Document #: TMDA/DMD/MDA/G/001
Rev #:03

THE UNITED REPUBLIC OF TANZANIA

MINISTRY OF HEALTH

TANZANIA MEDICINES AND MEDICAL DEVICES AUTHORITY

COMPENDIUM OF GUIDELINES FOR MARKETING AUTHORIZATION OF MEDICAL DEVICES, DIAGNOSTICS AND LABORATORY EQUIPMENT

June 2024

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ABBREVIATIONS

CAB	-	Conformity Assessment Body
DoC	-	Declaration of Conformity
ENT	-	Ear, Nose and Throat (Otorhinolaryngology)
FSCA	-	Field Safety Corrective Action
GHTF	-	Global Harmonization Task Force
GMDN	-	Global Medical Devices Nomenclature
HAS	-	Health Sciences Authority
IFU	-	Instructions for Use
IMDRF	-	International Medical Devices Regulatory Forum
ISO	-	International Organization for Standardization
IVDDs	-	In Vitro Diagnostics Devices
LRP	-	Local Representative Person
MA	-	Market Authorization
MAH	-	Marketing Authorization Holder
SAL	-	Sterility Assurance Level
QMS	-	Quality Management System
TMDA	-	Tanzania Medicines and Medical Devices Authority
TMDCA	-	Tanzania Medicines and Medical Devices Act, Cap 219
WHO	-	World Health Organization

ACKNOWLEDGEMENTS

This compendium marks a significant milestone as the first comprehensive resource for marketing authorization for medical devices, diagnostics, and laboratory equipment developed by the Tanzania Medicines and Medical Devices Authority (TMDA). The development process involved an extensive review and synthesis of existing guidelines.

I extend my heartfelt appreciation to the dedicated TMDA staff, particularly Ms. Rehema F. Mariki, Ms. Gudula S. Mpanda, Dr. Shani M. Maboko, Ms. Engerasia T. Mtui, Ms. Edina Z. Nyasana, Mr. David A. Mwakyoma and Mr. Abel J. Walelo, whose diligent efforts were instrumental in perfecting this document. I am also deeply grateful to the esteemed stakeholders whose valuable feedback contributed to the enhancement of this compendium.

Special thanks are also due to the international organizations whose guidelines were adopted or adapted during this process. These include the EU Medical Devices Coordination Group (EU-MDCG), Therapeutic Goods Administration (TGA) Australia, Health Sciences Authority (HSA) Singapore, International Medical Devices Regulators Forum (IMDRF), World Health Organization (WHO), Health Canada, and the United States Food and Drug Administration (US-FDA). Their accessible guidelines were invaluable in shaping this document.

Kissa W. Mwamwitwa
Director Medical Devices and Diagnostics

FOREWORD

The Tanzania Medicines and Medical Devices Authority (TMDA) was established under the Tanzania Medicines and Medical Devices Act, Cap 219 of 2003. Among its responsibilities is the regulation of the quality, safety and performance of medical devices and diagnostics. This regulatory function includes the registration process, which serves as an official authorization allowing the marketing and free distribution of a medical device following an assessment of its safety and performance.

This has been implemented by using the third edition of the *Guidelines on Submission of Documentation for Registration of In-Vitro Diagnostic Medical Devices* and the third edition of the *Guidelines on Submission of Documentation for Registration of Medical Devices* in Tanzania. To adhere to good practices, these guidelines have been reviewed and combined to develop a comprehensive compendium guideline for the marketing authorization of medical devices, diagnostics, and laboratory equipment.

This compendium introduces new guidelines on Grouping of Medical Devices, Labelling and Information for Use, Clinical Evidence of Medical Devices, Borderline Products and Software as Medical Devices. Additionally, various ISO standards have been referenced to ensure that applicants are provided with the necessary requirements for compiling marketing authorization applications.

In this compendium, we have also introduced the overall dossier summary for applications submitted as a single device, system, family, group, or kit. This aims to ensure that adequate and comprehensive technical information for marketing authorization is provided, which will expedite the assessment process and consequently speed up the authorization of medical devices, diagnostics, and laboratory equipment for marketing in Tanzania.

Applicants are henceforth advised to read the compendium and submit their applications based on the requirements stipulated in this document. It should be noted that the requirements outlined in this compendium are considered minimal; therefore, applicants may be required to submit additional data or information to substantiate the quality, safety, and performance claims made in their applications.

The Authority will continue to review and update the compendium in line with current international and national requirements.

Dr. Adam M. Fimbo
Director General

INTRODUCTION

This compendium intends to prescribe the procedures and regulatory requirements that need to be fulfilled in order for a medical device, in vitro diagnostics and laboratory equipment to be granted marketing authorization. The compendium consists of eleven parts (XI) consisting of individual guidelines. These guidelines provide detailed information on specific aspects the marketing authorization procedures including a description of how applicants can comply with the regulatory requirements.

The overall objective is to provide applicants with a single document that contains all required information for ease of reference during dossier compilation. The compendium consists of the following guidelines: -

Part I: Guidelines on General Procedural Aspects for Applications for Market Authorization of Medical Devices, In-Vitro Diagnostic Devices and Laboratory Equipment

Part II: Guidelines on Technical Documentation Requirements for Registration of Medical Devices

Part III: Guidelines on Technical Documentation Requirements for Registration of In-Vitro Diagnostic Devices

Part IV: Guidelines for Notification of Medical Devices Exempted from Registration

Part V: Guidelines on Classification of Medical Devices

Part VI: Guidelines on Classification of In-vitro Diagnostic Devices (IVDDs)

Part VII: Guidelines on Clinical Evidence of Medical Devices

Part VIII: Guidelines on Labelling Requirements for Medical Devices, In-vitro Diagnostic Devices and Laboratory Equipment including Electronic IFU

Part IX: Guidelines on Grouping of Medical Devices and In-vitro Diagnostic Devices

Part X: Guidelines for Software Medical Devices

Part XI: Guidelines for Borderline Products

Adherence to these guidelines by the manufacturers/applicants will facilitate timely assessments and approvals of medical devices hence ensuring that Tanzanians

have access to quality and safe medical devices and diagnostics that perform as intended by the manufacturer.

DEFINITION OF TERMS

Active Medical Devices

Means a medical device that depends for its operation on a source of energy other than energy generated by the human body or gravity.

Accessory

Means an article that is intended specifically by its product owner to be used together with a particular medical device to enable or assist that device to be used in accordance with its intended purpose. An accessory is typically intended to be used for one or more of the purposes as described in the definition of medicaldevice and therefore should be considered a medical device.

Applicant

Means a person who owns a formula or trademark of a product, who may be a manufacturer or a person to whose order and specifications, the product is manufactured and who shall be the marketing authorization holder and have the primary responsibility of the product on the Tanzanian market.

Authority

Means the Tanzania Medicines and Medical Devices Authority.

Brand name

Means a unique name given by the product owner to identify a medical device as a whole product, also known as the trade name or brand name.

Confirmatory device

Means a device intended to be used for the confirmation of a reactive result from a first line assay.

Detecting the exposure to an agent

Means the indirect detection of an agent (present or past exposure) by detecting the presence of surrogate markers, such as antibodies against components of the agent.

Detecting the presence of an agent

Means the direct detection of the agent, by detecting the presence of the agent itself (e.g. bacterial, viral, fungal, parasitic, protozoal agents), or the presence of structural components derived from the agent, such as antigens or nucleic acids.

Device

Means a medical device, in-vitro diagnostic device or laboratory equipment.

Devices for monitoring

Means devices that are used for the measurement of the analyte (measurand) levels for the purpose of adjusting treatments/interventions as required. Devices for monitoring include the following:

a) Devices which are used to assess whether an analyte remains within physiological levels or within an established therapeutic drug range. These types of devices are designed to evaluate an individual's current state.
b) Devices which are used for serial measurement, whereby multiple determinations are taken over time. These types of devices are typically used for the detection/assessment of disease progression/regression, disease recurrence, minimum residual disease, response/resistance to therapy, and/or adverse effects due to therapy. These types of devices are designed to evaluate changes in an individual's state.

Devices for screening

Means devices that are used to detect the presence of or the predisposition to a disease, disorder or other physiological state in a specimen from an individual, embryo or foetus not demonstrating clinically evident symptoms.

Depending on the nature of the condition and the targeted patient population, screening devices may be used routinely or may be restricted to "at risk" patients. This also includes (for example) devices intended to assess the suitability of blood, blood components, cells, tissues or organs, or in any of their derivatives for transfusion, transplantation or cell administration, with respect to transmissible agents.

Devices for self-testing

Means any device intended by the manufacturer to be used by lay persons, including devices used for testing services offered to lay persons by means of information society services.

Embryo or foetus

Means to stages in human development after zygote formation. A zygote is considered an embryo in particular from the period of conception to approximately the eighth week, and considered a foetus following this period until birth. Samples from the embryo or foetus include samples from the embryonic/foetal membranes, fluids and excretions, the umbilical cord, and maternal samples (e.g. blood) containing embryonic/foetal material to be examined.

First-line device

Means a device intended to be used to detect a marker or analyte, and which may be followed by a confirmatory assay. Devices intended to be used solelyto monitor a previously determined marker or analyte are not considered first-line assays.

Intended purpose/use

Means the objective intended use or purpose, as reflected in the specifications, instructions and information provided by the manufacturer of the medical device.

Infective/infectious agent

Means is an agent capable of producing infection. This includes iatrogenic infections, i.e. those infections transmitted during medical treatment and care.

In Vitro Diagnostic Medical Device

Means a 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. This includes reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles.

Label

Means any tag, brand, mark, pictorial or other descriptive matter, written, printed, stenciled, marked, embossed or impressed on or attached to a container of any medical devices.

Labeling/ Information Supplied by the Manufacturer

Means written, printed or graphic matter affixed to a medical device or any of its containers or wrappers or, accompanying a medical device, related to identification, technical description, and use of the medical device, but excluding shipping documents.

Laboratory equipment

Means technological system or device or any tool that is used in health laboratories for any purpose other than diagnosis and does not fall under the definition of a medical device or in-vitro diagnostic device. Example: Laboratory refrigerator; water bath.

Life-threatening

Means diseases, conditions or situations that in general result in death. These are often untreatable; treatment options are limited or require major medicalinterventions.

Local Responsible Person (LRP)

Means a person residing in Tanzania mainland or corporate body registered in Tanzania mainland who has received a mandate from the Applicant to act on his behalf with regard to matters pertaining to registration of medical devices.

Market Authorization

Means registration or notification that is an official approval of a medical device, diagnostic or laboratory equipment for circulation on the market.

Market Authorization Holder (MAH)

Means a person who supplies the health product under his own name, or under any trademark, design, trade name or other name or mark owned or controlled by him.

Manufacturer

Means a person who sells medical devices under their own name, or under a trademark, design, trade name or other name or mark owned or controlled by the person, and who is responsible for designing, manufacturing, assembling, processing, labeling, packaging, refurbishing or modifying the device, or for assigning to it a purpose, whether those tasks are performed by that person or on their behalf.

Manufacturing Site

Means an authorized space where designing, manufacturing, assembling, processing, labeling, packaging, refurbishing or modifying the device take place.

Medical Device

Means an instrument, apparatus, appliance, material, implement, medical equipment, machine, contrivance, implant, in vitro reagent or other similar or related article, including any component, part of accessory, which is: -

a) Recognized in the official National Formulary, or Pharmacopoeia or any supplement to them;
b) Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease, in man or other animals; or
c) Intended to affect the structure or any functions of the body of man or other animals and which does not achieve any of its principal intended purposes through chemical action within the body of man or other animals and which is not depended upon being metabolized for the achievement of any of its principle intended purposes.

Medical Devices with Measuring Function

Device has a measuring function if;

a) The device is intended by the manufacturer to measure: - quantitatively a physiological or anatomical parameter, or - a quantity or a qualifiable characteristic of energy or of substances delivered to or removed from the human body.

b) The result of the measurement - is displayed in legal units or other internationally acceptable units or - is compared to at least one point of reference indicated in legal units or other acceptable units.

c) The intended purpose implies accuracy, claimed explicitly or implicitly, where a non-compliance with the implied accuracy could result in a significant adverse effect on the patient's health and safety.

Medical Device Accessories

Means a separate, finished device intended to "support, supplement, and/or augment the performance" of at least one parent device. Accessories might be marketed individually for use with a specific device type and may be a different class than their parent device.

Medical Device Family

Means a group of medical devices that are made by the same manufacturer that differ only in shape, color, flavor or size, that have the same design and manufacturing process and that have the same intended use.

Medical Device Group

Means a collection of medical devices, such as a procedure pack or tray that is sold under a single name.

Medical Device Procedure Pack

Means a combination of products packaged together and placed on the market with the purpose of being used for a specific medical purpose.

Medical Device Spare Parts / Components

Means "any, substance, piece, part, software, firmware, labeling, or assembly which is intended to be included as part of the finished, packaged, and labeled device." For example, a stethoscope contains multiple parts, including a diaphragm, bell, and tubing. When packaged in whole with the stethoscope, these parts would be considered medical device components that comprise a finished medical device.

Medical Device System

Means a number of components or parts intended to be used together to fulfill some or the entire device's intended functions and that is sold under a single name.

Medical Gases

Means any gases that are intended for therapeutic use for:

a) Treatment and prevention of diseases;
b) Performing diagnostic tests;
c) Calibrating machines used for making diagnostic tests; and/or
d) Restoration, correction and modification of physiological functions in human beings

These include oxygen, medical air, nitric oxide, and mixtures of helium and oxygen and oxygen and carbon dioxide.

Newborn

Means a newborn, or neonate, refers to an infant in the first 28 days after birth.

Offspring

Means the result of conception, at all stages of development, embryo and foetus, premature and full term neonates, child and adults.

Quality Management System

Means a management system to direct and control an organization with regard to quality, from establishing quality policy, quality objectives and implementing and maintaining quality system.

Recognized Standards

Means national or international standards deemed to offer the presumption of conformity to specific essential principles of safety and performance.

Specimen

Means a discrete portion of a body fluid or tissue taken from an individual for examination, study or analysis of one or more quantities or characteristics to determine the character of the whole. This also includes other materials, for example, hair, nails excretions, secretions, or a sample from the skin surface.

Transmissible agent

Means a biological substance or entity capable of causing disease or infection in individuals through individual to individual, animal to individual, or other modes of contact.

PART I

GUIDELINES ON PROCEDURAL ASPECTS FOR MARKETING AUTHORIZATION OF MEDICAL DEVICES, IN VITRO DIAGNOSTIC DEVICES AND LABORATORY EQUIPMENT

1. Scope

This guidance is applicable for applications for marketing authorization (registration and notification) of medical devices, in-vitro diagnostic devices and medical laboratory equipment. The procedures cover new applications, applications for renewal of market authorization and changes to approved products.

2. General Requirements

2.1. Language

All applications and supporting documents shall be in Kiswahili or English.

2.2. Applicant

The applicant shall be a person who is a resident of Tanzania and must be licensed by TMDA as a medical device dealer. Applicants are expected to be conversant in international regulatory requirements as well as TMDA specific requirements.

If the applicant is not resident in Tanzania, he/she shall appoint a Local Responsible Person (LRP) also referred to as Authorized Representative or Local Agent who must be a company incorporated in Tanzania and authorized by TMDA to deal in medical devices. Proof of official appointment shall be submitted to TMDA during the marketing authorization process.

The applicant shall be responsible for the product as well as the information supplied in support of the application for marketing authorization, renewal and changes thereof. If an applicant is a resident of Tanzania, he/she shall take on the duties outlined in part 2.2.2 of these guidelines.

2.2.1. Responsibility of Applicant

The applicant is the legal entity responsible for the product when on the Tanzanian market. It is thus the responsibility of the applicant to: -

a) Provide authentic and complete scientific documents to support their applications;

b) Ensure that all submissions (of additional data) are submitted within the deadlines; and

c) In case of marketing authorization;
   i. Ensure that their product meets all requirements to be retained in the register of registered medical devices and in-vitro diagnostics;
   ii. Submit any variations to the Authority in line with the requirements stated in the variation guidelines;
   iii. Renew their registration every five (5) years; and
   iv. Conduct market surveillance activities once the product has been granted marketing authorization.

v. Monitoring the device on the market and inform the Authority immediately after the detection of any problem relating to a registered device such as serious manufacturing defects which may endanger public health
vi. Handling device recalls.
vii. Providing technical support and services to users of registered device (s).

2.2.2. Responsibility of Local Responsible Person

The Local Responsible Person shall be responsible for:

a) Monitoring the device on the market and inform the Authority immediately after the detection of any problem relating to a registered device such as serious manufacturing defects which may endanger public health.

b) Facilitating communication between the applicant and the Authority on matters relating to the product.

c) Handling device recalls.

d) Providing technical support and services to users of registered device (s).

3. Applications for Marketing Authorization

3.1. Classification of Medical Devices

Medical devices are classified into four (4) classes based on the level of risk and the intended purpose of the device. The manufacturer is responsible for classifying the device. However, the Authority reserves the right to decide on the class of the device.

Classification of medical devices and in-vitro diagnostic devices is based on the classification rules outlined in *the Guidelines for Classification of Medical Devices and Guidelines for Classification of In-vitro Diagnostic Devices found under part V and part VI of this compendium.*

CLASS	RISK LEVEL	DEVICE EXAMPLES
A	Low Risk	Surgical retractors/tongue depressors
B	Low- moderate Risk	Hypodermic Needles/suction equipment
C	Moderate – high Risk	Lung ventilator/bone fixation plate
D	High Risk	Heart valves / implantable defibrillator

In the incidence that more than one classification rule is applicable to the device, the rules resulting in the highest risk classification shall be applicable to the device.

3.2. Routes for Marketing Authorization

There are two main routes for marketing authorization of medical devices, in-vitro diagnostic devices and laboratory equipment i.e. registration or notification. Registration is the main route and is applicable to all class B, C and D medical

devices and in-vitro diagnostic devices as well as select class A devices that possess the following characteristics:

a) Active devices;
b) Measuring function; and
c) Sterile.

Notification is the marketing authorization route that is reserved for class A medical devices and in-vitro diagnostic devices that do not meet the criteria for registration process.

3.3. Types of applications

There are three main types of applications for registration of medical devices and in-vitro diagnostic devices as follows: applications for registration of new devices, applications for re-registration of devices and applications for changes to registered devices.

For purposes of submission to TMDA, applications are categorized as follows:

3.3.1. New applications

These are applications for registration of medical devices that are intended to be placed on the Tanzanian market for the first time. A new application may only be made by the applicant and he shall be the person who signs the application form.

A separate application is required for each medical device. Nevertheless, grouping of multiple medical devices is permissible provided that the manufacturer has demonstrated that the devices submitted together meet the criteria for grouping. Guidance on grouping of medical devices can be obtained in the *Guidelines for Grouping of Medical Devices and In-Vitro Diagnostic Devices found in part IX* of this compendium.

Therefore, each application submitted to TMDA shall contain one of the following:

a) A single medical device
b) One medical device family
c) One medical device system
d) One medical device group

3.3.2. Applications for Change of a Registered Medical Device

After a medical device has been granted market authorization, it is the responsibility of the applicant to ensure that all changes made to the product are reported to TMDA. The marketing authorization holder must provide scientific evidence to prove that any changes made do not negatively affect the quality, safety, or performance of the device.

For detailed requirements for changes of a registered medical device and the required information to be submitted, applicants may refer to ***Guidelines on Submission of Applications for Changes to Approved Medical Devices and In-vitro Diagnostics*** (TMDA/DMD/MDA/G/003).

3.3.3. Applications for renewal of registration

Applications for renewal of registration shall be made at least 90 days before the expiry of existing registration by submitting the following: -

a) Summary of any changes made to the device since registration. Note that, all approved changes as well as changes that are pending approval should be reported;
b) Specifications of the device along with batch certificates of analysis;
c) Product information including artwork or mock up label of the device and instructions for use/user manual
d) Post Marketing Surveillance Reports; and
e) Two samples of the commercial pack(s) from the same batch.

3.4. Application process

3.4.1. Lodging applications

All applications shall be submitted online through the TMDA Trader's Portal. An application consists of documentation in electronic form, samples and fees. The applicant should have the following information before submitting the dossier to TMDA: -

a) Class of the device
b) Intended purpose of the device
c) GMDN code and term
d) Conformity assessment certification
e) Declaration of conformity

In some cases, it may be difficult to determine whether a product is a medical device particularly when the product has features similar to medicines, cosmetics, food supplements or biocidal. Furthermore, when a product consists of two or more regulated components (a medical device and a medicine) that are combined/integrated as a single product or co-packed and sold together, applicants may face challenges in understanding if the product should attain authorization as a medical device or medicine.

Such products are referred to as borderline products. For guidance on how to determine if a borderline product is a medical device refer to *Guidelines on Borderline Products found under part XI* of this compendium.

3.4.2. Screening of applications

After receipt of the application, the Authority shall conduct a screening of submitted documents to confirm the completeness of submission before issuing an invoice for payment of the respective fees within 1 - 2 working days.

Incomplete applications will be queried for additional data, and returned back to the applicant for rectifications. Applications for incorrect products applied for notifications will be rejected and returned to the applicant.

Once the application has been accepted, an invoice shall be generated and sent to applicants via TMDA Traders' Portal.

3.4.3. Payment

Application invoices shall be sent to applicants via the TMDA Trader Portal. Every application shall be accompanied by appropriate fees as specified in the Fees and Charges Regulations currently in force at the time of application. All fees are non-refundable and shall be paid by the control number issued through TMDA invoice

When payment is made by bank transfer all bank charges shall be borne by the applicant who shall also make sure he sends an advice note giving details of the payment in particular the name of the applicant, the medical device paid for and the amount of fees paid. If the device is already registered in addition to the aforementioned details, the registration number of the device must also be quoted.

Once payment has been received, a receipt shall be sent to the applicant through TMDA Trader's Portal.

3.4.4. Scheduling for assessment

A complete application includes the product dossier and required product samples. Once TMDA receives a complete application, the application is scheduled for assessment. The time taken to schedule assessment is dependent on the complexity of the device and availability of assessors. Nevertheless, the scheduling stage may not exceed 10 working days for class A and B devices and 20 working days for class C and D devices.

3.4.5. Assessment Process

Each process shall undergo first and second assessment whereby assessors shall review the documents to confirm whether the device complies with TMDA requirements of quality, safety and performance.

The assessment stage is expected to take 23 working days for class A and B devices and 40 working days for class A and B devices.

Note: Quality Audit of the manufacturing facilities is also incorporated into the assessment process however, the timelines reflected above do not include the time for conducting site inspections.

3.4.6. Quality Assurance

Quality assurance of the assessment reports shall be done to verify the recommendations and any request for additional data (queries). This stage is expected to take 5 working days for class A and B devices and 8 working days for class C and D devices.

In case queries are raised the processing shall halt until after the response to the query has been received. If no response to the query or request has been received within **60 working days**, it will be deemed that the application has been withdrawn by the applicant.

3.4.7. Administrative Procedures

After a final conclusion is reached and the product is recommended for registration or refused registration, the application under goes administrative procedures. These procedures attaining approval from the Director General. This stage shall not exceed 5 days for class A and B devices and 25 days for class C and D devices.

3.4.8. Applications for notification

Applications for notification shall only undergo first assessment. The time frame for processing of notification is 5 working days.

4. Sample submission

Sample submission is a requirement for marketing authorization. Thus, all samples shall be submitted after payment of applications. Applications that are not accompanied by samples shall not proceed with the assessment process. Nevertheless, sample submission may be waived in certain circumstances. Instructions on quantity of samples required is as follows:

a) For all single use devices, all new applications and applications for re-registration shall be accompanied by two commercial packs of the samples. Additional samples may be requested during evaluation of the application;

b) For re-usable devices that are small in size, two samples shall be submitted similarly to single use devices;

c) For medical devices that are intended for general use by untrained people (layman), two samples shall be submitted; and

d) For large medical devices and any devices that are part of hospital infrastructure or cardiac implants submission of label artwork and scaled pictures of the device from different angels giving a 360^{o} view shall suffice in lieu of physical samples.

5. Registration of the device

When a device is found to have complied with all the prescribed marketing authorization requirements, the applicant will be informed to that effect. A certificate of registration together with such conditions as the TMDA may determine shall be issued for registrable devices and an approval letter for notifiable devices.

5.1. Validity of registration

The registration of a medical device shall be valid for five (5) years and notification approval for three (3) years unless suspended or revoked by TMDA or terminated by the registrant. The validity of registration shall be subject to:-

a) Payment of annual retention fees as prescribed in the current Fees and Charges Regulations in force;

b) Submission of biannual post-marketing surveillance reports; and

c) Submission of adverse effect reports associated with the use of device.

5.2. Termination of registration

The TMDA may by giving reasons in writing suspend or revoke the registration of a device, or amend the conditions of its market authorization. The registrant may issue TMDA 60 days written notice and reasons to terminate marketing authorization of a device.

5.3. Appeals

Any person aggrieved by a decision of the Authority in relation to any application for registration of a medical device may make representations in writing to TMDA. If after consideration of the representations, the Authority is satisfied it may approve registration of a medical device and if not satisfied it shall reject the application. In case the applicant is not satisfied with the decision, he may appeal to the Minister responsible for Health.

PART II
GUIDELINES ON TECHNICAL DOCUMENTATION REQUIREMENTS FOR REGISTRATION OF MEDICAL DEVICES

Scope

This guidance provides requirements for submissions of technical documents to support applications for the registration of class A, B, C and D medical devices. Classification of medical devices is based on the classification rules outlined in the *Guidelines for Classification of Medical Devices found under part V* of this compendium.

This guidance document is not applicable for class A medical devices supplied in non-sterile state, non-active and non-measuring function. Such devices are exempted from registration thus attain marketing authorization through notification. An application for notification of a medical device, diagnostic or laboratory equipment shall be made through an online portal in accordance with the *Guidelines for Notification of Medical Devices Exempted from Registration found under part IV* of this compendium.

Submission of applications for registration of Medical Devices

All applications for registration of medical devices shall be made online through the TMDA Traders Portal. For detailed information on the application procedures, refer to the *Guidelines on Procedural Aspects for Marketing Authorization of Medical Devices, In Vitro Diagnostic Devices and Laboratory Equipment found under part I* of this compendium.

Technical Requirements for Registration of Medical Devices

Applicants are required to submit the following information regardless of the class of the device: -

Device Details

Name(s)
State the generic and brand name of the device.

Description
Provide a summary of information on design, characteristics and performance of the device. The description should also include information on device packaging.

Category
State the GMDN category of the device. If the device is not categorized according to GMDN and is coded based on other system, please specify.

Intended Use/Indication(s)
State the intended use(s) of the device and/or provide a general description of the disease or condition that the device will diagnose, treat, prevent, cure or mitigate. The description of the target patient population for which the device is intended should also be included.

The statement of intended use should specify the therapeutic or diagnostic function provided by the device and may describe the medical procedure in which the device is to be used and whether the device is intended for single use or multiple uses.

Instructions for Use
Give a concise summary of information for safe use of the device including procedures, methods, frequency, duration, quantity and preparation to be followed.

Contraindications
State conditions under which the device should not be used. The statement should specify the clinical conditions of a patient that would make use of the device inadvisable.

Warnings
State the specific hazard alert information that a user needs to know before using the device.

Precautions
State briefly precautions to be taken and any special care necessary for the safe and effective use of the device.

Adverse Effects
Describe all adverse and side effects associated with the device under normal conditions of use.

Alternative Use
Describe any alternative practices or procedures for diagnosing, treating, curing or mitigating the disease or condition for which the device is intended.

Storage conditions
State the storage conditions for the device. This should be based on results of stability studies conducted (where applicable).

Recommended shelf-life (where applicable)
State the recommended shelf-life of the device.

Summary Technical Documentation

Device description and features including description of variants and accessories

Provide the name of the device and detailed description of the device attributes that are necessary to explain how the device functions. If it is part of a system, the relationship of the components in the system should also be described. The details should include: -

a) The principle of operation of the device;

b) Risk class and applicable classification rule for the medical device;

c) Description of the key functional elements of the device including software and its release version, if applicable. e.g. its parts/components, formulation, composition and functionality;

d) A description of the accessories, other medical devices and other products that are not medical devices, which are intended to be used in combination with the medical device.

e) Components or accessories that can be sold separately and used with other medical devices, systems or units should be identified. Variants of the device must be identified, as well as the parameter ranges of variants [for example (e.g.), hip implants with varying coatings].

f) Labelled pictorial representation of the device in the form of diagrams, photographs or drawings with sufficient explanation should be provided.

Evidence of Conformity to Essential Principles

Provide evidence of conformity to Essential Principles of Safety and Performance (EPSP) by completing the checklist and its guidance appended as *Annex I* of this guideline.

Note:

a) Manufacturer should identify the essential principles of safety and performance that are applicable to the device and the general methods used to demonstrate conformity to each applicable Essential Principle. The methods that may be used include: -
   i. Compliance with a recognized or other standard(s)
   ii. Internal industry methods
   iii. Comparison to another similar marketed device

b) When the manufacturer uses national, international or other standards to demonstrate conformity with the Essential Principles, full title of the standard, identifying numbers, date of the standard and the organization that created the standard should be provided.

Materials

Details of material identifications and specifications including raw materials and components should be provided. The description of the materials of the device and their physical properties should be sufficient to demonstrate the conformity with the relevant Essential Principles. The information shall include complete chemical, biological and physical characterization of the materials of the device especially for materials contacting the patient or when the material chosen is considered critical for the design or function of that component. Reference to applicable material standards may be useful in this description.

Device Specification

Describe functional characteristics and technical performance specifications for the device including as relevant, accuracy, sensitivity, specificity of measuring and other specifications including chemical, physical, mechanical, electrical and biological.

Note: A list of the features, dimensions and performance attributes of the medical device, its variants and accessories that would typically appear in the product specification should be made available to the end user e.g in brochures and catalogues.

Device Verification and Validation

Summarize the results of verification and validation studies undertaken to demonstrate compliance of the device with Essential Principles that apply.

The following documentation should be submitted;

a) Declarations/ certificates of conformity to the recognized standards listed as applied by the manufacturer; and

b) Summaries or reports of tests and evaluations based on other standards, manufacturer methods and tests or alternative ways of demonstrating compliance.

Whenever applicable the information should cover:

a) Engineering tests
b) Laboratory tests
c) Biocompatibility tests
d) Animal tests
e) Simulated use
f) Soft-ware validation

For sterile medical devices the following information should be provided in this section:

a) Detailed information of the initial sterilization validation including bio- burden testing, pyrogen testing, testing for sterilant residues (if applicable) and packaging validation. If initial sterilization validation is not performed, adequate justification must be provided. For example, if reference to the sterilization validation conducted for another medical device is made for the medical device in the application, the justification for the applicability of the previously conducted validation to the current medical device must be provided. In addition, the initial sterilization validation report for the reference medical device must be provided;

b) Evidence of the ongoing revalidation of the process; typically, this would consist of arrangements for, or evidence of, revalidation of the packaging and sterilization processes;
c) Detailed validation information should include the method used, sterility assurance level attained, standards applied, the sterilization protocol developed in accordance with those standards, and a summary of results;

d) Post-sterilization functional test on the medical device; and

e) If the sterilant is toxic or produces toxic residuals (e.g. ethylene oxide residues), test data and methods that demonstrate that post-process sterilant and/or residuals are within acceptable limits must be presented.

Shelf life of the device

For medical devices with a shelf-life, data demonstrating that the relevant performances and characteristics of the medical device are maintained throughout the claimed shelf-life which the "expiry" date reflects is to be provided under this section. This may include:

a) Prospective studies using accelerated aging, validated with real time degradation correlation; OR
b) Retrospective studies using real time experience, involving e.g. testing of stored samples, review of the complaints history or published literature etc.; OR
c) A combination of (a) and (b).

If real time shelf-life data is not available, shelf-life data collected from accelerated studies can be used to support the initial shelf-life claim. The rationale for the parameters selected for the accelerated studies must be provided. Shelf-life data collected from accelerated studies must be supported by real time testing to confirm the initial shelf-life claim. The final real time study report must be submitted when completed.

As the absence of an "expiry" date constitutes an implicit claim of an infinite shelf-life, evidence demonstrating the following shall be provided:

a) That there are no safety-related performances or characteristics which are likely to deteriorate over time; OR

b) That the extent of any likely deterioration does not represent an unacceptable risk; OR

c) That the period over which unacceptable deterioration occurs is far beyond the likely time of the first use of the medical device e.g. 30 years.

For devices that do not have expiry dates (e.g. infusion pump, digital thermometer), the projected useful life of the medical device must be provided. Manufacturers may refer to the current TS/ISO 14969 (Medical devices – Quality Management Systems – Guidance on the application of ISO 13485) for information on how to determine the projected useful life.

For medical devices with a measuring function where inaccuracy could have a significant adverse effect on the patient, studies demonstrating conformity with metrological requirements shall be provided.

If the device requires special packaging (e.g. considerations related to sterility, humidity, light sensitivity, pressure or oxidative reaction under irradiation), evidence should be provided that this has been addressed. Likewise, evidence should be provided to demonstrate that the integrity of the device and the internal environment can be maintained by the device packaging during handling, transport and storage (i.e., for claimed shelf life). In the case of sterility, ensure that the test methods address both seal integrity and sterility (e.g., bubble tests, dye penetration test, etc.).

Biocompatibility (if applicable)

Biocompatibility testing characterizes the biological response to the material. If the device comes in contact with the patient, then the biocompatibility of all materials which are potentially patient contacting is required. Tests should be conducted on samples from the final product after all manufacturing and processing has been completed (e.g., sterilization). Deviations from this should be justified; generic claims from the raw material supplier are generally insufficient.

Reports describing the tests, the results and the analyses of data should be presented. For each test, the predefined acceptance criteria and the results should be clearly provided (e.g., tabular form). In general, ISO 10993 standards are taken as the gold standards for biocompatibility. If testing was not conducted from a currently recognized standard, the validated alternative method should be provided along with a justification for its use (e.g., devices incorporating nanotechnology). Any deviations from a standard method should also be specified.

Software Verification and Validation (if applicable)

Provide information on the software design and development process and evidence of the validation of the software, as used in the finished device. This information should typically include the summary results of all verifications, validation protocols and report and testing performed both in-house and in a simulated or actual user environment prior to final release. It should also address all of the different hardware configurations and where applicable, operating systems identified in the labelling. Submission of such devices shall be in accordance with the *Guidelines for Software Medical devices provided under Part X* of this compendium.

Devices containing Biological Material (if applicable)

Provide results of studies substantiating the adequacy of the measures taken with regards to the risks associated with transmissible agents. This will include viral clearance results for known hazards. Donor screening concerns must be fully addressed and methods of harvesting must also be fully described. Process validation results are required to substantiate that manufacturing procedures are in place to minimize biological risks.

To fulfil the requirements under this section, the following information shall be submitted:

a) A list of all materials of animal, human, microbial and/or recombinant origin used in the medical device and in the manufacturing process of the medical device. This includes animal or human cells, tissues and/or derivatives rendered non-viable and cells, tissues and/or derivatives of microbial or recombinant origin;

b) Detailed information concerning the selection of sources/donors;

c) Detailed information on the harvesting, processing, preservation, testing and handling of tissues, cells and substances;

d) Process validation results to substantiate that manufacturing procedures are in place to minimize biological risks, in particular, with regard to viruses and other transmissible agents;

e) Full description of the system for record keeping allowing traceability from sources to the finished medical device; and

f) Evidence that demonstrates a system is in place for animals and tissue traceability; and quality control processes and procedures are in place to prevent contamination with potential infectious/transmissible agents, including Transmissible Spongiform Encephalopathies (TSEs) should be provided. Disinfection/decontamination procedures in the event of contamination should also be outlined along with appropriate validation.

Pre – clinical Studies (if applicable)

Provide detailed information on pre-clinical animal studies conducted to justify the probability of effectiveness in humans. These studies must follow Good Laboratory Practices. The objective, methodology, results, analysis and manufacturers conclusions must be presented. The study conclusion should address the device's interactions with animal fluids and tissues and the functional effectiveness of the device in the experimental animal model(s). The rationale (and limitations) of selecting the particular animal model should be discussed.

Clinical Evidence (If applicable)

An evaluation of clinical evidence is necessary to help establish the clinical safety and effectiveness of a medical device for each claimed indication for use. Guidance is provided under the *Guidelines for Clinical Evidence of In Vitro Diagnostics Medical Devices found under Part VII* of the compendium.

A clinical evaluation considers available, relevant clinical data from published sources, or device-related investigations. It may be necessary to generate additional clinical data to address specific issues for certain medical devices.

If a clinical history has been well established with a given device technology, evidence may be provided in the form of a literature review of relevant publications in the peer-reviewed scientific literature. Reference to devices other than the subject device in support of safety or effectiveness requires a thorough comparison to the subject device design, features and performance capabilities to demonstrate relevance. This may be provided in a table format.

The clinical evaluation report should be summarized as per the current IMDRF guidance documents.

Risk Analysis

A risk assessment should be based on an analysis and an evaluation of the risks inherent in the use of the device, as well as the risk reduction measures adopted to satisfy safety and effectiveness requirements. The manufacturer should identify the individual or organization that carried out the risk analysis and it should be conducted on the version of the device under review.

The information provided should include a description and identification of the devices and accessories under consideration in a risk assessment. Design aspects should be evaluated. The method of risk analysis must be appropriate for the device and the level of risk involved. A brief description of the technique used to perform the risk assessment, definitions of risk and any standards used in this process should be stated. A list of critical hazards should be provided, which includes how the risks associated with these hazards have been evaluated and what risk reduction measures have been taken. An evaluation of the risks as compared with the claimed benefits of the device and steps taken to reduce the risks to acceptable levels should also be presented.

Manufacturing Information

Provide details of the manufacturing process for the device in the form of a list of resources and activities that transform inputs into the desired output. The manufacturing process should include the appropriate manufacturing methods and procedures, manufacturing environment or conditions and the facilities and controls used for the manufacturing, processing, packaging, labelling and storage of the device. A manufacturing process flow chart should be submitted.

Sufficient details must be provided to enable a person generally familiar with quality systems to judge the appropriateness of the controls in place.

If multiple facilities are involved in the manufacture of the device, the physical address of the manufacturing site and manufacturing activities for each facility should be provided. The sites where design and manufacturing activities are performed shall be identified. For example:

a) If the manufacturing process of a product consists of a number of subassembly processes, the manufacturing sites where each of these subassembly processes are carried out must be identified, and the relationship between these processes must be shown; or

b) If multiple sites manufacture the same product, each of these sites must be identified.

The sites (including contract manufacturers) where design and manufacturing activities are performed shall be identified. Quality Management System certificates are to be provided for the design and manufacturing sites (including contract manufacturers as Annexes to the submission).

For those multiple facilities involved in the manufacture of medical device, the applicable information (e.g. quality assurance certificates issued by an accredited third-party inspection body) for each facility must be submitted. Firms that manufacture or process the medical device under contract to the manufacturer may elect to submit all or a portion of the manufacturing information applicable to their facility directly to the Regulatory Authority in the form of a master file.

The manufacturer should inform these contractors of the need to supply detailed information on the medical device. However, it is not the intent of this section to capture information relating to the supply of sub-components (i.e. unfinished medical device) that contributes towards the manufacture of the finished medical device itself.

Details of the sterilization method and processing should be included, if the device is sold sterile or is to be sterilized, process validation data should include sterility test data, reference to a standardized test method, and attestation or evidence of successful validation under real- life conditions under which the product is to be sterilized. Bioburden determination, culture media used, time and temperature of incubation, controls, number of samples examined and frequency of testing should also be presented. A Sterility Assurance Level (SAL) of 10-6 is generally required.

If a biological indicator was used, its placement needs to be described and rationalized (e.g., most difficult to sterilize location). If a group of devices are to be sterilized together, the worst- case scenario or most difficult to sterilize product should be validated. Attestation of validation may be used. The manufacturer should also demonstrate that they have a process in place to monitor bioburden levels on a regular basis to confirm that the sterilization method remains valid.

Alternatively, a method of parametric release may be proposed and validated. If a process challenge device was used to assess the sterilization process it must be shown to have comparative resistance or a greater challenge to sterilization than the biological indicators placed inside the product/packaging.

If the product is to be re-sterilized by the end-user, a description of the recommended sterilization process for the end-user should be provided, and evidence of validation provided. Validation should be for sterility and also to confirm that the process does not compromise integrity or performance of the product. The recommended, validated sterilization method should be stated in the device labeling information.

Labelling Requirements

The product dossier should contain a complete set of labelling associated with the product. This includes:

a) Mock up labels for the primary and secondary packaging materials;

b) Instructions for use (IFU);

c) If applicable, the instrument manual; and

d) Any other instructional materials provided to the user.

Requirements for product labelling is provided under *the Guidance on Labelling Information for Medical Devices and In-Vitro Diagnostics* ***under Part VIII of the compendium.***

Post-Marketing Surveillance Activities

Post Market Surveillance Plan

The product dossier shall contain a post market surveillance plan. The post market surveillance plan describes the systems are in place to ensure appropriate post market surveillance data is collected. This section shall include:

a) Sources of potential post-market surveillance data:

b) a proactive and systematic process to collect any information referred to in point (a). The process shall allow a correct characterization of the performance of the devices and shall also allow a comparison to be made between the device and similar products available on the market.

c) Effective and appropriate methods and processes to assess the collected data, consideration should also be given to statistical methods.

d) Ensure suitable indicators and threshold values been chosen that will be used in the continuous reassessment of the benefit-risk analysis and of the risk management.

e) Effective and appropriate methods and tools to investigate complaints and analyze market- related experience collected in the field

f) Methods and protocols to manage the events subject to the trend report, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period.

g) Methods and protocols to communicate effectively with TMDA, stakeholders and users regarding medical device issues.

Periodic Safety Update Report and Post Market Surveillance Reports

Post-market surveillance report

The product dossier shall contain copies of any available post-market surveillance reports for the jurisdictions where the product has already been marketed.

Post- market authorization, the MAH shall prepare a post-market surveillance report summarizing the results and conclusions of the analyses of the post-market surveillance data gathered as a result of the post-market surveillance plan together with a rationale and description of any preventive and corrective actions taken. The report shall be updated when necessary and made available to the TMDA upon request.

Periodic safety update report

MAH shall prepare a periodic safety update report (PSUR) for each device and where relevant for each category or group of devices summarizing the results and conclusions of the analyses of the post-market surveillance data gathered as a result of the post-market surveillance plan together with a rationale and description of any preventive and corrective actions taken. Throughout the lifetime of the device concerned, that PSUR shall set out:

a) The conclusions of the benefit-risk determination; and
b) The main findings of the post-market clinical follow-up.

Requirements for Registration of Specialized Medical Devices

Special requirements are prescribed in this section for certain specialized devices such as MRI, Diagnostics Ultrasound Systems and Transducers, X-ray machines, ECHO and other similar machines. These devices are classified in either class B, C and D but their documentation requirements differ from other devices due to their complexity. TMDA require the applicants who intend to register such devices in Tanzania to submit the following minimum information as applicable to the device. An application for these Medical Devices shall be made through an online portal and shall be accompanied by the following:

a) Certificate of market approval from any other country and market history. Brief description of the foreign marketing history, if any, of the device, including a list of all countries in which the device has been marketed and a list of all countries in which the device has been withdrawn from marketing for any reason related to the safety or effectiveness of the device. The description shall include the history of the marketing of the device by the applicant and, if known, the history of the marketing of the device by any other person;

b) Manufacturer’s Declaration of Conformity;

c) Certificate of Analysis to confirm safety and performance of the device;

d) Operator's manual;

e) The User or Operator's Manual of the devices must address the contraindications, warnings, precautions, and general risks associated with the device. Moreover, the User or Operator's Manual for a Device should contain the following. The indications for use statement in the user manual should be identical to the Indications for Use statement in application form and device details section;

f) Summaries of non-clinical and clinical data supporting the intended use and performance characteristics;

g) A label must provide sufficient details to satisfy the requirements prescribed in the Tanzania Regulation of Medical Devices, 2015 and section 4.0 of these guidelines;

h) In case of medical device adverse report. TMDA requires manufacturer/ importers who have received complaints of device malfunctions, serious injuries or deaths associated with medical devices to notify TMDA of the incident. The requirements for medical device reporting are defined in Tanzania Medical Devices Regulations, 2015; and

i) All other details as per section 3 of these guidelines.

Cleaning, Disinfection, Sterilization, and Pyrogenicity for Specialized Medical Devices

If the medical device supplied is non-sterile or is intended to be reused between patients, you should provide clearly written recommended procedures on how to clean, disinfect and sterilize the medical device between uses if necessary. These recommended procedures should be validated and summary validation procedures provided in the submission. The level of disinfection or sterilization should be appropriate for the intended clinical use. E.g. For sterilization, which should be used for transducers in contact with the bloodstream or normally sterile tissues, the use of an appropriate sterilization process should be recommended and its use validated.

For device components or accessories provided sterile to the user, TMDA recommends that the applicant should provide sterilization information (Sterilized with a sterility assurance level (SAL) of 1 x 10-6).
If the device is labelled pyrogen-free, then the applicant must provide a description of the method (standard method) used to assess pyrogenicity. TMDA recommends the following endotoxin endpoint: 0.5 EU/mL for general medical devices (e.g. blood contacting) and 0.06 EU/mL for devices that contact cerebrospinal fluid.

