EAST AFRICAN COMMUNITY

REGULATORY FRAMEWORK FOR MEDICAL DEVICES INCLUDING IN VITRO DIAGNOSTIC MEDICAL DEVICES

JUNE 2020

FRAMEWORK DEVELOPMENT HISTORY

STEP	**DATE**
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FOREWORD

The East Africa Community Regulatory Framework for medical devices including in vitro diagnostic medical devices (IVDs) recommends principles, requirements and harmonized definitions to guide the National Medicines Regulatory Authorities (NMRAs) when developing regulatory systems for regulating medical devices including IVDs in the East African Community (EAC).

The framework was developed by a team of experts on medical devices and IVDs from the seven NMRAs of the EAC Partner States. Reference from the WHO Model Regulatory Framework on Medical Devices Including IVDs and other relevant documents such as those developed by the International Medical Devices Regulators Forum (IMDRF) formerly known as Global Harmonization Task Force was made.

It is recognized that there is no single solution that will address to the needs of every partner state, some are ahead of others and some have not started regulating these products and in worst case there are some which do not have established regulatory authority to oversee quality and safety of medical device including IVDs. The framework therefore provides recommendations to partner states on how they can begin regulation at the basic level and gradually advance to expanded levels of control taking into consideration availability of both human and financial resources.

I would like to extended our sincere appreciation to the World Health Organization (WHO) for the supporting the development of this framework document. I would also like to acknowledge the work done by the experts, regional stakeholders including the respective Ministries responsible for the EAC Affairs and Health for their valuable contributions and inputs into this framework document.

Amb. Liberat Mfumukeko
EAC Secretary General

PREFACE

According to the baseline survey conducted in East Africa from October to November 2012 by the Pan-African Harmonization Working Party (PHWP) in collaboration with EAC NMRAs and EAC Secretariat on the status of regulation of in vitro diagnostics in the Eastern African Partner States, it was revealed that there were inadequacies in regulating medical devices in all countries and countries are at different levels in terms of regulation of medical devices and IVDs.

The survey also revealed that although some countries have laws, regulations and systems in place to regulate medical devices and diagnostics, there is limited capacity to do so. Some countries have different institutions carrying out parallel regulation resulting in duplication of work. Existing regulatory bodies have limited capacity to regulate medical devices and diagnostics. Some regulatory bodies do not have tools such as guidelines and procedures to systematically carry out their work. It was also observed that, control of medical devices and diagnostics is largely confined to those used by national disease programs such as Tuberculosis (TB), Human Immunodeficiency Virus (HIV) and malaria.

The situation called for a need to have systems in place for regulation of medical devices as in medicines. Medical devices range from very simple tools such as tongue depressors to very risky and complicated machines such as Pacemaker, CT scan, Mammography machine and Ultra sound just to mention a few that requires Authorities to verify their safety and performance for the purposes of protecting the public against health risks that may result after using such devices.

EAC partner states NMRAs have been mandated to regulate amongst other products medical devices including IVDs and therefore a need to put in place policies and mechanisms that will address all elements related to medical devices and IVDs ranging from access to high quality, affordable products, their use and appropriate disposal. The general objective of the the framework document is to recommend principles, harmonized definitions and other attributes for effective regulation of medical devices including IVDs.

Streamlining and harmonizing regulatory processes for medical devices including IVDs in EAC Partners States can reduce delays, reduce unnecessary regulatory costs and improve access to new medical devices including IVDs within the EAC countries. In 2019, EAC with the support from the World Health Organization published a framework for regulation of medical devices including IVDs providing recommendations for stepwise approach in regulation of medical devices for EAC NMRAs who wish to begin regulating and those who wish to expand to advanced levels of regulation. The EAC EAC partner states are expected to follow these principles for successful introduction of I medical devices including IVDs regulatory systems within their respective jurisdictions and expand further to advanced

elements of regulation. The Framework for medical devices including IVDs document contains seven (7) chapters and sections.

I wish to express my gratitude to all individuals from EAC Partner States' NMRAs, regional and international organizations who actively participated in the development of this framework document. I therefore urge all technical experts from the Partner States National Medicines Regulatory Authorities and EAC Secretariat to use this document as a tool to guide regulation of medical devices including IVDs in a stepwise approach.

Hon. Christophe Bazivamo
EAC Deputy Secretary General
Productive and Social Sectors

RESPONSIBILITY FOR THE IMPLEMENTATION OF THE FRAMEWORK FOR REGULATION OF MEDICAL DEVICES INCLUDING IN VITRO DIAGNOSTIC MEDICAL DEVICES

The EAC Sectoral Council of Ministers of Health recognizes the work done by the EAC Secretariat in collaboration with the lead EAC Partner States National Medicines Regulatory Authorities (NMRAs), Tanzania Medicines and Medical Devices Authority (TMDA) for coordinating the development of harmonized framework for regulation of medical devices including in vitro diagnostic medical devices. Implementation of the framework will facilitate uniformity in performance assessment of medical devices and reduce duplication of efforts between National Medicines Regulatory Authorities in the region.

Harmonization of medical product and health technologies is an explicit policy priority under Chapter 21 (Article 118) of the EAC Treaty and vital in enabling the free movement of goods in line with the EAC Common Market Protocol. Streamlining safety and performance evaluation of medical devices will have a positive impact to public health by increasing access to good quality and safe medical devices in the region.

The EAC Sectoral Council of Ministers of Health approves the use of framework for regulation of medical devices in the East African Community Partner States' National Medicines Regulatory Authorities (NMRAs) in accordance with the existing regional legal instruments. Implementation of the framework will facilitate mutual recognition of regulatory decisions and attestation of the quality and safety of medical devices including in vitro diagnostics manufactured, produced, imported, exported or traded in East African Community.

The EAC Partner States Ministries responsible for Health shall be responsible for the enforcement of this framework for regulation of medical devices including in vitro diagnostic medical devices in the East African Community through the respective National Medicines Regulatory Authorities (NMRAs).

SIGNED by the Leaders of Delegation

Hon. Dr. Daniel Ngamije	**Hon. Mutahi Kagwe,EGH**		**Hon. Ummy Ally Mwalimu**	**Hon.Elizabeth Achuei Yol Kuol**	**Hon.Sarah Aceng Opendi**
Minister of Health	Cabinet Secretary	Minister of Public Health and	Minister of Health	Minister of Health	State Minister for

		Fight against HIV/AIDS			Health
Ministry of Health	Ministry of Health	Ministry of Public Health and Fight against HIV/AIDS	Ministry of Health, Community Development, Gender, Elderly and Children	Ministry of Health	Ministry of Health
REPUBLIC OF RWANDA	**REPUBLIC OF KENYA**	**REPUBLIC OF BURUNDI**	**THE UNITED REPUBLIC OF TANZANIA**	**REPUBLIC OF SOUTH SUDAN**	**REPUBLIC OF UGANDA**

Acronyms and abbreviations

AHWP	Asian Harmonization Working Party
ASEAN	Association of Southeast Asian Nations
ATMP	Advanced therapy medicinal products
CAB	Conformity assessment body
CLSI	Clinical and Laboratory Standards Institute
EAC	East African community
FSCA	Field safety corrective action
GDP	Good distribution practice
GHTF	Global Harmonization Task Force
GMDN	Global Medical Device Nomenclature
IEC	International Electrotechnical Commission
IMDRF	International Medical Device Regulators Forum
ISO	International Organization for Standardization)
IVD	In vitro diagnostic medical device
NMRA	National Medicines Regulatory Authority
QMS	Quality Management System
SF	Substandard and Falsified Medical Products
SUMD	Single-Use Medical Device
UN	United Nations
UNFPA	United Nations Population Fund
US FDA	United States Food and Drug Administration
WHO	World Health Organization
WHA	World Health Assembly

1.0 Introduction

1.1 Regulation of IVD Medical devices including IVDs in EAC

The six EAC Partner States have seven (7) National Medicines Regulatory Authorities (NMRAs) namely Department of Pharmacy and Medical Laboratories (DPML) of Burundi, Rwanda Food and Medicine Authority (RFMA) of Rwanda, Pharmacy and Poisons Board (PPB) of Kenya, Tanzania Medicines and Medical Devices Authority (TMDA), Zanzibar Food and Drugs Agency (ZFDA), National Drug Authority (NDA) of Uganda and South Sudan Drug and Food Control Authority (DFCA).

In the Republic of Burundi, regulation of medicines, medical devices including IVDs were being enforced by the Department of Pharmacy, Medicines and Laboratories (DPML) in the Ministry of Public Health and Fight Against AIDS. In May 2020, the Republic of Burundi enacted an Act for establishment of Burundi Medicines Regulatory Authority (ABREMA) which will oversee regulation of medicines and medical devices.

