decrees, etc.) issued by the national regulatory authority pursuant to, and implementing, the legislation
3. Administrative controls (e.g. guidelines, forms and templates published by regulatory body)
4. Stakeholder-regulator communication avenues (e.g. training sessions, phone, email)

Member economies that have yet to introduce comprehensive legal provisions may draw from a diversity of national regulatory frameworks in determining their own requirements. However, it is important that the framework is adequately designed based on available resources and adapted to the local medical device market.

In developing legislation and regulation, Member economies should also bear in mind international principles of good regulatory practice such as those in the *APEC-OECD Integrated Checklist on Regulatory Reform*[14, 15], jointly produced by the Asia-Pacific Economic Cooperation (APEC) and Organization for Economic Co-operation and Development (OECD). Amongst other recommendations is performance of a regulatory impact assessment as part of development of regulation.

Member economies are encouraged to perform a gap analysis of existing controls prior to planning for the regulatory framework. This may be done by first reviewing existing national controls, if any, of medical devices and considering where existing controls are inadequate to address all medical device activities. With the review, a plan can then be constructed for a regulatory framework to introduce such controls that may address the gaps identified. By their nature, medical devices cannot be treated as most consumer commodities. The regulatory framework must therefore reflect the special considerations to be applied to such products. While the aim of the framework is to minimize regulatory gaps as far as possible, consideration should be made to prevent overlapping or contradicting regulatory controls that will otherwise unnecessarily increase regulatory burden.

An example flowchart of how the process of development of legislation may be carried out as is given below.

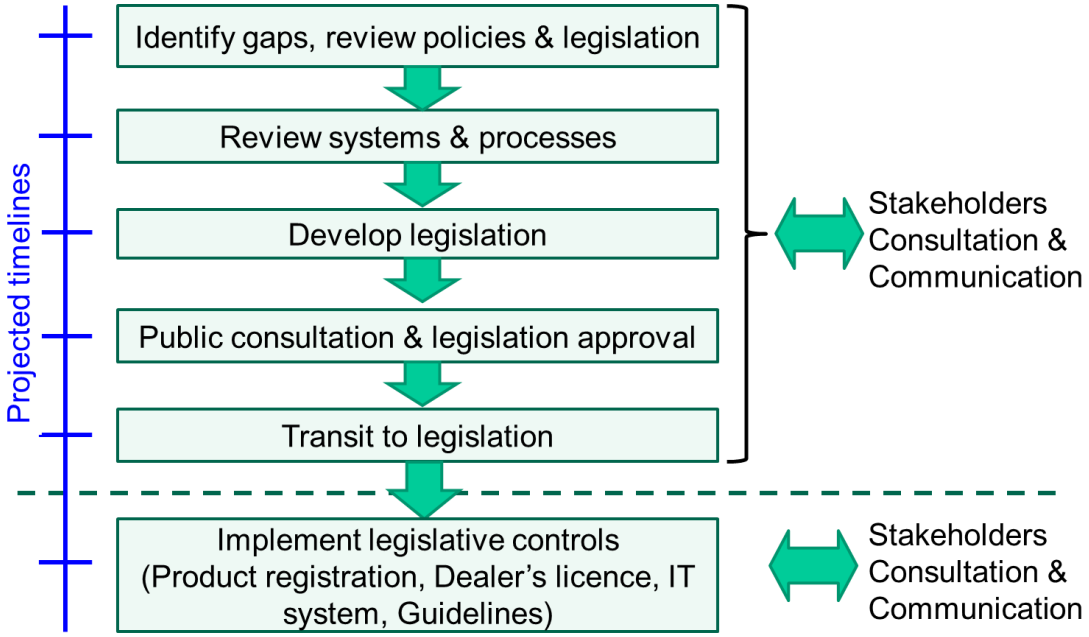


Figure 2: Example process of development of legislation

In the process of gap identification and policy review, it is critical for member economies to identify and engage the relevant stakeholders who would be affected by the regulatory controls to be introduced (e.g. medical device manufacturer, product owner, authorized representative, importer, distributor, clinicians, end-users, etc.).

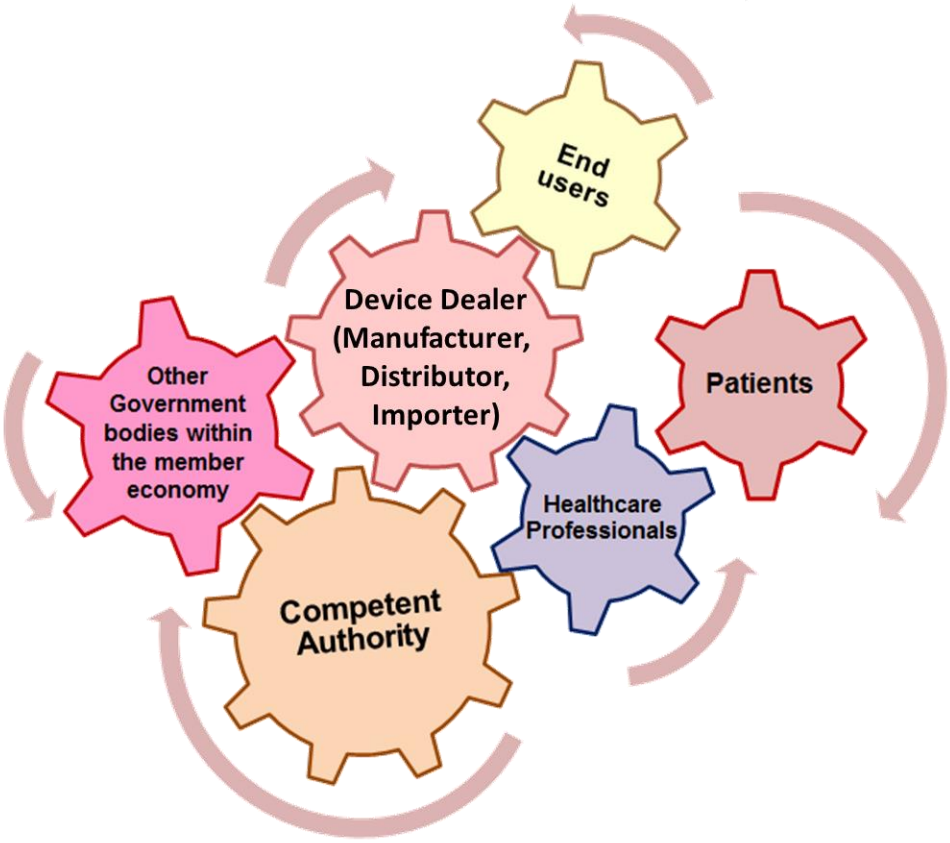


Figure 3: Identifying stakeholders, understanding their interaction and communication of their regulatory roles is crucial for effective regulations

Periodic consultation sessions with the identified medical device stakeholders during the process will allow better understanding of the member economy's clinical practices and medical device industry activity profile. They can help ensure that controls are developed in a manner that can be practically implemented in the member economy, while still achieving the aim of ensuring quality, safety and performance of medical devices.