Borderline Medical Devices

Many manufacturers have difficulties in interpreting whether or not their product would be considered a medical device within the terms defined in these guidelines. Manufacturers should always refer to the definition of a medical device when making any borderline determinations. Any such decision will be based on the

stated intended purpose of the product and its mode of action. Guidance on these products is provided under ***Part XI on*** *Guidance for Borderline Products.*

Medical / cosmetic / toiletry purpose

Where there is a specific intended medical purpose, products may be considered to be medical devices. For example:

a) breast pumps for treatment of inverted nipples;

b) external heat pads claiming pain relief, e.g. for the treatment of period pains;

c) Incontinence products (e.g. adult nappies);

d) muscle toning products with medical claims (such as treatment of incontinence);

e) slimming products indicated for the treatment of clinical obesity which do not act in a metabolic, pharmacological or metabolic manner;

f) baby nappies;

g) breast pumps; and

h) feminine hygiene products (sanitary towels, tampons).

Assistive technology products (aids for daily living)

Equipment intended for alleviation of, or compensation for a disability may or may not be considered as medical devices. The determining factor will be whether or not there is a direct link between the corrective function of the equipment and the individual concerned and whether there is a stated medical purpose.
The following products are considered to be medical devices as there is such a direct link:

a) baths with integral hoists;

b) external limb prostheses and accessories;

c) hearing aids;

d) mobility aids for the visually impaired;

e) orthopaedic footwear;

f) orthoses (lower/upper limb, spinal, abdominal, neck, head);

g) patient hoists;

h) rehabilitation tricycles / mobility carts;

i) walking / standing frames;

j) walking sticks/crutches; and

k) wheelchairs.

Products for sports or leisure

In general, products for sports or leisure purposes are not considered to be medical devices. However, in some cases, products aimed for sports may be considered to be medical devices. This is usually the case where specific claims are made for the treatment of pain or injury and the product acts in a physical manner. Examples of products considered to be medical devices under this section:

a) heat / cold pads for pain relief;

b) bandages for sprains and similar;

c) support bandages; and

d) Blood pressure monitors, even if intended to be used in a gym.

Software As Medical Devices

Software may be considered to be medical devices provided that the purpose fits the definition of a medical device. The definition of a medical device includes standalone software and specifies that when software is used in combination with a device which is intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes" that it will be considered to be a medical device. Submission of such devices shall be in accordance with the *Guidelines for Software Medical devices provided under Part X* of this compendia.

For example:

a) Software intended to enhance images from x-ray or ultrasound would be considered to be medical devices; and

b) Software that is simply a patient management system or a records storage system would not, however be considered to be a medical device.

Accessories

Accessories should be classified in their own right as medical devices and do not necessarily take the classification of the device with which they are intended to be used. A product can only become an accessory to a medical device if there is an established intended use in conjunction with a medical device. The registration of accessories will follow the requirements of these guidelines.
Examples of such potential accessories are:

a) Sterilizer for use with medical equipment;

b) Pouches for packaging re-sterilized medical devices;

c) Specific battery chargers for battery-driven electro-medical devices;

d) Contact lens care products;

e) Disinfectants specifically intended for medical devices;

f) Specialized water treatment devices for use with dialysis machines;

g) Gas cylinders / pressure release devices for use in conjunction with anaesthesia machines.

Spare parts

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

Re-used Medical Devices

Repairs

Where a registered device is „repaired" and returned to its original owner after the repair the components used in the repair would not require registration. The device should not be placed on the market" but returned to its owner. If the repaired device was not registered then registration process will be required.

Second-hand and fully refurbished devices

Second-hand medical devices are those which are already on the market and have been pre- owned and used and that are subsequently sold on" for the same continued use. These products are considered to be already registered and do not require second registration by their new owner.

A medical device that has been fully refurbished is not the same as one that has been repaired or undergone maintenance. Therefore, it requires to be registered as a new medical device.

They will be considered to be the manufacturer" under the regulations and are required to place the product on the market under their own name. „Fully refurbished" is considered to mean that a device has been completely rebuilt / made

as new from used devices and is assigned a new “useful life“. It would also be considered as a new device if a new intended purpose was assigned.

Medical devices that require final processing

Some devices may not be supplied in their final state (i.e. may not be immediately available for use) once placed on the market. They may require some further processing prior to being „usable“, for example processing, preparation, installation, assembly or fitting. These activities are not usually undertaken by the manufacturer but are carried out by the healthcare professional or the final user.
Examples of such activities are:

a) sterilization of medical devices supplied non-sterile;

b) assembly of systems;

c) configuration of electronic equipment;

d) preparation of dental fillings;

e) fitting of contact lenses; and

f) adaptation of a prosthesis to the needs of the individual patient.

NOTE: The type of documentation for the registration and application process for borderline medical devices shall depend on the declared intended use and risk class declared by the manufacturer.

PART III
TECHNICAL DOCUMENTATION REQUIREMENTS FOR IN VITRO DIAGNOSTICS REGISTRATION

1. Scope

This guidance provides requirements for submissions of technical documents to support applications for the registration of class A, B, C and D in-vitro diagnostic devices. Classification of in-vitro diagnostic devices is based on the classification rules outlined in *the Guidelines for Classification of In Vitro Diagnostics found under part VI* of this compendium.

This guidance document is not applicable for class A in-vitro diagnostic devices supplied in non-sterile state, non-active and non-measuring function. Such devices are exempted from registration thus attain marketing authorization through notification. An application for notification of a medical device, diagnostic or laboratory equipment shall be made through an online portal in accordance with *the Guidelines for Notification of Medical Devices Exempted from Registration found under part IV* of this compendium.

2. Submission of applications for registration of In-vitro Diagnostic Devices

All applications for registration of In Vitro Diagnostics shall be made online through the TMDA Traders Portal. For detailed information on the application procedures, refer to *the Guidelines on Procedural Aspects for Marketing Authorization of Medical Devices, In Vitro Diagnostic Devices and Laboratory Equipment found under part I* of this compendium.

3. Technical Requirements for Registration of In-vitro Diagnostic Devices

Applicants are required to submit the following information for all registrable Classes of the IVD such as Class A-registrable (supplied in sterile, active and have measuring function), B, C and D: -

3.1. Device Details

a) **Name(s):**
State the brand and generic name of the IVDD.

b) **Description**
Provide a general summary of information on design, characteristics and performance of the IVDD. The description should also include information on device packaging.

c) **Category**
State the class of the IVDD and the applicable classification rule as prescribed under Part II and III of the compendia.

d) **Intended Use/Indication**

State the intended use of the IVDD and/or provide a general description of the disease or condition that the device will diagnose. The description of the target patient population for which the device is intended should also be included.

The statement of intended use should specify the diagnostic function provided by the device and may describe the medical procedure in which the device is to be used and whether the device is intended for single use or multiple uses.

e) **Instructions of Use**

Give a concise summary of information for safe use of the device including procedures, methods, frequency, duration, quantity and preparation to be followed.

f) **Contraindications**

State conditions under which the IVDD should not be used. For example, a limitation of an assay using specimens from patients who have received preparations of mouse monoclonal antibodies for therapy when tested with assay kits which employed mouse monoclonal antibodies. It may show either false elevated or depressed values.

g) **Warnings**

State the specific hazard alert information that a user needs to know before using the IVDD. e.g. for products containing biological material, radioactive material, explosive material and any other hazardous material, safety warnings must be included.

h) **Precautions**

State briefly precautions to be taken and any special care necessary for the safe and effective use of the IVDD.

i) **Adverse Effects**

Describe all adverse and side effects associated with the IVDD under normal conditions of use.

j) **Alternative Use**

Describe any alternative practices or procedures for diagnosing, treating, or mitigating the disease or condition for which the IVDD is intended.

k) **Storage conditions**

State the storage conditions for the IVDD.

l) **Recommended shelf-life (where applicable)**

State the recommend shelf life of the IVD.

3.2 Summary of Technical Documentation

3.2.1 Device description and features

Provide a detailed description of the device attributes that are necessary to explain how the device functions. These details should include:

a) Intended use of the IVDD. This may include:

i. What is detected;

ii. The function (e.g. screening, monitoring, diagnostic or aid to diagnosis, staging or aid to staging of disease);

iii. The specific disorder, condition or risk factor of interest that is intended to detect, define or differentiate;

iv. Whether the product is automated or not;

v. Whether the test is qualitative or quantitative;

vi. The type of specimen(s) required (e.g. serum, plasma, whole blood, cerebrospinal fluid (CSF), sputum, urine);

vii. The intended testing population (e.g. neonates, antenatal women); and

viii. If applicable the environmental condition during operation (temperature range and attitude).

b) The intended user (laboratory professional and/or at point-of-care).

c) general description of the principle of the assay method or instrument principles of operation.

d) A description of the components of the assay (e.g. reagents, assay controls and calibrators), and where appropriate, a description of the reactive ingredients of relevant components (such as antibodies, antigens and nucleic acid primers).

e) Description of the specimen collection and transport materials provided with the product or description of specifications recommended for use.

f) For instruments of automated assays: a description of the appropriate assay characteristics or dedicated assays.

g) For automated assays: a description of the appropriate instrumentation characteristics or dedicated instrumentation.

h) If applicable, a description of any software to be used with the device.

i) If applicable, a description or complete list of the various configurations/variants of devices that will be made available. For example, a family of pregnancy rapid test can consist of device available in different configurations, such as test strip or in a cassette.

j) If applicable, a description of the accessories, and other non- IVDD products that are intended to be used in combination with the diagnostic.

k) Risk class and the applicable classification rule for the IVDD according to these guidelines.

The instruction for use may be used to provide some of this information on the condition that a cross-reference to the different requirements is supplied in conjunction with the instructions-for-use.

3.2.2 Evidence of conformity to Essential Principles

Provide evidence of conformity to Essential Principles of Safety and Performance (EPSP) by completing the checklist appended as *Annex I* of the compendium.

a) Manufacturer should identify the essential principles of safety and performance that are applicable to the device and the general methods used to demonstrate conformity to each applicable Essential Principle. The methods that may be used include:

   i. Conformity with a recognized or other standard(s)
   ii. Conformity with a commonly accepted industrial test method (reference method)
   iii. Conformity with appropriate in-house test methods that have been validated and verified;
   iv. Comparison to a diagnostic already available on the market.

b) When the manufacturer uses national, international or other standards to demonstrate conformity with the Essential Principles, full title of the standard, identifying numbers, date of the standard and the organization that created the standard should be provided.

c) The IVDD, to which the Essential Principles (EP) conformity checklist is applicable, should be identified by the brand name, common name and risk class on the checklist itself. The columns of the checklist should be completed as follows:

i. Applicable to the IVDD?

Either a “Yes” or “No” answer is required. If the answer is “No” there should be a brief explain

ii. Method of conformity

State the title and reference of the standard(s), industry or in-house test method(s), comparison study(ies) or other methods to demonstrate compliance. For standards, this should include the date of the standard and where a standard is referred to more than once in the checklist, the reference number and date can be repeated.

iii. Identity of specific documents

The column should contain the reference to the actual technical documentation that demonstrates compliance to the essential principle, i.e. the certificate number(s),

test reports, study reports or other documents that resulted from the method used to demonstrate compliance, and its location within the technical documentation or dossier.

3.2.3 Risk analysis

Provide a summary of the risks identified during the risk analysis process and how such risks have been controlled to an acceptable level. Preferably, the risk analysis should be based on recognized standards and be part of the manufacturer's risk management plan.

The summary should address possible hazards for the IVDD such as the risk from false positive or false negative results, indirect risks which may lead to erroneous results, or from user-related hazards, such as reagents containing infectious agents. The results of the risk analysis should provide a conclusion with evidence that remaining risks are acceptable when compared to the benefits**.**

3.2.4 Design and manufacturing information

3.2.4.1 Product design

Provide information such as to give a general understanding of the design applied to the IVDD. It should include a description of the critical ingredients of an assay such as antibodies, antigens, enzymes and nucleic acid primers provided or recommended for use with the IVDD:

a) For instruments include a description of major subsystems, analytical technology (e.g. operating principles, control mechanisms), dedicated computer hardware and software.

b) For instruments and software, give an overview of the entire system, including an Architecture Design Chart, which is typically a flowchart of the relationships among the major functional units in the software, including relationships to hardware and to data flows such as networking.

c) For standalone software, include a description of the data interpretation methodology (i.e. algorithms).

d) For self-testing devices the design should include a description of the design aspects that make it suitable for lay person use.

e) If design takes place at multiple sites, a controlling site must be identified.

3.2.4.2 Formulation and composition

Provide formulation/composition for each of the ingredients:

a) Materials

Provide complete details of material specifications, including raw materials;

i. All components of the IVDD should be listed and chemically and biologically characterized, including antibodies, antigens, and assay controls, substrates used to detect antigen-antibody complexes, and test reagents. Appropriate references should be cited.

ii. If synthetic peptides are used, the peptide sequence should be provided

iii. If components are of biological origin or recombinant, the source must be indicated and details on production must be provided. These details would include the strain of the virus, the cell line for cultivation of the virus, sequences of relevant nucleic acids and amino acids, etc., used in the manufacturing process of viral lysate, purified proteins, recombinant and synthetic proteins.

iv. If applicable, process validation results to be provided to substantiate that manufacturing procedures are in place to minimize biological risks, in particular, with regard to viruses and other transmissible agents. This also includes inactivation of infectious organisms in reagents and the production of reagents.

v. If applicable, information to be provided on irradiating components, non-ionizing or ionizing (e.g. Iodide- 131 in the Radioimmunoassay kit, radio-labeled Phosphorus-32 DNA probes in Southern blots).

vi. If applicable, information should be provided on the poison or controlled substance e.g. Buprenorphine in drug assay kit).

vii. Given the nature and specification of the packaging material(s) including complete chemical and physical characterization of the packaging material making either direct or indirect contact with the IVDD.

viii. Identify the sources of the materials from which the components are constructed.

b) Biological safety

List all biological components included in the IVDD to include material of bacterial, viral, parasitic, animal, or human origin or their derivatives where applicable. Indicate the name of the biological component, details of its use in the product and description of steps taken for the reduction of transmission or infection risk.

c) Documentation of design change

Provide records of each design change, if any, with reasons for these changes along with associated validation/verification data. Include evidence that the change achieves the desired effect, and that the product continues to comply with the Essential Principles of Safety and Performance.

3.2.5 Manufacturing processes

3.2.5.1 Overview of manufacturing process

Provide information on the manufacturing process, which may be in form of a process flow chart, showing an overview of production including technologies used, assembly and packaging of the finished IVDD. Include details of any in-process and final product testing (e.g. the manufacturer's QC release program).

3.2.5.2 Sites of manufacture

Provide the following information;

a) Name of site;

b) Physical address of the site;

c) Description of the component manufacture/stage of manufacturing process carried out at the site;

d) A simple sight plan highlighting production areas and number of employees at the site; and

e) A description of any other manufacturing that occurs at the site.

For all the critical manufacturing sites that are involved in the manufacture of this product (i.e. including design, warehousing and quality control stages of manufacture).

3.2.5.3 Key suppliers

Provide a list of key suppliers of ingredients/products/services for the manufacture of the IVDD, indicating the:

a) Name of the supplier;

b) Supplier's manufacturing site physical address;

c) A description of the ingredient/product/service supplied; and

d) Evidence of purchasing and verification procedures for the ingredients /products/services sourced from these suppliers.

3.2.6 Device Specifications

a) Describe functional characteristics and technical performance specifications for the device including as relevant, accuracy, sensitivity, specificity of

measuring and other specifications including chemical, physical, mechanical, electrical and biological.

b) A list of the features, dimensions and performance characteristics of the IVDD its variants and accessories should be provided in the dossier and also made available to the end user.

3.2.6.1 Device validation and verification

Summarize the results of validation and verification studies undertaken to demonstrate compliance of the IVDD with Essential Principles that apply to it. Whenever applicable the information should cover: -

a) The complete study protocol;

b) The method of data analysis;

c) Complete study report;

d) The study conclusion;

e) Any published literature regarding the device or substantially similar devices; and

f) Summaries or reports of tests and evaluations based on other standards, manufacturer methods and tests or alternative ways of demonstrating compliance. Declarations/certificate of compliance to a recognized standard as applied by the manufacturer should be provided.

When a recognized standard exists that contains the protocol and the method of data analysis, this information can be substituted by a declaration/certificate of conformity to the recognized standard. However, a summary of the data and conclusions should be provided. Where appropriate actual test results summaries with their acceptance criteria should be provided and not just pass/fail statements.

3.2.6.2 Specimen type

This section should describe the different specimen types that can be used, including their stability (and storage) conditions and is typically applicable to all systems and assay types.

a) Stability includes storage and where applicable transport conditions. Storage includes elements such as duration, temperature limits and freeze/thaw cycles.

b) Summary information for each matrix and anticoagulant when applicable, including a description of the measurement procedure for comparison or determination of measurement accuracy. This includes information such as specimen type tested, number of samples, sample range (using spiked

samples as appropriate) or target concentrations tested, calculations and statistical methods, results and conclusions.

3.2.7 Analytical performance characteristics

3.2.7.1 Accuracy of measurement

Provide information to describe both trueness and precision studies.

a) **Trueness of measurement**

Provide information on the trueness of the measurement procedure and summarize the data used to establish the trueness measures for both quantitative and qualitative assays.

b) **Precision of measurement**

Provide information to describe repeatability and reproducibility studies.

i. Repeatability

Provide details on repeatability estimation and information about the studies used to estimate, as appropriate, within-run variability. Repeatability data is obtained for instrumentation in conjunction with an appropriate assay.

For products to be used at point-of-care, where the testing may be undertaken by non- laboratory trained personnel (for example, clinic nurses), repeatability should be established in two steps, first, with professional laboratory personnel to establish the optimal repeatability of the IVDD under controlled laboratory conditions then followed by a consumer field evaluation to determine the product's performance when used by non-laboratory trained personnel, unassisted, following instructions provided with the product.

ii) Reproducibility

Provide information on reproducibility estimates and information about the studies used to estimate, as appropriate, variability between days, runs, sites, lots, operators and instruments. Such variability is also known as "Intermediate Precision".

For products to be used at point-of-care, where the testing may be undertaken by non- laboratory trained personnel (for example, clinic nurses), reproducibility should be established in two steps, first, with professional laboratory personnel to establish the optimal reproducibility of the IVDD under controlled laboratory conditions then followed by a consumer field evaluation to determine the product's performance when used by non-laboratory trained personnel, unassisted, following instructions provided with the product.

3.2.7.2 Analytical sensitivity

Provide information about the study design and results. Give a detailed description of specimen type and preparation including matrix, analyte (measured) levels, and how levels were established. The number of replicates tested at each concentration should also be provided as well as a description of the calculation used to determine assay sensitivity. For example:

a) Number of standard deviations above the mean value of the sample without analyte (measurand), commonly referred to as 'Limit of Blank' (LoB).
b) Lowest concentration distinguishable from zero, based on measurements of samples containing analyte (measurand), commonly referred to as 'Limit of Detection (LoD).
c) Lowest concentration at which precision and/or trueness are within specified criteria, commonly referred to as 'Limit of Quantitation' (LoQ).

3.2.7.3 Analytical specificity

a) Give information to describe interference and cross reactivity studies to determine the analytical specificity, defined as the ability of a measurement procedure to detect or measure only the analyte (measurand) to be detected, in the presence of other substances/agents in the sample.

b) Provide information on the evaluation of potentially interfering and cross-reacting substances/agents on the assay. Information should be provided on the substance/agent type and concentration tested, sample type, analyte (measurand) test concentration, and results.

c) Interferents and cross-reacting substances/agents, which vary greatly depending on the assay type and design, could derive from exogenous or endogenous sources such as: Substances used for patient treatment (e.g. therapeutic drugs, alcohol, vitamins, foods, etc.), substances added during sample preparation (e.g. preservatives, stabilizers), substances encountered in specific specimen types (e.g. haemoglobin, lipids, bilirubin, proteins), and; analytes of similar structure (e.g. precursors, metabolites) or medical conditions unrelated to the test condition including specimens negative for the assay but positive for a condition that may mimic the test condition (e.g. for a hepatitis A assay: test specimens negative for hepatitis A virus, but positive for hepatitis B virus).

3.2.7.4 Metrological traceability of calibrator and control material values

Where applicable, summarize the information about metrological traceability of values assigned to calibrators and trueness control materials. Include, for reference materials and/or reference measurement procedures and a description of value assignment and validation.

a) Measuring range of the assay

Provide a summary of studies, which define the measuring range (linear and non-linear measuring systems) including the limit of detection and describe information on how these were established. The summary should include a description of specimen type, number of samples, number of replicates, and preparation including information on matrix, analyte (measurand) levels and how levels were established. If applicable, add a description of high dose hook effect and the data supporting the mitigation (e.g. dilution) steps.

b) Validation of assay cut-off

Provide a summary of analytical data with a description of the study design including methods for determining the assay cut-off, including: the population (s) studied, method or mode of characterization of specimens and statistical methods e.g. Receiver Operator Characteristic (ROC) to generate results and if applicable, define gray- zone/equivocal zone.

c) Validation of assay procedure – reading time

Provide information on how the reading time (either end point or reading window) claimed in the Instructions for Use was determined.

3.2.8 Stability (excluding specimen stability)

Stability is the ability of an IVD reagent to maintain its performance characteristics over a defined time interval *(1, 2)*. The purpose of most stability studies is to establish or verify the time interval, and the storage conditions that can maintain stable IVD performance characteristics.

The stability of an IVD is fundamental to its reliable performance over a defined period of time. It is a regulatory requirement for the manufacturer to provide objective, scientifically sound evidence to support all claims made regarding the stability of an IVD. In addition, a manufacturer can use stability studies to demonstrate the probability that lots manufactured up to the end of the life-cycle of the IVD will meet predetermined user needs (as identified in design inputs)

The requirements for claimed shelf life, in use stability and shipping studies, the summary of requirements is provided below: -

3.2.8.1 Claimed shelf life

Provide information on stability testing studies, to support the claimed shelf life, performed on at least three different lots manufactured under conditions that are essentially equivalent to routine production conditions (these lots do not need to be consecutive lots). The summary should include the study report (i.e. protocol, number of lots, acceptance criteria and testing intervals):

a) When accelerated studies have been performed in anticipation of the real time studies;

b) Identify the method used for accelerated studies; and

c) Conclusion and claimed shelf life.

Note: Shelf life can be derived from the lot with the longest real time stability data as long as accelerated or extrapolated data from all three lots are comparable.

3.2.8.2 In use stability

Provide information on in use stability studies for one lot reflecting actual routine use of the device (real or simulated). This may include open vial stability and/or, for automated instruments, on board stability.

In case of automated instrumentation if calibration stability is claimed, supporting data should be included sufficient to describe: the study protocol (i.e. protocol, acceptance criteria and testing intervals), conclusions and claimed in use stability.

3.2.8.3 Shipping stability

Provide information on shipping stability studies for one lot to evaluate the tolerance of products to the anticipated shipping conditions, describing the study report (i.e. protocol, acceptance criteria), method used for simulated conditions, conclusion and recommended shipping conditions.

Shipping studies can be done under real and/or simulated conditions and should include variable shipping conditions such as extreme heat and/or cold.

3.2.8.4 Robustness studies

Provide information to demonstrate that the product design is robust e.g. insensitive to environmental and usage variation. Robustness (flex) studies are designed to challenge the system under conditions of stress to identify potential device deficiencies, including failures, and determine the robustness of the product.

The manufacturer must consider multiple skill levels of users, as well as potential instrument and reagent problems. Below is a list of factors that may need to be considered when performing robustness studies:

a) Operator error/ human factors, including not limited to;
    i. Use of incorrect specimen type,
    ii. Incorrect application of the specimen to the device (e.g., incorrect placement, incorrect volume),
    iii. Incorrect handling of reagents including those in self- contained unitized test devices, incorrect placement of device (e.g., non-level surface),
    iv. Incorrect placement of reagents, including strips, or other components that contain reagent, use of incorrect reagents (for example, reagents that are not specific for the particular device or lot or generic reagents),

v. Incorrect order of reagent application, use of incorrect amount of reagent, incorrect timing of procedures (e.g., specimen application, running the test, or reading results),
vi. Incorrect reading of test results, incorrect reading due to color blindness etc

b) Specimen integrity and handling including errors in specimen collection, use of inappropriate anticoagulant, clotted specimens, error in specimen handling, incorrect specimen transport and/or storage, presence of interfering substances, presence of bubbles in the specimen etc.

c) Reagent integrity (Reagent viability) including use of improperly stored reagents, use of outdated reagents, use of improperly mixed reagents, use of contaminated reagents etc.

d) Hardware, software, and electronics integrity including power failure, power fluctuation, incorrect voltage, repeated plugging and unplugging of the device, hardware failure, software failure, electronic failure, physical trauma to unit etc.

e) Stability of calibration and internal controls including factors that affect calibrator and calibration stability, factors that may interfere with calibration.

f) Environmental factors including impact of key environmental factors (heat, humidity, barometric pressure changes, altitude (if applicable), sunlight, surface angle, device movement, etc.) on reagents, specimens, and test results, impact of key environmental factors (including changes in parameters such as pH or temperature) etc. The following should be provided:

i. A summary of the evidence that falls within this category,
ii. State the test environment and relation to the intended use environment,
iii. A discussion of what tests were considered for the device and why they were or were not performed,
iv. A discussion to demonstrate why the evidence presented is sufficient to support the application,
v. If a performance study has been conducted that includes human factors/usability end points, reference to the studies and endpoints should be made, but full results do not need to be repeated.

3.2.9 Software verification and validation (if applicable)

Provide information on the software design and development process and evidence of the validation of the software, as used in the finished device. This information should typically include the summary results of all verification, validation protocol and report and testing performed both in-house and in a simulated or actual user environment prior to final release. It should also address all of the different hardware configurations and, where applicable, operating systems identified in the labelling. *Submission shall be in accordance with the Guidelines for Software Medical devices provided under Part X* of this compendium.

3.2.10 Clinical performance

Provide evidence of assessment and analysis of data generated from the clinical use of the product sufficient enough to verify the clinical safety of the IVDD. In Vitro Diagnostics that are used for testing diseases of public health importance such as HIV, Malaria, Hepatitis, Syphilis and Tuberculosis require in-country performance evaluation where the test will be conducted in the country by using samples collected from Tanzania population. The submission shall be in accordance with the *Guidelines for Clinical Performance of In Vitro Diagnostics Medical Devices (TMDA/DMD/MDA/G/006)*. The evidence shall include claims for clinical/diagnostic sensitivity and specificity. All claims should be supported by well-designed performance evaluations which should include:

a) A detailed written plan and protocol of the evaluation study.

b) Dates on which the study was performed and by which site.

c) A written report on the outcome of the study; all anomalous results should be explained and justified. The report outline should contain:
    i. The technology on which the medical device is based, the intended use of the device and any claims made about the device's clinical performance or safety.
    ii. The nature and extent of the clinical data that has been evaluated; and,
    iii. How does the referenced information (recognized standards and/or clinical data) demonstrate the clinical performance and safety of the device in question.

d) Details of the IVDD lots/batches used for the evaluation including lot number date of expiry, and the storage conditions of the product prior to and during study.

e) The clinical evaluation report should be signed and dated by evaluator(s) and accompanied by the manufacturer's justification of the choice of evaluator.

f) The clinical evaluation report should be summarized as per the required information elaborated above.

4. Labelling Requirements

The product dossier should contain a complete set of labelling associated with the product. This includes:

a) Labels;

b) Instructions for use (IFU);

c) If applicable, the instrument manual; and

d) Any other instructional materials provided to the user.

Requirements for product labelling is provided under *the Guidance on Labelling Information for Medical Devices and In-Vitro Diagnostics under Part IX of the compendium.*

5. Post-Marketing Surveillance Activities

5.1. Post Market Surveillance Plan

The product dossier shall contain a post-market surveillance plan. The post-market surveillance plan describes the systems that are in place to ensure appropriate post-market surveillance data is collected. This section shall include:

a) Sources of potential post-market surveillance data:

h) a proactive and systematic process to collect any information referred to in point (a). The process shall allow a correct characterization of the performance of the devices and shall also allow a comparison to be made between the device and similar products available on the market.

i) Effective and appropriate methods and processes to assess the collected data, consideration should also be given to statistical methods.

j) Ensure suitable indicators and threshold values been chosen that will be used in the continuous reassessment of the benefit-risk analysis and of the risk management.

k) Effective and appropriate methods and tools to investigate complaints and analyze market-related experience collected in the field

l) Methods and protocols to manage the events subject to the trend report, including the methods and protocols to be used to establish any statistically significant increase in the frequency or severity of incidents as well as the observation period.

m) Methods and protocols to communicate effectively with TMDA, stakeholders and users regarding medical device issues.

5.2. Periodic Safety Update Report and Post Market Surveillance Reports

5.2.1. Post-market surveillance report

The product dossier shall contain copies of any available post-market surveillance reports for the jurisdictions where the product has already been marketed.

Post- market authorization, the MAH shall prepare a post-market surveillance report summarizing the results and conclusions of the analyses of the post-market surveillance data gathered as a result of the post-market surveillance plan together with a rationale and description of any preventive and corrective actions taken. The report shall be updated when necessary and made available to the TMDA upon request.

5.2.2. Periodic safety update report

MAH shall prepare a periodic safety update report (PSUR) for each device and where relevant for each category or group of devices summarizing the results and conclusions of the analyses of the post-market surveillance data gathered as a result of the post-market surveillance plan together with a rationale and description of any preventive and corrective actions taken. Throughout the lifetime of the device concerned, that PSUR shall set out:

c) The conclusions of the benefit-risk determination; and

d) The main findings of the post-market clinical follow-up.

PART IV

GUIDELINES FOR NOTIFICATION OF MEDICAL DEVICES EXEMPTED FROM REGISTRATION

1. Scope

This guidance provides requirements for submissions of technical documents to support applications for the notification of selected class A medical devices and in-vitro diagnostic devices and other devices that meet the following criteria:

a) Class A medical devices and in-vitro diagnostics (IVDDs) which are ***NOT*** active, non-sterile or without measuring function. Class A medical devices and IVDDs that do not possess the above characteristics may be notified provided that they are not used directly in diagnosis and/ or they are designed for home use only. Example: body scales for monitoring weight, equipment for height measurement;

b) Medical devices and IVDD kits that contains devices already registered or notified in Tanzania;

c) Medical devices and in-vitro diagnostic devices for veterinary use;

d) Laboratory equipment and apparatus; and

e) Medical gases.

Classification of medical devices and in-vitro diagnostic devices is based on the classification rules outlined in the Guidelines for Classification of Medical Devices and Guidelines for Classification of In-vitro Diagnostic Devices found under part V and part VI of this compendium.

2. Submission of applications for registration of Medical Devices

All applications for registration of medical devices shall be made online through the TMDA Traders Portal. For detailed information on the application procedures, refer to ***the*** *Guidelines on Procedural Aspects for Marketing Authorization of Medical Devices, In Vitro Diagnostic Devices and Laboratory Equipment found under part I* of this compendium.

Each submitted application shall contain only one of the following:

a) A single medical device;

b) One medical device family;

c) One medical device system; and

d) One medical device group.

3. Technical Requirements for Registration of Medical Devices

3.1 General requirements

3.1.2 Appointment Letter for Local Responsible Person (LRP)

Applicant who is not resident of Tanzania should appoint LRP who is residing in Tanzania and who is registered by TMDA as dealer of Medical Devices.

Imported product submitted by local applicants should include an official letter from the manufacturer of the product as a testimony of no objection to notification of their product in Tanzania.

The letters should bear company letter head, signed, stamped and dated by the applicant or manufacturer (*applies for local applicants*).

3.2 Medical Devices, In-Vitro Diagnostic Devices and Laboratory Equipment

3.2.1 Product details

a) Description of the product including features, accessories and intended uses and users. The description should state:

   i. The intended uses of the product (i.e. conditions that require its usage);
   ii. The intended users (i.e. professional or general users);
   iii. The targeted population (Children, Adults, Elderly, any Gender criteria);
   iv. Any associated products that work together with the product (examples; reagents, controls, accessories etc); and
   v. Description of the commercial pack and the number of unit products in a commercial pack.

b) Pictures of the device in the commercial pack whereas, all sides of the devices are clearly visible.

3.2.2 Product Label

a) Mock-ups of the primary and secondary packaging labels; and

b) Copies of instructions for use, user manual or package insert.

Labelling of products should comply with the requirements stated in *Guidelines on Labelling Requirements for Medical Devices, In-Vitro Diagnostics and Laboratory Equipment Including Electronic IFU* ***found in part VIII*** of this compendium.

3.2.3 Manufacturer Information

Provide a valid certificate of compliance with ISO 13485 standards or its equivalent from the manufacturer(s) of the devices. Certificate should be issued by recognized Conformity Assessment Body (CAB).

Manufacturers in Tanzania have to be registered by TMDA prior to notification of their products. This also applies to the manufacturers involved in the final manufacturing process like assembly, resizing, cutting, and or packing.

Used product which have been refurbished by a third party who is not the original manufacturer of the devices, then, that third party shall bear the responsibility of the manufacturer described in this guideline.

3.2.4 Other Requirements

a) Declaration of Conformity (DoC) to TMDA Control of Medical Devices Regulations. The declaration (***Annex I***) of the compendium should be filled, signed and stamped by the manufacturer. ***Annex II*** provide general guidance for meeting the essential principles of safety and performance
b) Medical Devices Specifications including the list of standards that the product complied with.
c) Submission of samples as required in the ***Guidelines for Procedural Aspects for Marketing Authorization of Medical Devices, found in part I*** of this compendium.
d) Instructions for use or user manual.

3.3 Medical devices and IVD groups, family and kits

Medical device groups, family or kits may be notified under a single application. In addition to the technical requirements outlined in section 2.2 above, the applicant is also required to:

a) Provide a complete description of each component of the group, family or kit;

b) State the intended use of each component of the group, family or kit; and

c) For kits or groups that contain devices that require registration (such as sutures), state the registration number issued by TMDA for the product.

3.4 Medical Gases

a) Medical gases are gases for therapeutic purposes that are used within healthcare facilities. They include the following elements and compounds:

    i. **Oxygen**, used to provide supplemental oxygen to the respiratory system; in dentistry in combination with nitrous oxide; and as an emergency standby;
    ii. **Nitrous oxide**, used as an anaesthetic agent in surgery; mixed with oxygen to help patients relax during dental procedures; and in cryosurgery (the use of extreme cold to destroy tissue);
    iii. **Nitrogen**, used to provide pneumatic pressure in medical equipment; to prevent combustion and other chemical reactions; and as a component of many gas mixtures;
    iv. **Carbon dioxide**, used to inflate areas of the body for "keyhole" surgery (small incisions made to accommodate surgical instruments); mixed with

air or oxygen to stimulate breathing; and in cryosurgery or testing tooth sensitivity in dentistry;

v. **Medical air**, used in administering breathing treatments and as a mixing component for other respiratory gases; and
vi. **Helium**, used in breathing mixtures for patients with impaired lung functions

b) The following information should be submitted along with all applications for notification of medical gases:

i. Controlled copies of the valid standard operating procedures or protocols for the production of the medical gases including procedures for storage, transportation and distribution;
ii. Results of the daily quality of gas checks of consecutive batches manufactured over a period of at least 3 months *(if applicable*);
iii. A comprehensive plan for ensuring tracking of the recipients of each batch to enable follow up of the product in the market;
iv. Mockup labels of the finished product as packaged for sale/distribution; and
v. Evidence of premises certification (domestic) or GMP compliance (foreign)

c) Notification is not applicable for aerosol preparations or mixtures of solids that are used to generate gases for fire departments, ambulance services, hospitals or health care facilities that produce medical gases for their own use or administration to a patient.

3.5 Medical Devices for Veterinary Uses

a) Medical devices (MDR) and In-vitro Diagnostics (IVDDs) intended to be used in animals have been exempted from registration. This applies to those products which are specifically intended by the manufacturer to be used in animal care and must be labelled as such.

b) The applicant is required to submit all the technical information outlined under section 2.2 above.

4. Labelling Requirement

The product dossier should contain a complete set of labeling associated with the product. This includes:

e) Mock-up labels for the primary and secondary packaging materials;

f) Instructions for use (IFU);

g) If applicable, the instrument manual; and

h) Any other instructional materials provided to the user.

Requirements for product labelling is provided under ***the Guidance on Labelling Information for Medical Devices and In-Vitro Diagnostics*** ***under Part VIII of the compendium.***

4.1 Mock-up Labels for primary

a) Labels must minimally include the following information:

i. Product name and product identification number (product code/catalogue number),
ii. Name of manufacturing site and physical address,
iii. Contents and if the contents are not readily apparent, an indication of what the package contains, expressed in terms appropriate to the device such as size, net weight, length, volume or number of units, volume after reconstitution shall be indicated,
iv. Manufacturing and expiry dates shall be indicated where applicable and shall follow the requirements of ISO 8601,
v. Storage conditions necessary to maintain the stability of the product shall be indicated. If there are any other conditions that may affect the handling or storage of the products shall be specified e.g. fragile,
vi. Warning and precautions: If a product is considered hazardous, the outer container label shall include the appropriate danger wording or symbol(s) e.g. chemical, radioactive and biological hazards,
vii. Lot/batch and/or serial number,
viii. The words "**Sterile**" if the manufacturer intends to sell the product in a sterile condition,
ix. Names of all included reagents, and components in each box on the outer package label, where possible,
x. The word "**For Single Use Only**" shall be included if the product is intended for single use,
xi. The In vitro diagnostics use of the device shall be indicated e.g. "**For In vitro diagnostics use**" or graphical symbol: "**In vitro diagnostic medical device**",
xii. All devices intended for animal uses it shall be indicated "**For Veterinary Use**" or "**Device for Veterinary Uses Only**"
xiii. Where a component is too small to contain all the above information, it must at a minimum contain Name, lot number, expiration date, volume, and storage conditions,
xiv. If the product requires associated instrumentation, the above requirements also apply to the instrument,
xv. The instrument should clearly display information regarding its status as a new or reprocessed product.

4.2 Instructions for use *(if applicable)*

A copy of the current instructions for use must be submitted in the dossier and should include the following minimum information:

a) The product name and product code;

b) The name and contact details of the manufacturer or an authorized representative of the manufacturer, in order for the user to obtain assistance;

c) A clearly stated intended use, including:

i. What is detected by the assay (that is, the analytical use of the assay e.g. the marker or nucleic acid sequence being detected)

ii. the clinical indication for the test (e.g. if it is for a specific disorder or a condition or risk factor of interest that the test is intended to detect, define or differentiate)

iii. the function of the product (screening, monitoring, diagnostic or aid to diagnosis, staging or aid to staging of disease)

iv. the intended user (laboratory professional and/or at point-of-care)

v. the intended testing population (e.g. neonates, antenatal women)

vi. What the instrument is intended for and whether the test is qualitative or quantitative

vii. An indication that the product is for ***in vitro use, Veterinary Uses***

viii. A general description of the principle of the assay method or instrument principles of operation

ix. A description of all components of the assay (e.g. reagents, assay controls and calibrators) and a description of the reactive ingredients of relevant components (e.g. antibodies, antigens, nucleic acid primers etc.)

x. A description of the specimen collection and transport materials provided with the product or recommended for use

xi. If applicable, a description of any software to be used with the product

xii. If applicable, a description or complete list of the various configurations/variants of product that will be made available

xiii. If applicable, a description of the accessories, and other products that are intended to be used in combination with the product but are not provided with the product

xiv. Storage conditions, including storage conditions and stability of both the unopened and opened product, and working solutions. When applicable, these instructions should include such information as conditions of temperature, light, humidity, and other pertinent factors

xv. If the test kit includes sterile accessories, an indication of that condition and any necessary instructions in the event of damage to sterile packaging

xvi. If the test kit includes accessories that have been specified by the manufacturer as intended for single-use only, an indication of that stat

xvii. Clear instructions on how to perform the assay, including instructions on specimen collection, handling, preparation and storage of reagents, the use of assay calibrators and controls and the interpretation of results

xviii. Recommendations for quality control procedures

xix. Clear instructions on the correct usage of any equipment or software that is required for the performance of the assay

xx. Any warning and precautions to be considered related to the use of the assay including but not limited to interpreting the results, the disposal of the assay and/or its accessories (e.g. lancets), to any consumables used with it (e.g. reagents) that may be carcinogenic, mutagenic or toxic, or to any potentially infectious substances of human or animal origin

xxi. Any residual risks.

xxii. Precautions and measures to be taken in the event of performance changes or product malfunction

xxiii. Limitations of the assay, including information on interfering substances that may affect the performance of the assay

xxiv. Any requirements for special training or particular qualifications of the assay user

xxv. Any requirements for routine maintenance. Include details of frequency of maintenance and who should perform this maintenance (for example: the user, a representative of the manufacturer, or a third party

xxvi. Where relevant, a bibliography

xxvii. Document control details, such as a document version number and release date.

4.3 Instrument manual

If the product requires associated instrumentation, include a hard copy and softcopy of the instrument manual and/or associated operator manuals. If the instrument manual is large, an electronic version may be included instead of a hard copy.

4.4 Any other instruction material provided to the user

a) Provide copies of any other instructional materials that need to be provided to the user.

b) In case the device is intended to be sold to the general public, labeling information: -

i. Shall be set out on the outside of the package that contains the device; and be visible under normal conditions of sale.

ii. Where a package that contains a device is too small to display all the information in accordance with (i) above, the directions for use shall accompany the device but need not be set out on the outside of the package or be visible under normal conditions of sale.

iii. Specimen label(s), promotional material(s) and user manual(s) should be provided.

Note: *Requirements that have been described in a respective standard should also be followed when labeling the product.*

Symbols commonly used in medical devices have been attached in ***Annex III*** *(*Examples of Symbols Used in Medical Devices Based on ISO 15223-1) *of this compendium).*

PART V:

GUIDELINES ON CLASSIFICATION OF MEDICAL DEVICES

4. Scope

This document applies to all products that fall within the definition of medical device that has been specified in the TMDA (Control of Medical Device) Regulations other than those used for the *in vitro* examination of specimens derived from the human body for which a separate document will be referred.

The purpose of this document is to provide guidance on how to determine the classification of medical device which has been specified in TMDA (Control of Medica Devices) Regulations, GN.315

5. Risk-based Classification of Medical Devices

Regulatory controls are intended to safeguard the health and safety of patients, users and others by ensuring that manufacturers of medical devices follow specified procedures during design, manufacturing and marketing.

The level of controls will depend on the identified risks associated with devices, and the identification of a suitable way of generating a sustainable set of rules is an important feature of any regulatory control system.

The risk associated with using medical devices can range from little to significant potential risks inherent in the type of device. The level of premarket intervention by the regulator is proportional to the level of potential risk and established through a classification system based on that potential risk. The level of regulatory control increases with the increasing degree of risk, considering of the benefits offered by use of the device.

The classification of medical device is determined from:

a) The manufacturer's intended purpose for the medical device; and

b) A set of classification rules. These rules shall classify medical devices into one of 4 classes with the main purpose of:

   i. Ensuring that the regulatory controls applied to a medical device are proportionate to risk; and

   ii. Assisting a manufacturer to allocate its medical device to an appropriate risk class.

For the purposes of this document, the following terms and definitions apply:

2.1. Active Medical Device

Any medical device, operation of which depends on a source of electrical energy or any source of power other than that directly generated by the human body or gravity and which acts by converting this energy but does not include medical devices

intended to transmit energy, substances or other elements between an active medical device and the patients, without any significant change.

2.2. Active Therapeutic Device

Any active medical device, whether used alone or in combination with other medical devices, to support, modify, replace or restore biological functions or structures with a view to treatment of alleviation of an illness, injury or handicap.

2.3. Active Device Intended for Diagnosis

Any active medical device, whether used alone or in combination with other medical devices, to supply information for detecting, diagnosing, monitoring or to support in treating physiological conditions, states of health, illnesses or congenital deformities.

2.4. Body Orifice

Any natural opening in the body, as well as the external surface of the eyeball, or any permanent artificial opening, such as a stoma or permanent tracheotomy.

2.5. Central Circulatory System

The major internal blood vessels including the following: Pulmonary veins; pulmonary arteries; cardiac veins; coronary arteries; common carotid artery; external carotid artery; internal carotid artery; cerebral arteries; brachiocephalic artery; superior vena cava; inferior vena cava; aortic arch; thoracic aorta; abdominal aorta; ascending aorta; common iliac arteries; and descending aorta to the bifurcation of aorta.

2.6. Central Nervous System

The brain, meninges, spinal cord and cerebrospinal fluid.

2.7. Cleaning

Removal of contamination from an item to the extent necessary for its further processing and its intended subsequent use.

2.8. Continuous Use

(a) The entire duration of use of the device without regard to temporary interruption of use during a procedure or, temporary removal for purposes such as cleaning or disinfection of the device.

(b) The accumulated use of a device that is intended by the manufacturer to be replaced immediately with another of the same type

2.9. Disinfection

Reduction of the number of viable microorganisms on a product to a level previously specified as appropriate for its intended further handling or use.