The South Sudan Drug and Food Control Authority (DFCA)Act No.37, 2012 has well stated the role of DFCA to regulated medical devices including IVDs line together with medicines regulations guideline and polices. But has not developed guidelines to regulate medical devices including IVDs. The Authority has plans to develop some guidelines for medical devices including IVDs.

Tanzania Medicines and Medical Devices Authority (TMDA) Act Cap 219 section 51 (1) gives TMDA the mandate to regulate among other products, medical devices including IVDs to ensure that these products are correctly evaluated for quality, safety and performance before being approved for use. TMDA is also responsible for import and export control, post marketing surveillance (PMS) and adverse events monitoring, inspection, licensing of manufacturers and importers of medical devices including IVDs.

The Act empowers the health minister to make regulations and the Director General to make technical guidelines. The Tanzania Food, Drugs and Cosmetics (Control of Medical devices including IVDs) Regulations, 2015 has been made. Furthermore, TMDA has developed the following guidelines; submission of documentation for registration of medical devices including IVDs, submission of documentation for registration of medical devices including IVDs, importation and exportation of medical device including IVDs and medical devices including IVDs vigilance systems.

The National Drug Policy and Authority (NDA) Act (Cap 206 of the laws of Uganda), Section 64 on Regulation, sub section (g), provides for regulating, restricting or prohibiting the importation, sale or advertising of surgical instruments and appliances. The current legal framework does not cover other medical devices including IVDs. Nevertheless, the NDA undertakes regulation of medical devices including IVDs through import control, PoE inspection, licensing of premises and to some extent, quality control testing. Registration of devices is not currently being done. The proposed National Food and Medicine Authority Bill, 2016, seeks to establish the National Food and Medicines Authority with mandate to, among others, regulate medical devices including IVDs.

Rwanda Food and Drugs Authority (Rwanda FDA) is a semi-autonomous authority, established by the law Nº 003/2018 of 09/02/2018. Rwanda FDA is headed by the Ag Director General officially nominated in July 2018 in which all matters pertaining to the control of food, medicines, medical devices including IVDs are handled by this newly established institution. Rwanda has started regulation on medical devices including IVDs and soon after approval of draft guidelines on medical devices including IVDs and diagnostic registration will start.

Regulation of medical devices including IVDs in Kenya is domiciled in the department of standards, regulation and quality assurance of the Ministry of Health under Pharmacy and Poisons Board (PPB) and Kenya Medical Laboratory Technicians and Technologists Board (KMLTTB). PPB is the national medicines regulatory authority responsible for regulation of health products and technologies in Kenya. KMLTTB is responsible for validation for medical laboratory, equipment, reagents and in vitro diagnostic devices to ensure compliance to the set standards in Kenya.

Zanzibar Food, Drugs and Cosmetic Agency ZFDA is a regulatory body responsible for controlling the quality, and safety of food, drugs, herbal drugs and medical devices including IVDs for the purpose of protecting public health. Established under section 3(1) of the Zanzibar Food, Drug and Cosmetic Act No.2 of 2006, ZFDA is a semi-autonomous body under the Zanzibar Ministry of Health, and became operational on 1 January 2007.

A baseline survey on regulatory activities for medical diagnostics in EAC and other selected African countries undertaken in 2012 found that there was either no regulatory framework or if available it was fragmented with multiple institutions doing the same work. However, the capacity to regulate medical devices including IVDs was limited in terms of skills and human resource[1]. The survey noted that in some

countries the regulation of medical devices including IVDs had been delegated to the NMRAs while in other countries, Ministry of Health departments were involved. Control of medical devices including IVDs was largely confined to those used by national disease programs such as Human Immunodeficiency Virus (HIV) and malaria. In addition, some activities to evaluate medical devices including IVDs were performed in research laboratories but post market surveillance was rarely done. Mori M, et al[2] reported that there were limited reports and evidence with regards to poor quality medical devices including IVDs and this was mainly due to:

i. the poor regulatory oversight of medical devices including IVDs in resource-limited settings;
ii. a general lack of awareness of the problem of poor-quality medical devices including IVDs amongst the scientific community and decision-makers; and
iii. poor quality assurance in diagnostic laboratories in resource-poor settings, precluding tracing quality problems of IVDs from the other potential causes of diagnostic inaccuracy.

The EAC Partner States have decided to adopt the WHO regulatory framework to strengthen their regulatory capacity based on the WHO Global Model Regulatory Framework for Medical devices including IVDs. Critical elements for adoption will include definition of medical devices including IVDs, risk classification of medical devices including IVDs as applicable to EAC countries and adoption of Essential Principles of Safety and Performance. This will require the partner state governments to-buy- in and take a leading role and provide enabling environment for effective regulation of medical devices including IVDs as described below.

1.2 WHO Global Model Regulatory Framework for Medical devices including IVDs

In 2016 WHO published the WHO Global Model Regulatory Framework for Medical devices including IVDs[3]. The Model recommends guiding principles, harmonized definitions and specifies 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)[4].

The Model is particularly relevant for WHO Partner Statess such as EAC Partner States with little or no regulation for medical devices including IVDs currently in place but with the ambition to improve this situation. It foresees that such countries will progress from basic regulatory controls towards an expanded level to the extent

that their resources allow. The Model is written for the legislative, executive and regulatory branches of government as they develop and establish a system of medical devices including IVDs regulation. It describes the role and responsibilities of a country's regulatory authority for implementing and enforcing the regulations. Also, it describes circumstances in which a regulatory authority may either "rely on", or "recognize" outcomes from trusted regulatory sources (such as assessments, audit and inspection reports) or from the WHO Prequalification of Diagnostics Team.

The Model outlines a general approach but does not provide country-specific guidance on implementation. While it does not offer detailed guidance on regulatory topics it contains references to relevant documents where further information may be found. Also 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 including IVDs. The Model recommends establishing a regulatory system for medical devices including IVDs taking a staged or stepwise approach. It suggests starting with basic controls and as the technical and human capacity is strengthened to include expanded controls. The basic controls will therefore form the foundation for the expanded controls.

1.3 Definition and classification of medical devices including IVDs including IVDs

14.1 Definition of medical devices including IVDs

EAC Partner States have adopted the definition of both medical devices including IVDs as developed by GHTF. Many jurisdictions have accepted the principles of the GHTF definition and in the interest of international convergence partner states are encouraged to promote it's 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 including IVDs;*
- *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.*

IVD: 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.
There may also be products on the market that are similar to medical devices including IVDs in function and risk that do not fit within these definitions. For reasons of protecting public health they are regulated as if they were medical devices including IVDs. Examples include: impregnated bed nets to protect against malaria-bearing mosquitoes; personal protective devices to avoid cross-infection; lead aprons to protect against radiation; some medical gases; and implantable or other invasive products for a cosmetic rather than a medical purpose.

1.4.2 Classification of medical devices including IVDs

Medical devices including IVDs are separable into groups or classes, typically four, A, B, C and D, by applying a set of classification rules (2) and specifying separately the different conformity assessment procedures that should apply to each group of devices (Figure 1)

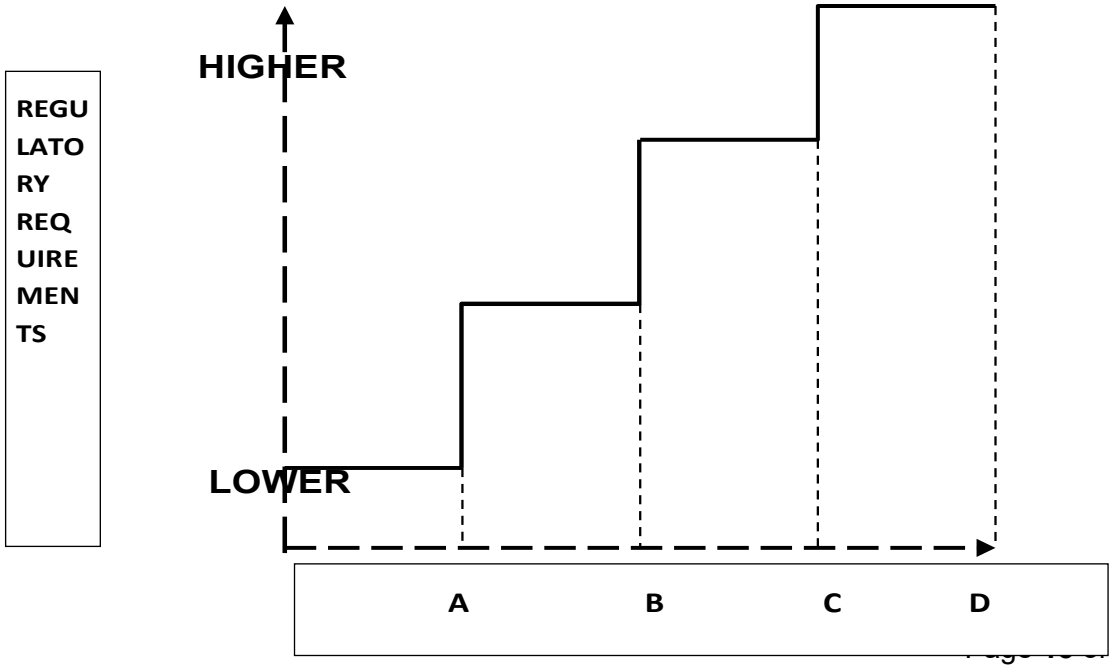

Figure 1. Impact of device classification on regulatory scrutiny

Note: As the regulatory requirements increase, so does the scrutiny by the regulatory authority. Source: Reproduced from Principles of medical devices including IVDs classification (2).