In addition, such consultations provide an opportunity to identify and address specific device activities and needs in the member economy early in the policy planning process. For example, a member economy with a high amount of import-export activity may consider incorporating in their proposed framework a means for transshipment companies to readily import unregistered medical devices - that would otherwise not be permitted –solely for export.

Member economies will also need to communicate and coordinate across government bodies to ensure that regulatory controls are optimized with minimal unnecessary overlap and contradiction. Some non-exhaustive examples of potential existing general controls are:

1. Advertisement and promotion
2. Import-export procedures
3. General business licensing
4. Clinical practice or IVD diagnostic guidelines
5. Environmental controls (e.g. irradiating apparatus, explosives)
6. Disposal procedures (e.g. biohazards)
7. Transboundary movement of used parts and devices for the purpose of repair or refurbishment

Member economies will also have to consider an appropriate transition time for implementing a regulatory framework for the first time or for changes based on the significance of the changes.

An implemented legislation and policy framework will rarely remain stagnant and needs to be reviewed and refined from time to time in response to changes and new information and advances in technology and clinical practices. A process flow is illustrated below of a possible approach to the refinement of an existing framework.

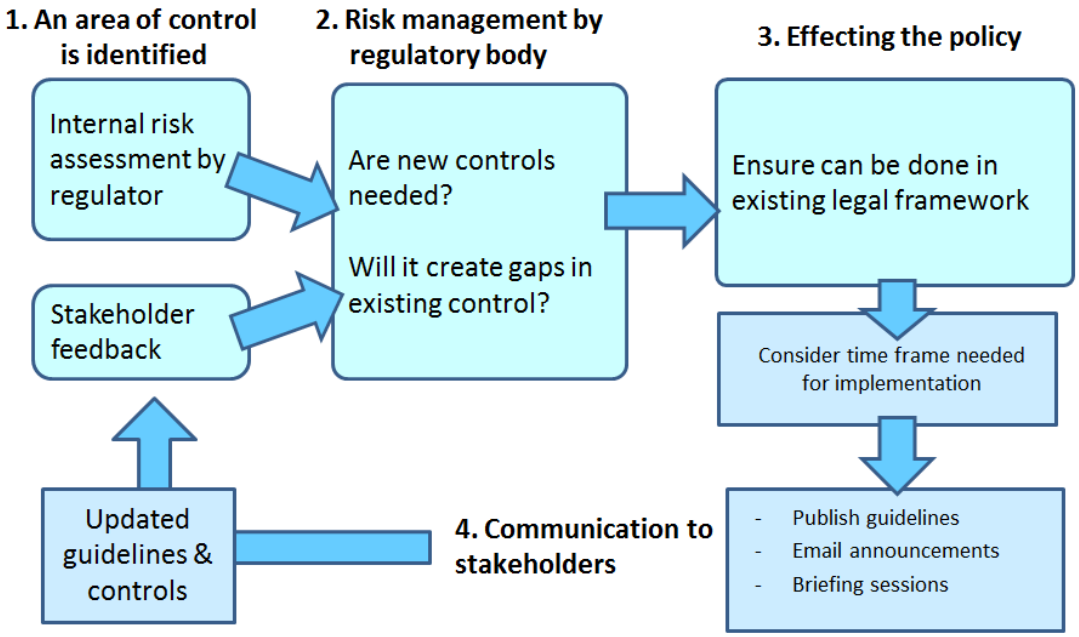


Figure 4: Example process flow for policy refinement of existing regulatory framework

The ongoing refinement ensures a balance in facilitation of market access to medical devices while protecting of public health and safety.

Finally, appropriate legal penalties should be tagged with regulatory requirements to ensure the effective administration and enforcement of regulatory requirements. Having clear enforcement policies on an operational level also enhances enforcement actions, allowing action against violators to be carried out in a fair and uniform manner. This is critical to effective compliance to the regulations in the interest of protecting public health.

Chapter 4: Phased Implementation Considerations

To effectively implement the elements of the regulatory framework, the responsibilities of stakeholders in the member economy should be first clearly defined.

Member economies may opt to select different regulatory systems, depending on available resources. One system is where the national regulatory authority is responsible for the national medical device regulatory activities and also undertakes a majority of them itself. The other utilizes designated CABs to carry out some of the tasks on behalf, and under the supervision, of the national regulatory authorities [3].In both systems, the responsibility for ensuring that a medical device complies with the regulations that apply to it, ultimately resides with the manufacturer.

The implementation and maintenance of the regulatory framework for ensuring safety and performance of medical devices is enhanced via the participation and cooperation of each stakeholder. As such, transparency, consistency and clarity in communication of regulatory requirements are paramount in achieving a high level of compliance from device dealers. Unpublished or ambiguous requirements leave device dealers uncertain of existing controls and suspicious of preferential treatment and/or corrupt practices. Lack of clarity and consistency in requirements also discourages trade as device dealers refrain from establishing businesses in the jurisdiction.

Formal consultation mechanisms and public notice and opportunities for submission of comments remain important elements of the process during implementation and changes. It is also important that the regulatory authority coordinates closely with other ministries and government departments, e.g., customs and health ministries, to ensure consistency and to avoid conflicting requirements.

When the elements of a regulatory framework have been decided and assigned to responsible parties, clear communication between all parties is essential to ensure smooth implementation. The regulatory authority, who will eventually lead the implementation in accordance to national policy/law, will be the central figure in communicating the intended implementation plan to all stakeholders. This may include such forms of communication, but not limited to:

- published guidance documents that are readily available to all stakeholders (e.g. internet)
- periodic training and briefing sessions on the regulatory controls implemented
- establish a mailing list that stakeholders may subscribe to for periodic updates
- communication and feedback mechanism from stakeholders to regulatory authority (e.g. phone, email)

Progressive implementation can be done via the Progressive Regulatory Framework illustrated in the Global Harmonization Task Force Regulatory Model [3].