2.10. Duration of Use

3.10.1 Transient Use: Normally intended for continuous use for less than 60 minutes.

3.10.2 Short-term Use: Normally intended for continuous use for between 60 minutes and 30 days.

3.10.3 Long-term Use: Normally intended for continuous use for more than 30 days.

2.11. Harm

Physical injury or damage to the health of people or damage to property or the environment.

2.12. Hazard

Potential source of harm.

2.13. Immediate Danger

A situation where the patient is at risk of either losing life or an important physiological function if no immediate preventative measure is taken.

2.14. Implantable Medical Device

Any device, including those that are partially or wholly absorbed, which is intended to be totally introduced into the human body or to replace an epithelial surface or the surface of the eye, by surgical intervention which is intended to remain in place after the procedure or any device intended to be partially introduced into the human body through surgical intervention and intended to remain in place after the procedure for at least 30 days is also considered an implantable device.

2.15. Intended Use

The objective intent of the manufacturer regarding the use of a product, process or service as reflected in the specifications, instructions and information provided by the manufacturer.

2.16. Invasive Medical Device

A device, which, in whole or in part, penetrates inside the body, either through a body orifice or through the surface of the body.

2.17. Life Supporting or Life Sustaining Medical Device

A device that is essential to, or that yields information that is essential to, the restoration or continuation of a bodily function important to the continuation of human life.

2.18. Reusable Surgical Instrument

An instrument intended for surgical use by cutting, drilling, sawing, scratching, scraping, clamping, retracting, clipping or other surgical procedures, without connection to any active medical device and which are intended by the manufacturer to be reused after appropriate procedures for cleaning and/or sterilization have been carried out.

2.19. Risk

A combination of the probability of occurrence of harm and the severity of that harm.

2.20. Radiopharmaceuticals

Unique medicinal formulations containing radioisotopes which are used in major clinical areas for diagnosis and/or therapy.

2.21. Surgically Invasive Medical Devices

An invasive device which penetrates inside the body through the surface of the body, including through mucous membranes of body orifices with the aid or in the context of a surgical operation; and a device which produces penetration other than through a body orifice.

NOTE Devices other than those referred to in the previous subparagraph and which produce penetration other than through an established body orifice, should be treated as surgically invasive devices. The term surgical operation used in this definition includes all clinical intervention procedures in which a device is placed into the body through the surface in the context of a surgical operation or other clinical procedure.

3. Principles of classification

3.1. General principles

The classification of the device is based on the risk associated to it at the point of usage (The risk to patients, users and other persons). The risk presented by a particular device depends on:

a) Its intended purpose;
b) The effectiveness of the risk management techniques applied during design, manufacture and use;
c) Its intended user(s);
d) Its mode of operation; and
e) Technologies.

3.2. Factors influencing device classification

A number of factors may influence medical device classification. These include:

a) The duration of contact of the device with the body
b) The degree of, and site of, invasiveness into the body.
c) Whether the device deliver medicines or energy to the patient.
d) Whether the device is intended to have a biological effect on the body.
e) Intended action on the human body.
f) Local *versus* systemic effects.
g) Whether the device comes into contact with injured skin.
h) Whether for diagnosis or treatment,
i) The ability to be re-used or not, and
j) Combination of devices.

3.3. Application rules

3.3.1. The class of the medical device is determined by its intended use and mechanism of action, and not the specific technical characteristics of the medical device, unless the specific technical characteristics have a direct bearing on the intended use.

NOTES:

a) The accidental use of the medical device does not determine the class of the medical device. Similarly, if a medical practitioner uses the medical device in a manner not intended by the manufacturer, this does not determine or change the class of the medical device for the purpose of conformity assessment.

b) It is the intended use determined and assigned by the manufacturer to the medical device that determines the class of the medical device and not the class assigned to other similar medical devices. For instance, two sutures that have the same composition may have different intended uses.

3.3.2. If two or more rules are applicable to the medical device based on the manufacturer's intended use, the medical device is allocated the highest level of classification indicated.

3.3.3. The manufacturer must take into consideration all the rules in order to establish the proper classification for its device. It is quite conceivable for instance that one of the general rules that are not specific to active devices, nevertheless applies to such a device. All the device characteristics must be taken into consideration. The characteristic or combination of characteristics in accordance with the intended purpose of the device that rates the highest class determines the class for the device as a whole.

3.3.4. The duration of use should be specified for all invasive medical devices as it determines the class of invasive medical device.

3.3.5. Accessories intended to be used together with a 'parent' medical device to achieve its intended use should be classified separately from the medical device they are used with (as though it is a medical device in its own right).

3.3.6. If a medical device is not used in a specific part of the body, it should be classified on the basis of the most critical specified use.

NOTE: Classification of the medical device will have to be determined on the basis of claims contained in the information provided with the device. The manufacturer must be sufficiently specific in that regard. If the manufacturer wants to avoid the particular higher classification, then it must clearly define on the labelling the intended use in such a way that the device falls into the lower class. The manufacturer must provide as a minimum requirement either appropriate positive or negative indications for use. Otherwise, it is deemed to be intended to be used principally for the purpose that is accepted in general medical practice.

3.3.7. Software that is incorporated into the medical device itself and intended to drive or influence the use of a medical device should be classified the same classification as the medical device (e.g. software which is used for image enhancement).

3.3.8. Where the software is independent of any other medical device, it is classified in its own right using the classification rules for medical devices.

NOTE: Standalone software (to the extent it falls within the definition of a medical device) is deemed to be an active device.

3.3.9. Classification of an assemblage of medical devices that individually comply with all the relevant regulatory requirements depends on the manufacturer's purpose in packaging and marketing such devices.

For example:

a) If the intended use of combination of devices is different from the individual medical devices, it should be classified according to the new intended use.

b) If the combination does not change the intended use of the individual medical devices that make it up, the classification allocated to the assemblage for the purpose of a Declaration of Conformity is at the level of the highest classified device included within it.

If one or more of the medical devices that is in the assemblage has yet to comply with all the relevant regulatory requirements, the combination should be classified as a whole according to its intended use.

4. Classification of medical devices

Table 1 indicates the four risk classes of devices. The examples given are for illustration only and the manufacturer must apply the classification rules to each medical device according to its intended purpose.

Table 1: Classification system for general medical device

Class	Risk Level	Device Examples
A	Low Risk	Cotton wool
B	Low-moderate Risk	Hypodermic needle / suction equipment
C	Moderate-high Risk	Lung ventilator / orthopedic implants
D	High Risk	neuro-endoscopes/implantable defibrillator

In the event of any dispute between an establishment and conformity assessment body over a classification of a medical device, the establishment may request in writing to the Authority within thirty days from the date of dispute to decide on the matter. Authority shall decide on the proper classification of the medical device concerned, whose decision shall be final.

4.1. Determination of device class using rules-based system

The manufacturer shall:

a) Decide if the product concerned is a medical device, using the appropriate definition;

b) Determine the intended use of the medical device; and

c) Take into consideration all the rules that follow in order to establish the proper classification for the device, noting that where a medical device has features that place it into more than one class, classification and conformity assessment should be based on the highest class indicated.

4.2. Classification rules for medical devices

The actual classification of each device depends on the claims made by the manufacturer and on its intended use. While the provision of illustrative examples in the table that follows is helpful when interpreting the purpose of each rule, it must be emphasized that the actual classification of a particular device must be considered individually, taking account of its design and intended use.

Table 2: Graphical summary – medical devices classification guidance chart for initial identification of probable device class

SUBJECTS

Non-invasive medical devices – Rules 1, 2, 3, 4
Invasive medical devices – Rules 5, 6, 7, 8
Active medical devices – Rules 9(i), 9(ii), 10(i), 10(ii), 11, 12
Additional rules – Rules 13, 14, 15,16,17,18,19,20,21,22

Decision trees illustrating how these rules may be used to classify specific devices are shown in Appendix A.

Classification Rules for Medical Devices

RULE	**EXPLANATIONS**
Non-invasive Medical Devices	
Rule 1	
a) All non-invasive devices which come into contact with injured skin	Medical devices covered by rule are extremely claim sensitive
b) are in Class A if they are intended to be used as a mechanical barrier, for compression or for absorption of exudates only, i.e. they heal by primary intent;	Examples: • simple wound dressing • cotton wool • absorbent pads • wound strips • adhesive bandages (sticking plasters, band-aid) • gauze dressings • which act as a barrier, maintain wound position or absorb exudates from the wound Note. Primary intent implies that the edges of the wound are close enough or pulled together, e.g. By suturing, to allow to heal before formation of granulation tissue
c) are in Class B if they are intended to be used principally with wounds which have breached the dermis, including devices principally intended to manage the microenvironment of a wound.	Examples: • non-medicated impregnated gauze dressings • hydrogel dressing for wounds or injuries that have not breached the dermis or can only heal by secondary intent • polymer film dressing
d) unless they are intended to be used principally with wounds which have breached the dermis and can only heal by secondary intent, in which case they are in Class C.	Medical devices used to treat wounds where the subcutaneous tissue is as least partially exposed, and the edges of the wound are not sufficiently close to be pulled together. To close the wound, new tissue must be formed within the wound

	prior to external closure. The device manufacturer claims that they promote healing through physical methods other than 'primary intent' Examples: • dressing for chronic ulcerated wounds • dressing for severe burns • dressings for severe decubitus wounds • dressings providing a temporary skin substitute NOTES: i. Breached dermis: the wound exposes the subcutaneous tissue at least partly. ii. Secondary intent: the wound heals by first being filled with granulation tissue, subsequently the epithelium grows back over the granulation tissue and the wound contracts iii. For such devices incorporating a medicinal product, see Rule 13. For such devices incorporating an animal/human tissue derivative rendered non-viable, see Rule 14
Rule 2	
a) All non-invasive medical devices intended for channeling or storing body liquids or tissues, or liquids or gases for the purpose of eventual infusion, administration or introduction into the body are in Class A,	Such medical devices are 'indirectly invasive' in that they channel or store liquids that will eventually be delivered into the body (see Rule 4). Medical devices that provide a simple channeling function, with gravity providing the force to transport the liquid. Medical devices intended to be used for a temporary containment or storage function. Examples: Administration sets for gravity infusion Empty syringes without needles
b) Unless they may be connected to	Examples:

an active medical device in Class B or a higher-class, in which case they are Class B	• Syringes and administration set for infusion pumps • Medical devices used for channeling gases e.g. antistatic tubing for anesthesia and anesthesia breathing circuits NOTES: If a device, e. g tubing can be used for a purpose that would cause it to be connected to an active device such a device will be automatically in Class B, unless the manufacturer clearly state that it should not be connected to an active device of Class B or higher "May be connected to an active device" Such a connection is deemed to exist between a non-active device and an active device where the non-active device forms a link in the transfer of the substance between the patient and the active device and the safety and performance of one of the devices is influenced by the other device. For instance, this applies to tubing in an extracorporeal circulation system which is downstream from a blood pump and in the same blood flow circuit, but not directly in contact with the pump.
c) Unless they are intended for use of channeling blood, or storing channeling other body liquids or for storing or organs, parts of organs or body tissues in which case they are Class B	Examples: • Tube used for transfusion • Organ storage containers • to channel blood (e.g. in transfusion, extracorporeal circulation) • for temporary storage and transport of organs for transplantation (i.e. containers, bags) • for long term storage of biological substance and tissues such as corneas, sperm, human embryos, etc. (i.e. containers etc.
d) Unless they are blood bags, in which case they are Class C.	Example: Blood bags that do not incorporate ant-coagulant. NOTE: in some jurisdictions, blood bags have a special rule that places them

	within a different risk class
Rule 3	
a) All non-invasive medical devices intended for modifying the biological or chemical composition of blood, other body liquids, or other liquids intended for infusion into the body are in Class C	This rule covers mostly the more sophisticated elements of extracorporeal circulation sets, dialysis systems and autotransfusion systems as well as devices for extracorporeal treatment of body fluids which may or may not be immediately reintroduced into the body, including, where the patient is not in a closed loop with the device. Such medical devices are indirectly invasive in that they treat or modify substances that will eventually be delivered into the body. They are normally used in conjunction with an active device within the scope of either Rule 9 or 11. Examples: • Hemodialyzers • Devices to remove white blood cells from whole blood • Medical devices intended to separate cells by physical means, e.g. gradient medium for sperm separation • Hemodialysis concentrates NOTE: for the purpose of this part of the rule, 'modification' does not include simple, mechanical filtration or centrifuging which are covered below
b) Unless the treatment consists of filtration, centrifuging or exchanges of gas or of heat, in which case they are in Class B	Examples: • Devices to remove carbon dioxide; • Particulate filters in an extracorporeal circulation system • Centrifugation of blood to prepare it for transfusion or autotransfusion • Warming or cooling the blood in an extracorporeal circulation system
Rule 4	
All other non-invasive medical devices are in Class A	These medical devices either do not touch the patient or contact intact skin Examples: • urine collection bottles;

	• medical devices used to immobilize body parts and/or to apply force or compression on them (e.g. non-sterile dressings used to aid the healing of a sprain, cervical collars, gravity traction devices, compression hosiery) • non-invasive electrodes (electrodes for EEG or ECG) • non-invasive conductive gels • medical devices intended in general for external patient support (e.g. hospital beds, patient hoists, walking aids, wheelchairs, stretchers) • corrective glasses • stethoscopes • eye occlusion plasters incision drapes
Invasive Medical Devices	
Rule 5	
All invasive medical devices with respect to body orifices (other than those which are surgically invasive) and which: are not intended for connection to an active medical device, or; are intended for connection to a Class A medical device only	Such medical devices are invasive in body orifices and are not surgically invasive medical devices tend to be diagnostic and therapeutic instruments used in ENT, ophthalmology, dentistry, proctology, urology and gynecology. Classification depends on the duration of use and the sensitivity (or vulnerability) of the orifice to such invasion. NOTE: Invasiveness with respect to the body orifices must be considered separately from invasiveness that penetrates through a cut in the body surfaces (surgical invasiveness). For short term use, a further distinction must be made between invasiveness with respect to the less vulnerable anterior parts of the ear, mouth and nose and the other anatomical sites that can be accessed through natural body orifices. Surgically created stoma, which for example allows the evacuation of urine or faeces, should also be considered as a body orifice.
a) are in Class A if they are intended	Examples:

for transient use;	• examination gloves • enema devices • handheld mirrors used in dentistry to aid in dental diagnosis and surgery • dental impression materials • stomach tubes • impression trays • urinary catheters intended for transient use • embryo transfer catheter
b) are in Class B if they are intended for short-term use;	Examples: • Indwelling urinary catheters intended for short term use • tracheal tubes • short term corrective and non-corrective • contact lens
c) Unless they are intended for short-term use in the oral cavity as far as the pharynx, in an ear canal up to the ear drum or in a nasal cavity, in which case they are in Class A,	Examples: • dentures intended to be removed by the patient • a dressing for nose bleeds Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice are classified as Class B if they are applied in the nasal or oral cavity as far as the pharynx, and achieve their intended purpose on those cavities Example: Nasal solution sprays intended to penetrate, hydrate the nasal passages and sinus cavity for preventive or symptomatic nasal care are Class B. unless saline nasal solution intended for clear, clean, rinsing is Class A.
d) are in Class C if they are intended for long-term use	Examples: • urethral stent • corrective and non-corrective contact lenses for long-term continuous use (for this device,

	removal of the lens for cleaning or maintenance is considered as part of the continuous use) • urinary catheters intended for long term use
e) Unless they are intended for long-term use in the oral cavity as far as the pharynx, in an ear canal up to the ear- drum or in a nasal cavity and are not liable to be absorbed by the mucous membrane, in which case they are in Class B.	Examples: • orthodontic wire • fixed dental prosthesis • wetting or lubricating eye drops
f) all invasive medical devices with respect to body orifices (other than those which are surgically invasive) that are intended to be connected to an active medical device in Class B or a higher class, are in Class B.	Examples: • tracheal tubes connected to a ventilator • suction catheters for stomach drainage • dental aspirator tips. • powered nasal irrigators • some enteral feeding tubes • endoscope. See also Rule 2 b)
Rule 6	
All surgically invasive medical devices intended for transient use are in Class B,	A majority of such medical devices fall into several major groups: • surgical swabs • surgical gloves • those that create a conduit through the skin (e.g. syringe needles, lancets) • suckers • surgical instruments (e.g. single-use scalpels, single use scalpel blades, surgical staplers, single-use • aortic punch • drill bits connected to active devices • various types of catheter/sucker etc. NOTES i. A surgical instrument (other than that in Class D) is in Class A if reusable and in Class B if supplied sterile and intended for single use. Also, a surgical instrument connected to an active

	device is in a higher class than A. ii. If the device incorporates a medicinal substance in a secondary role refer to Rule 13 iii. If the device incorporates a medicinal substance in a secondary role refer to Rule 13
a) Unless they are reusable surgical instruments, in which case they Class A; or	Examples: • Manually operated surgical drill bits and saws • Manually operated surgical instruments e.g. scissors, forceps, clamps, blades, hand-held retractor NOTE: refer to definition of reusable surgical instrument
b) Unless intended to supply energy in the form of ionizing radiation, in which case they are in Class C; or	Example: • Incorporating/containing sealed catheter radioscope
c) Unless intended to have a biological effect or be wholly or mainly absorbed, in which case they are in Class C; or	Example: • insufflation gases for the abdominal cavity. NOTES: i. The 'biological effect' referred to is an intended one rather than unintentional. The term 'absorption' refers to the degradation of a material within the body and the metabolic elimination of the resulting degradation products from the body. ii. This part of the rule does not apply to those substances that are excreted without modification from the body.
d) Unless intended to administer medicinal products by means of a delivery system, if this is done in a manner that is potentially hazardous taking account of the mode of application, in which they are in Class C; or	Example: • insulin pen for self-administration (supplied without insulin) NOTES: i. the term 'administration of medicines' implies storage and/or

	influencing the rate/volume of medicine delivered not just channeling. ii. The term 'potentially hazardous manner' refers to the characteristics of the device and not the competence of the user
e) Unless they are intended specifically for use in direct contact with the central nervous system, in which case they are in Class D; or	Examples: • neuro-endoscopes • brain spatulas • direct stimulation canulae • spinal cord retractors • spinal needles
f) Unless intended specifically to diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with these parts of the body, in which case they are in Class D.	Examples: • angioplasty balloon and related guide wires • dedicated disposable cardiovascular instruments NOTES: i. The expression "correct a defect" does not cover devices that are used accessorily in heart surgery procedures, e.g. clamps, aortic punch instruments. The first indent of this rule does not apply to aortic punches and similar cutting instruments which perform a similar function to a scalpel. ii. Dedicated means that the intended purpose of the device or accessory is to specifically control, diagnose, monitor or correct a defect of the heart or of the central circulatory system
g) Unless they are intended specifically for use in direct contact with the central nervous system, in which case they are in Class D; or	Examples: • Neuro-endoscopes • Brain spatulas • Direct stimulation canulae • Spinal cord retractors • Spinal needles
Rule 7	
All surgically invasive medical devices intended for short-term use are in Class B,	Such medical devices are mostly used in the context of surgery or post-operative care, or are infusion devices, or are catheters of various types Examples:

	• infusion cannula • temporary filling materials • non-absorbable skin closure devices • tissue stabilizers used in cardiac surgery NOTES i. includes devices that are used during cardiac surgery but do not monitor or correct a defect. ii. if the device incorporates a medicinal substance in a secondary role refer to Rule 13
a) Unless they are intended to administer medicinal products, in which case they are in Class C; or	NOTE: the term 'administration of medicines' implies storage and/or influencing the rate/volume of medicine delivered not just channeling
b) Unless they are intended to undergo chemical change in the body (except if the devices are placed in the teeth), in which case they are in Class C; or	Example: surgical adhesive
c) Unless they are intended to supply energy in the form or ionizing radiation, in which case they are in Class C; or	Example: brachytherapy device
d) Unless they are intended to have a biological effect or to be wholly or mainly absorbed, in which case they are in Class D; or	Examples: • absorbable suture • biological adhesive NOTE: the 'biological effect' referred to is an intended one rather than unintentional. The term 'absorption' refers to the degradation of a material within the body and the metabolic elimination of the resulting degradation products from the body.
e) Unless they are intended specifically for use in direct contact with the central nervous system, in which case they are in Class D;	Example: • neurological catheter.
f) Unless they are intended specifically to diagnose, monitor or correct a defect of the heart or of the central circulatory system through direct contact with these parts of the body, in which case	Examples: • cardiovascular catheters • temporary pacemaker leads • carotid artery shunts

they are in Class D	
Rule 8	
All implantable medical devices, and long-term surgically invasive devices, are in Class C,	Most of the medical devices covered by this rule are implants used in the orthopedic, dental, ophthalmic and cardiovascular fields. Examples: • maxilla-facial implants • prosthetic joint replacements • bone cement • non-absorbable internal sutures • posts to secure teeth to the mandibular bone (without a bioactive coating). • intraocular lens • peripheral vascular grafts and peripheral stents • shunts • dental implants and abutments NOTE: if the device incorporates a medicinal substance in a secondary role refer to Rule 13
a) Unless they are intended to be placed into the teeth, in which case they are in Class B; or	Examples: • bridges; • crowns • dental filling materials
b) Unless they are intended to be used in direct contact with the heart, the central circulatory system or the central nervous system (CNS), in which case they are in Class D; or	Examples: • prosthetic heart valves • spinal stents • vascular prosthesis and stents • cardiovascular sutures • CNS electrodes • aneurysm clips • central vascular catheter for long term-use
c) Unless they are intended to be life supporting or life sustaining, in which case they are in Class D; or	
d) Unless they are intended to be active implantable medical devices, in which case they are Class D; or	Examples: • pacemakers, their pacemakers' electrodes and their pacemakers lead; • implantable defibrillators
e) Unless they are intended to have a biological effect or to be wholly or mainly absorbed, in which case they are in Class D; or	Examples: • adhesives and implantable devices claimed to be bioactive through the attachment of surface coatings such as phosphoryl

	choline) • long-term absorbable suture • elastoviscous fluids for joint movement (e.g. hyaluronan of non-animal origin) • biodegradable Bone Cements
f) Unless they are intended to administer medicinal products, in which case they are in Class D; or	Example: • rechargeable non-active drug delivery system.
g) Unless they are intended to undergo chemical change in the body (except if the devices are placed in the teeth), in which case they are in Class D; or	NOTE: bone cement is not within the scope of the term 'chemical change in the body' since any change takes place in the short rather than long term.
h) Unless they are breast implants, in which case they are in Class D.	Examples: • breast implants • breast tissue expanders
Active Medical Devices	
Rule 9(i)	
All active therapeutic medical devices intended to administer or exchange energy are in Class B,	Such medical devices are mostly electrically powered equipment used in surgery; devices for specialized treatment and some stimulators. Examples: • muscle stimulators • Transcutaneous electrical nerve stimulation (TENS) devices • powered dental hand pieces • hearing aids • neonatal phototherapy equipment • ultrasound equipment for physiotherapy • powered drills

a) Unless their characteristics are such that they may administer or exchange energy to or from the human body in a potentially hazardous way, including ionizing radiation, taking account of the nature, the density and site of application of the energy, in which case they are in Class C	Examples: • lung ventilators • baby incubators • electrosurgical generators • external pacemakers and defibrillators • surgical lasers • lithotripters • therapeutic X-ray and other sources of ionizing radiation. • blood warmers • electrically powered heat exchangers (with patient's incapable of reacting, communicating /or who are without a sense of feeling) NOTE: the term 'potentially hazardous' refers to the type of technology involved and the intended application.
Rule 9(ii)	
All active medical devices intended to control or monitor the performance of active therapeutic devices in Class C, or intended directly to influence the performance of such devices, are in Class C.	Example: external feedback systems for active therapeutic devices
Rule 10(i)	
Active medical devices intended for diagnosis are in Class B:	Such medical devices include equipment for ultrasonic diagnosis/imaging, capture of physiological signals, interventional radiology and diagnostic radiology
a) if they are intended to supply energy which will be absorbed by the human body (except for devices used solely to illuminate the patient's body, with light in the visible or near infra-red spectrum, in which case they are class A) or	Examples: • magnetic resonance equipment • ultrasound in non-critical applications • evoked response stimulators.
b) if they are intended to image in vivo distribution of radiopharmaceuticals, or	Examples: • gamma/nuclear cameras • positron emission tomography and single photon emission computer tomography

c) if they are intended to allow direct diagnosis or monitoring of vital physiological processes, unless they are specifically intended for: i. monitoring of vital physiological parameters, where the nature of variations is such that it could result in immediate danger to the patient, for instance variations in cardiac performance, respiration, activity of central nervous system, or ii. diagnosing in clinical situations where the patient is in immediate danger, in iii. which case they are in Class C	Examples: • electronic thermometers • stethoscopes and blood pressure monitors • electrocardiographs • electroencephalograph NOTE: Vital physiological processes and parameters include, for example respiration, heart rate, cerebral functions, blood gases, blood pressure and body temperature. Medical devices intended to be used for continuous surveillance of vital physiological processes in anesthesia, intensive care or emergency care are in Class C, whilst medical devices intended to be used to obtain readings of vital physiological signals in routine checkups and in self-monitoring are in Class B. A thermal imaging device intended to monitor blood flow is not considered to be a temperature measuring device. Examples: • monitors/alarms for intensive biological sensors • oxygen saturation monitor • apnea monitor • patient monitors (intended use: monitor intended for multi-parameter patient monitoring. The device will produce visual and audible alarms if any of the physiological parameters monitored vary beyond pre-set limits and timed alarm recordings will be produced.) for example in intensive care monitoring, • e.g. blood pressure, temperature, oxygen saturation. Example: ultrasound equipment for use in interventional cardiac procedures.
Rule 10(ii)	
Active medical devices intended to	Examples:

emit ionizing radiation and intended for diagnostic and/or interventional radiology, including devices which control or monitor such devices, or those which directly influence their performance, are in Class C	• these include devices for the control, monitoring or influencing of the emission of ionizing radiation • Diagnostic X-ray machine
Rule 11	
All active devices intended to administer and/or remove medicinal products, body liquids or other substances to or from the body are in Class B,	Such devices are mostly drug delivery systems or anesthesia equipment. Examples: • suction equipment • feeding pumps • jet injectors for vaccination • nebulizer to be used on conscious and spontaneously breathing patients where failure to deliver the appropriate dosage characteristics is not potentially hazardous
a) Unless this is done in a manner that is potentially hazardous, taking account of the nature of the substances involved, of the part of the body concerned and of the mode and route of administration, in which case they are in Class C	Examples: • infusion pumps • anesthesia equipment • dialysis equipment • hyperbaric chambers • nebulizer where the failure to deliver the appropriate characteristics could be hazardous.
Rule 12	
All other active devices are in Class A.	Examples: • examination lamps • surgical microscopes • powered hospital beds & wheelchairs • powered equipment for the recording, processing, viewing of diagnostic Images • dental curing lights

Additional Explanations:

4.2.1. The concept “act by converting energy” includes conversion of energy in the device and/or conversion at the interface between the device and the tissues or in the tissues**.** Electrodes intended for E.C.G or E.E.G are normally not active devices because they do not normally act by conversion energy.

4.2.2. The concept of “significant change” for energy includes changes in the nature, level and density of energy (see Rule 9(i) and Rule 9(ii)). This means that for

instance an electrode is not an active device under this classification system as long as the energy input is intended to be the same as the energy output. For instance, resistance in a wire that causes minor changes between input and output cannot be considered to constitute "significant change". However, electrodes used in electrosurgery for cutting tissues or cauterization are active devices because their operation depends on energy provided by a generator and their action is achieved by conversion of energy at the interface between the device and the tissue or in the tissue.

4.2.3. The application of energy from the human body does not make a device "active" unless that energy is stored within the device for subsequent release. For instance, energy generated by human muscle and applied to the plunger of a syringe (thus causing a substance to be delivered to a patient) does not make this syringe an "active device". However, if a drug delivery system depends upon manual winding to preload a spring which is subsequently released to deliver a substance, then the device incorporating the spring is an "active device".

4.2.4. Medical devices using prestored gases and/or vacuum as a power source are regarded as active devices, as long as they fulfil both criteria under the definition of e.g. gas mixers with anesthesia machines, aerosol pain relief sprays with a pre-stored propellant gas and gas-powered suction pumps.

4.2.5. Heating/cooling pads intended only to release stored thermal energy are not active devices because they do not act by conversion of energy. However, heating/cooling pads which act by chemical action (e.g. endothermic or exothermic reaction) are active devices as they are converting chemical energy into heat energy and/or vice versa.

4.2.6. Radioactive sources that are intended to deliver ionizing radiation are regarded as active medical devices (e.g. radioactive isotopes coated beads), unless they are radiopharmaceuticals which may be infused into the body

RULE	**EXPLANATIONS**
Additional Rules	
Rule 13	

All medical devices incorporating, as an integral part, a substance which, if used separately, can be considered to be a medicinal product, and which is liable to act on the human body with action ancillary to that of the devices, are in Class D.	These medical devices incorporate medicinal substances in an ancillary role. Examples: antibiotic bone cements heparin-coated catheters wound dressings incorporating antimicrobial agents to provide ancillary action on the wound blood bags incorporating an anti-coagulant drug eluting stents NOTES: Such medical devices may be subject to additional conformity assessment procedures according to the regional or national requirements of medicinal product Regulatory Authorities. For combination products, please refer to Guideline for Registration of Drug-Medical Device and Medical Device-Drug Combination Products.
Rule 14	
All medical devices manufactured from or incorporating animal or human cells/tissues/derivatives thereof, whether viable or non-viable, are Class D,	NOTES: In some jurisdictions such products: are considered to be outside the scope of the medical device definition; may be subject to different controls.
	It is likely the regulations controlling these
	devices will be the subject of future
	harmonization efforts.
	Examples:
	porcine heart valves catgut sutures.
	For all non-invasive medical devices consisting of a substance or a mixture of substances intended to be used in vitro in direct contact with human cells, tissues or organs taken from the human body or used in vitro with human embryos before their implantation or administration into the body are classified as Class D.

	Examples: substances or mixture of substances for transport, perfusion, storage of organs intended for transplantation that do not achieve the principal intended action by pharmacological, immunological or metabolic means IVF or ART products without principal pharmacological/metabolic action (substances or mixture of substances) IVF cell media without human albumin)
Unless such medical devices are manufactured from or incorporate non-viable animal tissues or their derivatives that come in contact with intact skin only, where they are in Class A.	Examples: leather components of orthopedic appliances.
Rule 15	
All medical devices intended specifically to be used for sterilizing medical devices, or disinfecting as the end point of processing, are in Class C.	Examples: denture disinfecting products washer-disinfector equipment specifically for disinfecting endoscopes or other invasive devices at the end point of processing (e.g. dental equipment) disinfectants for the fluid pathways of hemodialysis equipment NOTES They are specifically to be used for disinfecting invasive devices. This rule does not apply to products that are intended to clean medical devices by means of physical action e.g. washing machines.
a) Unless they are non-invasive which are intended for disinfecting medical devices prior to end point sterilization or higher-level disinfection, in which case they are in Class B; or	Examples: disinfectants specifically intended for non-invasive medical devices and equipment such as sterilizers specifically intended to sterilize medical devices in a medical environment and washer disinfectors washers-disinfectors intended specifically for disinfecting non-invasive medical devices.

	dry heat sterilizer ultraviolet sterilizer
b) Unless they are intended specifically to be used for disinfecting, cleaning, rinsing or, when appropriate, hydrating contact lenses, in which case they are in Class C.	Examples: contact lens solutions comfort solutions (also known as rewetting contact lens eye drop)
Rule 16	
All medical devices used for contraception or the prevention of the transmission of sexually transmitted diseases are in Class C,	Examples: condoms, contraceptive diaphragms.
Unless they are implantable or long- term invasive medical devices, in which case they are in Class D.	Example: intrauterine contraceptive device (IUD)
Rule 17	
This rule covers stand-alone X-ray detectors and sensors as recording devices used in several types or modalities of medical imaging procedures, each of which uses different technologies and techniques. It covers non-active devices and active devices used to record X-ray diagnostic images of the human body. The intention of the rule is to cover primarily digital devices and analogous recording media, but not media (including digital media) used for subsequent image processing and storage. Devices specifically intended for recording of diagnostic images generated by X-ray radiation are classified as class B.	Example: • Digital x-ray detectors for recording images • Photostimulable phosphor plates • X-ray films
Rule 18	
This rule covers devices manufactured utilizing tissues or cells of human or animal origin, or their derivatives, which are non-viable or rendered non-viable, i.e. where there is no longer any capacity for cellular metabolic activity. This includes devices containing derivatives of human origin that have an ancillary action to that of the device, as well as devices that contain or are made of animal tissues (non-derivative) that have been rendered non-viable, or their	• Animal derived biological heart valves • Porcine xenograft dressings • Devices made from animal sourced collagen/gelatine • Devices utilizing hyaluronic acid of animal origin • Substance-based devices containing collagen for use in body orifices • Collagen dermal fillers • Bone graft substitutes

derivatives All devices manufactured utilizing tissues or cells of human or animal origin, or their derivatives, which are non- viable or rendered non-viable, are classified as class D, unless such devices are manufactured utilizing tissues or cells of animal origin, or their derivatives, which are non-viable or rendered non-viable and are devices intended to come into contact with intact skin only.	
Rule 19	
All devices incorporating or consisting of nanomaterial are classified as: class D if they present a high or medium potential for internal exposure; class C if they present a low potential for internal exposure; and class B if they present a negligible potential for internal exposure.	Bone fillers with nanomaterials in their formulation (not polymerized before blood/tissue contact, and degradable) Superparamagnetic iron oxide nanoparticles (Intended use: thermal ablation of tumors or thermal modulation of the tumor microenvironment by submission to alternating magnetic fields) Intravascular catheter made of non-degradable polymer, with nano-coating31 Bone fixation screws/plates with a strongly bound nano-coating high potential Solution administration set made of non-degradable polymer, with a strongly bound nano-coating Intravascular catheter for short term use made of non-degradable polymer, with nanomaterial embedded in the polymer matrix Solution administration set made of non-degradable polymer, with nanomaterial embedded in the polymer matrix Dental filling materials
Rule 20	
All invasive devices with respect to body orifices, other than surgically invasive devices, which are intended to administer	Spacer intended for metered dose inhalers (attached to the inhaler) unless treating life threatening conditions

medicinal products by inhalation are classified as class B, unless their mode of action has an essential impact on the efficacy and safety of the administered medicinal product or they are intended to treat life- threatening conditions, in which case they are classified as class C.	Inhalers for nicotine replacement therapy (nicotine not included) Oxygen delivery system with a nasal cannula unless treating life-threatening conditions Inhalers and nebulizers in case their mode of action has probably no essential impact on the efficacy and safety of the administered medicinal product or which are not intended to treat life-threatening conditions For Class C Nebulizers (not pre-charged with a specific medicinal product) where the failure to deliver the appropriate dosage characteristics could be hazardous Spacer intended for metered dose inhalers attached to the inhaler.
RULE 21	
Devices that are composed of substances or of combinations of substances that are intended to be introduced into the human body via a body orifice or applied to the skin and that are absorbed by or locally dispersed in the human body are classified as: class D if they, or their products of metabolism, are systemically absorbed by the human body in order to achieve the intended purpose; class D if they achieve their intended purpose in the stomach or lower gastrointestinal tract and they, or their products of metabolism, are systemically absorbed by the human body; class B if they are applied to the skin or if they are applied in the nasal or oral cavity as far as the pharynx, and achieve their intended purpose on those cavities; and class C in all other cases.	Na/Mg alginate, xyloglucan, Fat absorbers that are systemically absorbed, themselves or their metabolites Substance-based formulations for skin treatment Salt water used e.g. as nose or throat sprays Oral cough treatments achieving their intended purpose in the oral cavity as far as the pharynx Simethicone preparations for oral administration Active coal for oral administration Gel for vaginal moisturizing / vaginal lubricants Eye drops for hydration Ear drops1, 2 Medical devices, for oral administration, for the treatment of diarrhoea, e.g. kaolin, diosmectite Medical devices, for oral administration, for

	the treatment of obesity, e.g. fructooligosaccharides, glucomannan
Rule 22	
Active therapeutic devices with an integrated or incorporated diagnostic function which significantly determines the patient management by the device, such as closed loop systems or automated external defibrillators, are classified as class D.	

10.0 Rationale for the inclusion of the additional rules

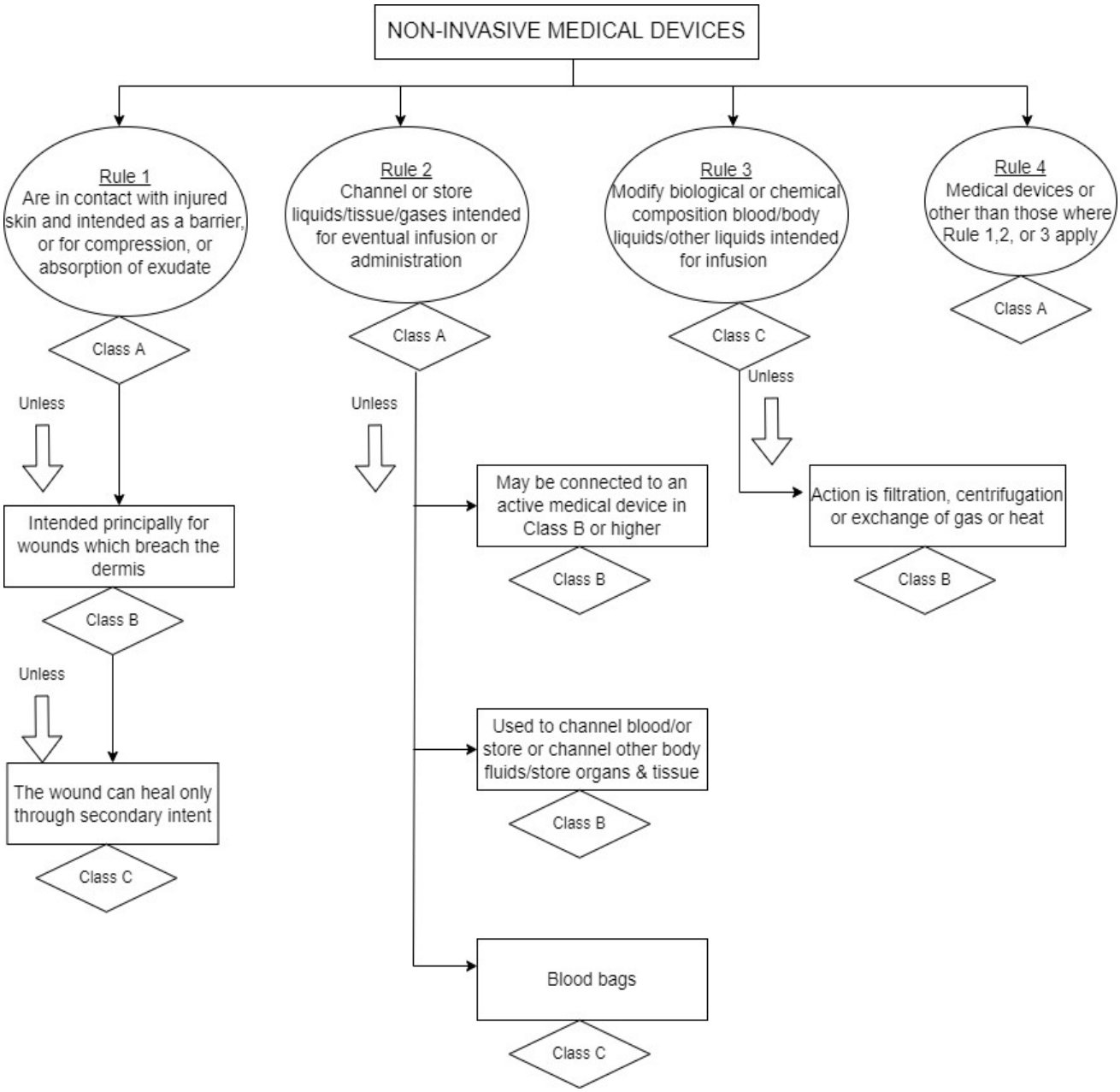
There are a small number of products that fall within the scope of the definition of a medical device and which may need to be classified to take account of factors other than those covered by the general rules (Rules 1 to 12). Therefore, ten Additional Rules are provided (Rules 13 to 22).
Matters that may need to be considered are:

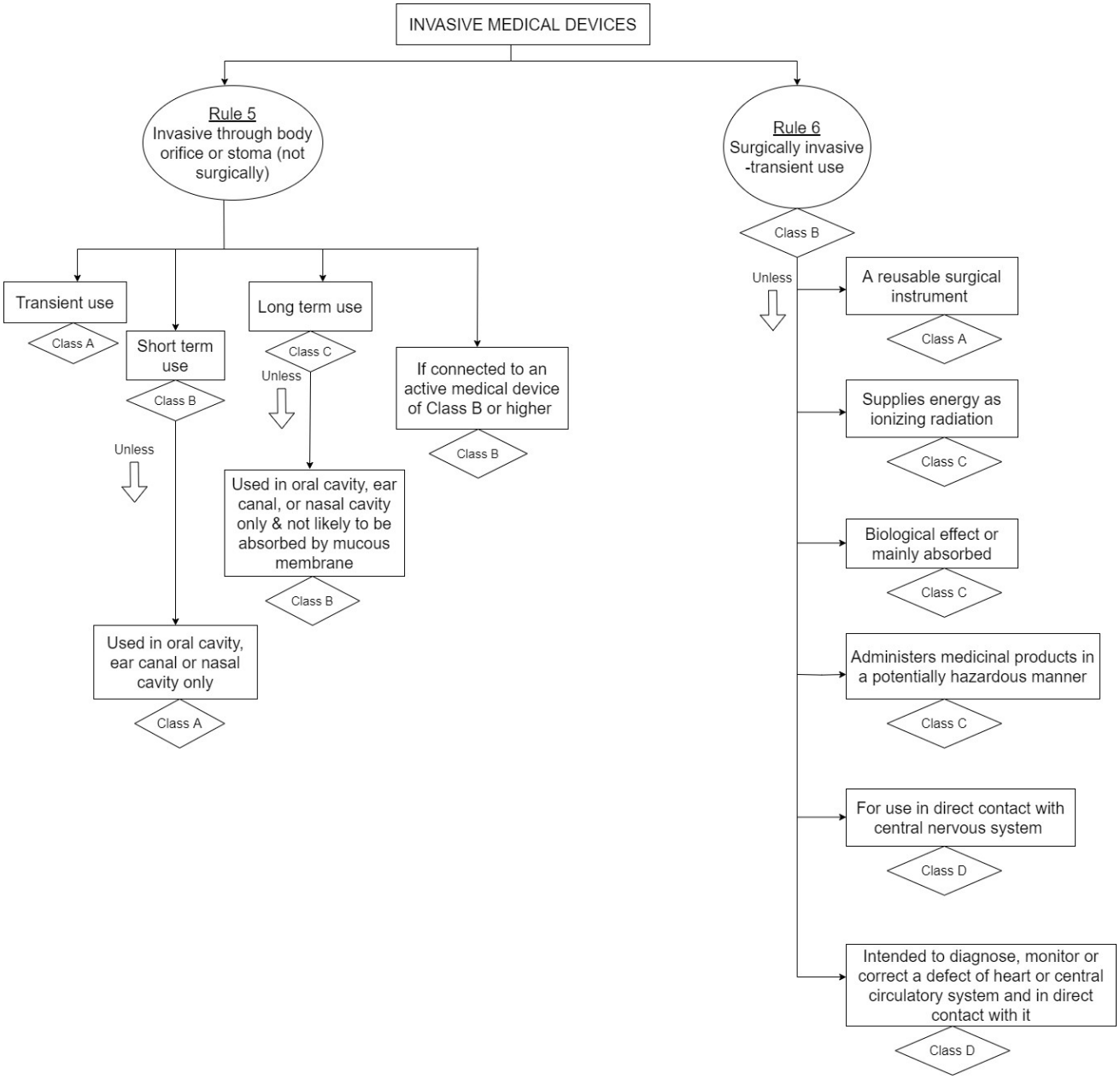
Rule 13:	Devices incorporating a medicinal product • The regulations applying to medicinal products require different acceptance procedures to those for medical devices. • The behavior of a medicinal product used in conjunction with a medical device may differ from that covered by its approved use as a medicinal product alone.
Rule 14:	Devices incorporating animal or human tissues • There is an absence of global regulatory controls for such devices. • Classification needs to acknowledge the diversity of opinions on such devices, globally. • The possible risks associated with the transmission of infectious agents through materials used in such devices, e.g. Bovine Spongiform Encephalopathy (BSE) and Creutzfeldt-Jacob disease (CJD), demand classification at a higher risk level.
Rule 15:	Disinfectants • The particular concerns relating to those disinfectants that are used with contact lenses, due to sensitivity and vulnerability of the eye.