The classification rules for medical devices including IVDs other than IVDs depend on the features of the device, such as whether it:

i. is life supporting or sustaining;

ii. is invasive and if so, to what extent and for how long;

iii. incorporates medicinal products;

iv. incorporates human or animal tissues or cells;

v. is an active medical device;

vi. delivers medicinal products, energy or radiation;

vii. could modify blood or other body fluids;

viii. is used in combination with another medical device.

Examples of the classes of medical devices including IVDs are shown in Table 1.

Table 1 Examples of medical device according to risk classes

Class	Risk level	Examples
A	Low	Syringes, examination gloves, patient hoists, stethoscopes, wheelchairs, IVD instruments, microbiological culture media
B	Low–moderate	Surgical gloves, infusion sets, pregnancy tests
C	Moderate–high	Condoms (unless with spermicide (class D)), infusion pumps, neonatal incubators, therapeutic and diagnostic X-ray, lung ventilators, haemodialysers, anaesthesia

		equipment, self-test glucose strips, IVDs for the diagnosis of Neisseria gonorrhea
D	High	Implantable cardioverter defibrillators, pacemakers, breast implants, angioplasty balloon catheters, spinal needle, IVDs for the diagnosis of HIV, hepatitis C or hepatitis B

The actual classification of each device depends on the claims made by the manufacturer for its intended use and the technology or technologies it utilizes. Classification also takes into the account the technical, scientific and medical expertise of the intended user (layperson or health- care professional). The GHTF has published documents on the classification of medical devices including IVDs that use the principles above to establish classification rules[4, 5]. Additionally, the regulatory authority may develop explanatory guidance to help a manufacturer apply the rules[7]. While the manufacturer has the primary obligation to classify its medical device, its decision may be challenged by the regulatory authority.

The GHTF risk classification rules determine the level of pre-market regulatory assessment that is required for an IVD, with the purpose that these controls are considered to be sufficient for each risk class to safeguard the health and safety of patients, users and other persons. The outcome of the rules is to group IVDs into one of four classes representing increasing individual and public health risk (Classes A to D), The basis for classification of in vitro diagnostic tests is shown in Table 2. Table 3 gives examples of IVD according to risk class.

Table 1 GHTF Classification Rules for in vitro diagnostic test

Classification Risk	Individual Health		Public Health Risk
Class A	Low	And	Low
Class B	Moderate	And	Low
Class C	High	and /or	Moderate
Class D	High	And	High

Table 3 GHTF Risk Classes and Risk Level of in vitro diagnostic Tests

Classification Risk	Examples
A	- Reagents or other articles which possess specific characteristics, intended by the manufacturer to make them suitable for in vitro diagnostic procedures related to a specific examination. - Instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures - Specimen receptacles - Selective/differential microbiological media (excluding the dehydrated powders which are considered not to be a finished IVD medical device), identification kits for cultured microorganisms, wash solutions, instruments and plain urine cup
B	- Blood gases, H. pylori and physiological markers such as hormones, vitamins, enzymes, metabolic markers, specific IgE assays and celiac disease markers - Pregnancy self-test, Fertility testing, Urine test-strips.
C	IVD medical devices including IVDs intended for use: - in detecting the presence of, or exposure to, a sexually transmitted agent. Examples: Sexually transmitted diseases, such as Chlamydia trachomatis, Neisseria gonorrhoeae. - in detecting the presence in cerebrospinal fluid or blood of an infectious agent with a risk of limited propagation. Examples: Neisseria meningitis or Cryptococcus neoformans. - in detecting the presence of an infectious agent where there is a significant risk that an erroneous result would cause death or severe disability to the individual or fetus being tested. Examples: diagnostic assay for CMV, Chlamydia pneumoniae, Methicillin Resistant Staphylococcus aureus. - in pre-natal screening of women in order to determine their immune status towards transmissible agents. Examples:

	Immune status tests for Rubella or Toxoplasmosis. - in determining infective disease status or immune status, and where there is a risk that an erroneous result will lead to a patient management decision resulting in an imminent life-threatening situation for the patient. Examples: Enteroviruses, CMV and HSV in transplant patients. - in screening for selection of patients for selective therapy and management, or for or for disease staging, or in the diagnosis of cancer. Example: personalized medicine. NOTE: those IVD medical devices including IVDs where the therapy decision would usually be made only after further investigation and those used for monitoring would fall into class B under rule 6. - in human genetic testing. Examples: Huntington's Disease, Cystic Fibrosis. - to monitor levels of medicines, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in an immediate life-threatening situation for the patient. Examples: Cardiac markers, Cyclosporin, Prothrombin time testing. - In the management of patients suffering from a life-threatening infectious disease. Examples: HCV viral load, HIV Viral Load and HIV and HCV geno- and subtyping. - In screening for congenital disorders in the fetus. Examples: Spina Bifida or Down Syndrome. - IVD medical devices including IVDs intended to be used for blood grouping, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation (HLA, Duffy system) - Blood glucose monitoring
D	- Devices intended to be used to detect the presence of, or exposure to, a transmissible agent in blood, blood components, blood derivatives, cells, tissues or organs in

	order to assess their suitability for transfusion or transplantation, - Devices intended to be used to detect the presence of, or exposure to, a transmissible agent that causes a life-threatening, often incurable, disease with a high risk of propagation - IVD medical devices including IVDs intended to be used for blood grouping - for ABO system [A (ABO1), B (ABO2), AB (ABO3)], rhesus system [RH1 (D), RH2 (C), RH3 (E), RH4 (c), RH5 (e)], Kell system [Kel1 (K)], Kidd system [JK1 (Jka), JK2 (Jkb)] and Duffy system [FY1 (Fya), FY2 (Fyb)] determinations - Tests to detect infection by HIV, HCV, HBV, HTLV

1.4 Essential principles of safety and performance

GHTF has established a list of Essential Principles of safety and performance for medical devices including IVDs[8]. 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 apply to all medical devices including IVDs and are supplemented by those principles specific to particular medical device types (e.g. implants or electrically powered devices). The general Essential Principles of safety and performance for medical devices including IVDs include the following.

i. 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.
ii. 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.
iii. Medical devices including IVDs should perform as the manufacturer intended when used under normal conditions.

iv. Performance and safety should not be affected during the lifetime of a medical device in such a way that it affects the safety of the patient or the user.
v. Performance and safety should not be affected by transport or packaging and storage, provided the instructions for packaging, transport and storage are followed.
vi. Known and foreseeable risks should be weighed against the benefits of the intended purpose.

Ensuring that a medical device conforms to all relevant Essential Principles (5) is the responsibility of the manufacturer. However, the manufacturer's evidence of conformity, recorded in its technical documentation, may be subject to review by the regulatory authority, either before or after market introduction. The medical device regulation shall specify the extent of the regulatory authority's involvement with different classes of device[9]. While retaining responsibility for the decisions it makes, the regulatory authority may appoint one or more conformity assessment bodies (CABs) to assist it in this task.

1.5 Clinical evidence for non-IVDs

One of the requirements of the Essential Principles is 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 together 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. In deciding whether to authorize a medical device, the regulatory authority may consider the acceptance of data from clinical investigations conducted outside its jurisdiction, provided that the applicant has demonstrated that the data are adequate and were obtained in accordance with applicable global standards.

Some technologies have been available for many years and their clinical safety and performance have been well characterized. Many devices, however, 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[8]. Certain technical elements of the regulatory framework may be delegated to “designated” or “recognized ” CABs. For example, they may be approved to perform initial certification and surveillance audits of a device manufacturer’s quality management system (QMS) and/or premarketing evaluation of device conformity with the Essential Principles. Satisfactory compliance with requirements is typically confirmed by the CAB issuing a design examination or QMS audit 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 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 shall perform a documented comprehensive evaluation of all the available clinical evidence under the control of its quality management system (QMS). 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[10]. A widely used international standard for the practice of clinical investigation is ISO 14155:2011 – Clinical investigation of medical devices including IVDs for human subjects – Good clinical practice[11].