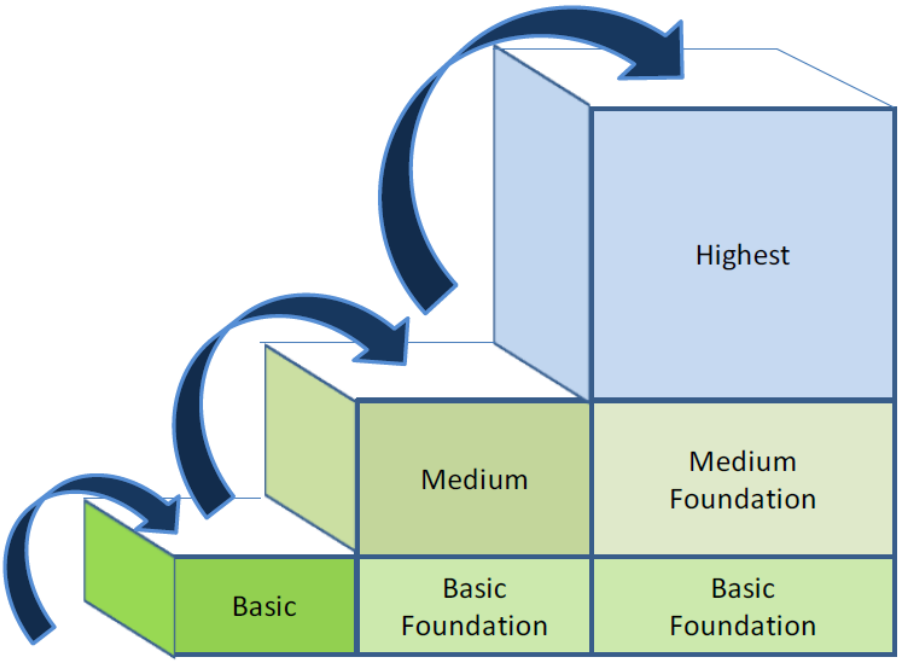


Figure 5: GHTF Progressive Regulatory Framework

Summarily, an example of a phased implementation plan for a medical device framework is given below. Note the below does not account for phase-out of existing regulatory controls, which will also need to be considered and may vary across member economies.

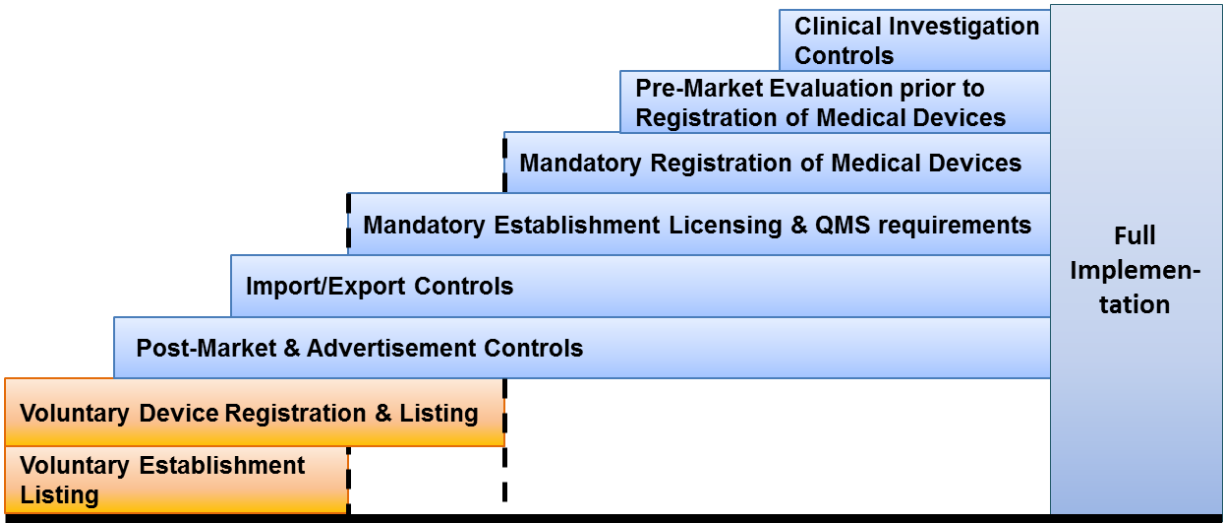


Figure 6: Possible phased implementation plan for a medical device framework

In addition, an example of the detailed activities and responsibilities mapped out for each party in each phase of the progressive regulatory framework is provided below. For certain framework elements, there may need to further phase implementation in tiers defined at the levels of individual elements. In the example below, for pre-market, post-market, QMS and clinical controls, this is shown phased in a three-tier approach.

Table 1: Three-Tiered Progressive Framework of Responsibilities

Legend:
1st tier – Basic
2nd tier - Intermediate
3rd tier - Advanced

	National Regulatory Authority (NRA)	**CAB (if applicable)**	**Device Dealers Manufacturer (M)/ Dealer (D)**
General	• Link government policies and priorities to regulatory system • Consult stakeholders • Draft and adopt laws and regulations • Appoint and oversee CABs • Maintain adequate resources • Enforce laws and regulations • Import/export controls	• Comply with CAB designation criteria (of NCA) • Maintain accreditation, if required • Maintain appropriate qualified resources	• Comply with national requirements(M or D) • Investigate and evaluate complaints and product experience information(M)
Post-Market	• Establish Adverse Event Report (AER) Requirements • Evaluate AER received • Monitor investigation and field safety corrective actions (FSCA) • Handle information concerning AERs.	• Assess device dealer's Post Market Surveillance (PMS) and vigilance reporting systems during QMS audits • Assess device dealer's Field Safety Corrective Action systems during QMS audits	• Establish and maintain post-market surveillance system (part of QMS) (M and D) • Prepare and submit AERs (M and D) • Conduct Field Safety Corrective Actions (FSCA) (M and D)
	• Increased robustness of the post-market surveillance system including a strong inspection program (there can be various levels of activities) • Establishment of a post-market testing ability – e.g. appropriate mixture of dedicated laboratory and contracting out of testing to accredited labs		

QMS	• Establish QMS requirements • Recognize QMS standards covering medical devices (e.g. ISO 13485) • Establish audit requirements including frequency	• Conduct device dealer QMS audits • Assess device dealer's Corrective actions from audit findings	• Establish and maintain appropriate and effective QMS, including risk management (e.g. ISO13485, ISO14971) (M) • Submit to periodic audits (M) • Respond to audit findings (M)
	• Oversight of audit of the device dealers' QMS		
Pre-Market	• Define 'medical device' • Define IVD medical device • Establish system for registration of and device dealers • Establish a device listing system		• Determine whether product is a "medical device"(M) • Registration of manufacturer and /or device dealer (M and/or D) • Provide listing of devices on the market (M and/or D)
	• Establish MD (general and IVD) classification rules • Establish 'essential principles' of safety and performancefor medical devices • Recognize standards • Recognize compliance with essential principles through market authorization by at least 1 respected regulatory authority • Registration of higher risk medical devices	• Assist in determination of medical device classification • Conformity assessment of device dossier • Verify standards appropriately applied to device	• Determine device class (general and IVD) (M) • Determine appropriate Essential Principles • Apply appropriate standards • Prepare, hold and maintain technical file(QMS) (M) • Prepare and hold Declaration of Conformity (M)
	• Define pre-market conformity assessmentsystem by class of medical device (based on general and IVD classification rules)		• Submit product dossier(M and/or D)