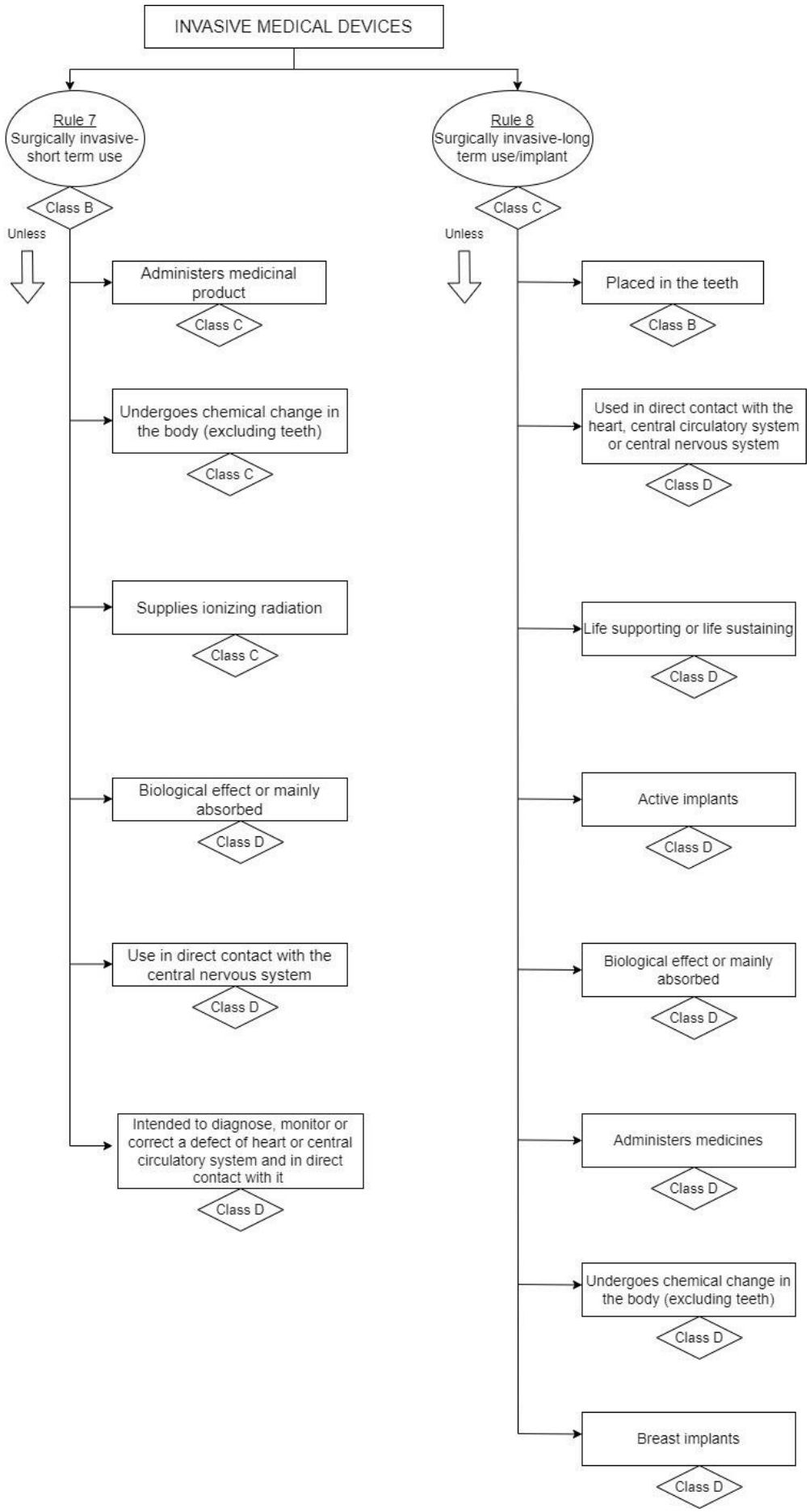
Rule 16:	Contraceptive devices • The risks associated with unwanted pregnancy if caused by mechanical failure of the device. • The need to safeguard public health through the use of condoms to reduce the prevalence of sexually transmitted diseases. • User expectation that contraceptive devices are perfectly reliable and safe despite published data to the contrary.
Rule 17:	Devices to record X-ray diagnostic images • This rule covers stand-alone X-ray detectors and sensors as recording devices used in several types or modalities of medical imaging procedures, each of which uses different technologies and techniques. • It covers non-active devices and active devices used to record X-ray diagnostic images of the human body. • The intention of the rule is to cover primarily digital devices and analogous recording media, but not media (including digital media) used for subsequent image processing and storage.
Rule 18:	Devices manufactured utilizing tissue or cells of human or animal origin or their derivatives • This rule covers devices manufactured utilizing tissues or cells of human or animal origin, or their derivatives, which are non-viable or rendered non-viable, i.e. where there is no longer any capacity for cellular metabolic activity. • This includes devices containing derivatives of human origin that have an ancillary action to that of the device, as well as devices that contain or are made of animal tissues (non-derivative) that have been rendered non-viable, or their derivatives.
Rule 19:	Devices incorporating or consisting of nanomaterial • The concept of internal exposure is a key element for the classification incorporating or consisting of nanomaterials. • The potential risk from the use of nanomaterials in medical devices is mainly associated with the possibility for release of free nanoparticles from the device and the duration of exposure. This estimates both external and internal exposure based on the type of device, type of application, type (location) of contact, and duration of contact. • The potential internal systemic exposure of all organ systems can be expected to occur after release of free nanoparticles from invasive devices as well as from non-invasive devices in contact with a breached or compromised body surface. • Every individual device needs to be classified taking into account its own specific characteristics with regard to the potential release of free nanoparticles taking also into account the exposure by the same nanomaterial via daily exposure routes., Also factors such as the number of nanomaterials in or on the product and the amount of product applied in the intended use have been taken into account. • Medical devices not incorporating or consisting of nanomaterials can still present a potential for internal exposure to nanomaterials due to degradation or wear processes. While it is very important to include this aspect in the risk assessment of such devices, it is not a factor to be

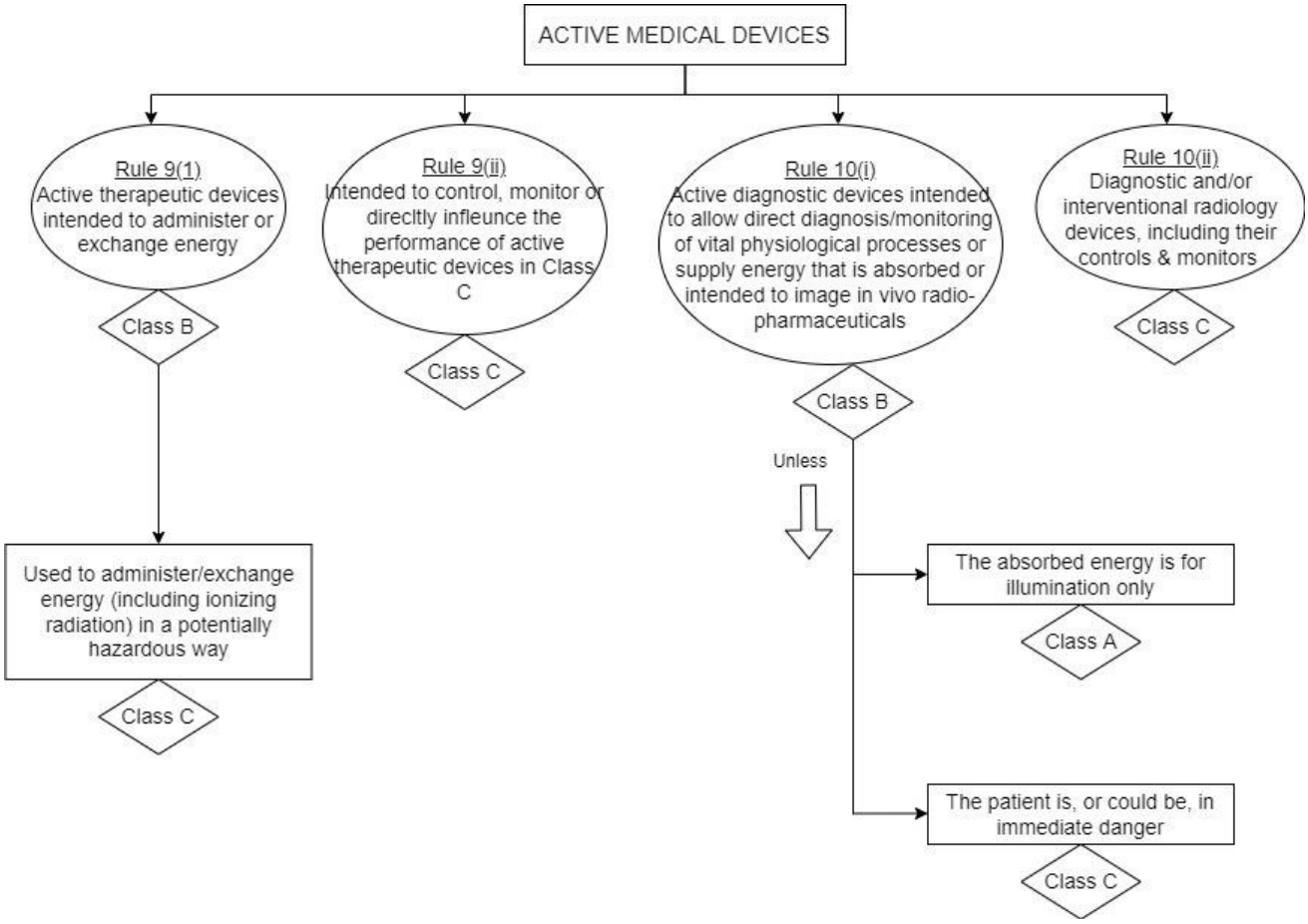
	considered when deciding the classification under Rule 19 since this rule is only applicable for medical devices incorporating or consisting of nanomaterials.
Rule 20:	Invasive devices, intended to administer medicinal product by inhalation • This rule covers active and non-active medical devices with a respiratory route of drug delivery. • In contrast to other rules covering devices that administer medicinal products, Rule 20 is also specifically intended to cover medical devices where the impact of the medical device on the efficacy and safety of the administered medicinal product is critical. The rule also covers drug delivery products that are intended to treat life-threatening conditions • Essential impact' includes drug delivery systems where the device has a significant impact on factors that influence inhaled medicinal product deposition within the airways including inhalation flow, aerosol velocity, the particle size of the inhaled drug and the amount of drug reaching the patient.
Rule 21:	Devices composed of substances that are introduced via a body orifice or applied to the skin • This rule covers a wide range of exclusively substance-based medical devices • The classification takes into account the site of application of the medical device as well as the site where the medical device performs its action in or on the human body. • Manufacturers of substance-based devices should provide clear information supporting the mode of action through which the substance achieves the intended specific medical purpose as a basis for the application of this rule, including the site of application as well as the site where the action is achieved in or on the body
Rule 22:	Active therapeutic devices, with an incorporated diagnostic function • This rule is intended for therapeutic devices whose intended functionality is dependent to a significant degree on an integrated or incorporated diagnostic function. • Automated or 'closed-loop' therapeutic systems are systems in which relevant biological conditions are automatically monitored (uses feedback from physiological sensors) and is used to adjust a therapy in order to maintain or achieve a particular physiological state. • Such devices are normally used in precision medicine and/or personalised therapies for obtaining optimal therapeutic efficacy. • This rule covers systems such as autonomic pharmacological (drug-delivery) and neuromodulation systems. • 'Integrated or incorporated diagnostic function' means the functionality of a system including a physiological sensor e.g., the AED electrodes/pads using a feedback control to process and record changes in the patient's physiological state to continuously adjust a therapy. The diagnostic function can be physically integrated or a component of an external sub-system

Annex A
Decision trees to demonstrate how the rules may be used to classify specific devices.

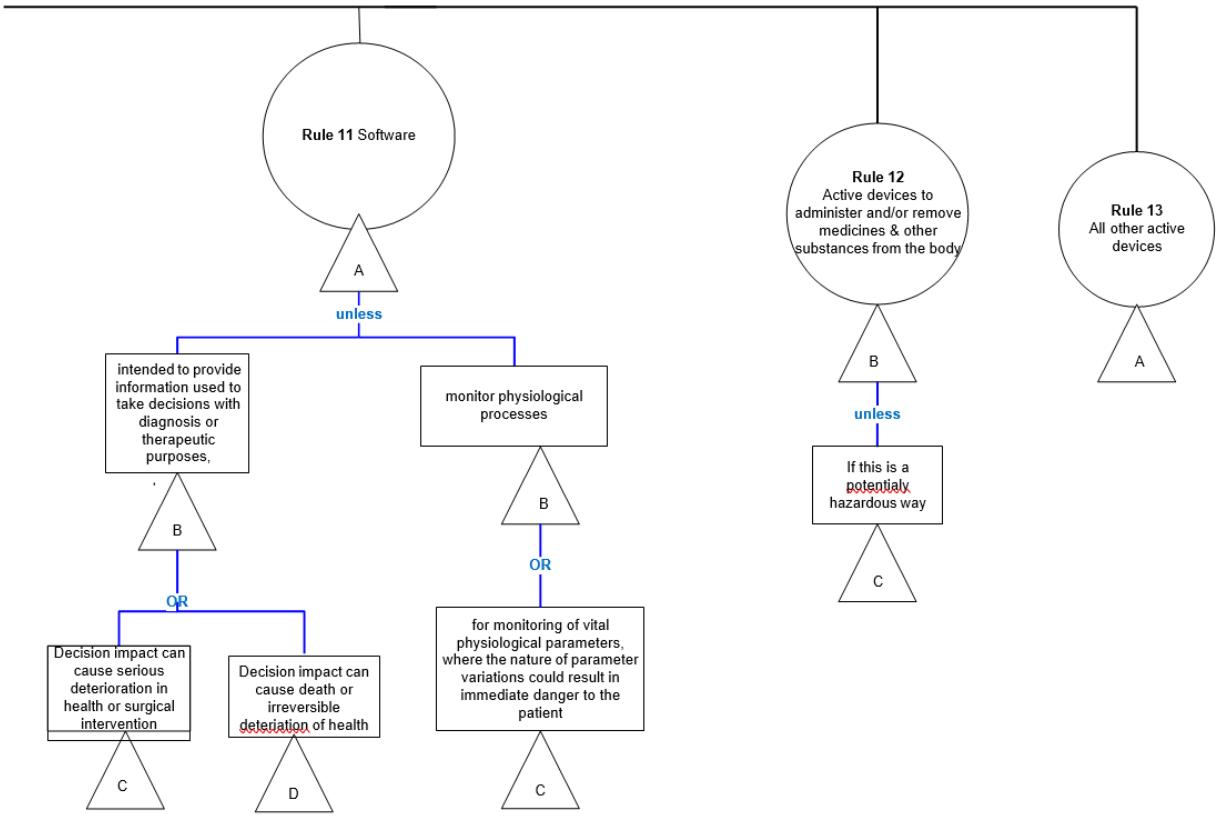



INVASIVE MEDICAL DEVICES
Rule 5
Invasive through body orifice or stoma (not surgically)
Transient use
Class A
Short term use
Class B
Unless
Used in oral cavity, ear canal or nasal cavity only
Class A
Long term use
Class C
Unless
Used in oral cavity, ear canal, or nasal cavity only & not likely to be absorbed by mucous membrane
Class B
If connected to an active medical device of Class B or higher
Class B
Rule 6
Surgically invasive -transient use
Class B
Unless
A reusable surgical instrument
Class A
Supplies energy as ionizing radiation
Class C
Biological effect or mainly absorbed
Class C
Administers medicinal products in a potentially hazardous manner
Class C
For use in direct contact with central nervous system
Class D
Intended to diagnose, monitor or correct a defect of heart or central circulatory system and in direct contact with it
Class D

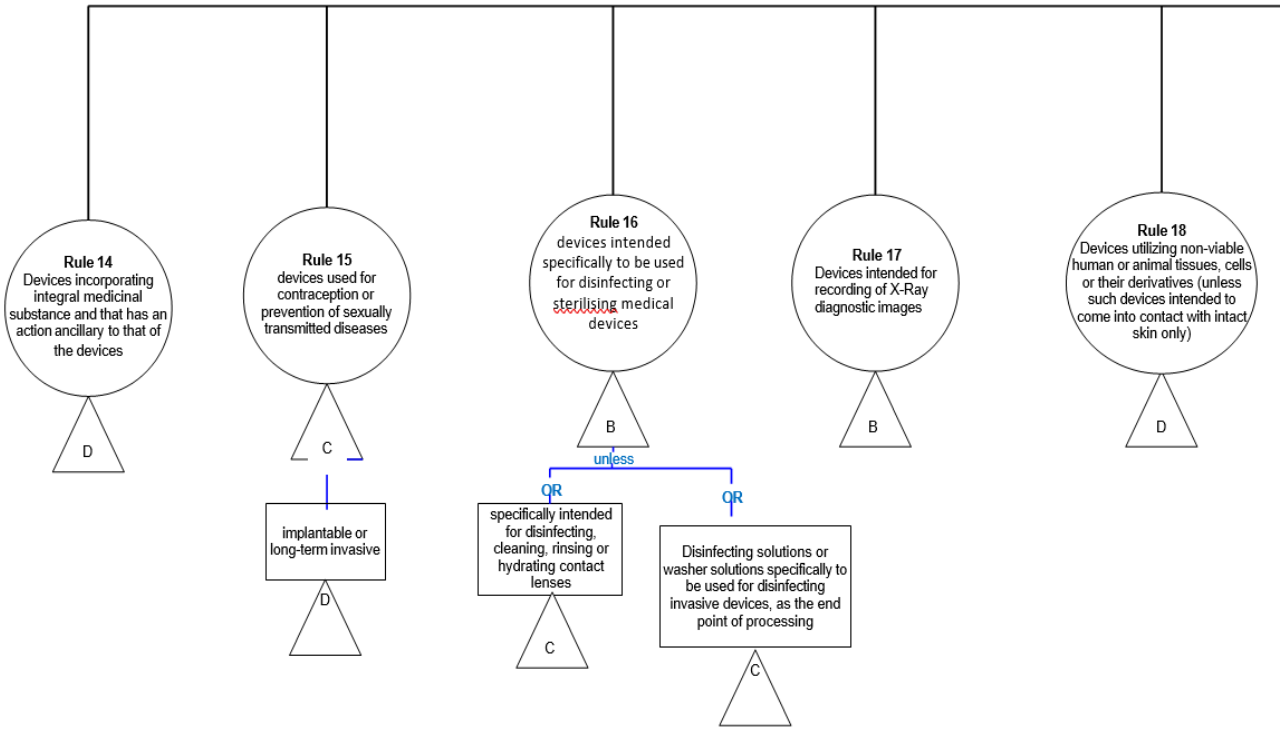

INVASIVE MEDICAL DEVICES
Rule 7
Surgically invasive-short term use
Class B
Unless
Administers medicinal product
Class C
Undergoes chemical change in the body (excluding teeth)
Class C
Supplies ionizing radiation
Class C
Biological effect or mainly absorbed
Class D
Use in direct contact with the central nervous system
Class D
Intended to diagnose, monitor or correct a defect of heart or central circulatory system and in direct contact with it
Class D
Rule 8
Surgically invasive-long term use/implant
Class C
Unless
Placed in the teeth
Class B
Used in direct contact with the heart, central circulatory system or central nervous system
Class D
Life supporting or life sustaining
Class D
Active implants
Class D
Biological effect or mainly absorbed
Class D
Administers medicines
Class D
Undergoes chemical change in the body (excluding teeth)
Class D
Breast implants
Class D


ACTIVE MEDICAL DEVICES
Rule 9(1)
Active therapeutic devices intended to administer or exchange energy
Class B
Used to administer/exchange energy (including ionizing radiation) in a potentially hazardous way
Class C
Rule 9(ii)
Intended to control, monitor or direclty infleunce the performance of active therapeutic devices in Class C
Class C
Rule 10(i)
Active diagnostic devices intended to allow direct diagnosis/monitoring of vital physiological processes or supply energy that is absorbed or intended to image in vivo radio-pharmaceuticals
Class B
Unless
The absorbed energy is for illumination only
Class A
The patient is, or could be, in immediate danger
Class C
Rule 10(ii)
Diagnostic and/or interventional radiology devices, including their controls & monitors
Class C

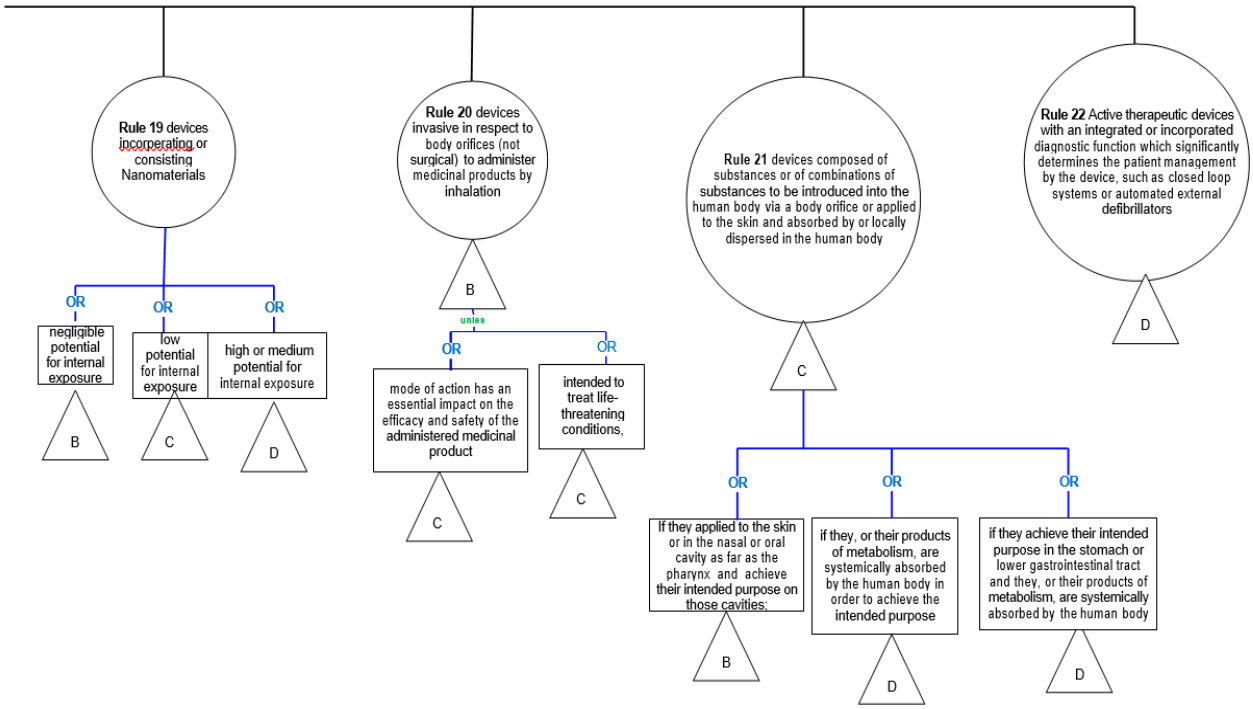
ACTIVE DEVICES



SPECIAL RULES



SPECIAL RULES



PART VI

GUIDELINES ON CLASSIFICATION OF IN-VITRO DIAGNOSTIC DEVICES (IVDDS)

1. Scope

This guidance applies to all in-vitro diagnostic devices (IVDDs) subject to regulatory oversight and as specified in the TMDA (Control of Medical Devices) Regulations. The document is intended to provide additional clarifications regarding the way IVD products should be classified, as well as recommendations to be considered by IVDDs manufacturers.

2. Principles of Classification

In vitro diagnostic devices shall be classified into classes A, B, C and D, taking into account the intended purpose of the devices and their inherent risks.

Robust risk-based classification rules are essential for the correct classification of devices to ensure the application of the correct market authorization procedure and accompanying fees and charges.

3. Intended purpose of the In-vitro Diagnostic Device

The classification of a device is defined by its intended purpose, as specified by the manufacturer. This covers the use for which a device is intended according to the data supplied by the manufacturer on the label, in the instructions for use, in the performance evaluation or in promotional or sales materials or statements.

It is therefore important that the manufacturer clearly indicates the purpose for which the device is intended. Where there is a foreseeable risk that a device may be used for purposes which are covered by other classification rules and which would result in classification of a device into a higher class, a clear limitation of use should be included in the Instruction for Use (IFU) and the technical documentation of the device.

For a device to be specifically intended for a purpose referenced in a particular classification rule, the manufacturer must clearly indicate that the device is intended for such a specific purpose in the information accompanying the device. Where several classification rules or sub-rules apply, the intended purpose of the device and its claims should be sufficiently specified to enable a clear attribution of the class. Ambiguous claims may lead to higher classification.

Example: A device intended to screen blood and tissue donations for syphilis would fall under class D according to rule 1 . Alternatively, a device intended to diagnose syphilis, a sexually transmitted agent, in the individual would fall under class C according to rule 3.

4. Application of the rules

All implementing rules, all classification rules, and all indents are to be taken into account for the classification of an IVD or an accessory for an IVD.

4.1. Technology

Unless otherwise specified, the rules presented below apply equally to all technologies, principles of detection or analytical procedures.

4.2. Specimen

Unless specified in the classification rule, the rules apply equally to all specimen types.

4.3. Software

Medical device software (MDSW) is software that is intended to be used, alone or in combination, for a purpose as specified in the definition of a “medical device” in the TMDA Act Cap 219.

Software which drives a device or influences the use of the device shall fall within the same class as the device.

4.4. Devices used in combination

When classifying devices that are used in combination, implementing rules play a key role in determining the classification of individual devices. Examples of devices used in combination include:

a) A control which is used in combination with a reagent or
b) Software which drives or influences the use of an analyzer.

Some devices may be classified based on the classification of another device; for example:

a) Software, which drives a device or influences the use of a device, shall fall within the same class as the device.
b) Calibrators intended to be used with a device shall be classified in the same class as the device.
c) Control materials with quantitative or qualitative assigned values intended for one specific analyte or multiple analytes shall be classified in the same class as the device. Controls without quantitative or qualitative assigned values are

classified as Class B per rule 7

d) Buffer/ washing solutions: Where the buffer/washing solution possesses no critical characteristic it is classified as Class A per rule 5a.

5. Classification rules for In Vitro Diagnostic Devices

Rule 1

IVDDs intended for the following purposes are classified as Class D:

a) 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, or

b) 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.

Rationale:

The application of this rule as defined above should be in accordance with the rationale that follows: Devices in this Class are intended to be used to ensure the safety of blood and blood components for transfusion and/or cells, tissues and organs for transplantation. In most cases, the result of the test is the major determinant as to whether the donation/product will be used. Serious diseases are those that result in death or long-term disability, that are often incurable or require major therapeutic interventions and where an accurate diagnosis is vital to mitigate the public health impact of the condition.

Examples:

Tests to detect infection by HIV, HCV, HBV, HTLV, Haemorrhagic fever viruses (e.g. Ebola, Marburg), Human T-Lymphotropic Virus I and II. - SARS CoV and SARS-CoV-2, Smallpox virus. This Rule applies to first-line assays, confirmatory assays, and supplemental assays.

Rule 2

IVDDs intended to be used for blood grouping or to determine foeto-martenal blood group incompatibility or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation or cell administration, are classified as Class C, except when intended to determine any of the following markers:

a) ABO system [A (ABO1), B (ABO2), AB (ABO3)],
b) Rhesus system [RH1 (D), RH2 (C), RH3, RH4 (c), RH5 (e)],

c) Kell system [Kel1 (K)],
d) Kidd system [JK1 (Jka), JK2 (Jkb)]
e) Duffy system [FY1 (Fya), FY2 (Fyb)] determinations which are classified as Class D.

Rationale:
The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: A high individual risk, where an erroneous result would put the patient in an imminent life-threatening situation places the device into Class D. The rule divides blood grouping devices into two subsets, Class C or D, depending on the nature of the blood group antigen the IVDD is designed to detect, and its importance in a transfusion setting.

Examples:
HLA, Duffy system (other Duffy systems except those listed in the rule as Class D are in Class C).

Rule 3
IVDDs are classified as Class C if they are intended for use:

a) In detecting the presence of, or exposure to a sexually transmitted agent. Examples: Sexually transmitted diseases.

Rationale:
Rule 3a applies to devices detecting agents whose main mode of transmission is sexual. The agents that cause sexually transmitted infections may pass from person to person through blood, semen, vaginal or other bodily fluids.

Examples:
Chlamydia trachomatis, Neisseria gonorrhoeae, haemophilus ducreyi, herpes simplex virus 1&2, human papilloma virus (HPV), mycoplasma hominis, mycoplasma genitalium, trichomonas vaginalis, treponema pallidum, ureaplasma urealyticum.

b) In detecting the presence of an infectious agent (e.g. bacterial, viral, fungal, parasitic, protozoal infectious agents) in cerebrospinal fluid or blood with a risk of limited propagation.

Rationale:
Rule 3b applies to devices intended for detecting the presence of an infectious agent (either the agent itself or component thereof) e.g. bacterial, viral, fungal, parasitic,

protozoal infectious agents, specifically in specimens derived from cerebrospinal fluid or blood.

Examples:

i. Bacterial pathogens: Streptococcus pneumoniae, Group B Streptococcus, Neisseria meningitidis, Haemophilus influenza type B, Listeria spp., Borrelia burgdorferi, Mycobacterium tuberculosis.
ii. Fungal pathogens: Cryptococcus neoformans, Aspergillus spp.
iii. Viral pathogens: Herpes simplex virus 1&2, human herpes virus 6, varicella zoster virus, enterovirus, West Nile virus, chikungunya, Dengue, Zika, hepatitis A, hepatitis E.
iv. Parasitic pathogen: Toxoplasma gondii.

c) 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.

Rationale:

Rule 3c applies to devices intended for detecting the presence of an infectious agent (either the agent itself or component thereof) e.g. bacterial, viral, fungal, parasitic, protozoal infectious agents. Devices intended for the detection of antibodies against the infectious agent are not covered by this rule. This rule does not have any specimen type restrictions and is applicable to specimens being tested from the individual, foetus or embryo. This rule applies if there is a significant risk that an erroneous result would cause death or severe disability. It is the risk of death or severe disability to an individual that must be considered. In this context, the risk of death or severe disability to the individual should take into account that an erroneous result in a healthy individual does not carry the same risk as an erroneous result in (for example) a pregnant, immunocompromised, or vulnerable individual. This rule also applies to an embryo or foetus being tested, or the individual's offspring where an infectious agent can be detrimental to the viability/development of the embryo/foetus leading to death or disability, both current and future e.g. developmental disability.

Examples:

Devices intended for detecting the presence of:

i. Bacterial pathogens: Treponema pallidum, Chlamydia trachomatis, Haemophilus influenzae type B meningitis, Neisseria meningitidis, Listeria meningitis (Listeria monocytogenes), Mycobacterium leprae, Mycobacterium spp., Legionella spp., Streptococcus agalactiae, methicillin-resistant Staphylococcus aureus (MRSA) and multi-resistant Enterobacteriaceae (MRE).

ii. Parasitic pathogens: Toxoplasma gondii.
iii. Viral pathogens: Herpes simplex virus 1&2, cytomegalovirus, Rubella, Measles, Poliomyelitis, Parvovirus B19, Zik

d) in pre-natal screening of women in order to determine their immune status towards transmissible agents.

Rationale:
Rule 3d applies to devices specifically intended to screen pregnant women for their immune status towards transmissible agents. These are in particular transmissible agents that may cause infections in the embryo and foetus. The term 'immune status' refers to the presence, absence or level of an immune response acquired by the women following an infection or vaccination.

Devices covered by this rule are intended for the screening of pregnant women before birth in order to identify the presence of an acquired appropriately targeted immune response to transmissible agents. The absence of such acquired maternal protection is associated with an enhanced risk of transmission of the agent to the embryo/foetus upon infection of the mother. These mothers may be recommended to take preventive measures.

Examples:
Devices intended to determine for prenatal screening the immune status of women towards: Cytomegalovirus; Rubella virus, Toxoplasma gondii, Varicella zoster virus, Zika na Parvovirus B19.

e) 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.

Rationale:
Rule 3e applies to devices for both the determination of the infective disease status and the determination of the immune status of a patient.

'Determination of infective disease status' The determination of the infective disease status provides information on the state, condition or evolution of a disease caused by an infective agent, which may include the effectiveness of a specific treatment. In this context, the determination of the infective disease status typically involves the measurement of infective agents, antibodies to infective agents, surrogate markers or analytes in specimens from patients.

'**Determination of immune status'** The determination of the immune status

provides information on the state or condition or evolution of the immune response acquired by the patient in relation to infection with a pathogenic agent, vaccinations, allergic, immunotoxic, autoimmune and alloimmune reactions such as transfusion reactions and transplant rejection reactions.

Examples:

Devices intended to determine:

i. Salmonella typhi in faeces, for the assessment of the carrier-status of patients.
ii. Antibodies from lymphocyte secretions immunoassay intended for the detection of active Mycobacterium tuberculosis infection.
iii. Quantitative virus-specific NAT tests (e.g. Cytomegalovirus, John Cunningham virus, Adenovirus, Enterovirus) to monitor an immunocompromised patient's (e.g. transplant patient) response to antiviral therapy.
iv. Methicillin-resistant Staphylococcus aureus and Staphylococcus aureus specific polymerase chain reaction assay for pre-surgical screening of patients to determine nasal carriage.
v. Assays intended for the detection of IgM antibodies against rubella virus to identify an acute infection in pregnant women in order to determine whether specific treatment is necessary for protecting the foetus from virus-induced damage due to a lack of previously acquired immunity.
vi. Assays intended for the detection of IgM antibodies against HEV.
vii. Enzyme immunoassay intended for the quantitation of intrathecal antibodies against rubella virus in the diagnosis of rubella virus-induced encephalitis
viii. Assays intended for the detection of antibodies in the recipient to potentially pathogenic viruses (e.g. anti-cytomegalovirus, anti-herpes simplex virus antibodies) to determine latent disease status of viral infection prior to organ or bone marrow transplantation.
ix. Screening assays comprising allergy panels, such as Multiple Allergen Simultaneous Tests (MAST), intended to detect IgE antibodies against several specific allergens that may lead to anaphylaxis, e.g. certain nutritional allergens or hymenoptera venom allergens. False-negative results with such MAST assays could increase the risk that the patient is not adequately managed for the occurrence of a life-threatening anaphylactic event.
x. Assays intended for the detection of alloantibodies in the recipient associated with transplant rejection reactions, such as antibodies against
xi. angiotensin II receptors type 1 (anti-AT1R) and against endothelin receptors type A (anti-ETAR).
xii. Interferon-Gamma Release Assays (IGRA)for Mycobacterium

tuberculosis.

f) 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 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.

Rationale:
Rule 3f applies to devices with the specific intended purpose to be used in screening, diagnosis or staging of cancer. ‘Cancer’ is the uncontrolled growth and spread of cells. It can affect almost any part of the body.

The scope of this rule is limited to cancer. Two distinct cases should be considered:

1. Cancer is a term for diseases (including malignant neoplasia or malignant tumours) characterised by abnormal cells which divide without control and invade nearby tissues. Additionally, these cells can also spread to other parts of the body through the blood and lymph systems, in the process that leads to the development of secondary tumours or metastases. Many cancers form solid tumours, which are masses of tissue. Cancers of the blood, such as leukaemia, generally do not form solid tumours.

2. Cells may present hyperplasia (increased density of cells) and dysplasia (abnormal appearance) or form a carcinoma in situ (no invasion of nearby tissues). These precancerous or premalignant cells may or may not develop into cancer.

This rule applies to devices for both cancerous and precancerous conditions, where the devices are intended to be used in screening, diagnosis, or staging of cancer.

Disease staging involves the determination of distinct phases or periods in the course of a disease, or level of severity of a disease that can be assessed by, for example, the life history of an individual, organism, markers or any biological or physiological process. The purpose of disease staging is to provide information with respect to patient management, the appropriateness and accuracy of treatment decisions, and/or for prognosis or prediction.

Non-malignant neoplasms or non-malignant tumours do not spread into, or invade, nearby tissues. Therefore, they do not fulfil the criteria of cancer. These benign tumours may grow larger, and the growth tends to be slow.

Devices that are intended to be used in screening, diagnosis, or staging of cancer, may have the following functions: screening, patient management, monitoring, diagnosis or aid to diagnosis, prognosis and prediction.

Examples:

i. A faecal occult blood screening test (FOBT) or faecal immunochemical test (FIT) specifically intended to be used in colon cancer screening.
ii. A device intended for the quantitative/qualitative determination of IgG antibodies to Helicobacter pylori in human blood samples specifically intended to be used in gastric cancer screening.
iii. Papanicolaou (Pap) stain automated cervical cytology screening system, intended to process Pap cervical cytology slides and classify the cervical specimen as either normal or abnormal.
iv. A qualitative real-time PCR test intended for the detection of high-risk genotypes of Human Papillomaviruses for use in cervical cancer screening.
v. Immunohistochemistry assay intended for the detection of c-KIT or CD117 tyrosine kinase receptor expression in normal and neoplastic formalin fixed, paraffin-embedded tissues for histological evaluation, and gene mutation testing for KIT and platelet-derived growth factor receptor alpha in (familial) gastro-intestinal stromal tumor.
vi. Assay for the quantitative determination of the cancer associated antigen CA 125 (celomic epithelium-related glycoprotein associated with epithelial ovarian cancer) in serum.
vii. Immunohistochemistry assay intended to detect progesterone receptor in breast tumours to be used as an aid in the management, prognosis, and prediction of therapy outcome of breast carcinoma.
viii. Fluorescence in situ hybridisation (FISH) panels intended for the diagnosis of e.g. lymphoma, multiple myeloma and leukaemia.
ix. Targeted next generation sequencing test intended to be used in (haemato)-oncology, to detect acquired somatic mutations in DNA isolated from formalin-fixed paraffin embedded (FFPE) tumour tissue specimens.
x. BRCA1 device intended for the detection of deletions or duplications in the human BRCA1 gene in order to confirm a potential cause and clinical diagnosis for hereditary breast and ovarian cancer and for molecular genetic testing of at-risk family members.
xi. Device applied in testing services intended for the analysis of 35 genes relevant to digestive tract tumours (various forms of colorectal cancer, stomach cancer and pancreatic cancer), breast cancer, ovarian cancer, skin cancer, thyroid tumours, and endocrine tumours (panel), intended to provide information on whether an individual carries genetic alterations that favour the onset of specific tumour diseases, identifying these genetic predispositions.
xii. Circulating Tumour Cell Kit (Epithelial) intended for the enumeration of

circulating tumour cells (CTC) of epithelial origin in whole blood. The test is to be used as an aid in the monitoring of patients with metastatic breast, colorectal or prostate cancer. Serial testing for CTC should be used in conjunction with other clinical methods for monitoring metastatic breast, colorectal and prostate cancer, to allow assessment of patient prognosis and is predictive of progression free survival and overall survival.

xiii. Breast carcinoma cell line (SK-BR-3) CTC Cell Control Kit intended as an assay control to ensure that the sample detection and identification systems are performing when using the CTC Kit. They express epithelial cell markers recognised by the antibodies in the Circulating Tumour Cell Kit and are used as a control for the performance of the assay

g) In human genetic testing.

Rationale:

Rule 3g applies to devices for human genetic testing. Genetic testing involves the detection of specific alleles, mutations, genotypes, karyotypes or epigenetic changes that are associated with heritable traits, diseases or predispositions to disease for the individual or their descendants.

Several methods can be used for genetic testing (for example)7 :

i. **Molecular genetic tests** (or **gene tests**) study single genes or short lengths of DNA to identify its constitution, or variations or mutations that lead to a genetic disorder.
ii. **Chromosomal genetic tests** analyse whole chromosomes or long lengths of DNA to see if there are large genetic changes, such as an extra copy of a chromosome which causes a genetic condition.

The results of a genetic test can provide a medical status, confirm or rule out a suspected genetic condition or determine a person's chance of developing or passing on a genetic disorder.

Some examples include devices intended for:

i. **Newborn Screening:** Newborn screening is used just after birth to identify genetic disorders, to detect potentially fatal or disabling conditions. Such early detection allows treatment to begin immediately, which can reduce or eliminate the effects of the condition.
ii. **Diagnostic testing:** Diagnostic testing is used to identify or rule out a specific genetic or chromosomal condition.
iii. **Carrier testing:** Carrier testing is used to identify people who carry one copy of a gene mutation that could result in a genetic disorder in one's offspring. For some genetic disorders, two copies of the gene mutation are required to

cause the genetic disorder (autosomal recessive). Whereas for others, one copy of the gene mutation is required either i) in the absence of a second normal copy resulting in the genetic disorder (X-Linked recessive) or ii) in the presence of a normal copy can result in a genetic disorder (autosomal dominant). This type of testing provides information about a couple's risk of having a child with a genetic condition.

iv. **Prenatal testing:** Prenatal testing is used to detect changes in a foetus's genes or chromosomes before birth.

v. **Preimplantation testing:** Preimplantation testing, also called preimplantation genetic diagnosis (PGD), is a specialised technique used to detect genetic changes in embryos obtained through in vitro fertilisation.

vi. **Predictive and presymptomatic testing:** Predictive and presymptomatic types of testing are used to detect gene mutations associated with disorders that appear after birth, often later in life. Predictive testing can identify mutations that increase a person's risk of developing disorders with a genetic basis. Presymptomatic testing can determine whether a person will develop a late-onset genetic disorder.

vii. **Direct-to-Consumer (DTC) genetic testing:** genetic testing provided through advertising and selling or (free) provision of genetic tests directly to consumers.

Examples:

Genetic testing may include devices intended to detect:

i. Chromosomal conditions e.g. trisomy 21, trisomy 18, XXX syndrome.
ii. Abnormalities in genes associated with thrombophilia e.g. genes which code for factor V and prothrombin.
iii. Hereditary cancer syndromes e.g. hereditary breast/ovarian cancer (BRCA1/BRCA2 genes).
iv. Genetic risk Factors e.g. rheumatoid arthritis HLA DRB1, ankylosing spondylitis HLA B27, osteo-arthritis, pre-senilin mutation.
v. Monogenetic disorders e.g. hemochromatosis, Huntington’s disease, Tay Sacs, cystic fibrosis.
vi. Pharmacogenomic tests e.g. CYP liver enzymes CYP2C9 and CYP2C19. - Preimplantation genetic diagnosis.
vii. XY disorders e.g. haemophilia, Duchenne muscular dystrophy, Fragile X

h) 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.

Rationale:

Rule 3h applies to devices intended to monitor an analyte with the purpose of

adjusting patient management, such as treatments/interventions, as required i.e. it is intended to be used for observing, checking, or keeping a record of the level, activity, presence, absence etc. of an analyte.

Monitoring tests may be intended to evaluate an individual's current state and/or changes in an individual's state. This is likely to be achieved by repeated or multiple determinations of an analyte over time, at appropriate intervals. These devices are intended to determine whether results are within expectation, for the detection/assessment of disease progression/regression, disease recurrence, minimum residual disease, response/resistance to therapy, and/or adverse effects due to therapy.

This rule does not apply to devices intended to be used in the diagnosis or screening of a condition where only a single measurement is required for this purpose, but would apply to diagnostic tests where multiple/serial measurements over time are intended by the manufacturer and where an erroneous result may result in a life threatening situation for the patient or their offspring e.g. when monitoring the change in concentration of a biological compound over time to aid diagnosis, such as with troponin to help determine an acute cardiac event.

Rule 3h is also applicable to the monitoring of non-life-threatening conditions. It covers a wide range of analytes where the device provides an important, critical, or sole determinant for the correct patient management decision and an erroneous result may result in the life of the patient or patient's offspring being at risk due to inappropriate treatment decisions.

Analytes measured by devices intended for monitoring may be medicinal products substances (drug, chemical, or biological entity/component) or biological components (pertaining to living organisms, or components of a living organism – this would include for example: antibodies, endogenous markers, platelets, cord blood, bone marrow, stem cells etc).

If the device is intended for a specific intended target population (e.g. paediatrics, pregnant women, immunocompromised individuals, etc.) then the risk to this population should be taken into account when determining if there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or their offspring. ith respect to the patient's offspring, the viability/development of the embryo/foetus, both current and future shall be taken into account.

Examples:
Devices intended for monitoring:

i. Cardiac marker for acute presenting patients: Troponin I, Troponin T, CKMB (when intended for monitoring cardiac muscle injury).
ii. Cortisol levels monitoring e.g. for patients with cortisol insufficiency.
iii. PT/APTT when used to assess major bleeds in acute presentations or patients with acute coagulopathy or for coumadin monitoring in patients without diagnosed coagulation disorder.
iv. Lithium for patients being treated for bipolar disorders.
v. Methotrexate when used for treating non-life threatening conditions such as vasculitis, rheumatoid arthritis and psoriatic arthritis).
vi. Immunosuppressive (anti-rejection) medicinal products e.g. cyclosporine, sirolimus, tacrolimus.
vii. Antibiotic where under/over treatment can have a serious impact on individual or offspring e.g gentamicin.
viii. Anti-RhD antibody levels in pregnant women given additional Anti-D.
ix. Blood amylase e.g. acute pancreatitis, perforated peptic ulcer, acute biliary obstruction.
x. Acute phase reactants e.g. C- reactive protein (CRP), procalcitonin when intended to be used to monitor infection response to therapy for life threatening conditions such as sepsis, necrotizing skin or tissue conditions, infective endocarditis, bacterial meningitis etc.
xi. Full blood count when used for monitoring the development of a life-threatening haematological disorder in patients being treated for other disorders/conditions, where this risk exists e.g. monitoring of patients with a diagnosis of schizophrenia for neutropenia/agranulocytosis. - Bilirubin in response to treatment of neonatal jaundice.

i) In the management of patients suffering from a life-threatening infectious disease.