1.6 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’s life cycle. In general, the manufacturer does this through implementation of a QMS. The degree of assessment of the QMS by the regulatory authority or CAB depends on the medical device risk class[9]. Depending on the class of the medical device, the evidence of conformity may be subject to regulatory assessment by the regulatory authority or CAB. The regulatory authority should have confidence that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization. The Conformity assessment of difference classes of medical devices including IVDs are summarized in Table 4.

Table 4: Conformity assessment of difference classes of medical devices including IVDs

Conformity assessment element	Class A	Class B	Class C	Class D
Quality management system (QMS)	Regulatory audit normally not required, except where assurance of sterility or accuracy of the measuring function is required.	The regulatory authority should have confidence that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.	The regulatory authority should have confidence that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.	The regulatory authority should have confidence that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.
Technical documentation	Premarket submission normally not requested.	Not normally reviewed premarket. The regulatory authority may request and conduct a premarket or post-marketing review sufficient to determine conformity with Essential Principles.	The regulatory authority will undertake a review sufficient to determine conformity with Essential Principles prior to the device being placed on the market.	The regulatory authority will undertake an in-depth review to determine conformity with Essential Principles, prior to the device being placed on the market.
Declaration of conformity	Submission normally not requested.	Review and verify compliance with requirements by the regulatory authority (see footnote to Table A4.1).	Review and verify compliance with requirements by the regulatory authority (see footnote to Table A4.1).	Review and verify compliance with requirements by the regulatory authority (see footnote to Table A4.1).

The GHTF has developed additional Essential Principles that apply to IVDs[8]. 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. Values assigned to calibrators and controls of IVDs need to be traceable to available reference measurement procedures and/or available reference materials of a higher order (ISO 17511:2003)

The main differences are that the Essential Principles for IVDs:

i. do not cover incorporation of substances considered to be a medicine as even if these substances are present, there is no effect on the human body;

ii. 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 infection is reduced due to the mode of use of IVDs;
iii. include a requirement for the design to ensure that performance characteristics support the intended use;
iv. do not include requirements in relation to protection against ionizing radiation, since this is not a function of IVDs;
v. have more limited requirements in relation to electrical safety and supply of energy, since IVDs do not connect to, or supply energy to the patient;
vi. include requirements for IVDs for self-testing;
vii. include requirements for performance evaluation of the IVD (whereas clinical evaluation is appropriate for non-IVD medical devices including IVDs).

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.

1.7 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 together 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 performance 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 including IVDs to be used on human patients. The application of ISO 14155:2011 – Clinical investigation of medical devices including IVDs for human subjects – Good clinical practice[11] is therefore not suited to IVDs. A standard specific to IVDs is being developed by the ISO Technical Committee 212[12].

1.8 Lot verification testing of IVDs

Some countries that have yet to implement effective regulation for medical devices including IVDs but need to import high-risk (Class D) IVDs, may implement a system of 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 premarket evaluation conducted. Where there are stringent controls on transport and storage, and the receiving laboratory has in place an effective quality control programme that will detect problems in the performance of a new batch on arrival, lot verification testing may not be needed.

The regulatory authority may designate a national reference laboratory or other recognized laboratory that is assigned the overall responsibility for coordinating and conducting lot verification testing on its behalf.

2.0 Enabling environment for regulation of medical devices including IVDs including diagnostics

The EAC framework for regulation of medical devices including IVDs will be implemented after creating suggested enabling environment for regulation of medical devices including IVDs including government continued support and commitment. The enabling environment will include stepwise approach and will include the following aspects.

2.1 Legal requirements

Each Partner State shall ensure that medical device regulation is guided by an established a legislative framework aligned with international best practices providing for:

i. establishing a national regulatory authority to regulate all medical devices including IVDs.
ii. defining the products within its scope and identifying the entities subject to regulation.
iii. creating a general requirement that medical devices including IVDs that are safe, perform as intended, and are of appropriate quality shall be authorized in the Partner States,
iv. defining the responsibilities of the regulatory authority and other stakeholders
v. addressing coordination with other bodies such as the justice ministry and the police and customs authorities.
vi. providing scope for administrative and enforcement discretion that allows the regulatory authority to apply the principles of “reliance” and “recognition”

vii. accommodating a transition from basic to expanded regulatory controls to the extent that resources allow as experience is gained.
viii. allowing the regulatory authority to respond to public health emergencies in an appropriate and timely manner.

The establishment of the legal framework will include the following; holding a consultative meeting of responsible ministries (Health, Justice, Finance, Customs, Internal affairs etc) to discuss and agree on formation of regulatory body for medical devices including IVDs. The same group will also oversee the establishment of legal framework for regulation of medical devices including IVDs. The consultative meeting should include other partner including those involved in procurement, storage and distribution of medical devices, central/national public health laboratory, research institutions and academia.

2.2 Gap analysis of existing controls

The true nature of the existing regulatory capacities and controls in EAC countries is patchy. Recently published surveys have to some extent tried to establish the existing capacities in EAC[1,2,3]. An extensive gap analysis needs to be conducted in each Partner State using the WHO Global Benchmarking Tool (GBT) for evaluation of national regulatory systems. The outcome of the gap analysis will allow the policy-makers to understand both the steps and resources needed to achieve national public health goals and to develop regulatory capacity. It will also be helpful in assessing the degree to which national regulations are aligned with international guidance and best practices.

Each EAC Partner Statess will then draw up an action plan for regulation of the medical devices including IVDs including diagnostics based on the findings of the gap analysis. The action plan should use the proposed WHO stepwise approach starting with basic control and driven by individual partner states under guidance of the MOH and involving all institutions involved in handling medical devices including IVDs including diagnostics.

2.3 Implementation plan

Once national legislation on medical devices including IVDs has been adopted, the appointed regulatory authority shall develop an implementation plan for adoption. The plan will be driven by public health priorities and needs and by the availability of resources, including trained competent staff to implement legislation. The plan should include time for promoting awareness, drafting proposals for implementing

regulations and seeking feedback from the public and other affected parties. Appropriate transition periods should be defined to allow industry to comply with new or amended requirements. The plan should also address how medical devices including IVDs already in the market, in the distribution chain, or in use will be handled, e.g. allowing well-defined exemptions and transition provisions. Provisions for donated medical devices including IVDs including in vitro diagnostics shall be addressed in the implementation plan. Regulatory strategy for rebranded medical devices including IVDs and in vitro diagnostics is to be provided for in the plan. 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 including IVDs during the transition period.

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 including IVDs regulation.

The National Medicine Regulatory Authority will exercise independent decision-making within the regulatory framework. The governance of the authority should be defined, together with appropriate checks and balances and a requirement to publish periodic public reports on performance. In countries where the law (or decree) consists 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.

2.4 Funding the regulatory system

Implementation of the regulatory system in EAC Partner States will require trained staff, infrastructure, facilities and information technology (IT). Resources allocated should be consistent with activities mandated in the law, with a legal provision enabling increase of financial resources as the regulatory system moves from the basic level to expanded-level controls. The Legal provision to enable fee collection by the NMRA can also be considered. The pre-implementation gap analysis should include an assessment of the financial resources required. Provisions should be made for management of resources by NMRAs.

2.5 Stepwise approach

The stepwise approach recommends establishing a regulatory system for these products taking a staged or stepwise approach – from basic to expanded controls. The basic controls will form the foundation for the expanded controls. In order to promote international regulatory convergence and harmonization it will be important for the EAC Partner States to adopt the principles recommended in internationally harmonized technical guidance into their legislation[13].

Basic regulatory controls fall into three broad groups:

i. those applied before a medical device is placed on the market;

ii. those applied when placing the device on the market;

iii. 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, needs and to progressively develop the capacity, knowledge, experience and expertise required. This approach helps the regulatory authority to 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. As NMRAs subsequently implements expanded-level controls, emphasis will shift to premarket controls such as authorizing devices to be placed on the market, while continuing to rely upon or recognize the work of other jurisdictions, where appropriate.

2.6 Reliance and recognition

The medical devices including IVDs regulatory law in each EAC partner state should establish to what extent the regulatory authority may reasonably use the work of regulatory authorities within and outside EAC jurisdictions in assessing evidence that a device conforms to national requirements. The two main examples of these techniques are:

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

ii. 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 within EAC countries or CAB audits a manufacturer and issues it with a QMS certificate. The NMRA of the importing country accepts certificates issued by another authority as proof of compliance with its own QMS requirements.

Partner States are encouraged to harmonize requirements with a view of bringing alignment in regulatory framework with EAC. In order for the regulatory authority to decide whether to use either the reliance or recognition option, it must have a clear understanding of the regulatory system that applies within the country where the medical device is manufactured.