Clinical	• Enforce human subject protection and ethical framework		• Medical devices -conduct clinical evaluation (ongoing) (M) • IVD medical devices – provide clinical evidence (scientific validity, analytical performance and where appropriate clinical performance) (M)
	• Establish and oversee ethics committees • Oversee clinical investigations • Enforce laws and regulations	• Audit/assess clinical investigator's process for clinical evaluation (MD) or performance studies (IVD)	• As needed conduct, monitor, report clinical investigations for general medical devices (per ISO 14155) • As needed conduct , monitor and report clinical performance studies for IVD medical devices (per ISO TC 212 standard – under development)
	• Evaluate adverse event reports	• Assess clinical evaluation and clinical evidence during conformity assessment	

In planning the phased implementation, a member economy would inevitably be faced with a vast range of unregulated medical devices already on the market. When phasing in mandatory registration regulations of medical devices, care must be taken to ensure the flow of manufacture, import, supply and maintenance of these devices are not unintentionally disrupted, and ensuring national healthcare needs are not compromised.

On the other hand, devices that have already been supplied on the market prior to implementation of regulatory controls, though impractical to call for termination of their use following implementation, would still require regulatory oversight to ensure they continue to perform as intended in a safe and performing manner. Similarly, competitive devices should all be subject to the same levels of control. To this end, a member economy may choose to identify this particular group of devices and impose a specified set of requirements on devices already supplied, such as post-market surveillance controls, and set reasonable transition periods (e.g. voluntary registration phase) to allow their manufacturers and distributors to come into compliance with the new requirements.

Member economies are also encouraged to consider priority implementation of post-market and advertisement controls in transitioning from voluntary to mandatory regulatory controls. This allows

the safety, quality and performance concerns of medical devices that are already in use on the market to be monitored and addressed soon as possible.

Chapter 5: Manpower Considerations

Successful implementation of a regulatory system will depend not only on the legal framework, but on human capacity and administrative systems. Manpower planning is a common challenge for regulatory bodies. Both headcount as well as expertise of the staff hired are important and need to be considered for overall operational effectiveness of the regulatory body. Similarly, motivation and retention of an experienced and skilled workforce is essential.

In the early stages of planning for the regulatory framework elements described in Chapter 2, member economies may start identifying the corresponding activities and organization structure needed to implement the framework element at an operational level, then plan for the training, expertise and headcount required for that activity. A simplified example is illustrated below.

Table 2: Example of identifying regulatory authority (or CAB) activities and allocating manpower

Mechanism	Activity by Regulatory Authority	Manpower
Stakeholder Communication & Relations	Communication with stakeholders on regulatory controls, provide advice & obtain feedback	Administrative manager Administrative staff
Product Qualification & Classification	Advise on qualification as a medical device or IVD medical device & classification of specific products	Technical specialists
Import / Export Monitoring & Control	Liaising with Customs officials Compliance checks of imports	Customs liaison officers
Standards Recognition	Review of standards & maintain recognized standards list	Technical specialists
QMS Audit	Assess and qualify QMS of device dealer	Auditors
Dealer's Licensing / Registration	Review of device dealer applications	Team leads Technical specialists Experts (may be external)
Product Registration	Screening and/or conformity assessment of submissions	
	Peer / Expert committee review	
Post market Monitoring & Control (both post-market & clinical activities)	Review of AE or FSCA reports	Team leads Review officers Enforcement officers
	Enforcement of regulatory controls	
Clinical	Audit or assess clinical evaluation process	Technical specialists Auditors
Finance	Billing, collection & refund of fees	Accountants
IT Support	Update and maintain IT infrastructure for submissions, registration databases and materials published online	Software & IT engineers

One of the first steps in estimating manpower needs is to map the market profile of the member economy. Such information may include the number of device dealers and medical devices on the market, from which manpower requirements for the processing of device dealer licenses and device

listing / registrations can be estimated. Such data may also aid in determining appropriate transition periods.

As noted in Chapter 4, where manpower constraints exist, outsourcing of activities, such as product review and QMS audits to CABs, may be done by the regulatory authority. However, there is consequently the added challenge of maintaining oversight, conveying requirements and ensuring uniformity, consistency and fairness of the CABs in their administration of controls.

It is important to note that the early stages of planning of the regulatory framework do not call for much manpower, and staff would be primarily involved in the planning of legislation and policies as well as communication with stakeholders. Resources can be conserved at the early phase. With each subsequent stage in the phased implementation, manpower can be gradually increased to accommodate the greater burden of activities that follow.

Medical device regulatory decisions must be based on objective science and sound analytical foundation. As such, regulators charged with the administration of regulatory controls need to have the requisite scientific expertise and knowledge of the law through which they act. With the diversity of medical devices in the market, recruiting regulators with appropriate fields of expertise – such as medical professionals, engineers and scientists - may be needed, depending on the type of regulatory activity to be implemented. In general, it is not sufficient simply to direct regulatory staff accustomed to evaluating medicines to evaluate medical devices. Staff with expertise in fields such as materials science, electrical and mechanical engineering, software, risk management, and telecommunications will be necessary.

Prospective staff with medical or scientific qualifications may, at present, be easier to find than staff with prior regulatory expertise, with the comparatively limited certifications and qualifications globally in this area. As such, training programs may need to be established by the regulatory body to educate new staff on basic regulatory science, the current regulatory framework through which they would operate and a fundamental understanding of the legal framework under which the controls are administered.

Even in a fully-implemented regulatory framework with an established regulatory workforce, ongoing refinements to the framework may be made in response to changes in the medical device industry and/or technology and clinical practices. Changes may include emergence of new technologies outside the expertise of current regulatory staff or an increase in product registrations as a result of a change in requirements. In anticipating such changes, member economies can plan for are-assessment in manpower distribution and expertise across regulatory activities, and provide training where necessary.

Chapter 6: Registration Databases

Establishing a medical device registration database and a registration of device dealers are fundamental elements of a medical device regulatory framework, and an important starting point in the implementation process. Such listing systems and registration systems may be used to capture information on the devices imported or manufactured and information on device dealers within the member economy. It is also used in establishing the identities of parties under the jurisdiction of the regulatory authority.