Rationale:
Rule 3i applies to devices intended for patients diagnosed with life-threatening diseases or conditions.

The device provides an important, critical, or sole determinant for the correct patient management decision, and provides information for the purpose of patient management, such as treatments/interventions, as required.

The classification of these devices is primarily based on the life-threatening nature of the disease or condition and the impact of the provided information on patient management (e.g. determining an initial course of therapy or erroneous decision resulting in life-threatening harm to the patient). This includes devices intended to detect drug resistant pathogens associated with a life-threatening condition (e.g.

sepsis, necrosing skin or tissue condition) directly from collected specimen such as blood, skin or tissues, in order to take a patient management decision. However, rule 3i does not apply to devices used in conjunction with microbiological culture methods that are only intended to test drug resistance of an already detected pathogen including drug sensitivity testing such as sensitivity discs and tablets or Minimum Inhibitory Concentration (MIC) panels, where such devices are not intended for the management of patients suffering from a life-threatening infection.

Examples:
Devices intended for:

i. Enumeration of CD4 T lymphocytes in HIV infected patients to initiate treatment and ascertain the anti-viral therapy response.
ii. Measurement of D-Dimers in patients with thrombotic disorders.
iii. Laboratory risk score calculator indicator for necrotising fasciitis in necrotising soft tissue infections.
iv. HbA1c and blood glucose tests for the management of patients with diabetes.
v. Monitoring anticoagulant therapy e.g. prothrombin Time/INR (warfarin), APTT (unfractionated heparin), anti-Xa chromogenic assays (low molecular weight heparin (LMWH), fondaparinux, rivaroxaban, and apixaban), anti-IIa chromogenic and clot-based assays (argatroban, bivalirudin, hirudin, and dabigatran).
vi. Digoxin monitoring.
vii. Anti-retroviral resistance testing in HIV infected patients.
viii. HCV viral load, HIV Viral Load and HIV and HCV geno- and sub-typing

j) In screening for congenital disorders in the fetus. Examples: Spina Bifida or Down Syndrome.

Rationale:
Rule 3j applies to devices for routine screening of embryo/foetus, and also specific screening for embryo/foetus whose families have known inherited conditions or where specific populations are at greater risk of an inherited condition e.g. Sickle cell. Rule 3i also applies to preimplantation and genetic screening tests.

Examples:

i. Devices intended for screening of foetal aneuploidies (e.g. trisomy 13, trisomy 18 and trisomy 21), which include devices intended for the measurement of biochemical maternal serum markers.
ii. Reagents and medical device software evaluating the risk of foetal aneuploidies based on biochemical markers and other information, non-invasive prenatal tests (NIPT).
iii. Devices intended to determine the foetal sex in cell-free foetal DNA in

maternal blood, in the remit of sex-depending congenital disorders.

iv. Genetic test for cystic fibrosis.
v. Genetic test for sickle cell disease.
vi. Huntington's chorea.
vii. Tay Sachs.
viii. Thalassaemia and other haemoglobin disorders

Rule 4

IVDDs intended for self-testing are classified as Class C, except those devices from which the result is not determining a medically critical status, or is preliminary and requires follow-up with the appropriate laboratory test in which case they are Class B.

IVDDs intended for blood gases and blood glucose determinations for near-patient testing would be Class C. Other IVDDs that are intended for near-patient should be classified in their own right using the classification rules.

Rationale:

The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: In general, these devices are used by individuals with no technical expertise and thus the labelling and instructions for use are critical to the proper outcome of the test.

Example for self-testing class C: Blood glucose monitoring, Self-testing devices for blood clotting, e.g. measurement of International Normalised Ratio (INR) are in Class C.

Example for self-testing class B: Pregnancy self test, Fertility testing, Urine test-strips.

Rule 5

The following IVDDs are classified as Class A:

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.

Rationale:

Rule 5a applies to general laboratory products like pipettes, stain powders, glass microscope slides, centrifuges, pipette tips or instrument liquid collection containers, buffers which usually do not fall under the definition of an IVDD.

Examples:

i. General microbiological culture media containing selecting agents, antimicrobial chromogenic agents, chemical indicators for colour

differentiation.

ii. Solutions like cleaners, buffer solutions, lysing solutions, diluents specified for use with an IVD.

iii. Pipette with a specific fixed one volume specifically intended for a particular IVD test with specified human sample, e.g. blood coagulation pipettes with automatic timing (Accessory of coagulometer).

iv. General staining reagents like hematoxylin, eosin, pap and grams iodine.

v. Kits for Isolation and purification of nucleic acids from human specimens. - Library Prep reagents for preparation of DNA for downstream analysis by NGS sequencing.

vi. Nucleic acid quantitation kits.

vii. General reagents (not assay specific) used with a Class A instrument, e.g. general sequencing consumable reagents used with a sequencer. Instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures.

Rationale:

Rule 5b applies to instruments specifically intended by the manufacturer for in vitro diagnostic procedures. These instruments are classified as class A, whereas reagents and kits are classified in their own right. Due to their interdependence, the performance of the reagent on this instrument will be part of the conformity assessment of the reagent. If the instrument has an independent measuring function which does not use any additional reagents, it is classified according to the intended purpose of the analysis (including instruments controls or instrument quality control). e.g. cell counting analyzers used in haematology, ion selective electrodes, instruments measuring blood gases or glucose via its sensors, specific gravity measurements in urine analysis, mass spectrophotometer for bacteria identification, erythrocyte sedimentation rate analyzer etc.

Examples:

i. Enzyme immunoassay analyzer, PCR thermocycler, sequencer for NGS applications, clinical chemistry analyzer.

ii. Instrument for automated purification of nucleic acids and PCR set-up

b) Specimen receptacles.

Examples:

Specimen containers or evacuated or non-evacuated tubes, empty or prefilled with a fixative solution or other general reagent to preserve the condition, stimulation, transport, storage and collection of biological specimens (e.g. cells, tissues specimens, urine, faeces) for the purpose of in vitro diagnostic examinations.

Note: Any product for general laboratory use not manufactured, sold or represented for use in specified in vitro diagnostic applications are not deemed to be IVDDs, as defined in this document. However, in certain jurisdictions products for general laboratory use are considered to be IVDDs.

Rule 6

IVDDs not covered in Rules 1 through 5 are classified as Class B.

Rationale:

The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: These devices present a moderate individual risk as they are not likely to lead to an erroneous result that would cause death or severe disability, have a major negative impact on patient outcome or put the individual in immediate danger. The devices give results that are usually one of several determinants. If the test result is the sole determinant however other information is available, such as presenting signs and symptoms or other clinical information which may guide a physician, such that classification into Class B may be justified. Other appropriate controls may also be in place to validate the results. This Class also includes those devices that present a low public health risk because they detect infectious agents that are not easily propagated in a population.

Examples:

i. Blood gases and physiological markers such as hormones, vitamins, enzymes, metabolic markers, specific IgE assays and celiac disease markers. Device intended to detect and measure magnesium to assess electrolyte / magnesium homeostasis.
ii. Test intended to detect and measure C-reactive protein or calprotectin to detect systemic inflammatory processes due to an active disease.
iii. Biochemical test for establishing the identification of microbiological culture isolates or for determining antimicrobial susceptibility of microbiological culture isolates except those permitting identification or determination of MIC associated with a life threatening condition.
iv. Test to detect Helicobacter pylori, Clostridium difficile, adenovirus, rotavirus and Giardia lamblia.
v. Non-typhoidal anti-salmonella antibodies to detect the exposure to an infectious agent. - FSH device for fertility testing in blood.
vi. Device intended for the detection of Candida albicans.
vii. Device intended for the detection of or exposure to Entamoeba histolytica.
viii. Device intended for the detection of Sarcoptes scabiei (genital scabies)

Rule 7

IVDDs that are controls without a quantitative or qualitative assigned value will be classified as Class B.

Rationale:
For such controls, the qualitative or quantitative value is assigned by the user and not the manufacturer. The manufacturer may indicate whether a specific analyte is present or absent in these controls without indicating expected assay results.

Examples:

i. Unassigned control sera.
ii. Control materials used to verify the migration of immunochromatographic assays.
iii. Unassigned QC Material as a heterozygous quality control to monitor analytical performance of the extraction, amplification, and detection.
iv. Non-assay specific control plasmas for use in coagulation.
v. Non-assay specific control serum containing multiple biochemical analytes.
vi. A DNA or RNA probe supplied for use as a non-assay specific normal control for in situ hybridization (ISH).

PART VII

GUIDILINES ON CLINICAL EVIDENCE OF MEDICAL DEVICES

1. Scope

This guideline is applicable to medical devices that require submission of proof of the device's clinical performance as part of the registration dossier. The guidelines aim at:

a) Introducing the concepts of clinical evaluation and clinical evidence;

b) Examining the relationship between clinical investigation, clinical data, clinical evaluation andclinical evidence; and

c) Serving as guidance to all those involved in the generation, compilation and review of clinical evidence sufficient to support the marketing of medical devices (regulatory authorities, conformity assessment bodies, manufacturers of medical devices and their associated industry groups).

This guideline is not applicable for in-vitro diagnostic devices. For requirements for submission of clinical evidence for in-vitro diagnostic devices, refer to ***the Guidelines on Clinical Performance of In-vitro Diagnostic Devices found in part VII of this Compendium***.

2. Key definitions and concepts

The definitions and concepts contained within this document are intended to apply to the establishment and maintenance of conformity with the relevant Essential Principles for medical devices generally:

2.1. Clinical investigation

Any systematic investigation or study in or on one or more human subjects, undertaken to assess the safety and/or performance of a medical device**.** It includes feasibility studies and those conducted for the purpose of gaining market approval, as well as investigations conducted following marketing approval. This term is synonymous with 'clinical trial' and 'clinical study'.

Routine post market surveillance and investigation of individual problem reportsdoes not constitute a clinical investigation.

2.2. Clinical data

Safety and/or performance information that are generated from the clinical use of a medical device. Clinical data may be generated through:

a) Results of pre- and post- market clinical investigation(s) of the device concerned;

b) Results of pre- and post- market clinical investigation(s) or other studies reported in the scientific literature of a justifiably comparable device; and

c) published and/or unpublished reports on other clinical experience of either the device in question or a justifiably comparable device

2.3. Clinical evaluation

The assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance of the device when used as intended by the manufacturer.

This is a process undertaken by manufacturers of medical devices to help establish compliance with the relevant Essential Principles for safety and performance. The result of this process is a report that can be reviewed by conformity assessment bodies and regulators and which details the extent of available data and its quality and demonstrates how the compliance with the Essential Principles is satisfied by the clinical data.

Clinical evaluation is an ongoing process; information about clinical safety and performance (e.g. adverse event reports, results from any further clinical investigations, published literature etc) should be monitored routinely by the manufacturer once the device is available on the market and the benefits and risks reassessed in light of this additional information.

The inputs for clinical evaluation are primarily clinical data in the form of clinical investigation reports, literature reports/reviews and clinical experience. The data required to establish the initial evidence of compliance with the Essential Principles may vary according to the characteristics of the device, its intended use, the claims made by the manufacturer, the existence and adequacy of warnings and other restrictions, and the extent of experience with its use. A key goal of the clinical evaluation is to establish that any risks associated with the use of the device are acceptable when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety. The clinical evaluation will, therefore, also need to cross-reference risk management documents.

2.4. Clinical evidence

The clinical data and the clinical evaluation report pertaining to a medical device.

This is an important component of the technical documentation of a medical device, which along with other design verification and validation documentation, device description, labelling, risk analysis and manufacturing information, is needed to allow a manufacturer to demonstrate conformity with the Essential Principles. It should be cross-referenced to other relevant parts of the technical documentation that impact on its interpretation.

The clinical evidence is used to support the marketing of the device, including any claims made about the clinical safety and performance of the device, and the labelling of the device. Figure 1 shows how the need for clinical evidence drives the processes of data generation and clinical evaluation, which produce clinical data and clinical evidence, respectively.

Clinical evidence should be reviewed and updated throughout the product life cycle by the manufacturer as new information relating to clinical safety and performance is obtained from clinical experience during marketing (e.g. adverse event reports, results from any further clinical investigations, formal post market surveillance studies) of the device in question and/or comparable devices.

3. Clinical evidence for medical devices

Clinical evidence is an important component of the technical documentation of a medical device which, along with other documentation (such as the device description, labelling, risk analysis and manufacturing information), is necessary for a manufacturer to demonstrate that the device complies with the essential principles, in particular essential principle 14. This provides assurance of the safety and performance of devices. Thus, all medical devices marketed in Tanzania must have demonstrated appropriate levels of safety and performance when used for their intended purpose(s).

The applicant and manufacturer must provide, or have available, clinical evidence to demonstrate compliance of the devices with the essential principles, if requested. The obligation to collect and compile clinical evidence lies with the manufacturer, who provides this to the applicant.

It should be noted that, clinical evidence is required to be available throughout the lifecycle of a device. It should be submitted at the time of application for market authorization, and as part of post-market surveillance reports. It should be evaluated and updated periodically as new information on safety and performance is obtained from clinical studies, literature or clinical experience in relation to the subject device and/or comparable devices.

NOTE: Clinical evaluation is an ongoing process conducted throughout the lifecycle of a medical device. Manufacturers must periodically review the performance, safety and benefit-risk profile of the device and update the clinical evidence accordingly.

Over the lifecycle of the device the clinical evaluation will change. For instance, when the device has been on the market for a number of years, the relevance of comparable device data is less significant, and direct clinical experience data is likely to be of greater relevance.

3.1. Clinical evidence requirements

Clinical evidence comprises clinical data and its evaluation pertaining to a medical device. It should provide the Authority with a current and accurate picture of both the state of scientific knowledge in relation to the treatment modality to which a device relates, and in relation to the subject device specifically. From this information, an acceptable benefit-risk profile may be demonstrated for a medical device, by showing that it performs as intended and that all identified undesirable effects and hazards, having been minimized during the design and development process, are outweighed by the benefits.

Submission of clinical evidence is mandatory for all devices regardless of their classification. Nevertheless, the extent and type of evidence submitted shall depend on the device under evaluation. Figure 1 depicts the sources of clinical data for different types of devices.

3.2. Requirements for different device classifications

Some Essential Principles are not applicable to certain classes of devices in certain circumstances (for example, Principle 13.4(2) in relation to when instructions for use need to be provided). Further, the principles may impose requirements subject to whether or not the device has a measuring function or whether the device is intended to be supplied in a sterile state, a non-sterile state, or both. Clinical evidence requirements must be met for applicable provisions of the Essential Principles (noting many aspects of the Essential Principles are applicable to all medical devices).

Greater scrutiny will be given to higher classification devices as part of ensuring safety and performance. Further, the classification, design and use of the device are relevant factors when considering the nature, type and range of evidence appropriate to being able to demonstrate compliance with applicable provisions of the Essential Principles. EP 14 itself notes that every medical device requires clinical evidence, **appropriate for the use and classification of the device**, demonstrating that the device complies with the applicable provisions of the Essential Principles.

3.3. Direct and indirect evidence

The following types of clinical evidence for the purpose of substantiating compliance with the Essential Principles are acceptable:

a) Direct clinical evidence - this is derived from an evaluation of clinical data pertaining to the subject device.

b) Indirect clinical evidence - this is derived from an evaluation of clinical data pertaining to a comparable device with which **substantial equivalence** has been demonstrated.

Evidence from comparable devices that are not substantially equivalent may support or supplement direct or indirect clinical evidence. However, it will not generally

constitute sufficient clinical evidence for substantiating compliance with the Essential Principles (except for certain low risk, well established technologies).

3.4. When there is no or limited clinical data

In some instances, it may be difficult to collect direct clinical data for a device due to very small numbers of eligible patients, high risk procedures limiting use, or practical or ethical considerations that limit the feasibility of conducting a high-quality clinical investigation. If there is no (or limited) clinical data for the specific device, depending upon the nature of the device, you may be able to provide a clinical justification for why clinical evidence is either not required or only partially required.

4. Sources of clinical data

Clinical data (meaning safety and performance information that is generated from the clinical use of a medical device) may be generated for either the subject device or a comparable device (including substantially equivalent devices). It includes:

a) data from clinical investigations (synonymous with trials and/or studies)
b) literature reviews
c) post-market data
d) other clinical experience data (also known as Real World Data).
e) The manufacturer is responsible for identifying relevant data and determining the extent of data needed for a complete clinical evaluation.

5. Clinical investigations

A clinical investigation is any systematic investigation or study in or on one or more human subjects, undertaken to assess the safety, clinical performance and/or effectiveness of a medical device. Clinical investigations include feasibility studies, studies conducted for the purpose of gaining market approval, and those conducted following market approval.

Clinical investigation data sourced directly from the device produces a higher level of confidence in its relevance and capacity to inform the safety and performance characteristics of the device and is the preferred option for fulfilling clinical evidence requirements.

It should be clearly indicated if the subject device has been modified since the clinical data were gathered, to clarify the device version and the nature of the changes.

In some circumstances direct clinical investigation data are not available for the subject device or are insufficient in quantity or quality. In this situation, provided that the devices are substantially equivalent, clinical investigation data from a comparable device may be used to support the safety and performance of the device under assessment (the subject device).

Reporting standards for clinical investigations

International guidance on reporting standards for clinical trials can be found in ISO 14155:2020 Clinical investigation of medical devices for human subjects – Good clinical practice. Annex D of this ISO provides useful information on what should go into a clinical trial report.

5.1. Format of Clinical Evaluation Report (CER)

Clinical Evaluation Reports (CER) should include the following:

a) scope and context of the evaluation;

b) clinical data;

c) data appraisal and analysis;

d) conclusions reached about performance, safety and presentation (including labelling, patient information and IFU) of the medical device when used for the intended purpose(s); and

e) a benefit-risk determination.

The clinical evaluation report should contain sufficient information to be read as a standalone document by the Authority for the purposes of assessing legislative compliance regarding clinical evidence requirements.

The following section provides an overview of the recommended content and format of the clinical evaluation report (CER), which is a standard component of pre-market applications and may also be required to be provided to the TGA in relation to post-market matters. The CER should be updated periodically through the lifecycle of the device to incorporate new evidence including clinical experience data and updated benefit-risk analyses. A record of reviews and amendments should be kept (along with a copy of each historical version and the most recent version).

5.2. CER content

The content and format of the CER should be as follows:

Part 1: General details

Part 2: Description of the medical device and its intended application

Part 3: Intended therapeutic and/or diagnostic indications and claims

Part 4: Context of the evaluation and choice of clinical data types

Part 5: Summary of relevant pre-clinical data

Part 6: Discussion regarding comparable devices including substantially equivalent devices

Part 7: Summary of the clinical data and appraisal

Part 8: Data analysis

Part 9: Conclusions

Part 10: Name, signature and curriculum vitae of the clinical expert and date of report

PART VIII

GUIDELINES ON LABELLING REQUIREMENTS FOR MEDICAL DEVICES, IN-VITRO DIAGNOSTICS AND LABORATORY EQUIPMENT INCLUDING ELECTRONIC IFU

1. Scope

This document applies to labelling requirements for medical devices, in-vitro diagnostic devices and laboratory equipment intended to be marketed in Tanzania mainland. This guidance is to be used in the preparation of labelling material for medical devices, (IVDs) in all risk classifications and laboratory equipment. Generally, the label and instructions for use should provide clear information on:

a) The identity and intended use/purpose of the device;
b) Maintenance (If applicable)
c) Storage of the device; and
d) Any residual risks, warnings or contra-indications.

The document provides guidance to manufacturers and marketing authorization holders on the requirements for medical device labelling.

Symbols to be included in the medical devices, IVD and laboratory equipment label shall meet the minimum requirements stated in the current ISO 15223 medical devices - symbols to be used with medical device labels, labelling and information to be supplied as provided in the **III** (Examples of Symbols Used in Medical Devices Based on ISO 15223-1) of this compendium**.**

2. Key Definitions

The definitions and concepts contained within this document are intended to apply to the product information that is supplied with the device. Therefore, for the sake of this document:

Clinical investigation means any designed and planned systematic study in human subjects undertaken to verify the safety and/or performance of a specific device.

Label means written, printed or graphic information provided upon the medical device itself. Where physical constraints prevent this happening, this term includes information provided on the packaging of each unit or on the packaging of multiple devices.

Labelling / information supplied by the manufacturer/product information means written, printed or graphic matter affixed to a medical device or any of its containers or wrappers, or, accompanying a medical device, related to identification, technical description, and use of the medical device, but excluding shipping documents.

Lay person means an individual that does not have formal training in a specific field or discipline.

Instructions for use means information provided by the manufacturer to inform the device user of the product's proper use and of any precautions to be taken.

Intended use / purpose means the objective intent of the manufacturer regarding the use of a product, process or service as reflected in the specifications, instructions and information provided by the manufacturer.

Performance evaluation means review of the performance of a medical device based upon data already available, scientific literature and, where appropriate, laboratory, animal or clinical investigations.

Primary packaging/container means the first level of packaging in direct contact/attached to the medical device, and is the element of packaging system that maintains the sterility and/or integrity of a medical device.

Refurbishment means to restore a used medical device or system to manufacturer defined safety and performance standards, which include actions such as repair, recondition, rework, software updates, replacement of worn parts with original parts. All actions are performed in a manner consistent with product specifications and service procedures defined by the manufacturer without changing its intended use

Reprocessing means all the steps performed to make a contaminated reusable device or a single-use device ready for use with a patient. The steps may include cleaning, functional testing, repackaging, re-labelling, disinfection or sterilization.

Re- processor means any entity that performs reprocessing activities.

Research use only means a medical device that has been made available to institutions/laboratories solely for their use in studies involving the collation of data. The device is not intended for any medical purpose or objective.

Secondary packaging means the process of repackaging of a medical device from its original packaging into another packaging, without breach of the primary package, before the medical device is supplied

Serial number means a unique serial number shall be given for IVD instruments.

Single use device means the medical device is intended to be used on an individual patient during a single procedure and then disposed of. It is not intended to be reprocessed and used again.

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

3. Labelling Requirements

3.1. General Requirements

3.1.1. The labelling for all medical devices shall adhere to these general requirements:

a) No person shall:
   i. Place any medical device in the market unless it has been appropriately labelled;
   ii. Use or operate any medical device to another person unless the appropriate label has been provided with the medical device when it is used on the other person; or
   iii. Use or operate any medical device to another person unless the appropriate label has been provided with the medical device when it is used to any other person in any investigational testing.

b) A registered medical device shall be labelled with TMDA medical device registration number. The use of QR code available from medical device registration certificate to indicate medical device registration number is encouraged.

c) The label shall not contain any statement to the effect, whether directly or indirectly, that the placement in the market, or usage or operation of the medical device is being promoted or endorsed by the Authority or the Ministry of Health or any of its organizational bodies.

d) The label of a medical device shall be legible, permanent and prominent.

e) The medium, format, content, readability and location of labelling should be appropriate to the particular device, its intended purpose and the technical knowledge, experience, education or training of the intended user(s). In particular, instructions for use should be written in terms readily understood by the intended user and, where appropriate, supplemented with drawings and diagrams. Some devices may require separate information for the healthcare professional and the lay user.

f) Paper versions of all labelling shall accompany all home use devices.

g) Any residual risk identified in the risk analysis should be reflected as contraindications or warnings within the labelling.

h) Where a component is too small to contain all required information, it must at a minimum contain Name, lot number, expiration date, volume, and storage conditions,

i) If the product requires associated instrumentation, the above requirements also apply to the instrument,

j) the instrument should clearly display information regarding its status as a new or reprocessed product

k) For more guidance on the inner and outer container label elements refer to the ISO 18113 standard series.

l) For guidance on the information to be incorporated within the label for Unique Device Identification (UDI) purposes,

3.1.2. Instructions for use (IFU) may not be needed or may be abbreviated for medical devices of low or moderate risk if they can be used safely and as intended by the manufacturer without any such instructions.

3.1.3. Labelling may be provided to the user in various media and by several means such as printed documents, through a display screen incorporated into the device, the manufacturer's website and magnetic or optical media. Whatever the media or the means, information should be targeted to the anticipated user population.

3.1.4. Labelling activities to meet the Medical Device Act and regulations, may be conducted post importation or manufacturing, but prior to placing in the market. Contents of labelling shall be as per submitted to the authority during medical device registration. There shall be no over labeling on the lot/batch or serial number, date of manufacturing and date of expiry.

3.2. Location of labelling

The label shall be appropriately located depending on a particular medical device and its intended use, in accordance with these following manners:

a) As far as it is practical and appropriate, the information needed to identify and use the medical device safely shall be provided on the medical device itself, and/or on the packaging for each unit (primary level of packaging), and/or the packaging of multiple medical devices (secondary level of packaging). If this is not practicable or appropriate, the information may be set out in the accompanying leaflet, manual, packaging insert, etc.

b) The medical device registration number, and manufacturer, applicant details, distributor and QR code (if available) shall be located where the information can be accessed at the point of sale by the customers/users.

c) in the case of medical devices that are packaged together because individual packaging of the medical devices is not practical, the label shall be provided as leaflet, packaging insert, document or other media supplied with a single or multiple medical devices; and

d) if multiple medical devices are supplied to a single user and/or location or

packaged together as one package, it may be appropriate to provide only a single copy of the label but more copies shall be supplied upon request.

e) Information to be translated into Kiswahili shall made next to the English version; or the location of the translation may be decided through a risk assessment exercise that shall be submitted during registration.

3.3. Format

The format of labelling shall be in accordance with the international standard for medical device labelling where applicable.

The use of internationally recognized symbols is encouraged provided that medical device safety is not compromised by a lack of understanding on the part of the patient or user. Where the meaning of the symbol is not obvious to the medical device user, e.g. for a home-used medical device or for a newly introduced symbol, an explanation shall be provided.

3.4. Language

The language to be used for labels and instructions for use for products intended to be marketed in Tanzania should be in English and/or Kiswahili, moreover the following shall be considered:

a) The use of Kiswahili shall be required for home use medical devices; and
b) Other languages may be used as necessary.

3.5. Use of TMDA Logo

Any logo of the TMDA is prohibited to be placed in the medical device labelling. Use of specific statements Statement such as “Tanzania Medicines and Medical Device Authority (TMDA)” and/or Ministry of Health Tanzania” (unless it required by Ministry of Health Tanzania) is prohibited in all labelling as it is considered as an endorsement from the Authority.

4. Electronic labelling

Product manual in electronic format for professional use medical device Product manual is recommended to be in printed form. However, electronic form is allowed to be provided subject to the following conditions
a) Manufacturers shall conduct and document a risk analysis for implementation of electronic manuals and maintain records of this analysis. Specific points to address include:

i) Does the intended user have the required level of experience and the means to use the electronic (e.g. a computer with internet access at or near the device’s point of use, CD/DVD Drive or a compatible web-browser)?

ii) Are there back-up methods for accessing the electronic/hard-copy manuals?

iii) Are there processes in place to ensure ongoing security of electronic manuals?

b) Manufacturers shall have defined procedures and processes for the establishment and revisions to electronic documents.

4.1. Electronic IFU (e-IFU)

a) Electronic IFU (e-IFU) is eligible for devices that are limited to those intended for use by professional users only.

b) Users should always have the choice to obtain the content of the eIFU in paper form on request, without undue delay or within the time period specified in the risk assessment, and at no additional cost.

c) For information downloadable from the internet, the internet web address shall be clearly printed on the physical label of the device and displayed in such a manner that highlights to the user its purpose. The manufacturer /AR shall ensure that the electronic label is identical with the printed IFU approved in the product registration.

d) Manufacturers shall conduct and document a risk analysis for implementation of electronic IFUs and maintain records of this analysis. Specific points to address include:
   i. Does the intended user have the required level of experience and the means to use the electronic IFU (e.g. a computer with internet access at or near the device's point of use, CD/DVD Drive or a compatible web-browser)?
   ii. Are there back-up methods for accessing the electronic/hard-copy IFU?
   iii. Are there processes in place to ensure ongoing security of electronic IFU?

e) Manufacturers shall have defined procedures and processes for the establishment and revisions to electronic documents.

f) Paper-form IFU is required and additional electronic IFU is optional for home use devices.

Note: Any changes to the electronic label shall comply with the specified requirements in Guidelines on Submission of Application for change (s) to approved Medical Devices and In Vitro Diagnostics

4.2. E-IFU for Kiswahili translation for home use device

a) E-IFU is eligible for medical device intended for use by professional users only.

b) Paper-form IFU is required and additional electronic IFU is optional for home use devices.

5. Content of Labelling for Medical Devices

5.1. Labelling and Instructions for use of Medical Devices

The labelling should bear the following particulars:

a) The brand and common name of the medical device

b) Identification number (product code/catalogue) (If applicable).

c) The details to identify the content of the device and its use, and if the contents are not readily apparent, an indication of what the package contains, expressed in terms appropriate to the device such as size, net weight, length, volume or number of units, volume after reconstitution shall be indicated.

d) The name and physical address of the manufacturing site that allows the location of the manufacturer to be established if appropriate, a phone number and/or fax number and/or website address to obtain technical assistance.

e) Where appropriate, an indication that the device contains or incorporates a medicinal or biological substance, e.g. heparin coated catheter.

f) An indication of the batch code/lot number (eg. On single use disposable medical devices) or the serial number of the device preceded by the word LOT or SERIAL NUMBER (e.g. on electrically-powered medical devices), or an equivalent symbol, as appropriate, to allow post-market action to be taken if there is a need to trace or recall the device

g) An unambiguous indication of the Manufacturing and expiry date (until when the device may be used safely), expressed at least as the year and month (e.g. on devices supplied sterile, single-use disposable devices or reagents), where this is relevant, format shall follow the requirements of ISO 8601

h) Storage conditions necessary to maintain the stability of the product shall be indicated. If there are any other conditions that may affect the handling or storage of the products shall be specified e.g. fragile

i) Where relevant, the storage conditions and shelf life following the first opening of the primary container, together with the storage conditions and stability of working solutions

j) If the device is supplied sterile, an indication of its sterile state and, where appropriate, the sterilization method.

k) Warnings or precautions to be taken that need to be brought to the immediate

attention of the user of the medical device as relevant, and to any other person where appropriate (e.g. 'CAUTION – HOT SURFACE' or 'THIS PRODUCT CONTAINS LATEX'). This information may be kept to a minimum in which case more detailed information should appear in the instructions for use.

L) warning and precautions If a product is considered hazardous, the outer container label shall include the appropriate danger wording or symbol(s) e.g. chemical, radioactive and biological hazards,

m) If the device is for use by a single individual and has been manufactured according to a written prescription or pattern (i.e. it is custom made), an indication of that fact preceded by a word or equivalent symbol, as appropriate

n) If the medical device is intended for single use the word "**For Single Use Only**" or equivalent symbol shall be included as appropriate

o) If the device is intended for premarket **clinical investigation** only or **research purpose only**, an indication of that fact preceded by word or equivalent symbol, as appropriate

p) If the device is intended for **non-clinical research**, teaching or testing purposes only, an indication of that fact preceded by word or equivalent symbol as appropriate

q) If the device is intended for **Demonstration** purposes only, for marketing or teaching an indication of that fact preceded by word or equivalent symbol as appropriate

r) If the device is intended for presentation or **demonstration** purposes only, an indication of that fact preceded by a word or equivalent symbol as appropriate

s) indication that the medical device is **refurbished** medical device. The refurbishment date shall also be indicated

t) If the devices intended for animal uses shall be indicated"For **Veterinary Use**" or "**Device for Veterinary Uses Only**

The Authority may require any other additional information to be included as medical device labelling whenever required

5.2. Content of the Instructions for use for Medical Devices

A copy of the current instructions for use for a medical device must be submitted along with the application and should include the following minimum information:

a) The Brand and Common name of the medical device

b) identification number (product code/catalogue).

a) The name and physical address of the manufacturing site that allows the location of the manufacturer to be established, together with a telephone number and/or fax number and/or website address to obtain technical assistance.

b) The device's intended use/purpose including the intended user (e.g. professional or lay person), as appropriate.

c) The performance of the device intended by the manufacturer.

d) Where the manufacturer has included clinical investigations as part of premarket conformity assessment to demonstrate conformity to Essential Principles, a summary of the investigation, outcome data and clinical safety information, or a reference as to where such information may be accessed.

e) Any residual risks, contraindications and any expected and foreseeable side effects, including information to be conveyed to the patient in this regard.

f) Specifications the user requires to use the device appropriately, e.g. if the device has a measuring function, the degree of accuracy claimed by manufacturer

g) If the device contains, or incorporates, a medicinal substance and/or material of biological origin, identification of that substance or material, as appropriate.

h) Details of any preparatory treatment or handling of the device before it is ready for use (e.g. sterilization method, final assembly, calibration, etc.).

i) Any requirements for special facilities, or special training, or particular qualifications of the device user and/or third parties.

j) The information needed to verify whether the device is properly installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant:

    i. details of the nature, and frequency, of preventative and regular maintenance, and of any preparatory cleaning or disinfection;

    ii. identification of any consumable components and how to replace them;

    iii. information on any necessary calibration to ensure that the device operates properly and safely during its intended life span;

iv. methods of eliminating the risks encountered by persons involved in installing, calibrating or servicing medical devices.

k) An indication of any special storage and/or handling condition that applies.

l) If the device is supplied sterile, instructions in the event of the sterile packaging being damaged before use.

m) If the device is supplied non-sterile with the intention that it is sterilized before use, the appropriate instructions for sterilization.

n) If the device is reusable, information on the appropriate processes to allow reuse, including cleaning, disinfection, packaging and, where appropriate, the method of re-sterilization. Information should be provided to identify when the device should no longer be reused, e.g. signs of material degradation or the maximum number of allowable reuses.

o) For devices intended for use together with other medical devices and/or general-purpose equipment or dedicated software:

    i. information to identify such devices or equipment or software, in order to obtain a safe combination, and/or

    ii. information on any known restrictions to combinations of medical devices and equipment.

p) If the device emits hazardous, or potentially hazardous levels of radiation for medical purposes:

    i. detailed information as to the nature, type and where appropriate, the intensity and distribution of the emitted radiation; Label and Instructions for Use for Medical Devices

    ii. the means of protecting the patient, user, or third party from unintended radiation during use of the device;

q) Information that allows the user and/or patient to be informed of any warnings, precautions, measures to be taken and limitations of use regarding the device. This information should cover, where appropriate:

    i. warnings, precautions and/or measures to be taken in the event of malfunction of the device or changes in its performance that may affect safety;

    ii. warnings, precautions and/or measures to be taken in regards to the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation

associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature;

iii. warnings, precautions and/or measures to be taken in regards to the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, therapeutic treatment or use (e.g. electromagnetic interference emitted by the device affecting other equipment);

iv. warnings or precautions related to potentially infectious material present in the medical device;

v. if the device administers medicinal or biological products, any limitations or incompatibility in the choice of substances to be delivered;

vi. warnings, precautions and/or limitations related to the medicinal substance or biological material that is incorporated into the device as an integral part of the device;

vii. precautions related to materials incorporated into the device that are carcinogenic, mutagenic or toxic, or could result in sensitization or allergic reaction of the patient or user.

viii. warnings, precautions or measures to be taken in regards to calibration and maintenance requirements that could result in inaccurate measurements, diagnostic results or therapeutic treatment or use; and

r) warnings or precautions on hazardous or potentially hazardous radiation, including:

i. the nature of the emitted radiation,

ii. the means of protecting the users, bystanders, or where appropriate, patients,

iii. including ways of avoiding misuse, and iv. including ways of appropriately reducing the risks inherent during transport, storage and installation where applicable.

s) Warnings or precautions to be taken related to the disposal of the device, its accessories and the consumables used with it, if any. This information should cover, where appropriate:

i. infection or microbial hazards (e.g. explants, needles or surgical equipment contaminated with potentially infectious substances of human origin);

ii. environmental hazards (e.g. batteries or materials that emit potentially hazardous levels of radiation);

iii. physical hazards (e.g. from sharps).

t) For devices intended for use by lay persons, the circumstances when the user should consult with a healthcare professional.

u) particular risks in connection with implantation of an implantable medical device

v) technical details concerning the medical device, e.g: device specification/ formulation, colour, size, compatibility, and etc.;

w) any necessary post-market servicing needs for the medical device; and

x) any decommissioning or disposal information (infection or microbial hazards, environmental hazards; physical hazards)

y) a specification of the clinical benefit to be expected

z) a summary of safety and clinical performance information relevant to the user or patient.

aa) instruction for the user and the patient to report any serious incident that has occurred in relation to the medical device to the manufacturer/ Applicant/LTR

bb) for medical device software, user instructions may be supplied in electronic data storage devices (e.g. compact disc, digital video disc, USB flash drive).

cc) Date of issue or latest revision of the instructions for use and, where appropriate, an identification number

5.3. Implant Card and Information to be Supplied to the Patient with an Implanted Device

The manufacturer of an implantable device shall provide together with the device the following:

a) information allowing the identification of the device, including the device name, serial number, lot number, the UDI, the device model, as well as the name, address and the website of the manufacturer;

b) any warnings, precautions or measures to be taken by the patient or a healthcare professional with regard to reciprocal interference with reasonably foreseeable external influences, medical examinations or environmental conditions;

c) any information about the expected lifetime of the device and any necessary

follow-up;

d) any other information to ensure safe use of the device by the patient, including the
e) information available in the Essential Principles.

The information referred to in the first subparagraph shall be provided, for the purpose of making it available to the particular patient who has been implanted with the device, by any means that allow rapid access to that information and shall be stated in Kiswahili and English language. The information shall be written in a way that is readily understood by a lay person and shall be updated where appropriate. Updates of the information shall be made available to the patient via the website mentioned in point (a) of the first subparagraph.

In addition, the manufacturer shall provide the information referred to in point (a) of the
first subparagraph on an implant card delivered with the device.

Health institutions shall make the information referred to in paragraph 1 available, by any means that allow rapid access to that information, to any patients who have been implanted with the device, together with the implant card, which shall bear their identity.

The following implants shall be exempted from the obligations laid down in this section; sutures, staples, dental fillings, dental braces, tooth crowns, screws, wedges, plates, wires, pins, clips and connectors. The Tanzania Medicines and Medical Devices Authority, when necessary, will amend this list by adding other types of implants to it or by removing implants therefrom.

6. Label and Instructions for use of In Vitro Diagnostic Medical Devices (IVDs)

6.1. Content of the Label

The label should contain the following particulars which may appear on the medical device itself, or on the packaging of each unit, or on the packaging of multiple devices.

a) The Common name and trade name of the IVD medical device

b) identification number (product code/catalogue).

c) Details to identify the IVD medical device and its use, e.g. ‘HIV-1/HIV-2 Antibody Test’ or ‘Blood Glucose meter’ or ‘Blood Gas Analyzer’.

d) The details to identify the content of the device and its use, and if the contents are not readily apparent, an indication of what the package contains, expressed in

terms appropriate to the device eg. Content of the IVD kits

e) The name and physical address of the manufacturing site that allows the location of the manufacturer to be established together with a telephone number and/or fax number and/or website address to obtain technical assistance

f) Name and postal address of either the authorized applicant, LTR, importer or distributor provided by the manufacturer, in which case, the additional label should not obscure any of the manufacturer's labels.

g) An indication that the device is for in vitro diagnostic use, preceded by a word. "**For In vitro diagnostics use**" or graphical symbol: "**In vitro diagnostic medical device** or equivalent symbol, as appropriate

h) An indication of the batch code/lot number (eg. On single use disposable IVD medical devices) or the serial number of the device preceded by the word LOT or SERIAL NUMBER (e.g. on electrically-powered medical devices) or an equivalent symbol, as appropriate, to allow post-market action to be taken if there is a need to trace or recall the IVD medical device. However, for accessories this may be substituted with a control number and for software it should be substituted with a version number.

i) An unambiguous indication of the date until when the IVD medical device may be used safely, expressed at least as the year and month (e.g. on reagents or consumables), where this is relevant, format shall follow the requirements of ISO 8601

j) For instruments, where there is no indication of the date until when it may be used safely, the year of manufacture. This year of manufacture may be included as part of the batch or serial number, provided the date is clearly identifiable.

k) Storage conditions necessary to maintain the stability of the product shall be indicated. If there are any other conditions that may affect the handling or storage of the products shall be specified e.g. fragile

l) Where relevant, an indication of the net quantity of contents, expressed in terms of weight or volume, numerical count, or any combination of these or other terms which accurately reflect the contents of the package.

m) An indication of any special storage and/or handling condition that applies.

n) If the IVD medical device is supplied as sterile, an indication of its sterile state and, where appropriate, the sterilization method.

o) Warnings or precautions to be taken that need to be brought to the immediate attention of the professional user, the lay person or other person (e.g. 'CAUTION – LASER' or 'CONTAINS POTENTIALLY INFECTIOUS MATERIAL'). This information may be kept to a minimum in which case more detailed information

will appear in the instructions for use.

p) Where relevant, if the IVD medical device is intended for single use and there is a potential risk of re-use, (e.g. blood collection tubes), an indication of that fact.

q) If the IVD medical device is intended for premarket performance evaluation only, an indication of that fact preceded by a word or symbol as appropriate.

r) If the IVD medical device is intended for non-clinical research or use, teaching or testing purposes only, an indication of that fact. That indication may be added by the LTR, importer or distributor within the country of import, rather than be provided by the manufacturer.

s) If the IVD medical device is intended for presentation or demonstration purposes only, an indication of that fact preceded by a word or symbol as appropriate. That indication may be added by the applicant, LRP, importer or distributor

t) IVD medical device kits include individual reagents and articles that may be made available as separate IVD medical devices. In this situation, these IVD medical devices should comply with the label content in this section

u) All In Vitro Diagnostic devices intended for animal uses shall be indicated "For **Veterinary Use**" or "**In Vitro Diagnostic Device for Veterinary Uses Only.**

6.2. Content of the Instructions for Use for IVDs

A copy of the current instructions for use for IVD must be submitted along with the application and should include the following minimum information:

a) The common name or brand name of the IVD medical device and identification number (product code/catalogue).

b) The name and physical address of the manufacturing that allows the location of the manufacturer to be established, together with a telephone number and/or fax number and/or website address to obtain technical assistance

c) The IVD medical device's intended use/purpose
   i. what is detected
   ii. The clinical indication for the test (e.g. if it is for a specific disorder, or a condition or risk factor of interest that the test is intended to detect, define or differentiate);
   iii. The function of the product (screening, monitoring, diagnostic or aid to diagnosis, staging or aid to staging of disease);
   iv. whether it is automated or not;
   v. whether it is qualitative or quantitative;
   vi. the type of specimen (s) required (eg. serum, plasma, whole blood, tissue biopsy, urine)

vii. the intended testing population (e.g. neonates, antenatal women);
viii. A description of the specimen collection and transport materials provided with the product or recommended for use;

d) An indication that the product is for ***in vitro diagnostic use***, ***Veterinary use.***

e) The intended user, as appropriate (e.g. self-testing by lay person, near patient at point of care by trained personnel or professionals).

f) Assay type (e.g. immunoassay, chemistry, cytochemistry, image analysis, immunohistochemistry, etc.)

g) A general description of the principle of the assay method or instrument principles of operation

h) A description of all components of the assay (e.g. reagents, assay controls and calibrators and any limitation upon their use) eg. Suitable for a dedicated instrument only and a description of the reactive ingredients of relevantcomponents (e.g. antibodies, antigens, nucleic acid primers etc.);

Note: IVD medical device kits include individual reagents and articles that may be made available as separate IVD medical devices. In this situation, where appropriate, these IVD medical devices should comply with the instructions for use content in this section.

i) A list or description of materials or accessories provided with a product and a list or description of special materials that are intended to be used in combination with the product but are not provided with the product

j) If applicable, a description of any software to be used withthe product;

k) If applicable, a description or complete list of the various configurations/variants of product that will bemade available;

l) the specific name of the instrument required for the assay, if any. For instruments, the intended use should also include the modes of operation for instruments e.g., random access, batch, stat, open tube, closed tube, automatic, manual

m) For IVD medical devices intended for use together with other medical devices, including IVD medical devices, and/or general-purpose equipment
   i. information to identify such devices or equipment, in order to obtain a safe combination, and/or
   ii. information on any known restrictions to combinations of medical devices and equipment.

n) An indication of any special storage (e.g. temperature, light, humidity, etc.) and/or handling conditions that apply.

o) In use stability which may include, the storage conditions, and shelf life following the first opening of the primary container, together with the storage conditions and stability of working solutions, where this is relevant.

p) If the IVD medical device or accessories in a kit is supplied as sterile, instructions in the event of the sterile packaging being damaged before use.

q) If the test kit includes accessories that have been specified by the manufacturer as intended for single- use only, an indication of that statement

r) Information that allows the user to be informed of any warnings, precautions, measures to be taken and limitations of use regarding the IVD medical device. This information should cover, where appropriate:

i. warnings, precautions and/or measures to be taken in the event of malfunction of the IVD medical device or its degradation as suggested by changes in its appearance that may affect performance;

ii. warnings, precautions and/or measures to be taken in regards to the exposure to reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, or temperature;

iii. warnings, precautions and/or measures to be taken in regards to the risks of interference posed by the reasonably foreseeable presence of the device during specific diagnostic investigations, evaluations, therapeutic treatment or use (e.g. electromagnetic interference emitted by the device affecting other equipment);

iv. precautions related to materials incorporated into the IVD medical device that are carcinogenic, mutagenic or toxic, or could result in sensitization or allergic reaction.

m) Any warnings and/or precautions related to potentially infectious material that is included in the IVD medical device.

n) Where relevant, requirements for special facilities (e.g. clean room environment) or special training (e.g. radiation safety), or particular qualifications of the device user.

o) Conditions for collection, handling, and preparation of the specimen.

p) Details of any preparatory treatment or handling of the IVD medical device before it is ready for use (e.g. reconstitution, calibration, etc.).

q) The information needed to verify whether the IVD medical device is properly

installed and is ready to perform safely and as intended by the manufacturer, together with, where relevant:

i. details of the nature, and frequency of preventative and regular maintenance (including cleaning and disinfection) and who should perform this maintenance (eg. The user, a representative of the manufacturer, or a third party;

ii. identification of any consumable components and how to replace them;

iii. information on any necessary calibration to ensure that the IVD medical device operates properly and safely during its intended life span;

iv. methods of mitigating the risks encountered by persons involved in installing, calibrating or servicing IVD medical devices, e.g. contaminated surfaces.

r) Where relevant, recommendations for quality control procedures.

s) The metrological traceability of values assigned to calibrators and trueness control materials, including identification of applicable reference materials and/or reference measurement procedures of higher order.

t) Clear instructions on how to perform the assay procedure including instructions on specimen collection, handling, preparation and storage of reagents, use of assay calibrators and controls, calculations and interpretation of results and where relevant if any confirmatory testing should be considered.

u) Clear instructions on the correct usage of any equipment or software that is required for the performance of the assay

v) Analytical performance characteristics, such as sensitivity, specificity, and accuracy (which is a combination of trueness and precision).

w) Where relevant, clinical performance characteristics, such as diagnostic sensitivity and diagnostic specificity.

x) Where relevant, reference intervals.

y) Information on interfering substances or limitations (e.g. visual evidence of hyperlipidaemia or haemolysis, age of specimen/sample) that may affect the performance of the assay.

z) Warnings or precautions to be taken related to the disposal of the device, its accessories, and the consumables used with it, if any. This information should cover, where appropriate:

i. infection or microbial hazards (e.g. consumables contaminated with potentially infectious substances of human origin eg. lancets);
ii. environmental hazards (e.g. batteries or materials that emit potentially hazardous levels of radiation);
iii. physical hazards (e.g. explosion).

aa) study design (population studies, N, type of sample, matrix, dilution, target, concentrations, etc.).

bb) For IVD medical devices intended for use by lay persons, the circumstances when the user should consult with a healthcare professional

cc) Document control details such as date of issue of latest revision of the instructions for use, version number and, where appropriate, document identification number.

dd) Any residual risk

6.3. Content of Laboratory equipment label

a) The brand and common name of the medical device

b) Identification number or product code/catalogue If applicable

c) The details to identify the content of the device and its use, and if the contents are not readily apparent, an indication of what the package contains, expressed in terms appropriate to the device such as size, net weight, length, volume or number of units, volume after reconstitution shall be indicated.

d) The name and physical address of the manufacturing site that allows the location of the manufacturer to be established if appropriate, a phone number and/or fax number and/or website address to obtain technical assistance.

e) An indication of the batch code/lot number (eg. On single use disposable medical devices) or the serial number of the device preceded by the word LOT or SERIAL NUMBER (e.g. on electrically-powered medical devices), or an equivalent symbol, as appropriate, to allow post-market action to be taken if there is a need to trace or recall the device

f) An unambiguous indication of the Manufacturing and expiry date (until when the device may be used safely) if applicable, expressed at least as the year and month (e.g. on devices supplied sterile, single-use disposable devices or reagents), where this is relevant, format shall follow the requirements of ISO 8601

g) Storage conditions necessary to maintain the stability of the product (if applicable) shall be indicated. If there are any other conditions that may affect the handling or storage of the products shall be specified e.g. fragile

6.4. Instrument manual

If the product requires associated instrumentation, include a hard copy and softcopy of the instrument manual and/or associated operator manuals. If the instrument manual is large, an electronic version may be included instead of a hard copy

7. Labelling Instructions for General Public

In case the device is intended to be sold to the general public, labeling information: -

a) Shall be set out on the outside of the package thatcontains the device; and be visible under normal conditions of sale.

b) Where a package that contains a device is too small to display all the information in accordance with (i) above, the directions for use shall accompany the device but need not be set out on the outside of the package or be visible under normal conditions of sale.

c) Specimen label(s), promotional material(s) and user manual(s) should be provided.