2.7 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, including vigilance reports; market surveillance activities; and communication and monitoring of field safety corrective actions (FSCA), prevention, detection and response to substandard and falsified medical devices including IVDs.

2.8 International, Regional, Sub Regional and Bilateral collaboration

Partner States are encouraged to participate in international forums to gain valuable regulatory skills, expertise, share experiences on best practices and their implementation, and knowledge transfer.

- Active participation in Strategic groups to further gain expertise.
- Twinning/ exchange programs between partner states with a view of learning from each other.

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.

2.9 Identification of existing expertise, areas for workforce improvement and capacity building

Legal and institutional arrangements can be effective only if they are backed-up with regulatory experts of appropriate qualification. Competence building and retention of the regulatory workforce requires appropriate arrangement for leveraging of expertise, relevant education, continuous learning, know-how and skills transfer and incentives to retain expertise.

3. Basic-level controls and their enforcement

3.1 Legal Framework

Each partner state will develop legal framework for regulation of of Medical devices including IVDs including in vitro diagnostics that will include basic level controls as follows:

The law will:

i. define the scope of regulation,
ii. define the responsibilities of the regulatory authority, manufacturers, importers, distributors and authorized,
iii. define conditions under which a medical device can be placed on the market, requires certain organizations to be registered,
iv. establishes import controls and requires post market surveillance activities.

The published law will include definition, and regulations with transition period. The national legislation for medical devices including IVDs will set out principles and broad requirements and mandate to carry out regulatory authority functions. In particular it will:

i. define the products and parties within its scope, in particular the terms medical device and IVD, using harmonized definitions[14];
ii. ensure that the regulatory framework is capable of adapting to new technologies and treatment modalities;
iii. designate the NMRA to enforce regulation, market oversight responsibilities, powers to issue implementing regulations and to act where the health of patients or users is compromised, and the responsibility for publishing guidance documents to aid understanding of legal requirements;
iv. provide the regulatory authority with administrative and enforcement discretion for reliance upon and recognition of the work or decisions of regulatory authorities in other jurisdictions;

v. require that only safe medical devices including IVDs that perform as the manufacturer describes in its labelling shall be placed on the market;
vi. specify market entry conditions for medical devices including IVDs;
vii. establish record keeping, registration and reporting requirements for all parties within the scope of the law, including the regulatory authority;
viii. 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 including IVDs to health facilities and other users.
ix. should foresee and include provisions covering the expanded levels of control, even though those provisions would not be likely to be implemented in the early stages.
x. Provision for resource mobilization for human, financial and others for regulation of medical devices including IVDs.
xi. Provide opportunities for synergies between multiple government bodies overseeing different components of the regulatory functions.
xii. Any other functions as deemed appropriate

Stakeholders must be allowed time to adapt to the new law, i.e. a transition period. Where the necessary prerequisites are in place, a reasonable transition period up to five 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.

3.1.1 Establish medical device and IVDs classification for regulatory purposes

The law should include a medical devices including IVDs classification scheme, based on internationally harmonized practice, to provide an efficient way of regulating each medical device according to its risk class (2). Each Partner States law should include provisions for the regulatory authority to issue implementing acts and guidance on the risk 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 section 2).

3.1.2 Establish Essential Principles of safety and performance

The law should also establish the fundamental requirement that all medical devices including IVDs be shown to be safe, to perform as intended and to 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 is in compliance with the Essential Principles (see section 2) (5).

3.2 Basic-level controls and enforcement – premarket

Only medical devices including IVDs 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 including IVDs requires that the manufacturer, through its labelling, provides the user with information on how to properly install, use and maintain them.

3.2.1 Establish a basis for reliance and recognition

The medical devices including IVDs law should encourage reliance and recognition techniques to be used by the regulatory authority to determine whether a medical device including IVDs complies with the regulatory requirements of another jurisdiction and to use this information as the basis for allowing the medical devices including IVDs to be placed on the domestic market and or collaboration within NMRAs on joint sessessment and registration of medical devices including IVDs. However, the NMRA is ultimately responsible for determining whether a medical device including IVDs may be supplied in its jurisdiction (see section 3.1).

3.2.2 Establish requirements for declaration of conformity

The medical devices including IVDs 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. At a minimum, this declaration should contain the following:

- the regulation under which the declaration is made;
- 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 or her name;
- description of the device including IVDs and its classification according to the regulation;
- the declaration that the medical device is of good quality, is safe and will perform as intended during its lifetime when used according to the manufacturer's instructions for the manufacturer's stated intended purpose;
- information sufficient to identify the device(s) to which the declaration of conformity applies;

- the list of standards used in demonstrating compliance with Essential Principles;
- the name, position and signature of the responsible person who has completed the declaration upon the manufacturer's behalf;
- the date on which the declaration is issued.

3.2.3 Establish requirement for manufacturers medical devices including IVDs to implement QMS

To ensure Medical devices including IVDs are designed and manufactured to meet safety and performance requirements during their lifetime, the law should require manufacturers of all classes of medical devices including IVDs 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 that the QMS requirements should be aligned with the specifications in the current ISO 13485 Medical devices including IVDs Quality management systems Requirements for regulatory purposes[15] and current ISO 14971. Medical devices including IVDs – Application of risk management to medical devices including IVDs[16].

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.

3.2.4 Establish requirements for labels and labelling

The safe and effective use of most medical devices including IVDs requires that the user be given information on how to use them properly and, where appropriate, how 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 including IVDs. The law should include a requirement that labels, and labelling are appropriate to the intended user of a device, especially for laypersons, and set language(s) requirements[7]. To begin establishing regulatory controls, regulatory authorities must provide specific guidance on the labelling and language requirements for medical devices including IVDs 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 also consider whether instructions for use may be provided in addition to or instead of the printed

instructions in alternative media such as via the Internet or on CD-ROMs[17]. However, printed instructions for use shall be provided if requested by the user.

Another function of labelling is to allow the identification of medical devices including IVDs for example, lot number, or serial number. This allows traceability to facilitate FSCA and helps in the reporting and investigation of adverse events. A recent development is the addition of an internationally harmonized unique device identifier to the label[18].

3.2.5 Prohibit deceptive, misleading and false advertising

In addition to requirements for labelling of medical devices including IVDs, consideration should be given to inclusion in the law of provisions and prohibitions with respect to advertising and promotion for medical devices including IVDs including explicit enforcement measures. The regulatory authority should issue clear guidance to make these requirements explicit. Those basic regulatory controls should ensure that promotion, including online promotion:

i. does not target inappropriate audiences;

ii. makes only claims that are supported by evidence;

iii. covers only medical devices including IVDs that have been authorized for marketing;

iv. is consistent with indications for use and other information in the product labelling;

v. 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 that a requirement is breached, it shall take appropriate enforcement actions, which could include preventing the medical device including IVDs from being placed on the market and/or recalling medical devices including IVDs already placed on the market.

3.2.6 Establish provisions for exceptional premarket situations

In situations such as public health emergencies, exemptions from some regulatory requirements may be needed. Such exemptions should, however, be applied 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. Such exemptions should be clearly stipulated and explained.

The law should establish defined exemptions from, and provide enforcement discretion for, compliance with certain requirements, for example, medical devices including IVDs for humanitarian use, public health emergencies, clinical investigations, exhibition use and medical devices including IVDs donated to the country by charities or the manufacturer. Regulators should issue clear guidance on such exemptions.

3.3 Basic-level controls and enforcement – placing on the market

Many of the EAC countries depend almost entirely on imported medical devices including IVDs. However, it is impractical for a medical device including IVDs manufacturer to have a physical or legal presence in every country. Therefore, the law should require a manufacturer outside the jurisdiction of the country concerned to appoint an authorized representative within the country[19].

3.3.1 Registration of establishments

A key element of basic-level controls is effective oversight of medical devices including IVDs placed on the domestic market and the parties responsible for bringing medical devices including IVDs to the market. The law should require local manufacturers, authorized representatives, importers and distributors (in some cases the authorized representative may also be the importer and/or distributor) who place medical devices including IVDs on the market or make medical devices including IVDs available for use in the jurisdiction, to register with the regulatory authority[20]. Significant changes in a registered establishment (e.g. ownership, location, name of the responsible person or scope of activities) should be notified to the authorities to ensure that registration information is current and correct. Among other purposes, the registration process allows the regulatory authority to determine who is responsible for a product's conformity with the regulatory requirements and for taking corrective actions in the event of a problem with a device. 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 action (FSCA) and for law enforcement purposes. Making registration and listing information publicly accessible allows device purchasers or users of medical devices including IVDs to identify products available to them and determine the identity and location of their manufacturers and/or distributors and/or importers.