Registration databases serve many useful purposes. Prior to implementation of regulatory controls, voluntary registration of device dealers and medical devices allows member economies to gauge the number and type of medical device activities and devices in their market. This is useful in establishing policies and planning for manpower early. Registration information also allows member economies to reach out to these device dealers early in the implementation process of the regulatory framework and efficiently communicate regulatory updates to affected parties.

Table 3: Types of registration databases for regulatory purposes

Types of registration databases	**Objective**	**Example of information captured in database**
Device Dealer	• Identify device dealers conducting medical device business in jurisdiction • Overall number of each device dealer type within jurisdiction & identification of specific activities (e.g. refurbishment) • Facilitate communication of policies, requirements and feedback • Follow-up of post-market actions • Plan for site inspections	• Name and address • Contact person &contact information • Medical device activity/activities conducted • Types of medical devices under scope of activities
Product	• Identify medical devices supplied in jurisdiction, both current and previous • Impose criteria for device safety, quality and performance prior to registration • Impose specific conditions for continued registered • Post-market vigilance and surveillance communication • End-user reference, raising transparency and public confidence	• Device name • Range of models (e.g. sizes of catheters) • Date of registration • Intended use & indications • Product owner/ legal manufacturer name and address (may be foreign entity) • Local registrant or representative • Manufacturing site(s)

Post-market (field safety alerts and actions)	• Disseminate field safety corrective action information • Alert to device safety issues • Vigilance monitoring for adverse event trends amongst medical device categories	• Device name • Device description • Affected models • Issues identified • Root cause • Details of corrective and preventive actions • Local registrant/representative or device dealer initiating action • Date of alert

It is vital that registration database details are up-to-date. A mechanism is thus needed for device dealers or product registrants to readily updating their details with the regulatory body.

Registration databases that are made available in the public domain facilitate identification of devices and, to the extent their data and formats are harmonized, strengthen communication and exchanges of information between regulatory bodies.

- A regulatory body that recognizes the approval of a device granted by another regulatory body may then readily check on an online registration database to verify whether the devices to be supplied in his jurisdiction have indeed obtained registration or marketing authorization with the recognized regulatory body.

- From a post-market viewpoint, a database maintained of locally-implemented medical device recalls and other field safety corrective actions that can be readily accessible between regulatory bodies ensures information is transmitted openly across jurisdictions where the devices are marketed, allowing local regulatory bodies to act swiftly to undertake the corrective actions to secure patient safety.

To this effect, the design of the registration database should consider the ease of retrieval of information, clear format and common language used to facilitate global transmission of information. A harmonized internationally recognized medical device nomenclature system, e.g., Global Medical Device Nomenclature (GMDN), based on an international standard and maintained in several languages, facilitates such exchanges.

Chapter 7: Essential Principles of Safety and Performance and Recognition of Standards

In prescribing fundamental design and manufacturing requirements for medical devices, member economies are recommended to consider adoption of the essential principles of safety and performance as developed by the GHTF[16]. The essential principles of safety and performance provide general requirements for design and production of all medical devices as guidelines for their safety and performance.

The essential principles comprise six general principles applicable to all medical devices and other principles which only apply, as relevant, to some medical devices. To ensure that the essential principles are met where relevant, standards recognized by the member economy may be used to address the essential principles. Alternatively, manufacturers may have the option to select other solutions to demonstrate their medical device meets the relevant essential principles, with the acceptability of such other solutions to be justified and may be subject to review by the regulatory authority or CAB, as appropriate.

The manufacturer would be responsible for identifying which of the design and manufacturing requirements are relevant to their medical device and documenting evidence of such conformity, as well as providing the reasons for excluding the others. This decision would be verified by the Regulatory Authority or CAB during mandatory conformity assessment, or as required on a compliance check basis in the case of devices exempted from registration.

The combination of implementation of the essential principles of safety and performance and a QMS with design and development activities in its scope ensures the implementation of a full cycle of design and development controls such that medical devices may meet the intended safety, quality and performance standards. Finally, as part of the manufacturer's QMS, a process to assess the continued conformity of the device to the Essential Principles of Safety and Performance through the post-marketing phase can be implemented prior to placing the product on the market. This process will include complaint handling, post-market vigilance reporting and corrective & preventive actions.

Once member economies have defined the harmonized Essential Principles that medical devices in their jurisdiction must fulfill before they can be legally placed on the market, guidelines for demonstrating conformity to the applicable Essential Principles are needed. In many cases, the use of (international) standards may prove very practical.

Various international standards exist today for different aspects of the device lifecycle, and member economies are strongly encouraged to establish a system for on the recognition of such standards. It should be emphasized again that the term "recognized standard" does not imply that such a standard is mandatory– rather, it means the member economy recognizes the standard as one that may be used to demonstrate conformity to the essential principles of safety and performance.

As defined by the GHTF guidance "Role of Standards in the Assessment of Medical Devices" developed by Study Group 1[17], a standard is 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. Standards should principally be based on the consolidated results of science, technology and experience, and aimed at the promotion of optimum community benefits.

The benefits of recognizing standards have been widely acknowledged and emphasized; see also the ISO/IEC Guide "Using and referencing ISO and IEC standards for technical regulations", reference [18].

From a regulatory perspective in safeguarding public health and safety, recognition of standards allow regulatory authorities and other stakeholders to:

1. Reduce the burden of regulatory compliance
2. Provide for high level of patient safety at reduced cost
3. Leverage on consolidated global expertise and experience
4. Build confidence and understanding internationally with regulatory authorities and device dealers.

In relation to global trade, the benefits are apparent to device dealers through reducing technical barriers to trade and easing entry into foreign and domestic markets based on common standards.

Conformance to recognized standards also benefits other stakeholders besides device dealers - patients, users, authorities – by building confidence in quality of products and/or activities and cost savings translated from lowered burden of regulatory conformance.