PART IX

GUIDELINES ON GROUPING OF MEDICAL DEVICES AND IN-VITRO DIAGNOSTIC DEVICES

1. Scope

This document applies to all medical devices, in vitro diagnostic devices and laboratory equipment intended to be registered in Tanzania.

This document is meant to provide guidance in determining the category of a medical device or IVDD an applicant is intending to register. It provides guidance through a decision tree on how to determine whether a device falls into a category of a single device, group, family, system or a kit. Furthermore, it provides submission requirements for each category. Applicants are urged to carefully read this guidance for a proper submission of an application to TMDA in order to avoid inconveniences

2. General Principles of Grouping

Grouping of medical devices is for the purpose of compiling an application for marketing authorization.

The manufacturer or product owner of a medical device may incorporate as part of their device,medical devices and/or accessories from other manufacturers or product owners or intend such devices to be used together to achieve a common intended purpose. By such design and/or intended purpose, the product owner of the medical device also assumes the responsibility for such use of the otherdevices and accessories.

The regulatory requirements apply to all medical devices to be authorized, regardless of the manner in which they are grouped for the marketing authorization application. Information on all medical devices within a grouping including data to substantiate the quality and performance of these devices must be submitted as part of the dossier/application.

Once the device has been issued marketing authorization, for products that include instruments/accessories from different manufacturers only the manufacturer of the primary device will be listed on the certificate and register of registered devices. Nevertheless, the documentation relating to other product manufacturers is required to be submitted as part of the registration submission.

The Market Authorization Holder shall undertake the following post-market duties and obligations for all medical devices and accessories they have registered or notified either individually or as part of a medical device group:

a) comply with the conditions applicable to the registered medical device and conditions imposed on the Registrant;
b) submit applications to the Authority for changes made to the registered medical device;
c) maintain records of supply;

d) maintain records of complaints;

e) report defects and adverse effects to the Authority; and

f) notify the Authority concerning field safety corrective action (FSCA), including recall.

3. Grouping Categories

3.1. Family

A medical device FAMILY is a collection of medical devices and each medical device FAMILY member:

a) is from the same product owner;

b) is of the same risk classification;

c) has a common intended purpose;

d) has a common design and manufacturing process; and

e) has variations that are within the scope of the permissible variants.

3.2. List of permissible variants in a family

The list of permissible variants is a closed list.

Specific products	**Permissible variants**
Abutments	Retention (e.g. cement or screw)
Active Implantable Devices	MR conditional and Non- MR Conditional
Antibiotic test (IVD)	Concentration
Biopsy Forceps	Formable or Non-formable
Blood Bags	(i) Anticoagulants with same composition but different concentrations (ii) Additives (different composition and concentrations)
Catheter	(i) Number of lumens in catheter (ii) Material of catheter: PVC (polyvinylchloride), PU (polyurethane), nylon and silicone (iii) Curvature (iv) Coating material for lubrication

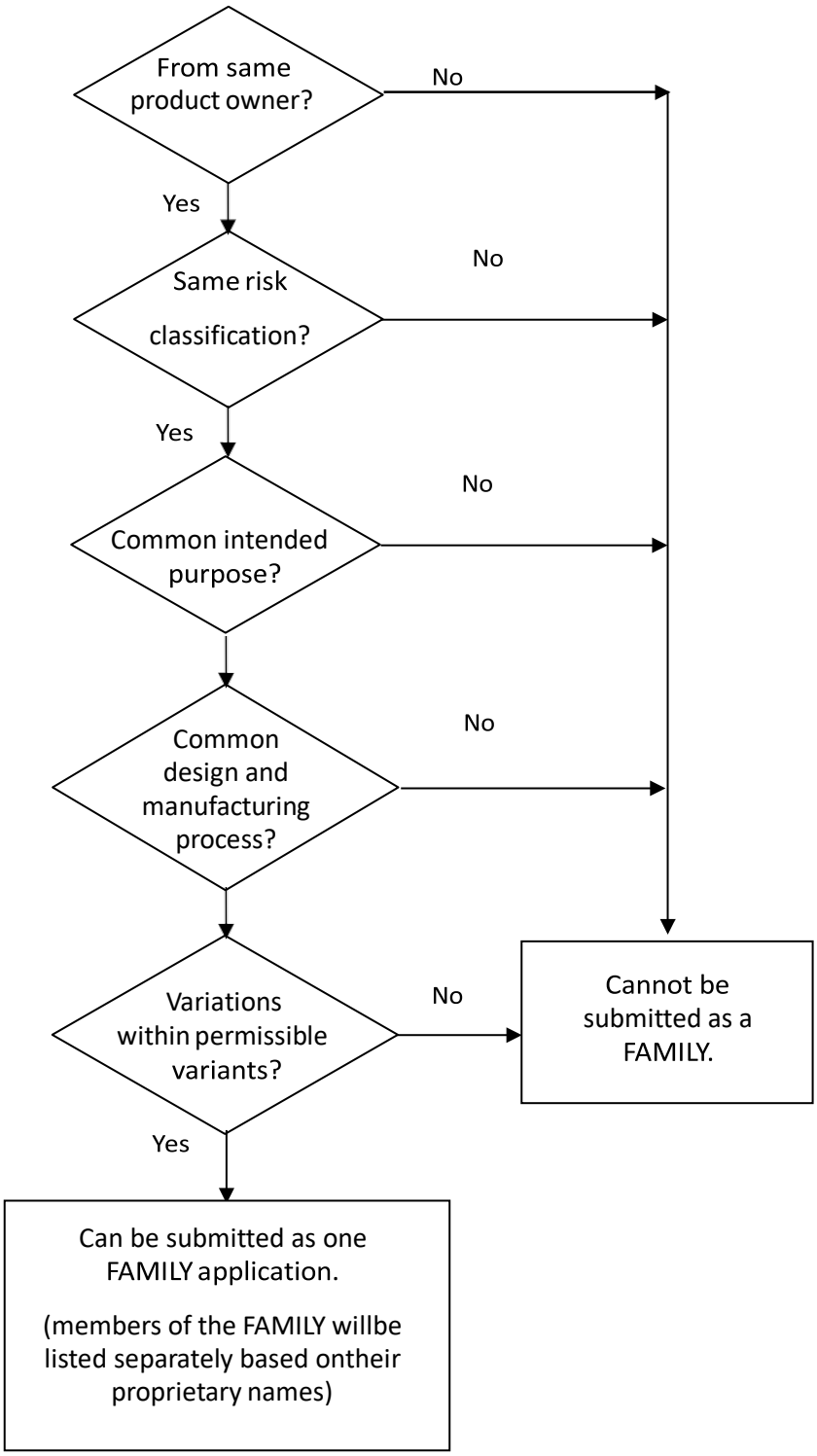
Condoms	(i) Texture (ii) Flavour
Contact lens	(i) Diopter, (ii) UV protection (iii) Tinting (iv) Colour (v) Wearing schedule (i.e. daily wear, extended wear) (vi) Replacement schedule (i.e. daily, weekly, monthly)
Defibrillators	Automatic or semi-automatic
Dental brackets	Material of bracket
Dental handpieces	(i) Rotational speed (ii) Material of handpiece
Dermal fillers	Same composition but different concentrations/densities
Diagnostic Radiographic systems	(i) Number of slices (ii) Digital vs Analog (iii) Biplane and Single Plane (iv) Flat Panel vs Cassette (v) PET ring size
Electrophysiological Catheter	(i) Electrode spacing (ii) Number of electrodes
Gloves	Powdered or powder-free
Gamma Camera	Number of detectors
Guide wire	With or without inert coating material
Orthopaedic/ Dental Implants	(i) Cemented or non-cemented fixation (ii) Collar

Intra-ocular Lens	(i) Monofocal or Multifocal (ii) Multi-piece or Single-piece (iii) Aspheric or Spheric
ImplantablePulse Generators	Number of Chambers (Cardio)
IV Cannula	(i) Presence of injection port (ii) Presence of safety wing
IVD rapid tests	Different assembly format: cassette, midstream, strip
IVD urinalysis strips	Different combination of testing configurations
Polymer products	With or without plasticisers (e.g. DEHP)
Stent	(i) Delivery system, that is over-the-wire or through the scope (ii) Flaps, Flares or sleeves
Suture	(i) Number of strands (ii) Pledgets (iii) Loops (iv) Dyes
Suture passer	Design of jaw, handle or needle
Tracheal Tube *(endotracheal tube, tracheostomy tube)*	With or without cuff
Wound Dressings	Different formats (e.g. solution, creams, gels loaded onto pads, etc)
X-ray detector	Scintillator material

Other permissible variants in general
Coating material for lubrication only
Colour

Diameter, Length, Width, Gauge
Concentration with same indication and mechanism (same composition different amount of constituent)
Dimensional design differences due to paediatric versus adult use (The differences due to the different patient populations are permissible, e.g. volume and length)
Flexibility
Holding force
Isotope activity level
Memory storage
Method of sterilisation (to achieve same sterility outcome)
Printing capability
Radiopacity
Shape, Size, Volume
Viscosity (The change in viscosity is solely due to changes in the concentration of constituent material)
Type of device mounting (e.g. ceiling mount, wall mount or standing)
Sterility status (sterile vs non-sterile)

Decision Flowchart for Grouping of Medical Devices as a FAMILY



3.3. Submission requirements

A single application shall be required for medical device family which shall be accompanied by a declaration of the differences in shape, colour, flavour or size. Data submission shall be in accordance with the requirements provided for medical devices and In Vitro Diagnostics.

3.3.1. Addition of New Models to a registered Medical Device FAMILY

The addition of new medical devices to a registered device through a submission of an application for change is only permissible if the new medical devices being added fulfill criteria for permissible variants under this guideline.

Although, the new medical devices may satisfy the criteria to be grouped as a FAMILY with the registered medical devices, a new product registration application has to be submitted for the registration of these new medical devices that have different brand names from those already registered. Refer to the Guidelines on Changes of Registered Medical Devices.

Examples:

- **Condoms** that differ in colour, size and texture but are manufactured from the same material, using common manufacturing process and share a common intended purpose can be grouped as a FAMILY.
- **IV administrative sets** that differ in features such as safety wings and length of tubing, but are manufactured from the same material, common manufacturing process and share a common intended purpose can be grouped as a FAMILY.
- **Steerable guidewires** that are available in various lengths and possess various tip shapes and tip flexibilities can be grouped as a FAMILY if their variations fall within the scope of permissible variants.
- **Cardiac catheters** that are available in a different number of lumens, lengths and diameters can be grouped as a FAMILY.
- **Contact lenses** with additional features of UV protection can be grouped as a FAMILY, as this feature does not affect the basic design and manufacturing of the lens.
- **Contact lenses** are available as toric lens or spherical lens. These productshave different intended purposes and performances. They are designed andmanufactured differently. Due to these differences, they shall <u>not</u> beconsidered as members of a FAMILY.

3.4. System

A medical device SYSTEM comprises of a number of medical devices and/or accessories that are:

a) from the same manufacturer;

b) intended to be used in combination to achieve a common intended purpose;

c) compatible when used as a SYSTEM; and

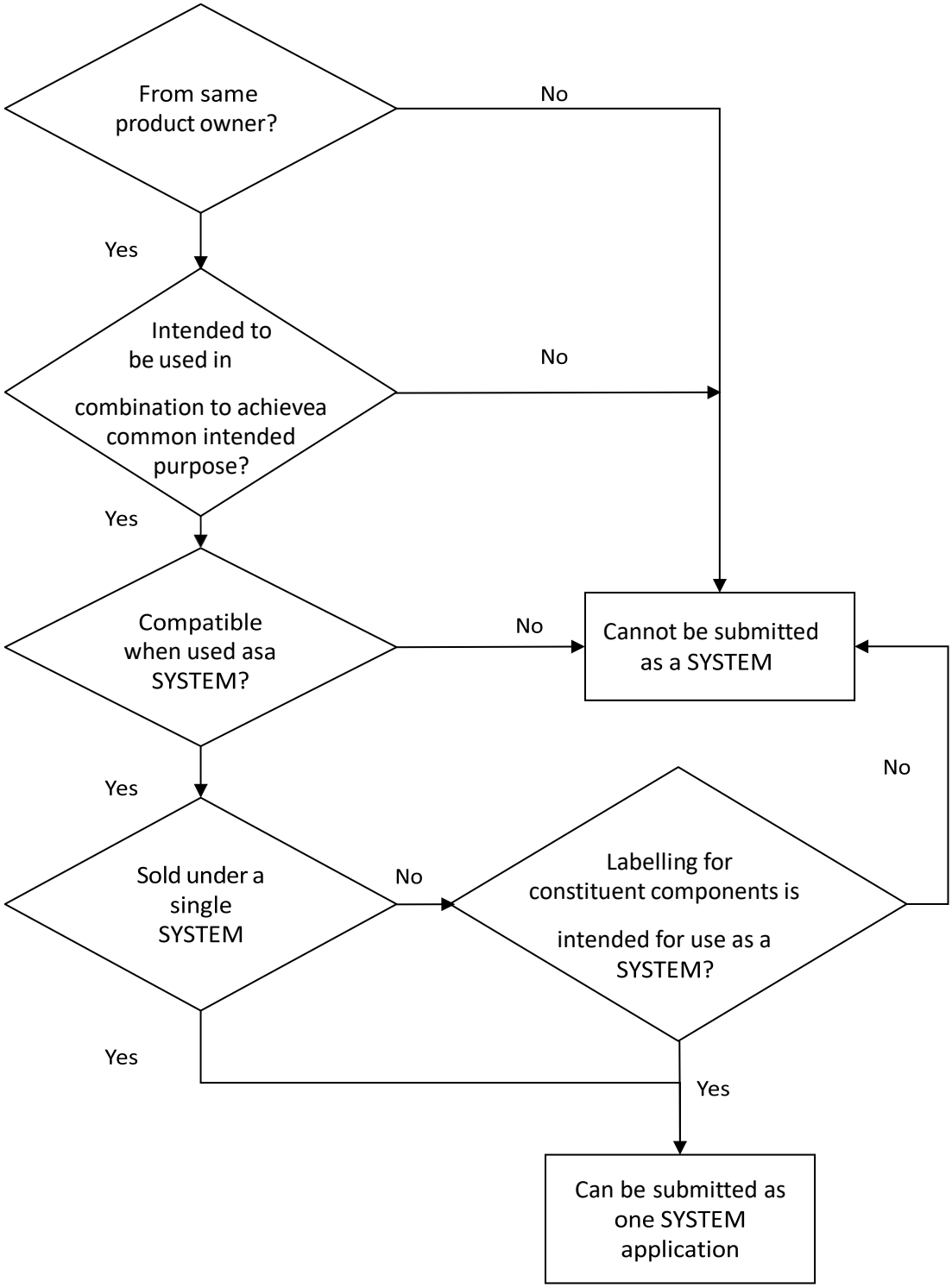
d) sold under a single SYSTEM name or the labelling, IFU, brochures or catalogues for each constituent component indicates that the constituent component is intended to be used together or for use with the SYSTEM.

3.4.1. Submission requirements for a System

Devices registered as part of a SYSTEM shall only be supplied specifically for use with that SYSTEM. Any device that is meant for supply for use with multipleSYSTEMs should be registered together with each of these other SYSTEMs. Alternatively, if these devices are compatible for use with one or multiple SYSTEMs from different product owners, they can be registered separately.

A single application shall be required for medical device system which shall be accompanied by a declaration of the different parts with function of each component in a system. Data submission shall be in accordance with the requirements provided for medical devices (Part V) and In Vitro Diagnostics (Part VI)

Decision Flowchart for Grouping of Medical Devices as a SYSTEM



An applicant, MAH or manufacturer of a medical device SYSTEM may incorporate medical devices and/or accessories from manufacturers as part of their SYSTEM to achieve the intended purpose of the device. These medical devices and/or accessories should be grouped together as a SYSTEM,and information on all these devices and accessories, such as

authorization from their product owners for registration with the SYSTEM, evidence on use and compatibility with the SYSTEM shall be submitted.

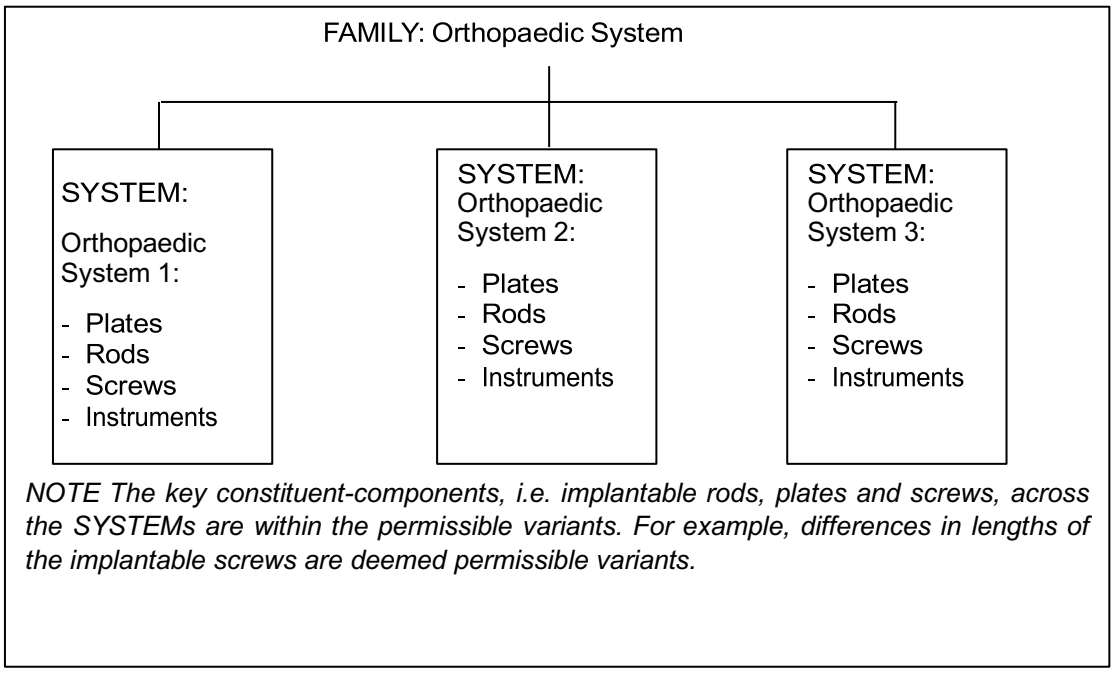
Example:

A patient monitoring SYSTEM from **manufacturer A** is intended to be used specifically with vital signs sensors and probes from **manufacturer B**. These accessories are used in combination to achieve a common intended purpose in accordance with **manufacturer A's** specifications, and can be grouped together with the patient monitoring SYSTEM in one application for registration.

In addition, if multiple SYSTEMs fulfil the following conditions to be grouped asa FAMILY, they may be grouped as a FAMILY (of SYSTEMs):

a) the SYSTEMs are from the same product owner;
b) the SYSTEMs are of the same risk classification;
c) the SYSTEMs have a common intended purpose;
d) the SYSTEMs have a common design and manufacturing process; and
e) key constituent components of the SYSTEMs have variations that are withinthe scope of the permissible variants.

Individual SYSTEM names may contain additional descriptive phrases.



NOTE The key constituent-components, i.e. implantable rods, plates and screws, across the SYSTEMs are within the permissible variants. For example, differences in lengths of the implantable screws are deemed permissible variants.

Examples:

- **A hip replacement SYSTEM** comprising of femoral and acetabular components can be grouped as a SYSTEM. The components must be used in combination to achieve a common intended purpose of total hip replacement. The size of the components may vary.
- **An electrosurgical unit and its accessories** that consist of forceps, electrodes, electrode holders, leads, plug adaptor, when used together for a common intended purpose, can be grouped as a SYSTEM.
- **A catheter placement set/kit** comprising of scalpels, syringes, needles, surgical gloves, gauze, drapes and flushing solution that is validated for compatibility and assembled by a single product owner under a single SYSTEM name for use in combination during a surgical catheter placementprocedure can be grouped as a SYSTEM.
- **Automated blood pressure monitors** with optional features such as memory storage and print capability for various models can be considered as part of a FAMILY of SYSTEMS.

3.5. IVD Test Kit

An IVD TEST KIT is an *in vitro* diagnostic device (IVDD) that consists of reagents or articles that are:

a) from the same manufacturer;

b) intended to be used in combination to complete a specific intended purpose;

c) sold under a single TEST KIT name or the labeling, instructions for use (IFU), brochures or catalogues for each reagent or article states that the component is intended for use with the IVD TEST KIT; and

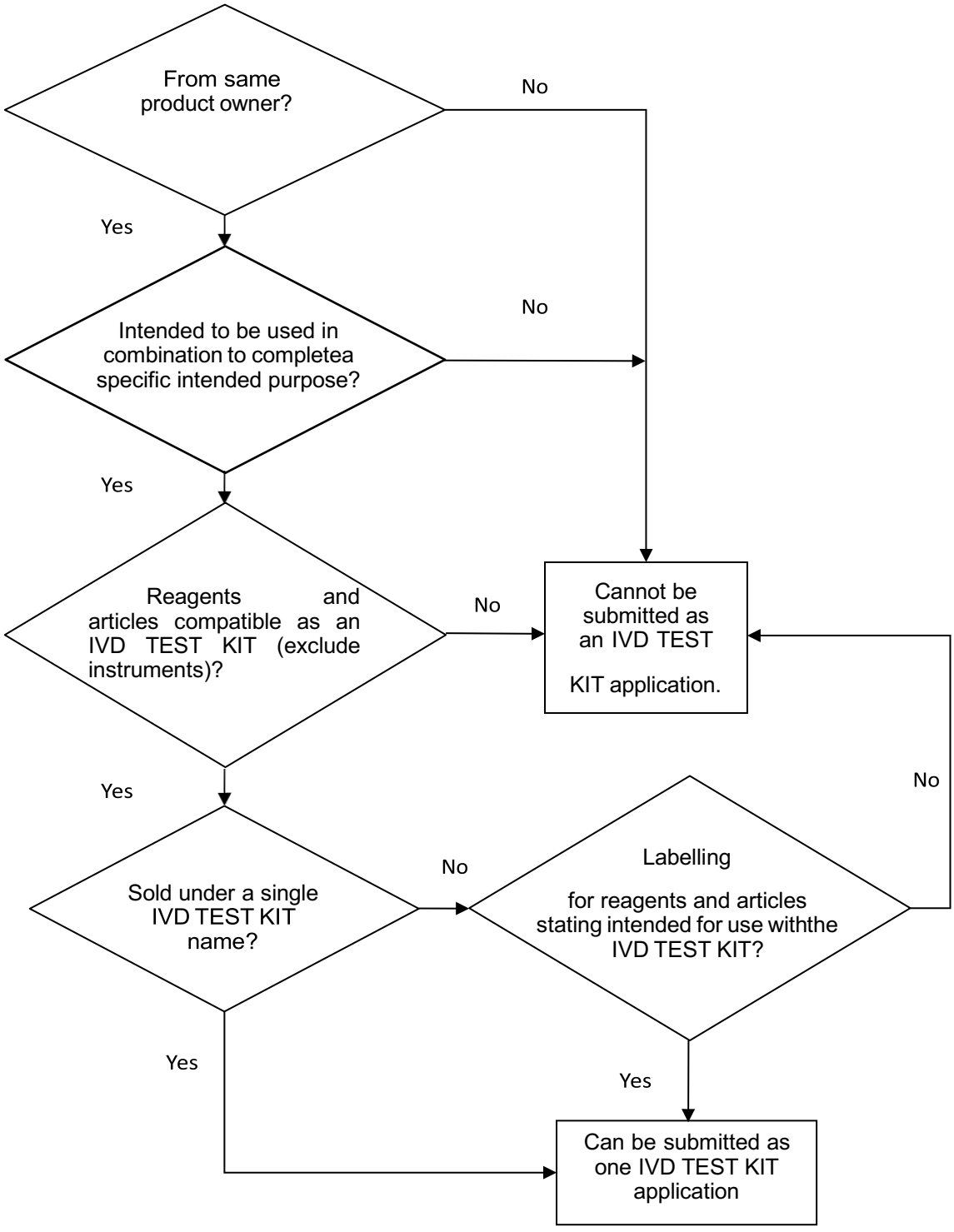
d) compatible when used as a TEST KIT.

An IVD TEST KIT <u>does not</u> include the instruments, such as analyzers, needed to perform the test.

An IVD Medical Device SYSTEM may typically consist of TEST KITs and instruments (e.g. an analyzer designed to be used with that TEST KIT). An IVD TEST KIT and its accompanying IVD analyzer can be listed together as an IVD SYSTEM **or** the IVD analyzer can be listed separately from the IVD TEST KIT(s) <u>as a SPLIT listing</u>.

<u>Example:</u> **A glucose monitoring SYSTEM** comprising of a glucose meter, test strips,control solutions and linearity solutions can be grouped as a SYSTEM.

Decision Flowchart for Grouping of Medical Devices as an IVD TEST KIT



Individual reagents or articles can be supplied separately as replacement items for the kit. If the reagents or articles in a TEST KIT are supplied for

use in more than one TEST KIT, such reagents or articles shall be included in the product registration application of each of the other TEST KITS.

Reagents or articles from another product owner may be grouped with the IVD TEST KIT if the applicant furnishes all information on these reagents or articles required for registration, such as authorization from the other product owners for registration and data to substantiate the performance of these reagents when used in the test kit.

Example: A **Human Immunodeficiency Virus (HIV) Enzyme Linked Immuno Sorbent Assay (ELISA) TEST KIT** may contain controls, calibrators and washing buffers. All the reagents and articles are used together to detect HIV and therefore can be grouped as a TEST KIT. These reagents and articles can be supplied separately as replacement items for that particular TEST KIT.

3.6. IVD Cluster

An IVD CLUSTER comprises of a number of *in vitro* diagnostic reagents orarticles that are:

a) from the same product owner;

b) is of the same risk classification (either Class A only or Class B only);

c) of a common test methodology as listed below; and

d) of the same IVD CLUSTER category as listed below.

The IVD CLUSTER may include analyzers that are designed for use with thereagents in the IVD CLUSTER.

Where IVD CLUSTERS also include the compatible IVD analyzer(s),an IVD TEST KIT and its accompanying IVD analyzer can be approved together asan IVD SYSTEM or the IVD analyzer can be listed separately from the IVD TEST KIT(s) as a SPLIT listing.

The IVD CLUSTER grouping is only to be used for product registration and would not be applicable as a grouping criterion for the addition of models through a Change Notification.

3.6.1. List Of IVD Cluster Categories

This list of IVD CLUSTER categories is only applicable to **Class A only or Class B only IVD** devices. It should be clearly stated in the label or IFUof each reagent or article that it is intended for use, whether alone or in combination, for the same category:

S/N	Methodology	CLUSTER Category(closed list)	Examples of Analytes(non-exhaustive list)
1	Clinical Chemistry	Enzymes	(i) Acid Phosphatase (ii) Alpha-Amylase (iii) Creatine Kinase (iv) Gamma-Glutamyl Transferase (v) Lactate Dehydrogenase (vi) Lipase
2		Substrates	(i) Albumin (ii) Bilirubin (iii) Urea/Blood Urea Nitrogen (iv) Cholesterol (v) Creatinine (vi) Glucose
3		Electrolytes Reagents	(i) Ammonia (ii) Bicarbonate (iii) Calcium (iv) Chloride (v) Magnesium (vi) Phosphate Inorganic/Phosphorus
4		Electrolyte Electrodes	(i) Ammonia Electrodes (ii) Carbon Dioxide (Bicarbonate) Electrodes (iii) Calcium Electrodes (iv) Chloride Electrodes (v) Magnesium Electrodes (vi) Potassium Electrodes

S/N	Methodology	CLUSTER Category (closed list)	Examples of Analytes (non-exhaustive list)

5		Substrate Electrodes/ Biosensors	(i) Creatinine Electrodes (ii) Glucose Electrodes (iii) Glycated Hemoglobin Electrodes (iv) Lactate Electrodes (v) Urea Electrodes (vi) Bilirubin Electrodes
6	Immunochemistry	Immunoglobulins (without IgE).	(i) Immunoglobulin A (ii) Immunoglobulin D (iii) Immunoglobulin G (iv) Immunoglobulin M (v) Immunofixation kits
7		Complement Components	(i) Complement Component C1q (ii) Complement Component C1 inactivator (iii) Complement Component C3/C3c (iv) Complement Component for Bb (v) Complement Component C4 (vi) Complement Component C5a
8		Transport Proteins	(i) Albumin (ii) Ceruloplasmin (iii) Haptoglobin (iv) Hemopixin (v) Lactoferrin (vi) Pre-albumin/Transthyretin
9		Lipoproteins	(i) Apolipoprotein A I (ii) Apolipoprotein A II (iii) Apolipoprotein B (iv) Apolipoprotein E Sub-typing (v) Lipoprotein (a)

S/N	Methodology	CLUSTER Category(closed list)	Examples of Analytes(non-exhaustive list)
10		Other Specific Proteins	(i) a1-Acid Glycoprotein (ii) a1-Antitrypsin (iii) a1-Microglobulin (iv) Fibronectin (v) Immuno Reactive Trypsin
11		Allergy	(i) Immunoglobulin E – Total (ii) Immunoglobulin E – Screen (iii) Immunoglobulin E – Specific, monotest/monoresult (iv) Allergen specific IgA (v) Allergen specific IgG
12		Cancer markers	(i) GI-marker CA242 (ii) p53
13		Thyroid Function Markers	(i) Free Triiodothyronine (ii) Free Thyroxine (iii) Thyroid Stimulating Hormone (iv) T – Uptake (v) Thyroglobulin (vi) Neonatal Thyroxine
14		Fertility/Pregnancy Hormones/ Proteins	(i) Androstenedione (ii) Estradiol (iii) Prolactin (iv) Human Placental Lactogen (v) Estriol

S/N	Methodology	CLUSTER Category(closed list)	Examples of Analytes(non-exhaustive list)
15		Diabetes Assays (Hormones)	(i) C-Peptide (ii) Glucagon (iii) Insulin (iv) Glycosylated/Glycated Haemoglobin (v) Islet Cell Ab (vi) Proinsulin
16		Renal Metabolism Assays	(i) Aldosterone (ii) Angiotensin I / II (iii) Angiotensin Converting Enzyme (iv) Cortisol (v) Renine
17		Bone and Mineral Metabolism Assays	(i) Bone Alkaline Phosphatase (ii) Calcitonin (iii) Cross-linked C-Telopeptides (iv) Cross-linkded N-Telopeptides (v) Cyclic Adenosin Monophosphate (vi) Hydroxyproline
18		Endocrine Hormones and Peptides	(i) Adrenocorticotropic Hormone (ii) Human Growth Hormone (iii) Insulin-like Growth Factor I (iv) Insulin-like Growth Factor Binding Protein 1 (v) Vasointestinal Peptide (vi) Vasopressin

19		Neuroendocrine Function Assays	(i) Bombesin (ii) 17-Hydroxy-Ketosterone (iii) β-Endorphin (iv) Neurotensin (v) Somatostatin (vi) Substance P

S/N	**Methodology**	**CLUSTER Category(closed list)**	**Examples of Analytes(non-exhaustive list)**
20		Other Individual and Specified Hormones	(i) Gastrin (ii) Gonadotropin-releasing hormone (iii) Melatonin (iv) Pepsinogen (v) Adrenalin (vi) Dopamine
21		Anaemia	(i) Erythropoietin (ii) Ferritin (iii) Folate (iv) Iron (v) Iron Binding Capacity (vi) Soluble Transferrin Receptor
22		Vitamins	(i) Vitamin B1 (ii) Vitamin B2 (iii) Vitamin B6 (iv) Vitamin B12 (v) Vitamin D (Cholecalciferol) (vi) Intrinsic Factor (BlockingAntibody)

23		Drug Monitoring	(i) Caffeine (ii) Benzodiazepines (iii) Penicillins (iv) Tetracyclines

S/N	Methodology	CLUSTER Category(closed list)	Examples of Analytes(non-exhaustive list)
24		Toxicology	(i) Amphetamines (ii) C ocaine (iii) Morphine (iv) Phencyclidine (v) Acetaminophen (vi) Catecholamines (vii) Ethanol (viii) Salicylate
25		Auto-immune Diseases	(i) Anti-nuclear antibodies (ANAs) (ii) Anti-topoisomerase (iii) Organ-specific autoantibodies (iv) Circulating Immuno-complex (v) TSH Receptor antibodies (vi) Anti-Cardiolipin antibodies
26		Rheumatoid-Inflammatory Diseases Markers	(i) Anti-Streptococcal Hyaluronidase (ii) Anti-Streptokinase (iii) Anti-Streptolysin O (iv) C-Reactive Protein (v) Anti-Staphylolysin (vi) Anti-Streptococcal Screening

27		Liver Function	(i) MEGX (ii) Carbohydrate DeficientTransferrin
28		Cardiac Markers	(i) Homocysteine (ii) ST2 (iii) Galectin-3 (iv) Myeloperoxidase (MPO)

S/N	**Methodology**	**CLUSTER Category(closed list)**	**Examples of Analytes(non-exhaustive list)**
29		Bacterial Infection - Immunology	*(i) Bacillus subtilis* *(ii) Pseudomonas Aeruginosa* *(iii) Helicobacter Pylori* *(iv) Lactobacillus casei*
30		Viral Infection - Immunology	(i) Norovirus (ii) Rotavirus (iii) Hantavirus
31		Parasitic Infection - Immunology	(i) *Leishmania*
32		Fungal Infection -Immunology	*(i) Candida albicans* *(ii) Aspergillus*

33	Haematology/ Histology/ Cytology (Blood tests for transfusions excluded)	Hemoglobin Testing	(i) Hemoglobin determinations(Total Hb) (ii) Fractional oxyhemoglobin (FO2Hb) (iii) Fractional carboxyhemoglobin (FCOHb) (iv) Fractional methemoglobin (FMetHb) (v) Fractional deoxyhemoglobin(FHHb)
34		General CoagulationTests	(i) Prothrombin Time (ii) Thrombin Time (iii) Activated Clotting Time (iv) Activated Partial ThromboplastinTime

S/N	**Methodology**	**CLUSTER Category(closed list)**	**Examples of Analytes(non-exhaustive list)**
35		Haemostasis (Coagulation)	(i) Fibrinogen (ii) Protein C and Protein S reagents (iii) C1-inhibitors (iv) Alpha-Antiplasmin (v) Fibrin (vi) Factor XIII (vii) Platelet Factor 4 (viii) Plasminogen
36		Other Hematology Tests	(i) Complete Blood count (ii) Hematocrit (iii) Erythrocyte Sedimentation rate

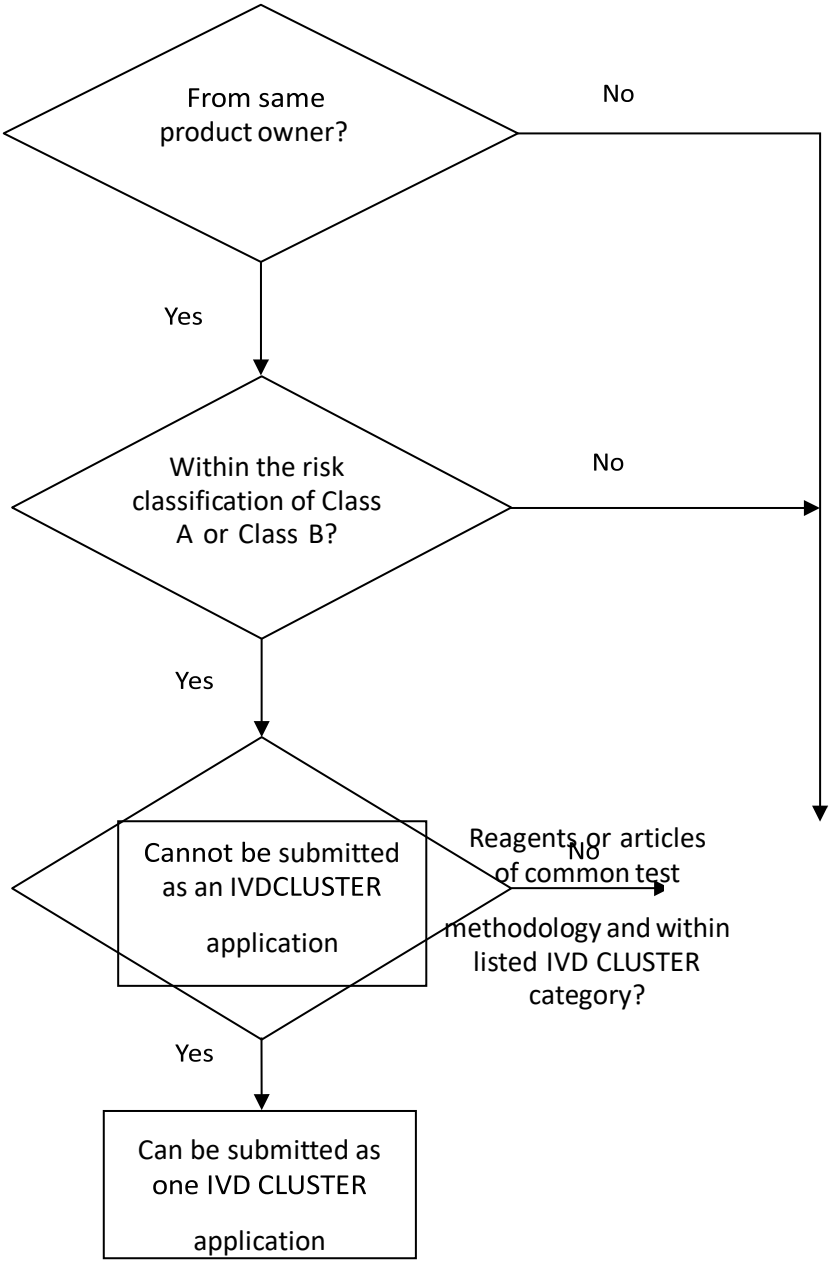
37		Cytokines (Lymphokines)/ Immunomodulators	(i) Interferons (ii) Soluble Antigens/Receptors (iii) Tumor Necrosis Factors (iv) Colony Stimulating Factors (v) Tumor Necrosis FactorsReceptors
38		Histology/ Cytology Reagents	(i) Cytochemical Staining (ii) Embedding, Fixing, Mountingmedia (iii) Stain solutions (iv) Immunohistology kits

S/N	**Methodology**	**CLUSTER Category(closed list)**	**Examples of Analytes(non-exhaustive list)**
39	Microbiology -culture	Culture Media	(i) Dehydrated culture media (DCM) (ii) Additives for DCM (iii) Prepared Media (Tubes, bottles,Plates) (iv) Cells, Media, Serum for Viralculture
40		Susceptibility Testing Testing for the susceptibility of thebacteria to certain antibiotics.	*(i)* Erythromycin susceptibility testfor *Staphylococcus aureus* (ii) Tobramycin susceptibility test for *Pseudomonas aeruginosa* (iii) Fungal susceptibility testing
41		Biochemical cultureIdentification (ID)	(i) Gram Negative Manual ID (ii) Gram Positive Manual ID (iii) Other ID Kits Manual -Anaerobes, Fastidious

		Immunological culture Identification(ID)	(i) Streptococci Grouping Slide tests (ii) Serotyping (Shigella etc.)
43		Nucleic Acid (NA) based culture identification (ID)	(i) Streptococci (ii) Shigella
44		Serological identification (ID)	For Parasitology and Mycology (Fungi and Yeast)
45		Bacterial Infections (Detection by NA Reagents)	(i) Streptococci (ii) Shigella

S/N	**Methodology**	**CLUSTER Category(closed list)**	**Examples of Analytes(non-exhaustive list)**
46		Viral Infections (Detection by NAReagents)	(i) Para-influenza NA Reagents
47		Fungal Infections	(i) Fungi NA Reagents (ii) Candida albicans (iii) Aspergillus

Decision Flowchart for Grouping of Medical Devices as an IVD CLUSTER



Information on all reagents or articles within an IVD CLUSTER must be submitted as part of the product registration application. Devices and articles that are listed as part of a CLUSTER can be supplied separately but solely for the registered intended purpose.

If a reagent or article is intended for multiple usage categories such that it can be grouped in more than one IVD CLUSTER, the Registrant can choose to group the reagent or article as part of any one of the IVD CLUSTERs it qualifies. Information to support all the intended purposes of the reagent or article mustbe submitted as part of the product registration

application.