3.3.1.1 Authorized representatives or Local representatives

The minimum requirements for registration shall be that the authorized/local 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]. Additionally, the regulation may require the applicant's authorized representative to attest that it will act on behalf of the manufacturer in its dealings with the regulatory authority by:

i. submitting a regularly updated listing of the medical devices including IVDs placed on the domestic market;
ii. providing the regulatory authority with the information it requires when the manufacturer seeks authorization to market its devices;
iii. 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;
iv. informing the regulatory authority of any FSCA to be taken within the local market;
v. cooperating with the manufacturer's importers and distributors;
vi. ensuring training is provided to the user by the distributor, manufacturer or third party, according to the manufacturer's requirements;
vii. cooperating with the regulatory authority and providing it with any information it requires during market surveillance activities.
viii. When required, to institute recall on defective of devices on the market on behalf of the manufacturer.

3.3.1.2 Importers and distributors

The minimum requirements for registration shall be that the importer and distributor provide 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. Beyond this, the regulation may require the applicant importer or distributor to attest that it will, for example:

i. ensure the medical devices including IVDs it imports or distributes comply with the medical devices including IVDs law and are accompanied by the proper documentation and labelling;
ii. trace medical devices including IVDs through that part of the supply chain with which it is directly involved;

iii. comply with the manufacturer's requirements for the storage, handling, transport and, as appropriate, maintenance of medical devices including IVDs.

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

3.3.2 Listing of medical devices including IVDs

The NMRA shall establish a requirement and information system for authorized representatives of manufacturers outside the jurisdiction, and importers and distributors, to submit a listing of medical devices including IVDs they place on the national market and to ensure information retained within the device listing system relating to those medical devices including IVDs in the market is up to date (24). Among other elements, the listing should provide the standardized generic descriptive names of those medical devices including IVDs, for example, those of the Global Medical Device Nomenclature (GMDN). Listing of medical devices including IVDs 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 including IVDs legally placed on the market.

It should be understood that listing is not of itself equivalent to, or evidence of a marketing authorization.

3.3.3 Import controls

Apart from the basic controls of registering establishments and listing marketed medical devices including IVDs, 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 including IVDs are to be imported provides 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, Lot verification testing of IVDs). 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 including IVDs will not be released from the port of entry unless there is proof that the regulatory authority has authorized them to be placed on the market. It may be helpful to designate official ports of entry for medical devices including IVDs so that the regulatory authority may better focus its enforcement activities.

3.4 Basic-level controls – post market

In clinical use medical devices including IVDs may not always perform as expected. This may indicate potential problems in their design, manufacture, labelling, storage or distribution. It could also reflect inappropriate device selection, installation, use or maintenance.

3.4.1 Establish a system for vigilance reporting

At the basic level the regulatory authority shall establish a system whereby users, patients and the manufacturer of medical devices including IVDs, either directly or through the authorized representative, can report complaints involving medical devices including IVDs, including malfunction at the device level and adverse events at the patient level, in particular those adverse events resulting in death or serious injury[21]. For IVDs, the risk of harm is usually indirect as the device is not used on the body: for instance, for high-risk IVDs a severe adverse event may include higher-than-expected false-negative results. Reports of adverse events received by the regulatory authority from the patient or end-user must be passed to the device manufacturer for investigation and trend analysis with possible FSCA and notification through a field safety notice. Vigilance reports may trigger investigation, trend analysis and/or possible FSCA or enforcement actions[22]. They may also prompt the regulatory authority to exchange information with regulatory authorities in other jurisdictions on similar occurrences elsewhere[23].

3.4.2 Require mandatory notification by the manufacturer of FSCA

The law should require a manufacturer, either directly or through its authorized representative, to report to the regulatory authority in a timely manner any FSCA 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 any newly identified 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 should prepare the regulatory authority to respond to questions from the public, clinicians, media or government and to exchange information with authorities in other jurisdictions.

3.4.3 Establish a procedure to withdraw unsafe medical devices including IVDs from the market

Regulatory authorities have an obligation to enforce laws and regulations on medical devices including IVDs 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.

Various approaches to enforcing regulations may be used, for example: suspension or withdrawal of registration of local manufacturers, authorized representatives, importers or distributors; withdrawal from the list of marketed medical devices including IVDs; or recall, quarantine and disposal of medical devices including IVDs. 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 whose labelling has been shown to be inadequate. Enforcement may also include issuance of public alerts, warning letters, prosecution and financial penalties. While the regulatory authority’s primary responsibility is for the health of its own citizens, where it believes an imported medical device is unsafe or of poor quality, it should consider sharing its opinion with the regulatory authority responsible for auditing the device manufacturer’s QMS, for the purpose of preventing similar devices being exported to other markets.

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

3.4.4 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 EAC framework recommends the regulatory authority to establish a procedure to directly notify health-care facilities that use the affected medical devices including IVDs, and other users, of serious adverse incidents and FSCA by issuing safety alerts and advisories[22]. Where possible, the text of any such alert should be discussed with the manufacturer or her or his authorized representative but the final decision lies with the regulator.

3.4.5 Undertake market surveillance

Market surveillance is the activity of the regulatory authority related to oversight of medical devices including IVDs on the domestic market. The regulatory authority may undertake targeted activities based on a risk assessment of the distribution chain, evaluation of complaints and adverse event reporting, and information from the post market surveillance systems of medical device manufacturers and their authorized representatives[23]. Table 5 summarizes the basic control elements

LEGAL FRAMEWORK		
Premarket	Placing on the market	Post market
Publish law, including definition, and regulation with the transition period	Registration of establishments	Establish system for vigilance report
Establish medical device classification for regulatory purposes	Listing of medical devices including IVDs	Require mandatory notification by the manufacturer of field safety corrective actions
Establish Essential Principles of safety and performance	Import controls	Establish a procedure to withdraw unsafe medical devices including IVDs from the market
Establish basis for reliance and recognition		Establish procedure to issue safety alerts to users

Establish requirements for declaration of conformity		Undertake market surveillance
Establish requirements for manufacturers for a QMS		
Establish requirements for labels and labelling		
Prohibit deceptive, misleading and false advertising		
Establish provisions for exceptional premarket situations		

Table 5. Basic control elements

4 Expanded-level controls

Once the basic-level controls have been implemented effectively and efficiently, the regulatory authority may consider implementing more advanced controls. To do so, the law should provide the legal basis for such expanded controls, the regulatory authority must have effectively enforced 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 the controls described below according to the priorities of the Partner State. A stepwise approach is recommended for the implementation of individual elements of expanded controls depending on the availability of technical expertise and resources

4.1 Expanded-level controls – premarket

4.1.1 Create oversight of clinical investigations

The regulatory framework should grant to 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 accepting responsibility and liability for the initiation or implementation of a clinical investigation, such as the 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[24]. 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.5 A widely used international standard for the practice of clinical investigation is: ISO 14155 – Clinical investigation of medical devices including IVDs for human subjects – Good clinical practice[11].

The NMRA should also establish a mechanism for periodic progress reports and for the reporting of serious adverse events that occur during clinical investigations[25]. In-country clinical investigations should generally not be required, unless there is are compelling and sound scientific reasons.

4.1.2 Appoint and have oversight of CAB

Certain technical elements of the regulatory framework may be delegated to designated or recognized third-party organizations, often private, generally known as CABs[26,27]. Authorities may establish criteria for designation of CABs. These bodies may perform initial certification and surveillance audits of device manufacturer QMS and/or premarketing reviews of the conformity of a device to the Essential Principles. The CAB may be designated by the regulatory authority to undertake conformity assessment of specific medical devices including IVDs where it is judged to have the necessary skills (e.g. active implantable and/or IVDs and/or electro-medical devices including IVDs). Satisfactory compliance with requirements is typically documented with a CAB certificate[28]. 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[29]. 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[30].

4.1.3 Recognition of standards

Conformity with voluntary standards is a means by which the manufacturer may demonstrate that a medical device conforms to one or more of the Essential Principles of safety and performance, consistently throughout its life cycle. Medical device standards can largely be grouped into three categories:

i. 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;
ii. 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;
iii. 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 and for IVDs.

At the expanded level, the regulatory authority may wish to establish a procedure to identify national versions of international standards that it accepts as providing presumption of compliance to specific Essential Principles, i.e. “recognized standards”.

Preference for recognition should be given to international standards, e.g. those of the International Organization for Standardization (ISO) 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 than placing the standards into legislation; they can then be updated to stay current and can be revised much faster than legislation can be updated.

4.1.4 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 including IVDs 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. It also facilitates the exchange of information among NMRAs. For these reasons the regulatory authority should adopt an international nomenclature system for medical devices including IVDs.