Medical device standards can be largely grouped into three categories. In strategizing their phased implementation approach for the regulatory framework, member economies may choose to gradually implement the recognition of standards, working their way from the bottom to the top:

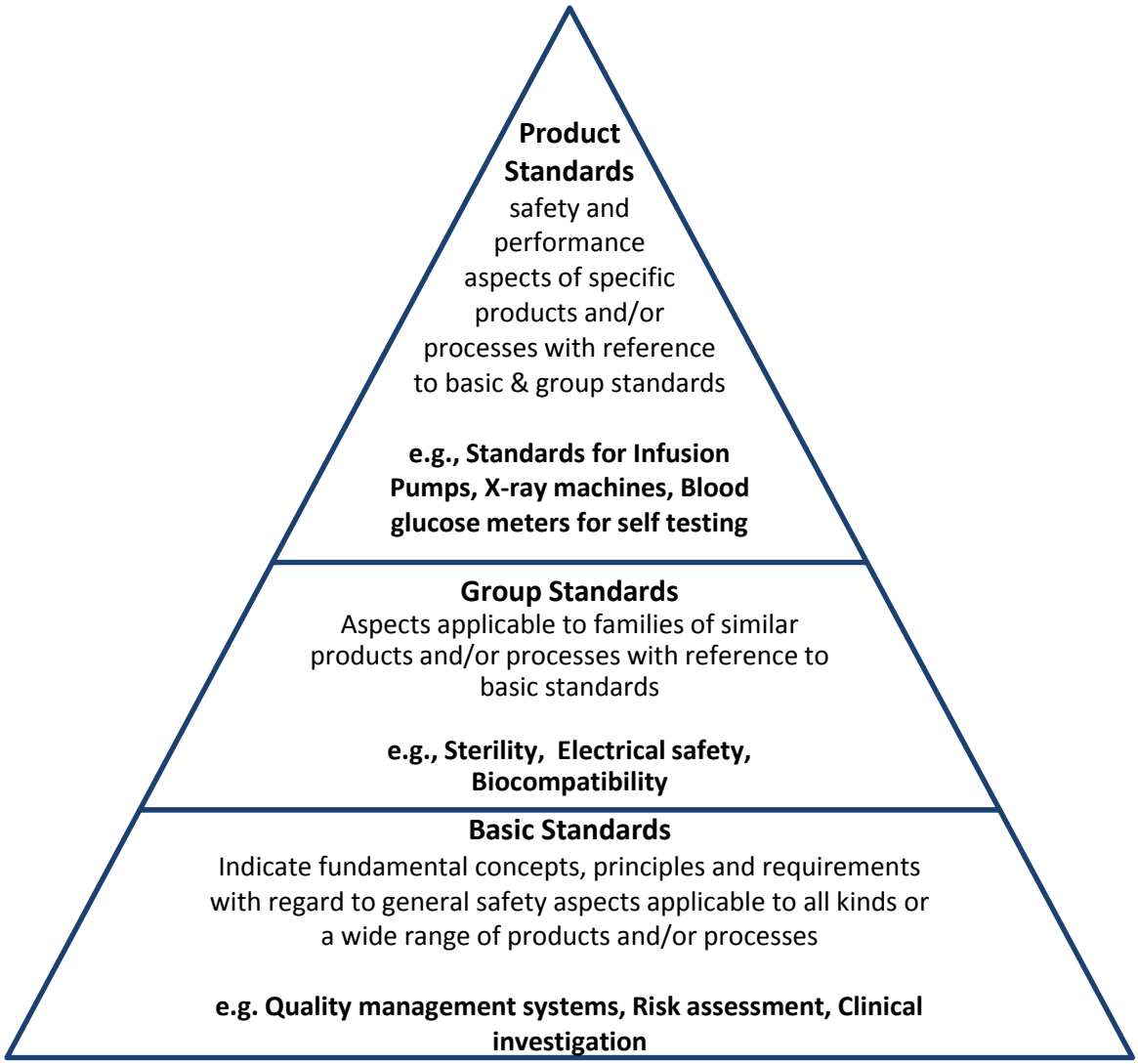


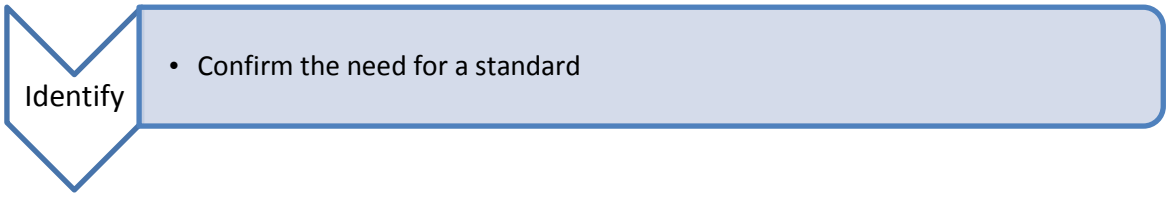
Figure 7: Categories of medical device standards

In the early process of regulatory implementation, a member economy may first recognize basic medical device standards, which are the foundation technical guidelines of compliance to the medical device regulatory framework. Coordination between the medical device regulatory authority and national standards authority are important in recognition of standards for regulatory purposes.

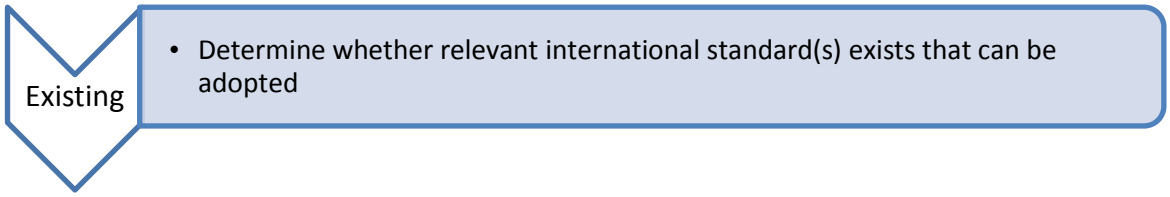
An example of a basic standard is the widely-adopted ISO 13485, a QMS standard covering design and manufacture of medical devices. A proper QMS covering the product lifecycle is fundamental to medical device regulatory compliance, and is the system in which evidence of conformity with regulatory requirements is generated. In Chapter 4, one of the basic regulatory controls is the establishing and recognizing QMS standards. This can be done by requiring an appropriate QMS – in this case, the ISO 13485 - in place for a manufacturer as a pre-requisite to obtaining his dealer's license. CABs may be appointed to perform the audit and certification of device dealers. Importers and distributors, with their scope of activities more limited than that of manufacturers, may conform instead to only select elements of the ISO 13485. The AHWP document "Guidance on the Quality Management System for Medical Device Distributor" [6], prepared by the AHWP Work Group 3, may

be used as reference for member economies in determining the clauses of ISO 13485 applicable to distributors.