3.7. Group

A medical device GROUP is a collection of two or more medical devices, that is labelled and supplied in **a single packaged unit** by a product owner.The medical device GROUP comprises of the following:

a) a single proprietary GROUP name;

b) labelled and supplied in a single packaged unit by the product owner; and

c) a common intended purpose.

For the purposes of grouping for product market authorization, the collection of medical devices in a GROUP is the **closed list** of devices included in a single submission. This closed list of medical devices in a GROUP (single packaged unit) may differ in the number (quantity) and combination (permutation within the closed list) of products that comprise the GROUP, while maintaining the same proprietary GROUP name and the GROUP's intended purpose.

Typically, for a medical device GROUP, the product owner intends to supply a collection of customized medical devices for a specific medical purpose within a single packed unit, such as a convenience pack or tray, which is under asingle name.

A product owner of the GROUP who assembles a GROUP together also assumes responsibility for the medical device GROUP and its intended purpose. The product owner of a medical device GROUP may incorporate medical devices obtained from other manufacturers/product owners as part oftheir GROUP to achieve the common intended purpose. In manufacturing and assembling this GROUP of medical devices, the evidence to substantiate the safety, quality and efficacy of the collection of devices shall be provided in the submission. Relevant information for submission may include sterility, shelf life, evidence on use and compatibility as a GROUP, quality management systems, etc. Labelling, particularly the instructions for use (IFU), where applicable, shall clearly describe the common intended purpose of the GROUP.

Only medical devices within a GROUP that are eventually approved as a single product shall be supplied on the market as a single packaged unit under the GROUP name.

If a medical device in a GROUP is supplied for use in another GROUP, such a medical device shall be included in the registration application of that other GROUP.

When the GROUP is registered, the product owner is able to customise

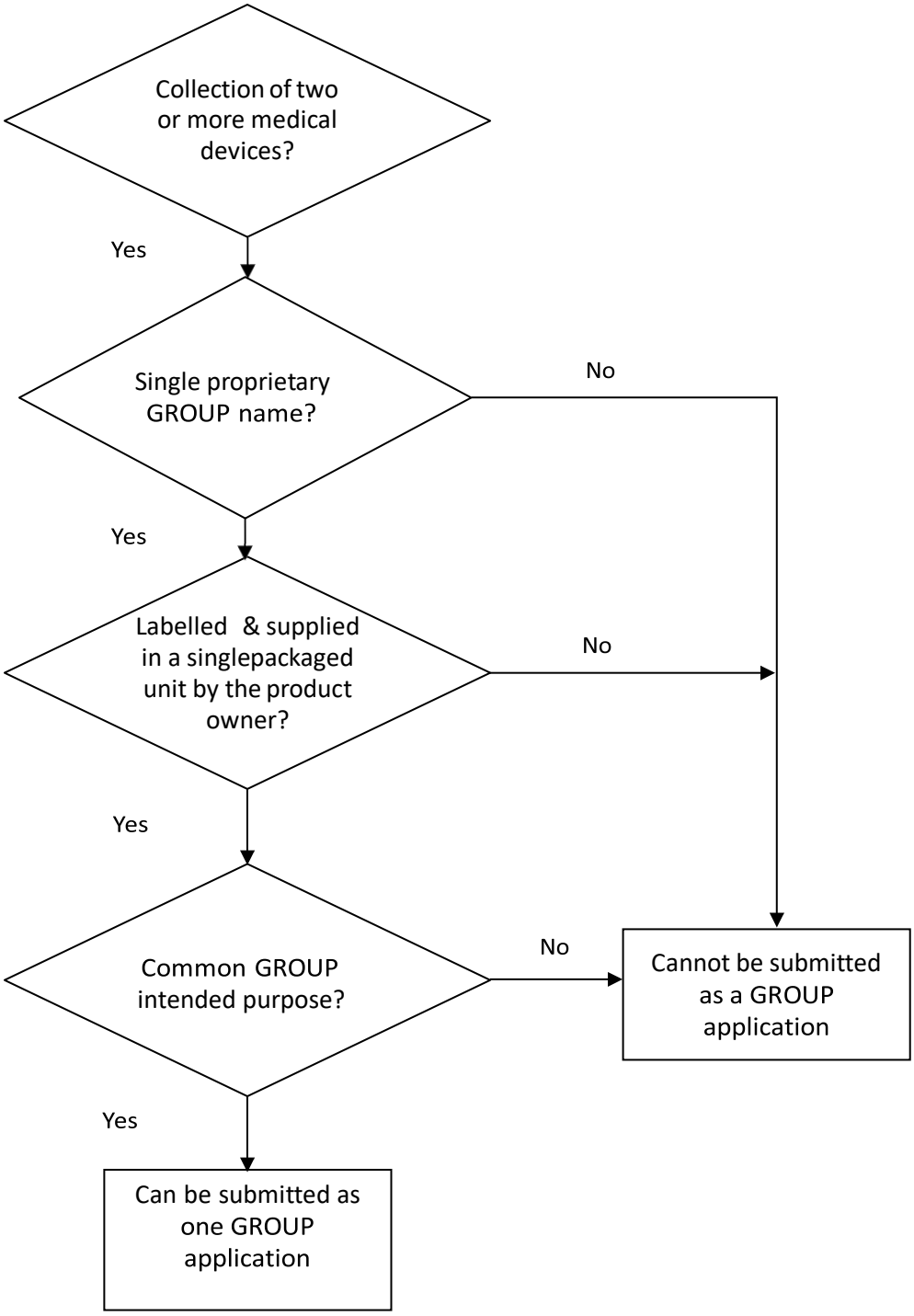
for supply, in a single packaged unit, from the closed list of devices for particular hospitals or physicians, while maintaining the same GROUP name and intended purpose. Thus, when the medical device GROUP is registered, any other single packaged unit combination (permutation of devices within the closed list) of devices in that GROUP can be supplied on the market for the registered intended purpose of the GROUP.

The GROUP name indicated for the medical device must appear in the productlabel affixed on the external package of the GROUP. The content list of devices within the single packaged unit for supply should also appear on the external package of the GROUP or supplied with the GROUP. Individual medical devices in the GROUP do not require to be labelled with that GROUP name. Individual medical devices in the GROUP may contain additional descriptive phrases.

Examples:

- A **first aid kit** consisting of medical devices such as bandages, gauzes, drapes and thermometers, when assembled together as one package for a common medical purpose by a product owner, can be grouped as a GROUP.
- A product owner supplies **dressing trays customized** with different quantity and type of gauze and sutures to different hospitals. When the closed list of medical devices in the GROUP are registered, the product owner is able to customize the trays, from the list of devices, for other hospitals, while maintaining the same GROUP name for the trays and the registered intended purpose. The product label for the trays shall bear the content list of devices within the package for supply. Some of the medical devices in the GROUP may be individually packaged and labelled, while others remain in bulk form and may not be labelled. The product owner shall account for these during the assembling of the GROUP and ensure compliance to existing regulatory requirements including traceability of individual devices packaged into the trays and record keeping.
- A **promotional pack or convenience pack**, without a GROUP name and without a common medical intended purpose, consisting of different number of medical devices, for example multi-purpose solution, saline solution, and contact lens case, will NOT qualify as a GROUP registration. Individual medical devices shall require registration as SINGLE medical devices.

Decision Flowchart for Grouping of Medical Devices as a GROUP



3.7.1. Submission requirements for a Group

A separate and complete dossier shall be required to be submitted for each single medical device or each device in a medical device group. The content of each dossier shall be in line with requirements for submissions of medical device or In-vitro diagnostic.

3.8. Single

A SINGLE medical device is a medical device from a manufacturer identified by a medical device brand name with a specific intended purpose. Medical devices that cannot be assigned to a FAMILY, SYSTEM, IVD TEST KIT, IVD CLUSTER, GROUP or any other device specific grouping category must be registered individually.

A SINGLE medical device is sold as a distinct packaged entity and may also beoffered in a range of package sizes.

Examples:

- Condoms that are sold in packages of 3, 12 and 144 can be grouped as a SINGLE medical device when submitting for registration.
- A company manufactures a standalone software program that can be used with a number of CT scanners produced by other product owners. The standalone software program itself is deemed a medical device, which can be used on different scanners. The software can be grouped as a SINGLE medical device.

  Requirements for submissions for single device shall follow requirements for submissions of medical device (Part V) or In-vitro diagnostic (Part VI)

PART X

GUIDELINES FOR SOFTWARE MEDICAL DEVICES

INTRODUCTION

Software plays an increasingly important role in medical devices as many medical devices rely on software for safe and effective function and for interoperability with other devices. In addition, emerging technologies like Artificial Intelligence and the Internet of Things (IOT) are being increasingly adopted for clinical applications, which introduces new and complex challenges (e.g. cybersecurity) to manufacturers who are developing medical device software.

To address this, all software medical device manufacturers are recommended to adopt an approach to managing the rapid changes in technology. This will include requirement management, risk assessment, software verification and validation, change management, traceability, and various aspects throughout a software's life cycle. This guideline is to be read in conjunction with National policy and Guidelines on Cyber Security stipulated by e-Government Agency which are accessed under www.ega.go.tz

1.1. Objective

These guidelines will provide clarity on the regulatory requirements for software medical devices in their entire life cycle. The requirements are presented starting from product development, all the way to post-market duties following product introduction in the market.

It is important to note that these guidelines reflect current thinking and practice, and should not be misconstrued as a new regulatory control on software medical devices.

1.2. Intended Audience

The document is intended for stakeholders who are involved in software medical device development and /or supplying such devices in Tanzania.

1.3. Scope

This document applies to software with an intended use that falls under the definition of a medical device as stipulated in the *TMDA Act. This will include software which is intended for medical purposes such as investigating, detecting, diagnosing, monitoring, treating or managing any medical condition, disease, anatomy or physiological process.*
This includes software supplied in the following forms:

Forms of Software	Examples
Software embedded in medical devices	• Imaging software in a diagnostic ultrasound system • Software to deliver pacing/defibrillation in a pacemaker/ ICD
Standalone software	• Image processing software that run-on general-purpose computer workstation(s) for the reviewing and diagnosis of x-ray images

Standalone mobile applications	• Mobile application running on a mobile computing device that is intended to remotely monitor a patient's vital signs For more examples, *please refer to Regulatory Guidelines for Telehealth Products. The guidelines can be found at https://www.hsa.gov.sg/medical-devices/guidance-documents*
Web-based software	• A software application that can be accessed through a web browserwhere users are able to upload patient images for diagnostic purposes without installation on their computing device

This document applies to the software of all risk classifications and is intended to cover regulatory requirements spanning the entire product life cycle. Additionally, it addresses key software-related regulatory requirements such as cybersecurity and requirements for Artificial Intelligence (AI) medical devices. These guidelines will also be reviewed and updated from time to time with the emergence of new software-related technologies and evolving risks.

Overall, the following topics will be covered in this document:

1.1.1 Pre-market product registration requirements
1.1.2 Change notification
1.1.3 Cybersecurity
1.1.4 Artificial Intelligence

1.4. Definitions

ARTIFICIAL INTELLIGENCE (AI): refers to a set of technologies that seek to simulate human traits such as knowledge, reasoning, problem solving, perception, learning and planning.

AI-MEDICAL DEVICE (AI-MD): an artificial intelligence application intended to be used for medical purposes, such as investigation, detection, diagnosis, monitoring, treatment or management of any medical condition, disease, anatomy or physiological process.

CLINICAL EVALUATION: The assessment and analysis of clinical data pertaining to a medical device to verify the clinical safety and performance of the medical device when used as intended by the productowner.

CYBERSECURITY: preservation of confidentiality, integrity and availability of information in the Cyberspace.

MANUFACTURE: in relation to a health product, means to make, fabricate, product or process the health product and includes:-

- any process carried out in the course of so making, fabricating, producing or processing the healthproduct; and

- the packaging and labelling of the health product before it is supplied.

MOBILE APPLICATION: a software application that runs on smartphones and other mobile communication devices.

OFF-THE SHELF (OTS) or COMMERCIALLY-OFF-THE-SHELF (COTS) SOFTWARE: refers to pre-built and ready-made software usually from commercial supplier.

PRODUCT OWNER: in relation to a health product, means a person who:

- supplies the health product under his own name, or under any trade mark, design, trade name or other name or mark owned or controlled by him; and
- is responsible for designing, manufacturing, assembling, processing, labelling, packaging, refurbishing or modifying the health product, or for assigning to it a purpose, whether those tasks are performed by him or his behalf.

REGISTRANT: in relation to a registered health product, means the person who applied for and obtained the registration of the health product under this *Act*.

STANDALONE SOFTWARE (also known as SaMD in IMDRF context): a software and/or mobile application that is intended to function by itself and are not intended for use to control or affect the operation of other hardware medical devices.

2.0 PRE-MARKET PRODUCT REGISTRATION REQUIREMENTS

Product registration applications for medical devices submitted to the Authority must be prepared in the format set out in the particular guidelines. The various sections of the dossier and the respective contents are presented in the *Guidelines on Submission of Documentation for Registration of Medical Devices and Guidelines on Submission of Documentation for Registration of In Vitro Diagnostics*. These guidelines can be found on the TMDA website.

This section provides guidance for particular sections of the dossier where there may be specific requirements for software medical devices. Following are the sections covered here:

- Essential Principles for the safety and performance of medical devices
- Labelling requirements
- Software versioning and traceability
- Software verification and validation
- Clinical evidence
- Risk management
- Supporting documents for cybersecurity

2.1. Essential Principles for Safety and Performance of Medical Devices

All medical devices must be designed and manufactured to ensure that they are

safe and perform as intended throughout the product life cycle. The Essential Principles for Safety and Performance checklist describes the fundamental design and manufacturing requirements. The design and manufacturing requirements that are relevant to a particular medical device must be identified and where requirements are deemed not applicable, the rationale has to be documented. This applies to all medical devices, including Class A medical devices.

The developer of a medical device can refer to the Essential Principles for Safety and Performance of Medical Devices available in the Guidelines on Submission of Documentation for Registration of Medical Devices and Guidelines on Submission of Documentation for Registration of In Vitro Diagnostics.
The essential design and manufacturing principles that may be relevant to software medical devices are listed in Table 1 against the respective forms of software for reference.

Essential design and manufacturing principles	**Software embedded in medical devices**	**) Standalone software i) standalone mobile applications (iii) Web-based software**
Essential Principles applicable to medical devices and IVD medical devices		
General requirements	√	√
Clinical evaluation	√	√
Chemical, physical and biological properties	If applicable	
Sterility, packaging and microbial contamination	If applicable	
Considerations of environment and conditions of use	√	√
Requirements for active medical devices connected to or equipped with an energy source	√	
Medical devices that incorporate software or are standalone software or mobile applications	√	√
Medical devices with a diagnostic or measuring function	√	√
Labelling and Instructions for use	√	√
Protection against electrical, mechanical and thermal risks	√	
Protection against radiation	√	
Protection against the risks posed by medical devices intended for use by lay persons		√

Medical devices incorporating materials of biological origin	If applicable	
Essential Principles applicable to medical devices other than IVD medical devices		
Particular Requirements for Implantable Medical Devices	√	
Protection against the Risks Posed to the Patientor User by Medical Devices Supplying Energy or Substances	√	
Medical Devices Incorporating a Substance Considered to be a Medicinal Product/Drug	√	
Essential Principles applicable to IVD medical devices		
Performance Characteristics	√	√

Table 1: Essential design and manufacturing principles

2.2. Labelling Requirements

Device labelling (e.g. physical label, instructions for use, implementation manual etc.) serves to help users: (i) identify the device; (ii) communicate safety and performance-related information; and (iii) ensure device traceability. Essential information such as the name of the device, software version number and product owner's information have to be presented on device labels for identification of the device. For safety and performance information, the intended purpose, instructions on proper use and safety information (e.g. contraindications) have to be clearly presented for users' reference.

Standalone software can be supplied in different forms and there may be difficulties in presenting device information for certain forms (e.g. web-based software). Generally, standalone software can be broadly categorized into two groups based on the mode of supply: i) supplied in physical form or ii) supplied without a physical form. The table below summarizes the minimum labelling information to be included for standalone software supplied in either one of the two aforementioned ways.

Supplied in physical form (i.e. CD/DVD)	Supplied without any physical form (i.e. downloadable software, web-based software)
Physical label and Instructions for Use	A screenshot of the software graphical interface (e.g. splash screen) which displays the elements for identification, including the software version number. In addition, for downloadable software where the downloading and installation are to be done by the end-user, the following information should be presented to the end user: a) Internet address or web link to allow the end-user to download the software; b) The software download procedure; and c) The software installation guide or procedure. This ensures that the user has sufficient information for the proper installation of such downloadable software. Although the software is supplied without physical form, the traceability of the software should not be compromised. An appropriate system for version controls and access rights controls should be in place to allow timely tracing of the software versions.

Table 2: Labelling requirements for the different forms of standalone software.

Please refer to *section 4: Guidelines on Submission of Documentation for Registration of Medical Devices and Guidelines on Submission of Documentation for Registration of In Vitro Diagnostics* for more information about labelling requirements for medical devices. The guidelines can be found on the TMDA website.

2.3. Software Versioning and Traceability

Software versioning is essential for identification and post-market traceability/follow-up in the event of software changes and field safety corrective actions. A description of the software versioning and traceability system implemented for the software may be required during the registration process.

In addition, information on the software version being registered and to be supplied

in Tanzania is to be clearly presented on the device labelling (if supplied in physical form) or software graphical interface (if supplied without physical form), depending on the mode of supply of the software. The software version information that represents all software changes/alterations (e.g. graphic interface, functionality, bug fixes) has to be submitted. This does not include Software version numbering that is **solely** for testing or internal use only (e.g. checking in of source code).

2.4. Design Verification & Validation

Software medical devices should be designed to ensure accuracy, reliability, precision, safety and performance, while fulfilling their intended use. Analytical validation is the process of generating objective evidence to support the safety and performance of the software medical device.

The analytical validation of software medical device(s) generally should be performed during the verification and validation phase of the software development life cycle. The software verification process ensures that software specifications are met, by demonstrating that the design inputs generate the expected design outputs. The software validation process serves to ensure that the specifications capture the user's needs.

Software Verification & Validation report should include the results of all verification, validation and tests performed in-house and/or in a simulated user environment for the software prior to its final release. It should also provide objective evidence that demonstrates specified requirements are fulfilled and that defined software specifications conform to user needs and intended use. Reference to International Standards such as *IEC 62304: Medical device software – Software life cycle processes* is encouraged to demonstrate conformity to the essential requirements.

Any unresolved anomalies and deviations after the verification and validation testing must be appropriately reviewed and addressed. Assessment and justification for accepting these deviations and unresolved anomalies must be documented and provided during submission as well.

In cases where the software version number tested in the validation reports is different from the version for registration, a comparison of the two versions of the software together with the applicability and relevance of the report to the version for registration to be provided. The need for specific validation to address significant differences between the two versions has to be considered.

Medical devices are also becoming increasingly inter-connected. Hence, for medical devices that work together or in conjunction with other medical devices or systems, issues relating to the interoperability between such medical devices or systems have to be carefully considered and addressed as appropriate. Measures to ensure safe, secure and effective transfer and utilization of information among these medical devices or systems have to be in place.

2.5. Clinical Evaluation

While software verification and validation ensure that specified software system requirements and users' needs are met, clinical evaluation of software medical devices is conducted to support the safety and effectiveness of the software when used in the intended clinical environment.

The clinical evaluation process establishes that there is a valid clinical association between the software output and the specified clinical condition according to the product owner's intended use.

Clinical association refers to the extent to which the software's output (concept, conclusion, measurements) is clinically accepted or well-founded (existence of an established scientific framework or body of evidence) that corresponds accurately in the real world to the healthcare situation and condition referred in the software's defined intended purpose.

The association between the software output and clinical condition can be substantiated by one or more of the following examples:

2.1.1 Referencing existing literature and well-established clinical guidelines;

2.1.2 Comparison with similarly established software medical devices in the market and/or;

2.1.3 Performing clinical studies for novel claims (e.g. new targeted population, new clinical condition)

In addition to establishing a valid clinical association, the software medical device should also be validated for its ability to generate accurate, reliable and precise output in the intended clinical environment, of the targeted patient population. Measures of clinical validation include sensitivity, specificity, positive and negative predictive values etc.

Table 4 below summarises the type of clinical evidence recommended to support the clinical evaluation process for software medical devices. The level of clinical evidence required depends on the significance of the information generated by the software medical device (to treat or diagnose, drive clinical management or inform clinical management) and the state of the healthcare situation or condition.

Device Characteristics	**Treat and Diagnose** Provide information that is the sole determinant to treat or diagnose a disease or condition.	**Drive Clinical Management** Provide information for aid in treatment, aid in the diagnosis, triage or identify early signs of a disease or condition that will be used to guide the next diagnostics or next treatment interventions.	**Inform Clinical Management** Provide information that is used in preventing/mitigating a disease or condition or to supplement the clinical management of a disease or condition. Such information will not trigger an immediate or near-term action.
Critical Situations or conditions where accurate and/or timely diagnosis or treatment action is vital to avoid death, long-term disability or other serious deterioration of health of an individual patient or to mitigate impact to public health.	• Literature Reviews • Clinical Experience • Clinical Studies	• Literature Reviews • Clinical Experience	• Literature Reviews • Clinical Experience

Serious Situations or conditions where accurate diagnosis ortreatment is of vital importance to avoid unnecessary interventions (e.g., biopsy) or timely interventions are important to mitigate long term irreversible consequences on an individual patient's health condition or public health.	• Literature Reviews • Clinical Experience • Clinical Studies	• Literature Reviews • Clinical Experience	• Literature Reviews • Clinical Experience
Non-Serious Situations or conditions where anaccurate diagnosis and treatment are important but not critical for interventions to mitigate long-term irreversible consequences on anindividual patient's health condition or public health.	• Literature Reviews • Clinical Experience • Clinical Studies	• Literature Reviews • Clinical Experience	• Literature Reviews • Clinical Experience

Table 3: Clinical evidence requirements for the software.

Where the software is assigned a novel intended purpose or is intended for use in new target populations, manufacturers should generate an appropriate association of the software output to the clinical condition/physiological state using clinical evidence described in Table 3.

It is important to note that clinical evaluation should be an ongoing process throughout the software life cycle. After the software medical device has been

deployed in the market, data should be collected to verify that the software continues to meet safety and effectiveness claims. Such continuous monitoring of the real-world clinical performance post-market allows for the timely detection of new or evolving risks arising from the use of the software and to assess and update the risk-benefit assessment, where necessary. In addition, this may result in changes to the software (e.g. design change) or labelling (e.g. limitations of use) to enhance its safety and/or performance or to address risks or limitations in a timely manner.

Please refer to GN-20 Guidance on Clinical Evaluation for more information about the presentation of clinical evidence for the purpose of product registration.

2.6. Risk Management

Risk management should review and address all foreseeable risks and failure modes of the software in its product life cycle. Risk assessment and evaluation should commensurate with the complexity and risk classification assigned to the software and also the defined intended purpose for the software. The principles described in "*ISO 14971 Medical Devices — Application of Risk Management to Medical Devices"* should be followed. In general, a systematic approach should be adopted in risk management:

(i) identify all possible hazards, (ii) assess the associated risks, (iii) implement mitigations or controls to reduce risks to acceptable level and (iv) observe and evaluate effectiveness of mitigation measures.

For embedded software, the evaluation should also be based on the medical device system, which includes the hardware components.

Where there are changes made to a software, these should be systematically evaluated to determine if any additional risk could arise from these changes. Where necessary, additional risk control measures should be considered.

2.7. Cybersecurity

Minimum necessary requirements concerning hardware, IT networks characteristics and IT security measures, including protection against un-authorised access, necessary to ensure the safe use of the software as intended should be implemented. For connected medical devices (e.g. with wireless features or internet-connected and network-connected functions), the following information should be submitted during product registration:

i. Cybersecurity control measures in place (e.g. design controls)
ii. Cybersecurity vulnerabilities (known and foreseeable), risk analysis focusing on assessing the risk of patient harm and mitigation measures implemented;
iii. On-going plans, processes or mechanisms for surveillance, timely detection and management of the cybersecurity related threats during the useful life of the device, especially when a breach or vulnerability is detected in the post-market phase.
iv. Evidence that the security of the device/ effectiveness of the security controls have been verified. It should contain the following information where applicable:
    a. Descriptions of test methods, results, and conclusions;
    b. A traceability matrix between security risks, security controls, and testing to verify those controls; and
    c. References to any standards and internal SOPs/documentation used.

Please refer to *section 8* for details on overall cybersecurity management for software medical devices.

2.8. Importance of Cybersecurity

Cybersecurity is critical in today's interconnected world, with medical devices becoming more connected (e.g. wireless, Internet, or network-connected). Cybersecurity attacks can fatally disrupt medical devices availability and/or functionality, and may render hospital networks unavailable, delaying patient care. Only with competent cybersecurity, medical devices functionality and safety can be effectively protected. For software medical devices that has the capability to communicate/connect with other systems, it is crucial for manufacturers to consider an effective cybersecurity strategy that addresses all possible cybersecurity risks not only during development but throughout the useful life of the software medical device.

Cybersecurity especially for medical devices cannot be achieved by a single stakeholder, it requires the concerted effort of diverse stakeholders (government agencies,

manufacturers, healthcare institutions, users of medical devices). Continuous monitoring, assessing, mitigating and communicating cybersecurity risks and attacks requires active participation by all stakeholders in the ecosystem.

2.8.1. Cybersecurity Considerations

When developing a software medical device, a cybersecurity plan should be devised to include the following considerations, (non-exhaustive): (i) a secure device design, (ii) having proper customer security documentation, (iii) conduct cyber risk management, (iv) conduct verification and validation testing and, (v) having an on-going plan for surveillance and timely detection of emerging threats

2.8.2. Secure Device Design

Cybersecurity should be considered from the early stages of device design and development. Manufacturers should take into account all possible cybersecurity hazards and consider design inputs that could reasonably secure the device and prevent, detect, respond and where possible recover from foreseeable cyber risks. Below are some possible design considerations.

Figure 8: Cybersecurity design considerations (non-exhaustive)

2.8.3. Customer Security Documentation

Besides supplying the end users with the Instructions for use (IFU) on the appropriate usage of the medical device, manufacturers should also consider providing a customer security documentation to communicate the relevant security information to mitigate

cybersecurity risks when operating the medical device in its intended use environment. The following information should be considered in the Customer Security Documentation (by the manufacturer):

- End users should be informed on the possible cybersecurity hazards that the software medical device poses. There should also be advice given on how and what they can do to mitigate the risk of those cybersecurity hazards (e.g. connecting only to protected network, anti-virus, firewall). This information to the end users could also be presented in the instruction manual or label of the device.

- Recommended infrastructure requirements to support the device in its intended use environment.

- A list of network ports and other interfaces that are expected to receive and/or send data, and a description of port functionality and whether the ports are incoming or outgoing. This may allow users to consider disabling unused ports to prevent unauthorised access to the device.

- The procedures to download and install updates from the manufacturer.

- Information, if known, concerning device cybersecurity end of support. This will allow the users to understand their responsibilities and device risks after the device has exceeded its end of support period.

3.0 ARTIFICIAL INTELLIGENCE MEDICAL DEVICES (AI-MD)

This section presents some additional regulatory considerations specific to medical devices incorporating Artificial Intelligence (AI) technology from a medical device regulatory standpoint. This includes AI applications, with medical purpose, that is incorporated into a hardware medical device. Please refer to section 1.3 for the various form of medical devices which can incorporate AI technology.

Developers and implementers of AI-MDs are to ensure that there are measures in place to ensure the responsible development and deployment of AI-MD. Other relevant legislation and guidelines applicable to the development and deployment of AI-MD in healthcare should be complied with. For e.g.:
Personal Data Protection Act
Human Biomedical Research Act
Healthcare Services Act

3.1. Regulatory Requirements for AI-MD

The regulatory principles for AI-MDs are comparable to software that are regulated as medical devices However, there are specific additional considerations such as continuous learning capabilities, level of human intervention, training of models, retraining etc. for AI-MD that need to be considered carefully and addressed.

All activities related to the design, development, training, validation, retraining and deployment of AI- MD should be performed and managed under an ISO 13485 based quality management system (QMS). Please refer section 2 in this document for further information.

The block diagram below illustrates the process of developing and deployment of the AI-MD.

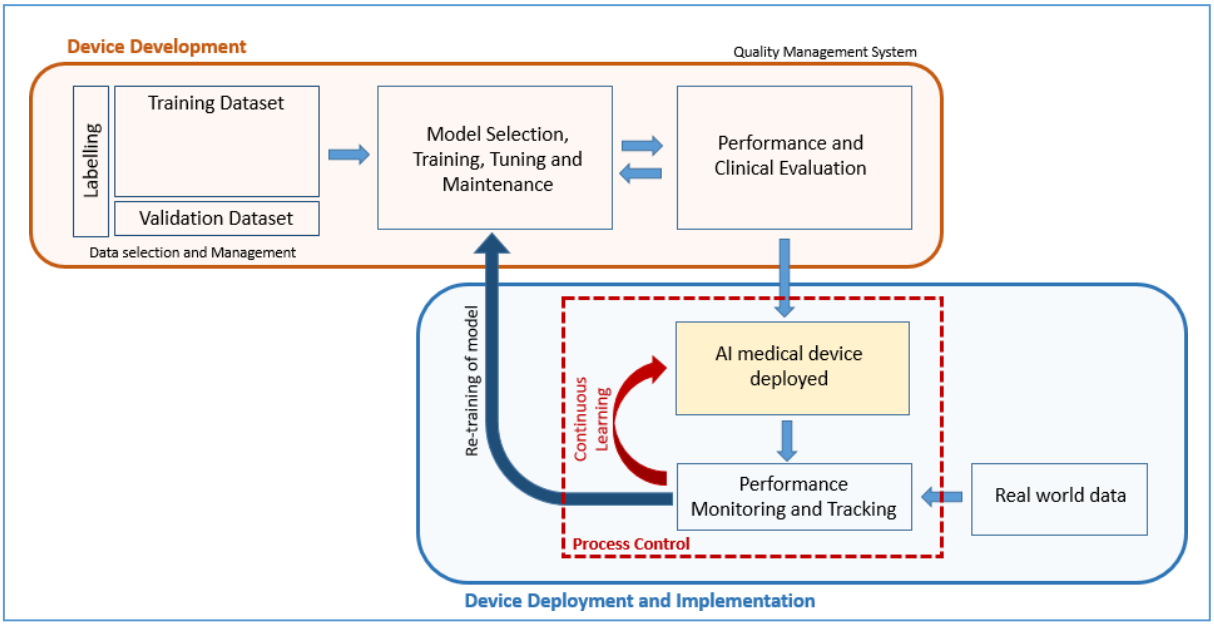


Figure 9: Typical illustration of an AI model

The following additional information should be submitted for pre-market registration of AI-MDs.

Requirements	Description
Dataset	
Input data and features/ attributes used to generate the corresponding output	This should include the various input data and features/ attributes selected for the AI-MD to generate the corresponding output result. This can be in the form of diagnostic images, patient's historical records, physiological signals, medication records, handwritten text by healthcare professionals, literature reviews, etc. The specifications or acceptance criteria for selecting the input data and features/ attributes have to be defined. In the event that pre-processing (e.g. signal pre-processing, image scaling,) of data is required, the process should be clearly defined and included in the submission. The rationale has to be provided for the pre-processing steps applied to the input data.

Source, size and attribution of training, validation and test datasets	The source and size of training, validation and test dataset should be provided. Information on labelling of datasets, curation, annotation or other steps should be clearly presented. Description on dataset cleaning and missing data imputation should be provided. Developer should also ensure that there is no duplication in training and validation datasets. Rationale for the appropriateness and adequacy of the dataset selected and possible factors that can potentially influence the output result must be provided. In addition, all potential biasness in selecting the training and validation dataset should be adequately addressed and managed.
AI Model	
AI model selection	A description on the machine learning model (e.g. convolutional neural network) used in the AI-MD, including any base model (e.g. Inception V3 model), should be provided. Appropriateness of the model for the AI-MD's intended purpose should be presented. Any limitations of the model and where applicable mitigating measures to manage any shortcomings should also be explained. Model evaluation should be performed using a test dataset that is separate from the training dataset. Metrics (e.g. classification accuracy, confusion matrix, logarithmic loss, area under curve (AUC)) selected to evaluate the performance of the machine learning model selected should be provided, including the results of model evaluation.
Performance and Clinical Evaluation	
Test protocol and report for verification and validation of the AI-MD, including the acceptance limits and information on the anomalies identified	Based on the performance specification of the AI-MD, the test protocol and test report should be provided. Please refer to section 3 of this document and where applicable this information should be provided. Information on control measures to detect extremes/outliers should be provided. Any limitation of the AI-MD and the operating system must be clearly evaluated and also communicated as appropriate to the user in the product labelling or instruction manual.
Performance of the AI-MD (e.g. diagnostic sensitivity/specificity /reproducibility where applicable	The performance specification such as accuracy, specificity and sensitivity of the device should be provided (e.g. Accuracy 90%, Sensitivity 91-93%, Specificity 95%). Validation and verification test report(s) has to be provided to substantiate such performance claims.

Clinical Association between the AI-MD's output and clinical conditions must be presented	Presence of a valid clinical association between the AI-MD's output and its targeted clinical condition should be presented. Please refer to Section 3.5 for more information.
Deployment	
Device workflow including how the output result should be used	The intended or recommended workflow during the deployment of the device should be presented and explained. When there is human intervention in the system (human-in- the-loop), the workflow should clearly indicate the degree of intervention and the stage(s) in the workflow for the intervention.
The interval for the training data update cycle (e.g. in months or years)	AI-MD (fixed-version) and these datasets are used to re-train the subsequent models of the AI-MD, information on the interval for training data update cycle has to be provided. If a new set of data collected changes the original specification and performance of the device, a Change Notification should be submitted to the Authority. Similar to other software, a Change Notification will be required for changes to registered AI-MDs. This includes any changes to the performance specifications, input data types, device workflow, degree of human intervention, choice of AI model, etc. The decision flow presented in section 5 of this document is also applicable to AI-MDs.
Software version to be supplied and the procedure or plan implemented to trace the software version for subsequent iterations	For the purpose of post-market traceability, the exact AI-MD version to be supplied and explanation on how the version numbers are designated and traced should be provided.

Table 7: Additional considerations for product registration for AI-MD

3.2. Additional Considerations for AI-MD with Continuous Learning Capabilities

AI-MD with continuous learning capabilities has the ability to change its behaviour post deployment. The learning process should be defined by the manufacturer and appropriate process controls should be put in place to effectively control and manage the learning process. For example, there should be appropriate quality checks to ensure that the quality of learning datasets are equivalent to the quality of the original training datasets. There should be validation processes incorporated within the system to closely monitor the overall learning and the evolving performance of the AI-MD post-learning. This is important to ensure that the learning does not compromise the defined specifications or output of the AI-MD. As the AI-MD with continuous learning capabilities can automatically change its behaviour post deployment, it is essential for the manufacturer to ensure there is a robust process control in place. This can ensure that the performance of the AI-MD does not deteriorate over time.

For continuous learning AI-MDs, complete information on the learning process including the process controls, verification, ongoing model monitoring measures shall be clearly presented for review in the application for registration of the AI-MD. The following information (non-exhaustive) in addition to those requirements described in Table 7 should be submitted.

- Description on the process of continuous learning of the AI-MD during deployment.

- Safety mechanism (can be built into the system) to detect anomalies and any inconsistencies in the output result and how these are mitigated. This can include process to detect and roll-back to the previous algorithm version which includes criteria by which the system is measured against (baseline).

- During deployment, the AI-MD will learn from real world data. The source, datatype collected, data pre-processing steps and parameter extracted should be defined to ensure there are no biasness in the process. The inclusion and exclusion criteria should be listed and this should be identical to the attributes of the original training dataset

- Process to ensure data integrity, reliability and validity of the new data set used for learning

- Software version controls should be in place as the system has the potential for frequent updates and the possibility for roll-back to the previous version in each of the deployment sites.

  If the AI-MD is deployed in a decentralized environment, there should be robust processes in place to address the risks involved in such a decentralized model. Other process controls for consideration include maintaining traceability, performance monitoring and change management.

- Process to ensure traceability between real world data for training, learning process, software version number and the AI-MD's output during clinical use. When there are inaccurate results during deployment due to bias real-world data, the manufacturer must be able to trace back to the specific data and remove such data from the AI model and retrain the models as necessary.

- Validation strategy and verification activities for continuous learning to ensure the performance is within the pre-defined boundaries / envelope

3.3. Cyber Risk Management

When managing cybersecurity risks, the principles described in ISO 14971 should also be followed. There may be some device specific cybersecurity risk involved but generally, manufacturers should include the following in their risk management plan: (i) identify all possible cybersecurity hazards, (ii) assess the associated risks, (iii) implement mitigations or controls to reduce risks to acceptable level and, (iv) observe and evaluate effectiveness of mitigation measures.

The risk management process should be carried out consistently throughout the software life cycle and there should be proper documentation (e.g. a report). Some critical components that should be incorporated into the risk management plan are as follows:

Employing tools such as threat modelling to identify vulnerabilities and develop mitigation after risk evaluation.

Cybersecurity risk management process should be conducted in parallel with safety risk management. The overall patient safety should be considered when introducing security measures prevent any unintentional patient harm. For instance, implementing multi-factor authentication before accessing a CT device, might cause the device to not be readily accessible during emergency, as such, an emergency mode may be considered to address the safety risk.

Establishing an on-going program for monitoring and surveillance of threats and vulnerabilities. If new cybersecurity vulnerabilities are discovered, manufacturers are strongly recommended to conduct vulnerability risk assessment to evaluate the potential for patient harm and compromise of device performance. The vulnerability can be analysed by taking into consideration (i) the exploitability of the vulnerability, and (ii) the severity of user/patient harm if the vulnerability were to be exploited. This can be achieved by using established vulnerability scoring methodology such as the Common Vulnerability Scoring System (CVSS). Additionally, this assessment should consider the existing compensating controls and mitigating measures to determine if the overall cybersecurity risk involved is of acceptable or unacceptable residual risk. If it is deemed that additional mitigating measures or compensating controls are required to mitigate the risk, manufacturer shall practice vulnerability disclosure to communicate to all affected users & stakeholders effectively. Such information could include identification of affected devices, vulnerability impact, mitigations/ compensating controls etc.).

- Monitoring all software (including 3rd party software) for new vulnerabilities and risks which may affect the safety and performance of the device.

- Implementing a process for timely detection and analysis of vulnerabilities and threats, including impact assessment and follow-up actions to take e.g. containment of threats, communication to affected parties, fixing of vulnerabilities.

3.4. Verification and Validation

Implemented cybersecurity risk control methods should be verified and validated against specified design requirements or specifications prior to implementation. The features and functions should remain operative for device to carry out its intended use even with the presence of those residual cybersecurity risks. Some possible cybersecurity tests include malware test, structured penetration test, vulnerability scanning etc.

3.5. On-going plan for surveillance and timely detection of emerging threats

As medical device systems are becoming more complex, the nature of cybersecurity threats has also evolved rapidly. Healthcare systems are especially vulnerable, given the number of medical devices that are connected to the hospital networks.

It is therefore, not possible to rely solely on premarket controls to mitigate all cybersecurity risks. Manufacturers of software medical devices should establish a comprehensive and structured cybersecurity risk management plan for the entire software life cycle.

Manufacturers should have an initiative to actively survey and detect possible threats as part of their post-market plan. There should be a plan outlined by the manufacturers on

how they can actively monitor and respond to evolving and newly identified threats.

Key considerations for this post-market plan include:

Post-market Vigilance	A plan to proactively monitor and identify newly discovered cybersecurity vulnerabilities, assess their threat, and respond
Vulnerability Disclosure	A formalized process for gathering information from vulnerability finders, developing mitigation and remediation strategies, and disclosing the existence of vulnerabilities and mitigation or remediation approaches to stakeholders.
Patching and Updates	A plan outlining how software will be updated to maintain ongoing safety and performance of the device either regularly or in response to an identified vulnerability
Recovery	A recovery plan for either the manufacturer, user, or both to restore the device to its normal operating condition following a cybersecurity incident.
Information sharing	Involve in the communication and sharing of updated information about security threats and vulnerabilities. For example, participation in Information Sharing Organizations (e.g., ISAOs, ISACs and etc.).

Table 6: Cybersecurity post-market planning

3.6. Patient Confidentiality and Privacy and Other Regulations

Medical device cybersecurity incidents can affect patient safety and privacy. There are increasing reports of breaches of data privacy. Software medical device developers, implementers and users should always be vigilant in handling confidential patient data. Local legislation and regulations on data protection and privacy should be complied with (e.g., TCRA Personal Data Protection Act). Please take note that it is the responsibility of the manufacturers and distributors to ensure that the medical device meets the requirements of any other applicable regulatory controls in Tanzania.

PART XI

GUIDELINES FOR BORDERLINE PRODUCTS

1.0 Introduction

The guideline is developed to address the dilemma that may arise when grouping certain ambiguous products as medical devices. This ambiguity may arise for products that do not meet the classic characteristics of medical devices or for products that may not have an immediate therapeutic application.

This guidance clarifies the demarcation between products that fall under the regulatory framework as stipulated in the Tanzania Medicines and Medical Devices Regulations for Control of Medical Products, 2015 and Registration of Medicinal Products, 2015. Thus, it aims at ensuring that there is a clear understanding of how borderline products that may be toeing the line between medicines and medical devices be addressed when it comes to marketing authorization.

2.0 Scope

This guidance applies to all products that may pose difficulty when being distinguished from medicinal products or cosmetics. This aims to guide applicants in determining whether such products fall under the regulatory framework of medical devices or medicinal products.

3.0 General principles and definitions

Borderline products are those where it is not clear from the outset whether they fall under the definition of medical devices, medicines or cosmetics. In order to fall under the umbrella of a medical device, it must fulfil the definition of a medical device and be excluded from the definition of a drug, pharmaceutical or medicinal product as per TMDA Act. It is therefore necessary to examine both sets of prerequisites.

Grouping a product as a medical device or a medicinal product will impact the market authorization procedure that the Authority will employ. Therefore, it is imperative that applicants confirm the type of product prior to lodging applications.

The definitions of relevant terminologies that should be used when concluding on whether the product is a medical device are reproduced here for reference. It should be noted that definitions for pharmacological, immunological or metabolic means are intended to provide guidance as to the meaning of these terms in the context of determining the principal mode of action of the product.

Medical device or device means an instrument, apparatus, laboratory equipment and reagents, implement, machine, appliance, implant, medical equipment, contrivance, in-vitro reagent or calibrator, software, material or other similar or related article which-

a) is intended by manufacturer to be used, alone or in combination for human beings or other animals for one more of the specific purpose(s) of-
b) diagnosis, prevention, monitoring, treatment or alleviation of diseases or compensation for an injury;
c) investigation, replacement, modification or support or the anatomy or of a physiological process;
d) supporting or sustaining life;
e) control of conception;
f) disinfection of medical devices;
g) providing information for medical or diagnostic purposes by means of in vitro examination or specimens derived from the human body or other animal; and does not achieve its primary intended action in or on the human body by pharmacological,

immunological or metabolic means, but which may be assisted in its intended function by such means.

Accessory for a medical device *means an article which, whilst not being itself a medical device, is intended by its manufacturer to be used together with one or several particular medical device(s) to specifically enable the medical device(s) to be used in accordance with its/their intended purpose(s) or to specifically and directly assist the medical functionality of the medical device(s) in terms of its/their intended purpose(s).*

Ancillary action of a medical device: the effect of the product on the body that completes (assists) the principal action to optimize performance, but is not necessary for achieving the claimed performance.

Medicinal product: *(a) Any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or*
(b) Any substance or combination of substances which may be used in or administered to human beings or animals either with a view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action.

Principal mode of action: The principal mode of action represents the means by which the product achieves its principal intended action, i.e. pharmacological, immunological, metabolic, physical or other. It is and must be based on state of the art scientific data.

Although the manufacturer's claims are important, it is not possible to place the product in one or other regulatory category in contradiction with current scientific data. Manufacturers will be required to justify scientifically in the technical file their rationale for the qualification of their product. A product cannot be qualified as a medical device within the meaning of the TMDA Act if it cannot be determined that the product's principal intended action is achieved by other than pharmacological, immunological or metabolic means. References to or making available by the manufacturer of information or data on safety or performance of the product is not relevant for the determination of its regulatory status.

Pharmacological means: is understood as an interaction typically at a molecular level between a substance or its metabolites and a constituent of the human body which results in initiation, enhancement, reduction or blockade of physiological functions or pathological processes. Examples of constituents of the human body may include, among others: cells and their constituents (cell membranes, intracellular structures, RNA, DNA, proteins, e.g. membrane proteins, enzymes), components of extracellular matrix, components of blood and components of body fluids. Examples of action via pharmacological means:

a) interaction between a ligand (e.g. agonist, antagonist) and a receptor;
b) interaction between a substance and membrane lipids;
c) interaction between a substance and components of the cytoskeleton.