The GMDN 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 including IVDs for regulatory purposes. There are other established nomenclature systems such as the Universal Medical Device Nomenclature System (UMDNS) and ISO 9999:2011– Assistive products for persons with disability – Classification and terminology.

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. listing, applications for marketing authorization, post market surveillance and 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.

4.1.5 Control advertising and promotion

As part of their market development efforts, manufacturers, importers and distributors generally seek to promote medical devices including IVDs to health-care professionals, users and/ or patients. At a minimum, advertising and promotion should not be false, misleading or deceptive. In countries where the presence of misleading and inaccurate advertisements is a particular problem, the regulatory authority may expand controls to include review of advertising and promotional material before it is placed on the market. At this time, the regulatory authority 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 IVDs, including online promotion. If not, they should consider whether specific guidance is required.

4.2 Expanded level controls – placing on the market

4.2.1 Perform in-country QMS 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 conformity of the device 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 Model recommends that the law should require manufacturers of all classes of medical devices including IVDs 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 an implementing act or ministerial decree that requires the **regulatory authority to verify that a QMS appropriate to the medical devices including IVDs under its control has been implemented**.

Although manufacturers of Class A medical devices including IVDs are required to implement a QMS, they are not subject to inspection by the regulatory authority prior to marketing approval nor routinely inspected by the regulatory authority after the devices have been placed on the market. The NMRA 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 CABs to perform QMS audits or otherwise gather and assess evidence of the manufacturer's effective implementation of the QMS requirements[9].

Because most medical devices including IVDs are imported, the option of reliance or recognition is likely to be appropriate: it will often be sufficient for the regulatory authority to rely upon evidence, including QMS certificates, of the manufacturer's compliance with internationally-recognized QMS requirements in other jurisdictions. The receiving country thereby relies upon the information from the QMS audit or recognizes the decision of the other jurisdiction regarding the QMS audit. The regulatory authority may also review and recognize the manufacturer's own declaration of conformity and current certificates of conformity with the current ISO 13485, issued by a recognized CAB. The regulatory authority should verify that such certificates remain valid and cover the scope of medical devices including IVDs and activities appropriate for the devices being imported.

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

4.2.2 Perform review of submissions for compliance with Essential Principles

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

At the basic level, assessing the safety and performance of medical devices including IVDs depends primarily on an assessment by another regulatory authority supported by the manufacturer's declaration of conformity. At the expanded level, the NMRA may establish a requirement for the premarketing review of a manufacturer's submission. Guidance on the process for application and approval should be provided. This will usually be through completion of a prescribed form or access to the authority's 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[41,42] and the Association of Southeast Asian Nations (ASEAN) Common Submission Dossier Template (CSDT)[43]. In addition, WHO has also developed several SOPs for submission which can be adapted. These formats provide guidance for the presentation of evidence that a medical device conforms to the regulatory requirements for safety and performance.

The IMDRF (GHTF) 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 including IVDs[44 45].

EAC NMRAs 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 technical documentation submitted by the manufacturer. For example, when:

i. the device incorporates innovative technology;
ii. an existing compliant device is being used for a new intended use;
iii. the device type is new to the manufacturer;

iv. the device type tends to be associated with an excessive number of adverse events, including use errors;
v. the device incorporates innovative or potentially hazardous materials;
vi. 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 premarket assessment, non- discriminatory country-specific requirements should be considered e.g. local language labelling, electrical supply, public health policies, 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[46].

The regulatory authority may be assisted in reaching its decision on premarket 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 regulatory authority should ensure that the necessary agreements for the exchange of confidential information are in place. The final decision rests at all times with the regulatory authority. EAC countries should consider conducting such assessment carefully. Decision to conduct such assessment should be guided by Class of IVD as established by the risk classification, and availability of competent and well-trained human resource.

In absence of the capacity the best option is leverage reliance and or recognition of work done by other stringent regulatory authorities such as FDA, CE marking, WHO PQ. WHO has established collaborative procedure which enables Partner States to access assessment data of WHO prequalified products in collaboration with the manufacturer.

4.3 Expanded-level controls – post market

4.3.1 Establish within the regulatory authority processes for post market surveillance and vigilance

At the basic level a system for reporting adverse events involving medical devices including IVDs to the regulatory authority, in particular those resulting in death or serious injury, shall be established. However, 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. Properly structured post marketing surveillance 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 premarket evaluation and provide for corrective actions. This may include exchange of alerts internationally in a standardized manner[47].

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

i. adverse event reporting and complaint handling systems with clear responsibilities for the regulator, manufacturer, authorized representative, importer and distributors;
ii. analysis and investigation of reported adverse events by the manufacturer and regulatory authority;
iii. maintenance by parties in the distribution chain (importers and distributors) of appropriate records of complaints and actions taken;
iv. oversight of 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 fulfils the national regulatory requirements and maintains records of the distribution of the device. The agreement should require the authorized representative to report serious adverse events, quality problems and complaints to the NMRA and manufacturer for investigation and corrective action.

4.3.2 Require mandatory reporting of adverse events

To the extent that 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 including IVDs in the jurisdiction. It should define the threshold for reporting (i.e. what kinds of events should be reported), reporting time limits, required information and which party (or parties) shall report. In general,

those criteria should be consistent with the EAC guidance on adverse event reporting[46].

4.3.3 Inspections of registered establishments

The regulatory authority may inspect periodically, scheduled or unannounced, all registered organizations to confirm they have the facilities, procedures and records in place to allow them to comply with the attestations made when they were registered. Additionally, the regulatory authority may issue licenses to the registered organization, renewable on a periodic basis. The registration or license if such has been issued may be withdrawn or suspended if non-conformities[48] are found during inspection.

4.3.3.1.1 Distribution of medical devices including IVDs

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 including IVDs may be affected after release from the manufacturer by various factors such as storage conditions, 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:

i. select appropriately qualified distributors (appropriate and adequate facilities, information systems and qualified staff);
ii. specify the requirements for medical device storage, handling, transport, installation, servicing and traceability of record keeping;
iii. 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, and implementation of FSCA for medical devices including IVDs may be conducted by the manufacturer through cooperation with its authorized representative and distributors. As with a manufacturer, a distributor would benefit from implementing a basic QMS to control its activities.

The NMRA shall prepare guidelines on distribution of medical devises including IVDs. In addition, it shall regularly inspect and verify implementation of the

established regulation including storage and distribution of the products, collection of post market surveillance data in collaboration with the manufacturer of the products.

4.3.3.1.2 Local production

The EAC Partner States import most of the medical devices including IVDs including IVDs, in the interests of safeguarding public health, local manufacturers should be subject to the same regulatory controls as manufacturers of imported medical devices including IVDs. 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 designate a CAB to act on its behalf. In the case of inspections to investigate suspected noncompliance or problems with products, the NMRAs shall undertake the inspection itself.

The NMRAs in the Partner States shall provide guidance specifically for local manufacturers.

4.3.4 Provide for testing laboratories

Testing Laboratories are utilized by all manner or business to provide objective analytical data on the quality of a product or a process (definitions.uslegal.com). Testing laboratory has great role in regulation of medical devices including IVDs. Tasks that may be undertaken by an appropriately qualified and equipped testing laboratories include:

i. Verification of performance of the medical devices especially IVDs as part of the premarket registration.
ii. institution of a programme of post market testing of specific imported devices according to specific national public health risks
iii. post-shipment lot verification testing of IVDs
iv. investigation of devices allegedly involved in a serious adverse event;

Given the diversity of medical devices including IVDs, it is unlikely that an NMRA will have all the necessary resources internally to establish and maintain its own laboratory. The WHO Model does not recommend that a regulatory authority sets up its own testing laboratory as, if it is to be effective, it requires a significant budget and qualified staff. When relying upon a testing laboratory, inside or outside the national jurisdiction, the authority should consider whether a laboratory has:

- accreditations to recognized current standards;

- technical competence;
- access to external experts, as needed;
- adequate resources, such as specialized equipment, specimen banks;
- QMS and instrument calibration facilities.

The summary of the expanded control of medical devices including IVDs are shown in Table 6.

LEGAL FRAMEWORK		
Premarket	**Placing on the market**	**Post market**
Create oversight of clinical investigations	Perform in-country quality management systems audit	Establish within the regulatory authority a post surveillance and vigilance reporting system
Appoint and have oversight of CAB	Perform review of submissions for compliance with essential Principles	Require mandatory reporting by manufacturers of adverse events
Recognize standards		Inspections of registered establishments
Adopt medical device nomenclature system		Provide for testing laboratories
Control advertising and promotion		

Table 6: Summary of the expanded level controls and enforcement

5 Stepwise approach, harmonization, reliance and 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 sub-regional 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 IVDs including

diagnostics" and "to promote the greater participation of Partner Statess in existing international and regional initiatives for collaboration and cooperation in accordance with WHO principles and guidelines".