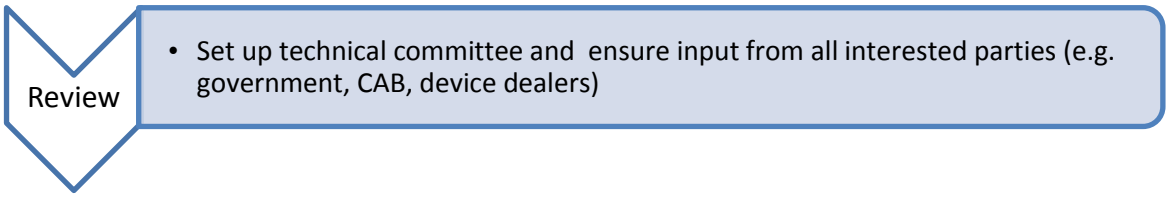
The mechanism of recognition of standards by the regulatory authority may be as follows:



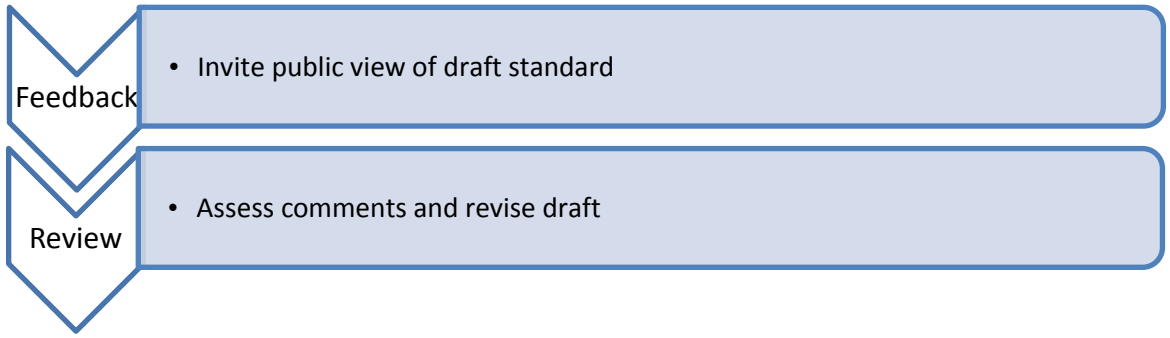
Consider the benefits to be achieved and key stakeholders that will benefit from the development of a new standard. Overall, benefits should exceed the costs likely to be imposed on dealers, patients, users, etc. as a result of its development and implementation.



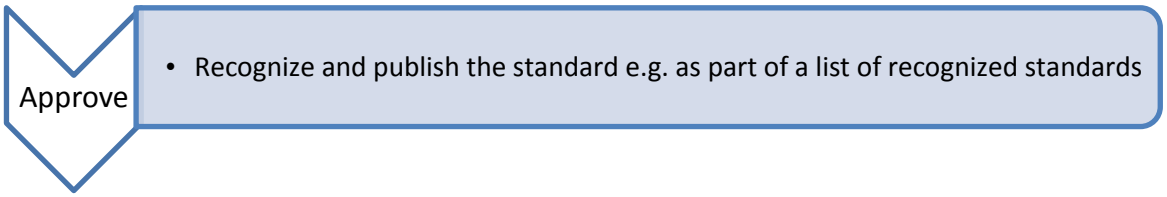
If a standard already exist for a certain product or process, the regulatory authority is to consider if it is acceptable; if multiple standards exist, the regulatory authority may need to select one that is best suited or combine desired elements of each standard. If no suitable or acceptable standards for the purpose exists, the regulatory authority may check if an existing standard can be adapted, by adding or modifying requirements, or whether a complete new needs to be drafted.



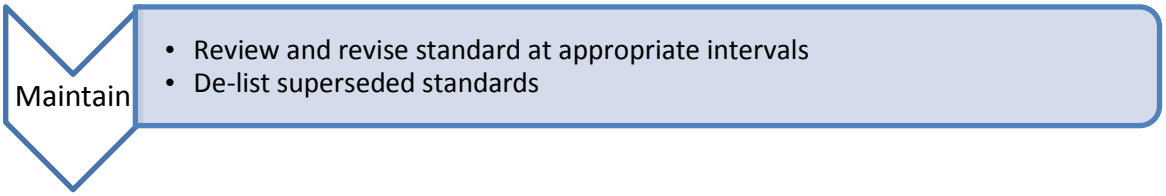
In general, each country or economy has a single recognized national standards body, with procedures in place for the recognition of new standards or adoption of international standards. An appropriately skilled and experienced committee would be appointed that fully represents all affected stakeholders, to ensure the standard retains widespread acceptance and relevance.



Feedback and review steps are relevant only when dedicated material is being developed. If development of a new standard is necessary, it is recommended member economies to do so preferably together with other member economies, and even more preferably, in close communication with the international standards organizations ISO or IEC.



This step is a formal task to be done by the regulatory authority. Recognition may occur by publication of lists identifying existing voluntary standards that the regulatory authority has found will meet specific requirements.



A mechanism of regular review and realignment of locally recognized standards to the international standards needs to be in place, especially when a recognized standard is updatedor an international standard is published or amended. Reasonable transition periods should also be established to allow manufacturers to adapt to the requirements of new standards or revised standards.

The ISO 13485 standard has been adopted in certain member economies, and sometimes even made mandatory. However, standards for use in regulatory contexts are being designed and developed to be voluntary tools to demonstrate conformity.

As such, member economies should consider the following when recognizing or mandating standards:

1. Making standards mandatory is, in general, not recommended. However, if mandating a standard is considered, take into account the potential consequences to **prevent creating additional regulatory burden and/or technical barriers to trade**, which may discourage new or improved diagnostic and treatment options from entering the local market
2. Be prepared also to **accept the use of global, national, regional or industry standards** as a means of demonstrating compliance. Such other solutions proposed by device dealers may be accepted as long as they can be demonstrated to fulfill the regulatory requirements set out.After all, recognized standards remain voluntary tools to demonstrate conformity.
3. In the case of **devices incorporating novel technologies**, international standards may not yet have been developed. Internal standards developed by the manufacturer or other sources that describe the state of technology and practice related to performance, material, design, processed or practices may be considered.

4. Devices **already in use or in distribution prior to implementation** of the medical device framework may continue to be placed on the market if essential safety and performance requirements are still met, unless it has been demonstrated otherwise through post-market activities.
5. Participate in and contribute to the **development of international standards** for medical devices. This is strongly recommended and can be done in several ways. ISO and IEC have mechanisms in place allowing member national committees to comment and vote on standards under development, without requiring extensive international travel.

For more details on the implementation of national standards recognition, member economies are encouraged to refer to the GHTF document "Role of Standards in the Assessment of Medical Devices" produced by GHTF Study Group 1 [17].

In recognizing the importance of standards in medical device regulatory convergence/harmonization, the AHWP has established the Work Group 7 (WG7) with an aim to guide member economies to utilize standards in an efficient, reasonable and economical way in their regulations. In relation to the recommendation of a mechanism of review and realignment of recognized standards, the AHWP WG7 has endeavored to encourage the use of international standards, especially in a bid to harmonize standard recognition across member economies. Updates on the work and progress of the WG7 can be obtained from the AHWP website [10].