Immunological means is understood as an action initiated by a substance or its metabolites on the human body and mediated or exerted (i.e. stimulation, modulation, blocking, replacement) by cells or molecules involved in the functioning of the immune system (e.g. lymphocytes, toll-like receptors, complement factors, cytokines, antibodies). Examples of action via 'immunological means':

a) replacement, reconstitution or introduction of natural or modified immune cells ormolecules;
b) triggering an immune response against the targeted tissues, cells or antigens

by immune-specific recognition;
c) targeting action of other linked or coupled substances.

Examples of substances acting via immunological means: vaccine, tetanus anti-serum, monoclonal antibodies, CAR-T cells, anti-venom, C1 esterase inhibitor.

When immunological recognition is used to target or direct the effects of linked or coupled substances, this recognition cannot be considered an ancillary action. Such products would therefore be deemed to act via immunological means and cannot be considered a medical device.

Metabolic means is understood as an action of a substance or its metabolites which involves an alteration, including stopping, starting or changing the rate, extent or nature of a biochemical process, whether physiological or pathological, participating in, and available for, function of thehuman body.

The term 'biochemical processes' is understood as reactions available for the human body including anabolic and catabolic reactions and transport of substances between compartments. An interaction with a known receptor is not a prerequisite for the metabolic means of action. Examples of action via 'metabolic means':

a) the movement of water due to active transport of electrolytes mediated by e.g. Na/KATPase pumps;
b) inhibition of endogenous enzymes, including the digestive enzymes;
c) altering the electrolyte balance of the serum.

The definitions above should be read in conjunction with the following notes.

Substance*: Any matter irrespective of origin which may be: human, e.g. human blood and human blood products; animal, e.g. micro-organisms, whole animals, parts of organs, animal secretions, toxins, extracts, blood products; vegetable, e.g. micro-organisms, plants, parts of plants, vegetable secretions, extracts; chemical, e.g. elements, naturally occurring chemical materials and chemical products obtained by chemical change or synthesis."*

This definition of substance includes cells or molecules involved in functioning in the immune system.

Diagnosis is the process of investigation of the anatomy, morphology, the condition or the functions of the human body irrespective if these are physiological or pathological, and subsequent interpretation of this information with a view to determining possible abnormalities. In this context investigation can include visualisation, detection or measurement.

4.0 Substance-based Medical Devices

A substance-based medical device is a medical device which is composed of substances that are permitted in a medical device, and does not achieve its principal intended action by pharmacological, metabolic or immunological means.

It should be noted that there may be ancillary pharmacological, metabolic or immunological action of one or more of the substance(s) the device is made of. The assessment of the ancillary nature of the pharmacological, immunological or metabolic action of such substances is a crucial element for the qualification of the product as a

medical device. Such devices may be similar in formulation to a medicinal product and may also be used in a similar way to a medicinal product *e.g.* ingested or applied to the skin. Substances that are not permitted in medical devices include, but are not limited to:

a) viable biological material or viable organisms, including living micro-organisms,bacteria, fungi or viruses;
b) viable animal tissues or cells or their derivatives;
c) viable human tissues and cells or their derivatives.

5.0 Medical Device and Medicinal Product Combinations

Some medical devices are intended for use with a medicinal product in different configurations. For such products to be considered a medical device, the medicinal product should an integral part of the device. In this incidence, the medicinal product is considered as an integral part of the device if it's presence is necessary to complete the functioning of the device.

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An **integral product** consists of at least two constituent parts, one of which is a device, which are combined (e.g. physically, chemically) in such a manner that they form a single entity when placed on the market. Nevertheless, it should be noted that,

a) If the relevant combination takes place at the time of administration, the product is not considered integral.
b) Medical devices co-packaged with a medicinal product, devices referenced in the medicinal product information, or medicinal products referenced in the information suppliedwith the device, are not considered integral products.
c) Devices for administration of medicinal products where the medicinal product is supplied separately are not integral products.
d) A device intended to administer a medicinal product and the respective medicinal product form a **single integral product**, if and only if the device and the medicinal product form an integral entity when placed on the market and, furthermore, the product is intended exclusively for use in the given combination and which is not reusable. A **single integral product** consists of at least two constituent parts, one of which is a device and the other a medicinal product, which are combined in such a manner that they are not intended to be separated prior to administration.

When deciding on the regulatory status of a product combination, the first step is establishing whether the product under consideration is an integral product according to the explanations provided above. As a second step, it should be determined if the action of the medicinal product incorporated in the device is principal or ancillary to that of the device part of the integral product.

If the principal intended action of the integral product is achieved by the substance, the entire product is regulated as a medicinal product, however if the principal intended action is achieved by the medical device the product is regulated as a medical device incorporating a medicinal product which has an ancillary action to that of the device.

6.0 Aesthetic medical devices

Aesthetic medical devices are devices that may not have an inherent medical purpose or therapeutic indication/use however they are utilized in a manner or has characteristics or risks that are comparable to those of medical devices. These include products used for cosmetic surgeries and other aesthetic procedures.

Aesthetic medical devices are regulated based on their intended use and whether they impact the structure or function of the body. Examples of aesthetic medical devices that are commonly used in the beauty industry are liposuction equipment, colored contact lenses, dermal fillers, collagen implants, tattoo removal equipment and skin resurfacing equipment.

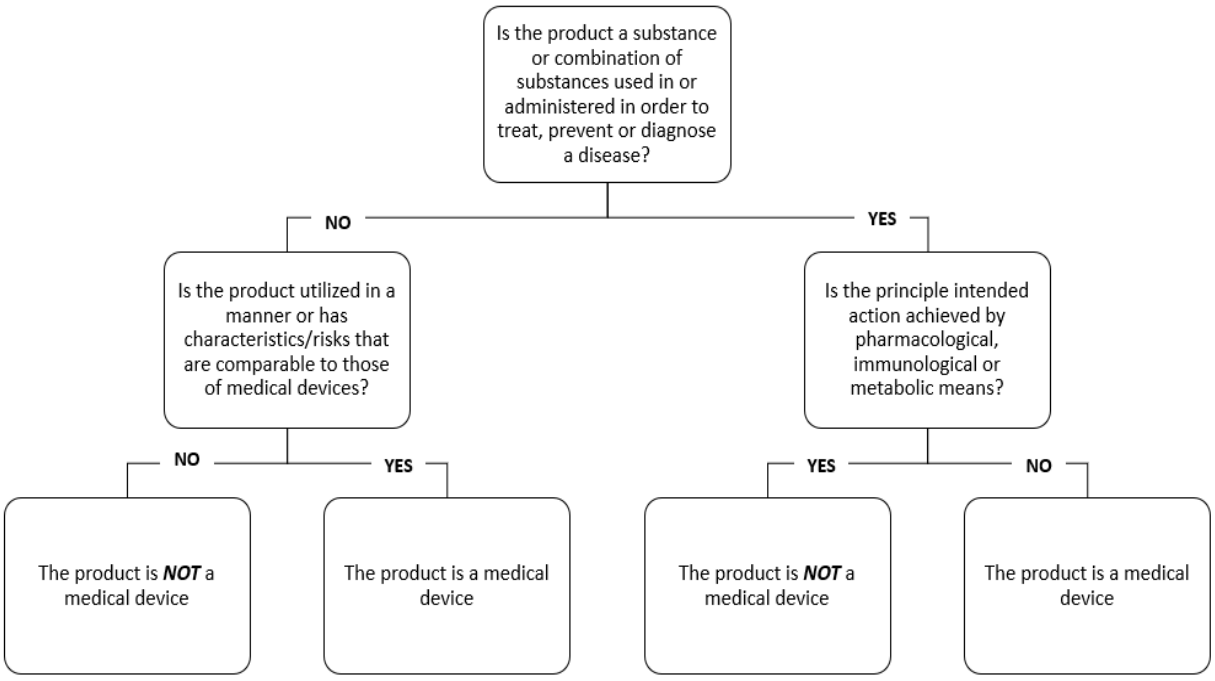
Applicants and manufacturers are required to consult the guidelines on classifications of medical devices (Part X of this compendium) prior to submission of an application for market authorization of these products.

7.0 Determining if a product fulfils the definition of a medical device

The definition of a medicinal product comprises two limbs, one relating to presentation and the other to function. A product constitutes a medicinal product if it is covered by one or the other or both of those limbs.

The first limb of this definition indicates that any substance presented as having properties for treating or preventing disease in human beings may be a medicinal product. In accordance with the TMDA Act, medical devices may also be intended to treat and prevent disease, along with other specific medical purposes. Therefore, the decisive criterion for the demarcation between the two categories is the second limb of the medicinal product definition, which concerns the 'principal mode of action' of the product.

Flowchart for determining if a product fulfils the definition of a medical device



Annex I

ESSENTIAL REQUIREMENTS CHECK LIST				
Brand name: _____		**Common name:**	**Risk class:** _____	
	Essential Principal	**Applicable to the device?**	**Method of Conformity**	**Identity of Specific Documents**
1	**ESSENTIAL PRINCIPLES APPLICABLE TO ALL MEDICAL DEVICES AND IVD MEDICAL DEVICES** The essential design and manufacturing principles listed in this Section are applicable to medical devices and IVD medical devices.			
1.1	**General Requirements**			
1.1.1	Medical devices and IVD medical devices should achieve the performance intended by their manufacturer and should be designed and manufactured in such a way that, during intended conditions of use, they are suitable for their intended purpose. They should be safe and perform as intended, should have risks that are acceptable when weighed against the benefits to the patient, and should not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons.			

1.1.2	Manufacturers should establish, implement, document and maintain a risk management system to ensure the ongoing quality, safety and performance of the medical device and IVD medical device. Risk management should be understood as a continuous iterative process throughout the entire lifecycle of a medical device and IVD medical device, requiring regular systematic updating. In carrying out risk management manufacturers should: a. establish and document a risk management plan covering each medical device and IVD medical device; b. identify and analyse the known and foreseeable hazards associated with each medical device and IVD medical device; c. estimate and evaluate the risks associated with, and occurring during, the intended use and during reasonably foreseeable misuse; d. eliminate or control the risks referred to in point (c) in accordance with the requirements of points 5.1.3 and 5.1.4 below; e. evaluate the impact of information from the production and postproduction phases, on the			

	overall risk, benefit-risk determination and risk acceptability. This evaluation should include the impact of the presence of previously unrecognized hazards or hazardous situations, the acceptability of the estimated risk(s) arising from a hazardous situation, and changes to the generally acknowledged state of the art. f. based on the evaluation of the impact of the information referred to in point (e), if necessary, amend control measures in line with the requirements of points 1.1.3 and 1.1.4 below.			
1.1.3	Risk control measures adopted by manufacturers for the design and manufacture of the medical device and IVD medical device should conform to safety principles, taking account of the generally acknowledged state of the art. When risk reduction is required, manufacturers should control risks so that the residual risk associated with each hazard as well as the overall residual risk is judged acceptable. In selecting the most appropriate solutions, manufacturers should, in the following order of priority: a. eliminate or appropriately reduce risks through safe design and manufacture; b. where appropriate, take adequate protection measures, including alarms, if necessary, in relation to risks that cannot be eliminated; and c. provide information for safety (warnings/precautions/contra-indications) and, where appropriate, training to users			

1.1.4	The manufacturer should inform users of any relevant residual risks			
1.1.5	In eliminating or reducing risks related to use, the manufacturer should: d. appropriately reduce the risks related to the features of the medical device and IVD medical device and the environment in which the medical device and IVD medical device are intended to be used (e.g. ergonomic/usability features, tolerance to dust and humidity); and e. give consideration to the technical knowledge, experience, education, training and use environment and, where applicable, the medical and physical conditions of intended users.			
1.1.6	The characteristics and performance of a medical device and IVD medical device should not be adversely affected to such a degree that the health or safety of the patient and the user and, where applicable, of other persons are compromised during the expected life of the device, as specified by the manufacturer, when the medical device and IVD medical device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained and calibrated (if applicable) in accordance with the manufacturer's instructions.			
1.1.7	Medical devices and IVD medical devices should be designed, manufactured and packaged in such a way that their characteristics and performance, including the integrity and cleanliness of the product and when used in accordance with the intended use, are not adversely affected by transport and storage (for			

	example, through shock, vibrations, and fluctuations of temperature and humidity), taking account of the instructions and information provided by the manufacturer. The performance, safety, and sterility of the medical device and IVD medical device should be sufficiently maintained throughout any shelf-life specified by the manufacturer			
1.1.8	Medical devices and IVD medical devices should have acceptable stability during their shelf-life, during the time of use after being opened (for IVDs, including after being installed in the instrument), and during transportation or dispatch (for IVDs, including samples).			
1.1.9	All known and foreseeable risks, and any undesirable side-effects, should be minimized and be acceptable when weighed against the evaluated benefits arising from the achieved performance of the device during intended conditions of use taking into account the generally acknowledged state of the art.			
1.2	**Clinical Evaluation**			
1.2.1	Where appropriate and depending on jurisdictional requirements, a clinical evaluation may be required. A clinical evaluation should assess clinical data to establish that a favorable benefit-risk determination exists for the medical device and IVD medical device in the form of one or more of the following: a. clinical investigation reports (for IVDs, clinical performance evaluation reports) b. published scientific literature/reviews c. clinical experience			

1.2.2	Clinical investigations should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. These principles protect the rights, safety and well-being of human subjects, which are the most important considerations and shall prevail over interests of science and society. These principles shall be understood, observed, and applied at every step in the clinical investigation. In addition, some countries may have specific regulatory requirements for pre-study protocol review, informed consent, and for IVD medical devices, use of leftover specimens.			
1.3	**Chemical, Physical, and Biological Properties**			
1.3.1	Regarding chemical, physical, and biological properties of a medical device and IVD medical device, particular attention should be paid to the following: a. the choice of materials and substances used, particularly with respect to: – toxicity; – biocompatibility; and – flammability; b. the impact of processes on material properties, c. where appropriate, the results of biophysical or modelling research whose validity of which has been demonstrated beforehand; d. the mechanical properties of the materials used, reflecting, where appropriate, matters such as strength, ductility, fracture resistance, wear resistance and fatigue resistance; e. surface properties; and			

	f. the confirmation that the device meets any defined chemical and/or physical specifications.			
1.3.2	Medical devices and IVD medical devices should be designed, manufactured and packaged in such a way as to minimize the risk posed by contaminants and residues to users and patients, taking account of the intended purpose of the medical device and IVD medical device, and to the persons involved in the transport, storage and use of the medical device and IVD medical device. Particular attention should be paid to tissues of users and patients exposed to those contaminants and residues and to the duration and frequency of exposure.			
1.3.3	The medical device and IVD medical device should be designed and manufactured in such a way as to appropriately reduce the risks posed by substance egress (including leaching and/or evaporation), degradation products, processing residues, etc. Special attention should be given to leaking or leaching of substances, which are carcinogenic, mutagenic or toxic to reproduction			
1.3.4	The medical device and IVD medical device should be designed and manufactured in such a way as to appropriately reduce the risks posed by the unintentional ingress of substances into the device, taking into account the medical device and IVD medical device and the nature of the environment in which it is intended to be used.			

1.3.5	Medical devices and IVD medical devices and their manufacturing processes should be designed in such a way as to eliminate or to appropriately reduce the risk of infection to users and all other persons who may come in contact with the medical device and IVD medical device. The design should: a. allow for easy and safe handling; b. appropriately reduce any microbial leakage from the medical device and IVD medical device and/or microbial exposure during use; c. prevent microbial contamination of the medical device and IVD medical device or its content (e.g., specimens); and/or d. appropriately reduce the risks from unintended exposure (e.g., cuts and pricks (such as needle stick injuries), eye splashes, etc.).			
1.4	**Sterilization and Microbial Contamination**			
1.4.1	Where necessary, medical devices and IVD medical devices should be designed to facilitate their safe cleaning,			
1.4.2	Medical devices and IVD medical devices labeled as having a specific microbial state should be designed, manufactured and packaged to ensure that they remain in that state when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.			
1.4.3	Medical devices and IVD medical devices, delivered in a sterile state should be designed, manufactured and packaged in accordance with appropriate procedures, to ensure that they are sterile when placed on the market and that, unless the packaging			

	which is intended to maintain their sterile condition is damaged, they remain sterile, under the transport and storage conditions specified by the manufacturer, until that packaging is opened at the point of use. It should be ensured that the integrity of that packaging is clearly evident to the final user (for example, through the use of tamper-proof packaging).			
1.4.4	Medical devices and IVD medical devices labelled as sterile should be processed, manufactured, packaged, and sterilized by means of appropriate, validated methods. The shelf-life of these medical devices and IVD medical devices should be determined by validated methods.			
1.4.5	Medical devices and IVD medical devices intended to be sterilized, either by the manufacturer or user, should be manufactured and packaged in appropriate and controlled conditions and facilities.			
1.4.6	Where the medical devices and IVD medical devices are provided non-sterile and are intended to be sterilized prior to use: a. the packaging system should minimize the risk of microbial contamination and should be suitable taking account of the method of sterilization indicated by the manufacturer; and b. the method of sterilization indicated by the manufacturer should be validated.			
1.4.7	For medical devices and IVD medical devices placed on the market in both sterile and non-sterile conditions, the label should clearly distinguish between these versions			

1.5	**Considerations of Environment and Conditions of Use**			
1.5.1	If the medical device or IVD medical device is intended to be used in combination with other medical devices or IVD medical devices and/or equipment, the whole combination, including the connection system should be safe and should not impair the specified performance of the medical device or IVD medical device. Any known restrictions on use applying to such combinations should be indicated on the label and/or in the instructions for use. Any connections which the user has to handle, such as fluid, gas transfer, electrical or mechanical coupling, should be designed and manufactured in such a way as to remove or appropriately reduce all possible risks, including incorrect connections or safety hazards.			
1.5.2	Medical devices and IVD medical devices should be designed and manufactured in consideration of the intended environment and conditions of use, and in such a way as to remove or appropriately reduce the: a. risks of injury to the users or other persons in connection with its physical and ergonomic/usability features; b. risks of user error due to the design of the medical device or IVD medical device user interface, ergonomic/usability features, and the environment in which the medical device or IVD medical device is intended to be used; c. risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity,			

	temperature, and/or variations in pressure and acceleration; d. risks associated with the use of the medical device or IVD medical device when it comes into contact with materials, liquids, and substances, including gases, to which it is exposed during intended conditions of use; e. risks associated with the possible negative interaction between software and the information technology (IT) environment within which it operates and interacts; f. environmental risks from unexpected egress of substances from the medical device or IVD medical device during use, taking into account the medical device or IVD medical device and the nature of the environment in which it is intended to be used; g. the risk of incorrect identification of specimens/samples/data and the risk of erroneous results due to, for example, confusing color and/or numeric coding on specimen receptacles, removable parts and/or accessories used to perform the analysis, test, or assay as intended; and h. the risks of interference with other medical devices or IVD medical devices normally used in diagnosis, monitoring or treatment			
1.5.3	Medical devices and IVD medical devices should be designed and manufactured in such a way as to remove or appropriately reduce the risks of fire or explosion during normal use and in single fault condition. Particular attention should be paid to medical devices and IVD medical devices whose			

	intended use includes exposure to or in association with flammable or explosive substances or substances which could cause combustion.			
1.5.4	Medical devices and IVD medical devices should be designed and manufactured in such a way that adjustment, calibration, and maintenance can be done safely and effectively. Specifically, a. When maintenance is not possible, for example, with implants, the risks from ageing of materials, etc. should be appropriately reduced. b. When adjustment and calibration are not possible, for example, with certain kinds of thermometers, the risks from loss of accuracy of any measuring or control mechanism are appropriately reduced.			
1.5.5	Medical devices and IVD medical devices that are intended to be operated together with other medical devices or IVD medical devices or products should be designed and manufactured in such a way that the interoperability and compatibility are reliable and safe.			
1.5.6	Medical devices and IVD medical devices should be designed and manufactured in such a way as to appropriately reduce the risk of unauthorized access that could hamper the device from functioning as intended or impose a safety concern.			
1.5.7	Any measurement, monitoring or display scale functions of medical devices and IVD medical devices should be designed and manufactured in line with ergonomic/usability principles, taking account of the intended purpose, users and the environmental conditions in which the medical devices and IVD medical devices are intended to be used.			

1.5.8	Medical devices and IVD medical devices should be designed and manufactured in such a way as to facilitate their safe disposal or recycling and the safe disposal or recycling of related waste substances by the user, patient or other person. The instructions for use should identify safe disposal or recycling procedures and measures.			
1.6	**Protection against Electrical, Mechanical, and Thermal Risks**			
1.6.1	Medical devices and IVD medical devices should be designed and manufactured in such a way as to protect users against mechanical risks connected with, for example, resistance to movement, instability, and moving parts			
1.6.2	Medical devices and IVD medical devices should be designed and manufactured in such a way as to appropriately reduce the risks arising from vibration generated by the medical devices or IVD medical devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.			
1.6.3	Medical devices and IVD medical devices should be designed and manufactured in such a way as to appropriately reduce the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance.			
1.6.4	Medical devices and IVD medical devices should be			

	designed and manufactured in such a way as to appropriately reduce the risk related to the failure of any parts within the device that are intended to be connected or reconnected before or during use			
1.6.5	Accessible parts of medical devices and IVD medical devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings should not attain potentially dangerous temperatures under normal use.			
1.7	**Active Medical Devices and IVD Medical Devices and Medical Devices Connected to Them**			
1.7.1	For active medical devices and IVD medical devices, in the event of a single fault condition, appropriate means should be adopted to eliminate or appropriately reduce consequent risks.			
1.7.2	Medical devices and IVD medical devices where the safety of the patient depends on an internal power supply should be equipped with a means of determining the state of the power supply and an appropriate warning or indication for when the capacity of the power supply becomes critical.			
1.7.3	Medical devices and IVD medical devices where the safety of the patient depends on an external power supply should include an alarm system to signal any power failure			
1.7.4	Medical devices and IVD medical devices intended to monitor one or more clinical parameters of a patient should be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health.			

1.7.5	Medical devices and IVD medical devices should be designed and manufactured in such a way as to appropriately reduce the risks of creating electromagnetic interference which could impair the operation of any devices or equipment in the intended environment.			
1.7.6	Medical devices and IVD medical devices should be designed and manufactured in such a way as to provide a level of intrinsic immunity to electromagnetic interference such that is adequate to enable them to operate as intended.			
1.7.7	Medical devices and IVD medical devices should be designed and manufactured in such a way as to appropriately reduce the risk of accidental electric shocks to the user or any other person, both during normal use of the medical device or IVD medical device and in the event of a single fault condition in the medical device or IVD medical device, provided the medical device or IVD medical device is installed and maintained as indicated by the manufacturer.			
1.8	**Medical Devices and IVD Medical Devices that Incorporate Software or are Software as a Medical Device**			
1.8.1	Medical devices and IVD medical devices that incorporate electronic programmable systems, including software, or are software as a medical device, should be designed to ensure accuracy, reliability, precision, safety, and performance in line with their intended use. In the event of a single fault condition, appropriate means should be adopted to eliminate or appropriately reduce consequent risks or			

	impairment of performance.			
1.8.2	For medical devices and IVD medical devices that incorporate software or are software as a medical device, the software should be developed, manufactured and maintained in accordance with the state of the art taking into account the principles of development life cycle (e.g., rapid development cycles, frequent changes, the cumulative effect of changes), risk management (e.g., changes to system, environment, and data), including information security (e.g., safely implement updates), verification and validation (e.g., change management process).			
1.8.3	Software that is intended to be used in combination with mobile computing platforms should be designed and developed taking into account the platform itself (e.g. size and contrast ratio of the screen, connectivity, memory, etc.) and the external factors related to their use (varying environment as regards level of light or noise).			
1.8.4	Manufacturers should set out minimum requirements concerning hardware, IT networks characteristics and IT security measures, including protection against unauthorized access, necessary to run the software as intended.			
1.8.5	The medical device and IVD medical device should be designed, manufactured and maintained in such a way as to provide an adequate level of cybersecurity against attempts to gain unauthorized access.			
1.9	**Medical Devices and IVD Medical Devices with a Diagnostic or Measuring Function**			

1.9.1	Medical devices and IVD medical devices with a diagnostic or measuring (including monitoring) function should be designed and manufactured in such a way as to provide, among other performance characteristics, sufficient accuracy, precision and stability for their intended purpose, based on appropriate scientific and technical methods. a. Where applicable, the limits of accuracy should be indicated by the manufacturer. b. Whenever possible, values expressed numerically should be in commonly accepted, standardized units, and understood by users of the medical device or IVD medical device. While generally supporting the convergence on the global use of internationally standardized measurement units, considerations of safety, user familiarity and established clinical practice may justify the use of other recognized measurement units c. The function of the controls and indicators should be clearly specified on the medical device and IVD medical device. Where a medical device or IVD medical device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information should be understandable to the user and, as appropriate, the patient.			
1.10	**Labelling** The following principle is a general recommendation for labelling. For additional guidance on the contents of the labelling, please refer to Guidelines for Labelling			

1.10.1	Medical devices and IVD medical devices should be accompanied by the information needed to distinctively identify the medical device or IVD medical device and its manufacturer. Each medical device and IVD medical device should also be accompanied by, or direct the user to any safety and performance information relevant to the user, or any other person, as appropriate. Such information may appear on the medical device or IVD medical device itself, on the packaging or in the instructions for use, or be readily accessible through electronic means (such as a website), and should be easily understood by the intended user			
1.11	**Protection against Radiation**			
1.11.1	Medical devices and IVD medical devices should be designed, manufactured and packaged in such a way that exposure of users, other persons, or where appropriate, patients, to radiation is appropriately reduced in a manner that is compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for diagnostic and therapeutic purposes.			
1.11.2	The operating instructions for medical devices and IVD medical devices emitting hazardous or potentially hazardous radiation should contain detailed information as to the nature of the emitted radiation, the means of protecting the users, other persons, or where appropriate, patients, and ways of avoiding misuse and of appropriately reducing the risks inherent to transport, storage and installation.			
1.11.3	Where medical devices and IVD medical devices are intended to emit hazardous, or potentially hazardous, radiation, they should be fitted, where possible, with			

	visual displays and/or audible warnings of such emissions			
1.11.4	Medical devices and IVD medical devices should be designed and manufactured in such a way that that the exposure of users, other persons, or where appropriate, patients, to the emission of unintended, stray or scattered radiation is appropriately reduced. Where possible and appropriate, methods should be selected which reduce the exposure to radiation of users, other persons, or where appropriate, patients, who may be affected.			
1.11.5	For medical devices and IVD medical devices emitting hazardous or potentially hazardous radiation and that require installation, information regarding the acceptance and performance testing, the acceptance criteria, and the maintenance procedure should be specified in the operating instructions.			
1.11.6	Where medical devices and IVD medical devices are intended to emit hazardous, or potentially hazardous, radiation, accessible to user, they should be designed and manufactured in such a way as to ensure that the quantity, geometry, energy distribution (or quality), and other key characteristics of the radiation emitted can be appropriately controlled and adjusted and, where appropriate, monitored during use. Such medical devices and IVD medical devices should be designed and manufactured to ensure reproducibility of relevant variable parameters within an acceptable tolerance.			
1.12	**Protection against the Risks posed by Medical Devices and IVD Medical Devices intended by the Manufacturer for use by Lay Users**			

1.12.1	Medical devices and IVD medical devices for use by lay users (such as self-testing or near-patient testing intended for use by lay users) should be designed and manufactured in such a way that they perform appropriately for their intended use/purpose taking into account the skills and the means available to lay users and the influence resulting from variation that can be reasonably anticipated in the lay user's technique and environment. The information and instructions provided by the manufacturer should be easy for the lay user to understand and apply when using the medical device or IVD medical device and interpreting the results.			
1.12.2	Medical devices and IVD medical devices for use by lay users (such as self-testing or near-patient testing intended for use by lay users) should be designed and manufactured in such a way as to: a. ensure that the medical device and IVD medical device can be used safely and accurately by the intended user per instructions for use. When the risks associated with the instructions for use cannot be mitigated to appropriate levels, these risks may be mitigated through training. b. appropriately reduce the risk of error by the intended user in the handling of the medical device or IVD medical device and, if applicable, in the interpretation of the results.			
1.12.3	Medical devices and IVD medical devices for use by lay users (such as self-testing or near-patient testing intended for use by lay users) should, where			

	appropriate, include means by which the lay user: a. can verify that, at the time of use, the medical device or IVD medical device will perform as intended by the manufacturer, and b. is warned if the medical device or IVD medical device has failed to operate as intended or to provide a valid result.			
1.13	**Medical Devices and IVD Medical Devices Incorporating Materials of Biological Origin**			
1.13.1	For medical devices and IVD medical devices that include tissues, cells, or substances of animal, plant, or bacterial origin or their derivatives, which are non-viable or rendered non-viable the following should apply: a. where appropriate, taking into account the animal species, tissues and cells of animal origin, or their derivatives, should originate from animals that have been subjected to veterinary controls that are adapted to the intended use of the tissues. Information on the geographical origin of the animals may need to be retained by manufacturers depending on jurisdictional requirements. b. sourcing, processing, preservation, testing and handling of tissues, cells and substances of animal origin, or their derivatives, should be carried out so as to provide safety for patients, users and, where applicable, other persons. In particular, safety with regards to viruses and other transmissible agents should be addressed by implementation of validated state of the art methods of elimination or inactivation			

	in the course of the manufacturing process, except when the use of such methods would lead to unacceptable degradation compromising the medical device or IVD medical device.			
1.13.2	For Regulatory Authorities, which regulate products manufactured utilizing tissues, cells, or substances of human origin or their derivatives as medical devices or IVD medical devices, the following should apply: a. donation, procurement and testing of the tissues and cells should be done in accordance with jurisdictional requirements; and b. processing, preservation and any other handling of those tissues and cells or their derivatives should be carried out so as to provide safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents should be addressed by appropriate methods of sourcing and by implementation of validated state of the art methods of elimination or inactivation in the course of the manufacturing process.			
1.13.3	For medical devices and IVD medical devices manufactured utilizing biological substances other than those referred to in Sections 1.13.1 and 1.13.2 (for example, materials of plant or bacterial origin), the processing, preservation, testing and handling of those substances should be carried out so as to provide safety for patients, users and, where applicable, other persons, including in the waste disposal chain. In particular, safety with regards to			

	viruses and other transmissible agents should be addressed by appropriate methods of sourcing and by implementation of validated state of the art methods of elimination or inactivation in the course of the manufacturing process. Other requirements can apply in specific regulatory jurisdictions			
2	**ESSENTIAL PRINCIPLES APPLICABLE TO MEDICAL DEVICES OTHER THAN IVD MEDICAL DEVICES** The essential design and manufacturing principles listed in this Section of the document are additional to the essential principles listed in Section 1. These essential principles are applicable to medical devices other than IVD medical devices.			
2.1	**Chemical, Physical and Biological Properties**			
2.1.1	With regards to chemical, physical, and biological properties of a medical device, particular attention should be paid to the compatibility between the materials and substances used and biological tissues, cells and body fluids, taking account of the intended purpose of the device and, where relevant (for example, for some absorbable products), absorption, distribution, metabolism and excretion.			
2.1.2	Medical devices should be designed and manufactured in such a way that they can be used safely with the materials, substances, and gases, with which they enter into contact during their intended use; if the devices are intended to administer medicinal products they should be designed and manufactured in such a way as to be compatible with the medicinal products concerned in accordance with the provisions and restrictions governing those			

	medicinal products and that the performance of both the medicinal products and of the devices is maintained in accordance with their respective indications and intended use.			
2.1.3	Medical devices should be designed and manufactured in such a way as to appropriately reduce the risks linked to the size and the properties of particles which are or can be released into the patient's or user's body, unless they come into contact with intact skin only. Special attention should be given to nanomaterials.			
2.2	**Protection against Radiation**			
2.2.1	Medical devices emitting ionizing radiation intended for medical imaging should be designed and manufactured in such a way as to achieve an image and/or output quality that are appropriate to the intended medical purpose whilst minimizing radiation exposure of the patient, user, and other persons.			
2.2.2	Medical devices emitting ionizing radiation should be designed to allow the accurate estimation (or monitoring), display, reporting, and recording of the dose from a treatment.			
2.3	**Particular Requirements for Implantable Medical Devices**			
2.3.1	Implantable medical devices should be designed and manufactured in such a way as to remove or appropriately reduce the risks associated with medical treatment, e.g. the use of defibrillators, high-frequency surgical equipment.			
2.3.2	Active programmable implantable medical devices			

	should be designed and manufactured in a manner that allows the unequivocal identification of the device without the need for a surgical operation.			
2.4	**Protection against the Risks Posed to the Patient or User by Medical Devices Supplying Energy or Substances**			
2.4.1	Medical devices for supplying the patient with energy or substances should be designed and manufactured in such a way that the amount to be delivered can be set and maintained accurately enough to ensure the safety of the patient, user, and others.			
2.4.2	Medical devices should be fitted with the means of preventing and/or indicating any inadequacies in the amount of energy delivered or substances delivered which could pose a danger. Devices should incorporate suitable means to appropriately reduce the risk of accidental release of dangerous levels of energy or substances from an energy and/or substance source.			
2.5	**Medical Devices Incorporating a Substance Considered to be a Medicinal Product/Drug**			
2.5.1	Where a medical device incorporates, as an integral part, a substance which, if used separately may be considered to be a medicinal product/drug as defined in the relevant legislation that applies in that Regulatory Authority and which is liable to act upon the body with action ancillary to that of the medical device, the safety and performance of the medical device as a whole should be verified, as well as the identity, safety, quality and efficacy of the substance in the specific combination product.			

3	**ESSENTIAL PRINCIPLES APPLICABLE TO IVD MEDICAL DEVICES** The essential design and manufacturing principles listed in this Section of the document are additional to the essential principles of safety and performance listed in Section 1. These essential principles are applicable to only IVD medical devices.			
3.1	**Chemical, Physical and Biological Properties**			
3.1.1	With regards to chemical, physical, and biological properties for IVD medical devices, attention should be paid to the possibility of impairment of analytical performance due to physical and/or chemical incompatibility between the materials used and the specimens, analyte or marker to be detected and measured (such as biological tissues, cells, body fluids and micro-organisms), taking account of the intended purpose of the device.			
3.2	**Performance Characteristics**			
3.2.1	IVD medical devices should achieve the analytical and clinical performances, as stated by the manufacturer that are applicable to the intended use/purpose, taking into account the intended patient population, the intended user, and the setting of intended use. These performance characteristics should be established using suitable, validated, state of the art methods. For example: a. The analytical performance can include, but is not limited to, i. Traceability of calibrators and controls ii. Accuracy of measurement (trueness and precision) iii. Analytical sensitivity/Limit of detection			

	iv. Analytical specificity v. Measuring interval/range vi. Specimen stability b. The clinical performance, for example diagnostic/clinical sensitivity, diagnostic/clinical specificity, positive predictive value, negative predictive value, likelihood ratios, and expected values in normal and affected populations. c. Validated control procedures to assure the user that the IVD medical device is performing as intended, and therefore the results are suitable for the intended use.			
3.2.2	Where the performance of an IVD medical device depends on the use of calibrators or control materials, the traceability of values assigned to such calibrators or control materials should be ensured through available reference measurement procedures or available reference materials of a higher order			
3.2.3	Wherever possible, values expressed numerically should be in commonly accepted, standardized units and understood by the users of the IVD medical device			
3.2.4	The performance characteristics of the IVD medical device should be evaluated according to the intended use statement which may include the following: a. intended user, for example, lay user, laboratory professional; b. intended use environment, for example, patient home, emergency units, ambulances, healthcare centers, laboratory; c. relevant populations, for example, pediatric,			

	adult, pregnant women, individuals with signs and symptoms of a specific disease, patients undergoing differential diagnosis, blood donors, etc. Populations evaluated should represent, where appropriate, ethnically, gender, and genetically diverse populations so as to be representative of the population(s) where the device is intended to be marketed. For infectious diseases, it is recommended that the populations selected have similar prevalence rates.			

I declare that the information provided in this form is accurate and correct and the device conforms to all applicable requirements stipulated above.

Name:_____

Signature:_____

Position _____

Date:_____

Annex II

GUIDANCE ON ESSENTIAL PRINCIPLES

The table below is intended to provide general guidance for meeting the essential principles of safety and performance. The standards and guidances below are not intended to encompass all of the requirements to meet a particular essential principle, but rather provide some overarching guidance. Depending on the specific medical device or IVD medical device additional product specific standards may need to be used. In addition, other Regulatory requirements must also be taken into consideration.

Essential Principle	Description of Principle	Guidances	Relevant standards
ESSENTIAL PRINCIPLES APPLICABLE TO ALL MEDICAL DEVICES AND IVD MEDICAL DEVICES			
General Requirements			
1.1	General Requirements for Medical Device and IVD	GHTF/SG3/N18:2010 Quality Management System –Medical Devices – Guidance on Corrective Action and Preventive Action and related QMS Processes GHTF/SG3/N17:2008 Quality Management System – Medical Devices – Guidance on the Control of Products and Services Obtained from Suppliers GHTF/SG3/N99-10:2004 Quality Management Systems - Process Validation Guidance GHTF/SG3/N15R8	ISO 13485 ISO 14971 ISO 23640 ISO 24971 CLSI EP25

		Implementation of Risk Management Principles and Activities within a Quality Management System. ISO 13485:2016 Handbook. TMDA Compendium Guidelines for Marketing Authorization of Medical Devices and Laboratory Equipment, June 2024.	
1.2	Clinical Evaluation for Medical Device and IVD	Declaration of Helsinki. GHTF/SG5/N1R8:2007 Clinical Evidence – Key Definitions and Concepts. GHTF/SG5/N2R8:2007 Clinical Evaluation GHTF/SG5/N3:2010 Clinical Investigations. GHTF/SG5/N6:2012 Clinical Evidence for IVD Medical Devices - Key Definitions and Concepts. GHTF/SG5/N7:2012 Clinical Evidence for IVD Medical Devices - Scientific Validity Determination and Performance Evaluation. GHTF/SG5/N8:2012 Clinical Performance Studies for In Vitro Diagnostic Medical	ISO 14155

		Devices. TMDA Compendium Guidelines for Marketing Authorization of Medical Devices and Laboratory Equipment, June 2024.	
1.3	Chemical, Physical, and Biological Properties for Medical Device and IVD		ISO 10993 IEC 60601 IEC 61010
1.4	Sterilization and Microbial Contamination for Medical device and IVD	TMDA Compendium Guidelines for Marketing Authorization of Medical Devices and Laboratory Equipment, June 2024	ISO 11135 ISO 11137 ISO 11138 ISO 11140 ISO 11607 ISO 10993 ISO 11737 ISO 13408 ISO 14644 ISO 14937 ISO 14698

			ISO 17664 ISO 17665
1.5	Considerations of Environment and Conditions of Use for Medical Device and IVD		IEC 60601 IEC 61010 IEC 62366-1 IEC/TR 62366-2 IEC 80001 ISO 80369 IEC 62304
1.6	Protection against Electrical, Mechanical, and Thermal Risks for Medical Device and IVD		IEC 60601 IEC 61010
1.7	Active Medical Devices and IVD Medical Devices and Medical Devices Connected to Them for Medical device and IVD		IEC 60601 IEC 61010
1.8	Medical Devices and IVD Medical Devices that Incorporate Software or are Software as a Medical Device	IMDRF/SaMD WG/N41FINAL:2017 Software as a Medical Device (SaMD): Clinical Evaluation. IMDRF/SaMD WG/N23 FINAL:2015 Software	IEC 62304

		as a Medical Device (SaMD): Application of Quality Management System. IMDRF/SaMD WG/N12 FINAL:2014 “Software as a Medical Device”: Possible Framework for Risk Categorization and Corresponding Considerations. IMDRF/SaMD WG/N10 FINAL:2013 Software as a Medical Device (SaMD): Key Definitions. TMDA Compendium Guidelines for Marketing Authorization of Medical Devices and Laboratory Equipment, June 2024.	
1.9	Medical Devices and IVD Medical Devices with a Diagnostic or Measuring Function		IEC 60601 IEC 61010 IEC 62366-1 IEC/TR 62366-2
1.10	Labelling for Medical device and IVD	TMDA Compendium Guidelines for Marketing Authorization of Medical Devices and Laboratory Equipment, June 2024. IMDRF/GRRP	ISO 15223-1 ISO 18113 ISO 20417

		WG/N52 Principles of Labelling for Medical Devices and IVD Medical Devices.	
1.11	Protection against Radiation for Medical device and IVD		IEC 60601 IEC 61010
1.12	Protection against the Risks posed by Medical Devices and IVD Medical Devices intended by the Manufacturer for use by Lay Users		IEC 62366-1 IEC/TR 62366-2
1.13	Medical Devices and IVD Medical Devices Incorporating Materials of Biological Origin		ISO 22442
ESSENTIAL PRINCIPLES APPLICABLE TO MEDICAL DEVICES OTHER THAN IVD MEDICAL DEVICES			
2.1	Chemical, Physical and Biological Properties for Medical devices other than IVD		ISO 10993 IEC 60601
2.2	Protection against Radiation for Medical devices other than IVD		IEC 60601
2.3	Particular Requirements for Implantable Medical Devices	Requirements depend on the type of implantable device.	
2.4	Protection against the Risks Posed to the Patient or User		IEC 60601

	by Medical Devices Supplying Energy or Substances		
ESSENTIAL PRINCIPLES APPLICABLE TO IVD MEDICAL DEVICES			
3.1	Chemical, Physical and Biological Properties for IVD medical devices		CLSI EP05 CLSI EP06 CLSI EP07 CLSI EP12 CLSI EP17 CLSI EP21 CLSI EP25 CLSI EP28 ISO 17511 ISO 23640
3.2	Performance Characteristics for IVD medical devices		ISO 10993 IEC 61010

Annex III

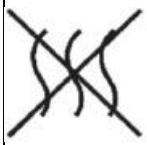
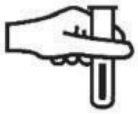
EXAMPLES OF SYMBOLS USED IN MEDICAL DEVICES BASED ON ISO 15223-1

Reference symbol	Title	Description
	Manufacturer	Indicates the medical device manufacturer, as defined in TMDA Guidelines
	Date of Manufacturer	Indicates the date when the device was manufactured
	Use by Date	Indicates the date after which the device is not to be used
	EC Representative	Indicates the Authorized Representative in the European Community
	Batch Code	Indicates the manufacturer's batch code so that the batch or lot can be identified
	Catalogue Number	Indicates the manufacturer's catalogue number so that the device can be identified
	Serial Number	Indicates a serial number so that a specific device can be identified
	Unique Device Identifier	The unique device identification (UDI) is a unique numeric or alphanumeric code related to a medical device. It allows for a clear and unambiguous identification of specific devices on the market and facilitates their traceability.
	Medical Device	Indicates that the product is intended to be used as a medical device

Reference symbol	Title	Description
	In Vitro Diagnostic	Indicates a device that is intended to be used as an in vitro diagnostic medical device
	Sterilize Use Steam Dry heat	Indicates a device that has been sterilized using steam or dry heat
	Sterilize	Indicates a device that has been subjected to a sterilization process
	Sterilize Use Irradiation	Indicates a device that has been sterilized using irradiation
	Sterilize Use Aseptic Processing	Indicates a device that has been manufactured using accepted aseptic techniques
	Sterilize Use Ethyleneoxide	Indicates a device that has been sterilized using ethylene oxide
	Sterile fluid Path	To identify the presence of a sterile fluid pathway within a medical device that might otherwise not be supplied sterile. Understanding that such a patheway is present is important to the safe use of the medical device.
	Sterilized Vaporized Hydrogen Peroxide	Indicates the presence of a sterile fluid path within the device when other parts of the device, including the exterior, may not be supplied sterile
	No Re-sterilize	Indicates a device that is not to be re-sterilized
	No Reuse	Indicates a device that is intended for one use or for use on a single patient during a single procedure
	Natural Rubber Latex	Indicates the presence of natural rubber or dry natural rubber latex as a material of construction within the device or the packaging of a device

Reference symbol	Title	Description
	Caution	Indicates the need for the user to consult the instructions for use for important cautionary information such as warnings and precautions that cannot, for a variety of reasons, be presented on the device itself.
	Instruction For Use	Indicates the need for the user to consult the instructions for use
	Nonsterile	Indicates a device that has not been subjected to a sterilization process
	Damaged Pack	Indicates a device that should not be used if the package has been damaged or opened
	Sunlight Away	Indicates a device that needs protection from light sources
	Heat Radioactive Away	Indicates a device that needs protection from heat and radioactive sources
	Keep Dry	Indicates a device that needs to be protected from moisture
	Temperature Low limit	Indicates the lower limit of temperature to which the device can be safely exposed

Reference symbol	Title	Description

	Temperature Upper limit	Indicates the upper limit of temperature to which the device can be safely exposed
	Temperature limit	Indicates the temperature limits to which the device can be safely exposed
	Humidity	Indicates the range of humidity to which the device can be safely exposed
	Atmospheric Pressure	Indicates the range of atmospheric pressure to which the device can be safely exposed
	Biological Risk	Indicates that there are potential biological risks associated with the device
	Non Pyrogenic	Indicates a device that is non-pyrogenic
	Sampling site	Indicates on a device or blood processing application that it includes a system dedicated to the collection of samples of a given substance stored in the device or blood container