National regulation of medical devices including IVDs is taking place in an increasingly globalized world, creating a need for closer alignment of regulatory requirements and practices. Accordingly, countries that align their medical device regulations with existing harmonization guidance documents will promote this necessary regulatory convergence.

WHA Resolution 67.20 also urges s to "engage in global, regional and sub-regional 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 contribute to more effective regulatory systems. They are an essential component of health system strengthening and contribute to better public health outcomes.

6.0 OTHER IMPORTANT REGULATORY ASPECTS FOR CONSIDERATION:

It is important as EAC Partner States to have common approach in other regulatory activities which are considered critical when developing and implementing regulations for medical devices including IVDs.

6.1 Determination to establish whether a medical product is a medical device including IVDs

Many products are used in the delivery of health care, yet not all fall comfortably within an existing definition for a medical product, more specifically the term "medical device". Some of the examples include medical gases, some laxatives, cosmetic articles, clinical laboratory reagents and articles of protective clothing worn by medical personnel during procedures. Products that may be considered to be medical devices including IVDs in some jurisdictions but not in others include disinfection substances, aids for persons with disabilities, devices incorporating animal and/or human tissues, and devices for in vitro fertilization or assisted reproduction technologies. A lack of clarity in such cases may lead to overlapping or conflicting regulatory requirements for a product, or in some jurisdictions, no separate regulation for such medical products. 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 including IVDs or for other regulated product sectors (e.g. medicines including advanced therapy medicinal products, biologicals and regenerative medicine products, cosmetics, food supplements or personal protective equipment).

To be predictable and transparent, the EAC regulatory authorities should develop criteria and mechanisms for determining the appropriate regulatory regime for such products through guidelines. It should describe considerations and the process whereby an applicant may obtain an advisory opinion from the regulatory authority before a product is applied for market authorization. Where necessary, that process should allow for consultation with subject matter experts as well as with regulatory authorities from other product sectors such as medicines or foods and with the manufacturers concerned. 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.

Borderline products such as sanitary pads, breast pumps are generally medical products for which it is unclear which legislation applies. Although they may have some of the attributes of two or more categories of regulated products, they are not combination products. A combination product is a product comprising two or more components which are regulated as medical products, i.e. medicine/medical device, or vaccine/medical device, which are physically, chemically or otherwise combined or mixed and produced as a single entity.

6.2 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 before the end of its 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 including IVDs should follow safety procedures to ensure that it does not cause harm to people or the environment. This is especially important for contaminated devices such as syringes or hypodermic needles, and devices that contain infectious, toxic or radiological materials. Medical device including IVDs labelling and instructions for use should include information on proper disposal at the end of device’s life, as appropriate for the type of device. Where the regulatory authority has identified substandard and falsified medical devices including IVDs, it shall itself dispose off

such products to ensure that they are not reused or exported to another country where they may cause harm.

Owing to their diversity and complexity, there are many ways that medical devices including IVDs 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 and followed. The responsible regulatory authority, in coordination with other concerned governmental bodies, should establish criteria for replacement and decommissioning 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 them.

6.3 Donations

Charitable donations of medical devices including 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 potential issue is a 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 including IVDs 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 including IVDs are "substandard" and have been "dumped" on a receiving country. For these reasons some countries have banned donations of used equipment.

To safeguard public health, medical devices including IVDs imported as donations should comply with all regulatory requirements on safety, quality and performance and should not differ from 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 including IVDs. 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. All donors are required to familiarize themselves with the donation requirements before they decide to donate medical devices including IVDs. Donations that do not comply with the requirements should be rejected and sent back to the donor at the donor's expense.

6.4 Reprocessing of single-use medical devices including IVDs

Single-use medical devices including IVDs (SUMDs) such as surgical forceps, stethoscope and endoscope etc. are designed and labelled for single use. They do not come with appropriate instructions for cleaning, disinfecting or sterilization procedures after use and the manufacturer has not investigated any deterioration in performance if they are subject to reprocessing. This may pose a danger to the patient when SUMDs are reprocessed and 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 as a result of the inability to assure the complete removal of viable microorganisms, inadequate cleaning, decontamination and removal of pyrogens and material alteration. Exposure to chemical cleaning agents may cause corrosion or changes in the materials of the device, and exposure to repeated sterilization processes may also change the properties or degrade the device material. The high temperature and harsh chemicals sometimes used during processing may impair the quality of reprocessed devices.

In addition to the potential health risks associated with the use of reprocessed SUMDs, ethical considerations arise. These considerations include whether it is justifiable to treat a patient with a reprocessed SUMD that may be of lower quality,

performance or cleanliness than it had when used for the first time, even with informed consent. Other considerations include liability: the entity that reprocesses a medical device becomes the new manufacturer with the associated responsibilities.

In adopting a policy on the reprocessing of SUMDs, the NMRAs 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. To allow their reuse, the entity that reprocesses and distributes medical devices including IVDs labelled by their original manufacturer for single-use only will be subject to the same requirements of safety, quality and performance as manufacturers of new devices. This applies equally to a health-care facility fully reprocessing SUMDs 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 their occurrence. The policy on the use of a reprocessed SUMD should only be enacted after appropriate risk–benefit analyses are performed on the potential risks described above.

6.5 Refurbishing electro-medical devices including IVDs

Some medical devices including IVDs, typically durable electro-medical devices including IVDs, are meant to be reused many times over a long design life. In some cases, they may be subject to refurbishing by an organization or entity 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 its condition when new. This includes reconditioning, repair, installation of certain software and/or hardware updates that do not change the intended use of the original device, and replacements of worn parts. Refurbished medical devices including IVDs should be identified as such on the labelling.

In adopting a policy on refurbishing, the regulatory authority should clearly state that the entity responsible for refurbishing or third party must meet the same regulatory requirements as applied to the original medical device. A party that refurbishes medical devices including IVDs will be subject to the same requirements of safety, quality and performance as manufacturers of new devices

6.6 Substandard and falsified products

Substandard and falsified medical devices including IVDs are harmful to the health of patients, damage confidence in medical products and health-care providers and increase the burden on health systems. SF medical devices including IVDs can result from genuine manufacturing errors or deliberate falsification of a product. The latter is usually a clandestine activity, is often difficult to detect and is designed to deceive a health-care provider or patient into believing that the device is the genuine article and has been carefully assessed in terms of quality, safety and effectiveness.

Reports of substandard and falsified medical devices including IVDs including IVDs have emerged from all over the world. The United States Food and Drug Administration (US FDA) has issued a letter concerning contaminated surgical hernia mesh. The United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) raided a business following a complaint about a portable dental X-ray unit available on eBay. The unit 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 *(72)*. The trade in SF medical devices including IVDs is driven and motivated by profit. Where a demand exists, those engaged in the manufacture and distribution of SF devices will respond. They will utilize online 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 may be required to distinguish the SF 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 including IVDs will assist in the prevention of SF devices reaching users and patients. Balanced awareness-raising among consumers, health-care providers and distributors can help to minimize the threat posed by SF medical products while 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 SF medical devices including IVDs early on. Regulatory authorities should establish mechanisms that enable and encourage reporting of suspicious medical devices including IVDs 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 SF 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 SF products. Strengthening capacity among 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.

6.7 WHO Prequalification Team for IVDs

Lack of access to quality health technologies, in particular IVDs, reduces the opportunity for progress towards addressing high-burden diseases in certain countries. The WHO Prequalification Team (PQT) 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 including IVDs (mostly IVDs), the regulatory authority may choose to rely upon evaluations conducted by the PQT for IVDs. This is a quality assurance programme that aims at promoting and facilitating access to safe, appropriate and affordable IVDs of good quality. The focus of this programme is on IVDs for priority diseases such as HIV/AIDS, malaria, hepatitis C and others, and their suitability for use in resource- limited settings.

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

• review of the technical documentation (product dossier) *(79)*;

• independent performance evaluation; • inspection of manufacturing site(s).

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, Clinical & Laboratory Standards Institute (CLSI) and IMDRF/GHTF, to ensure compliance with the Essential Principles. Like other stringent regulatory reviews, prequalification assessments cover 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:

i. the regulatory version marketed on the global market is assessed;

ii. the scrutiny level reflects individual and public health risks in resource- limited settings;

iii. data submitted by the manufacturer are assessed from the perspective of resource-limited settings in order to reflect the resource-limited settings' environment and users.

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

6.8 United Nations Population Fund Prequalification Programme for intrauterine devices and condoms

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

As for 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. Manufacturers of female condoms are expected to demonstrate the safety, efficacy and acceptability of new designs. 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/Reproductive Health and Research (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 TFs 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 PQTs.

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