In encouraging the recognition of international standards, member economies that are World Trade Organization (WTO) members also fulfill obligations set out under the WTO Agreement on Technical Barriers to Trade (commonly referred to as the WTO TBT Agreement)[19], which seeks to ensure that technical negotiations and standards do not create unnecessary obstacles to trade. In that regard, national standard bodies of the member economy may have accepted and are in compliance with the Code of Good Practice for the Preparation, Adoption and Application of Standards under Annex 3 of the WTO TBT Agreement, which member economies may refer to as guidelines in standards recognition.

For reference, a list of some sources of international standards is given below:

Name	**Scope**	**Website**
IEC: International Electrotechnical Committee	Electrical, electronics and related technologies	http://www.iec.ch
ISO: International Organization for Standardization	Large scope of technical fields, service sectors, management systems and conformity assessments	http://www.iso.ch
ITU: International Telecommunication Union	Telecommunications and radiocommunications	http://www.itu.int

Conclusion

In all chapters above, it is ultimately necessary for member economies to first identify and understand the activities of medical device manufacturers, importers, and distributors in their local markets and then to tailor and implement effective regulatory controls appropriate to local circumstances. Next, communication between all stakeholders involved is of critical importance in ensuring the regulatory framework implementation proceeds smoothly.

Where limited resources mean that a full framework implementation is not possible, strategic implementation of selected framework elements maybe done by identifying which regulatory controls are critical and need to be implemented first, as well as leveraging on existing regulatory bodies as reference.Basic controls are usually the registration of manufacturers and the listing of the medical device and IVD medical devices on the market in the member economy. Thereafter, continuous enhancements over time to the regulatory framework can be done to eventually reach implementation of all desired framework elements. Such an approach also allows an economy to develop the regulatory capacity, experience, and technical expertise required.

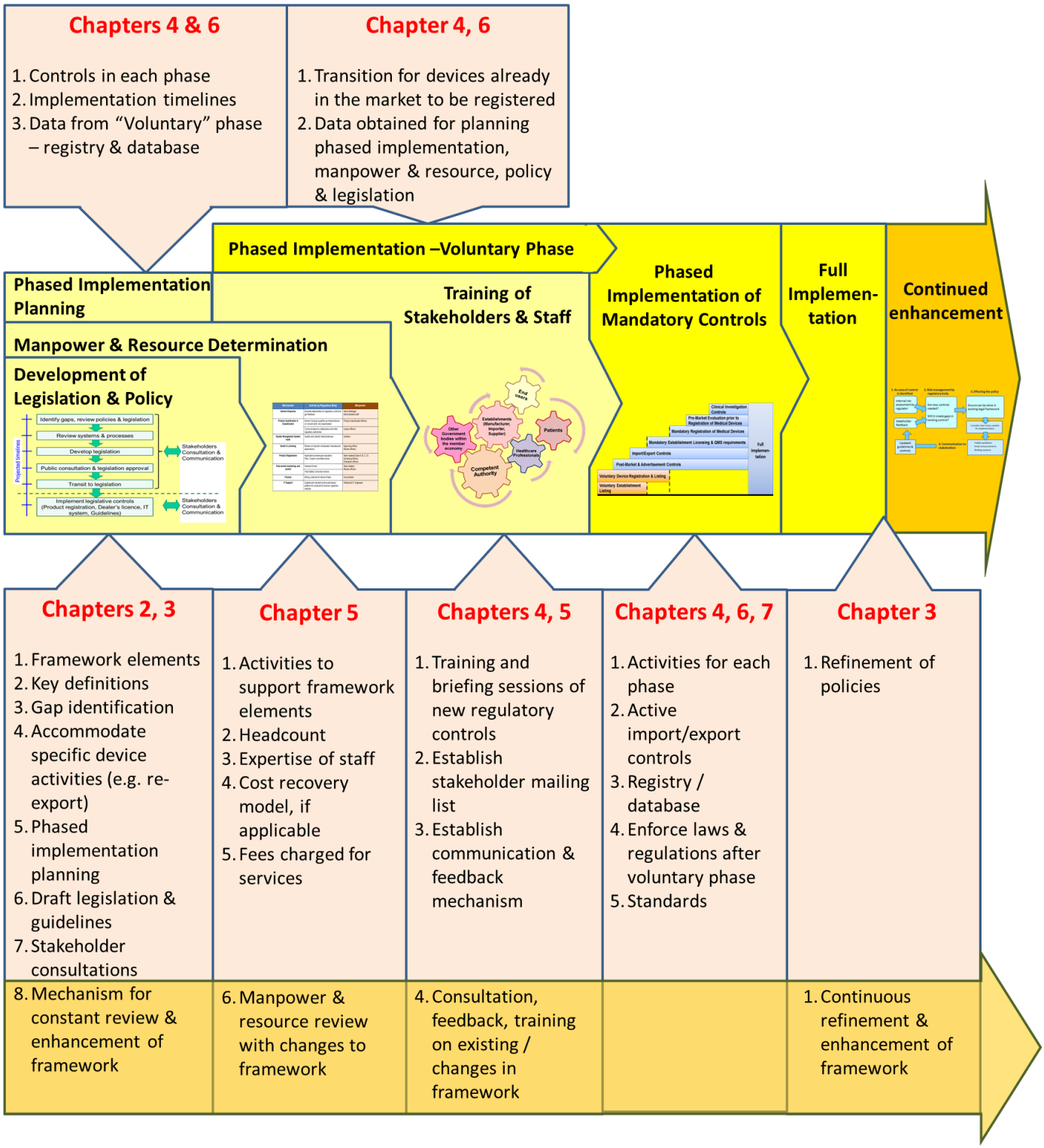
Summarily, a possible phased implementation approach is presented in the next page, taking into consideration aspects described in the various chapters above.

Even with full implementation, regulatory frameworks globally continue to evolve to maintain balance in monitoring devices for safety, quality and performance against the need to facilitate market access for new medical technologies. Member economies are thus encouraged to maintain active awareness of global interests and activities in the medical device regulatory field. This may be done by keeping up with developments of international organizations such as the WHO, IMDRF, APEC and the AHWP. The increasing cross-border trade in medical technology, as well as international public health challenges, will continue to require collaboration and cooperation amongst regulators, industry, and others to protect and promote public health.

This playbook set out to address a recognized need for guidelines to enable member economies to kick-start the framework implementation process. The next step involves the maintenance and continuous improvement of such a framework towards global best practices. As such, this playbook has tried as far as possible to serve as a complement to existing guidelines on medical device regulatory controls published by other organizations.

It is thus highly recommended to use this playbook as a ‘stepping stone’ to reference these existing guidelines, which provide greater detail on regulatory framework considerations. The references are provided below.

Figure 8: Possible phased implementation approach, mapped with the relevant chapters of this Playbook



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