



*FOOD, MEDICINE AND HEALTH CARE ADMINISTRATION AND CONTROL
AUTHORITY OF ETHIOPIA (FMHACA)*

GUIDELINE FOR REGISTRATION OF MEDICAL DEVICES

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ACRONYMS

BSE	Bovine Spongiform Encephalopathy
DOC	Declaration of Conformity
EP	Essential Principles
FMHACA	Food, Medicine and Health Care Administration and Control Authority (of Ethiopia)
GHTF	Global Harmonization Task Force
GMP	Good Manufacturing Practices
IVD	In Vitro Diagnostic
PQM	Promoting the Quality of Medicines Program
QMS	Quality Management System
STED	Summary Technical Documentation
TSE	Transmissible Spongiform Encephalopathy
USP	U. S. Pharmacopeial Convention
WHO	World Health Organization

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INTRODUCTION

The Food, Medicine and Health Care Administration and Control Authority (FMHACA) of Ethiopia was established to safeguard the health and safety of patients, users, and other persons by ensuring that manufacturers of medical devices follow specified procedures during the design, manufacture, and marketing as described in Proclamation No. 661/2009 for the regulation of medicines and healthcare products.

This Guideline have been revised based on the Authority's day-to-day experience as well as recommendations on the regulation of medical devices by other international organizations, such as the European Commission, Global Harmonization Task Force (GHTF), United States Food and Drug Administration (USFDA) and World Health Organization (WHO) guidelines. The main difference between the previous Guideline and this revised third edition of the Ethiopia Guideline are the introduction of the In Vitro Diagnostic (IVD) Medical Device Classification, Summary Technical Documentation (STED), and Essential Principles Checklist for Medical Device Safety and Conformity Assessment.

The method of classification for medical devices other than IVD medical devices stated in this Guideline depends on the intended use of the device, indications for use, duration of use, degree of invasiveness, and local vs. systemic effect of the device. The method of classification for IVD medical devices is based on individual vs. public health risk and on the intended use of the device either by lay persons and/or health professionals. The basic rationale for classification of the device is to proportionate the risk of the device and the technical requirement addition; the classification is risk-based, that is, the risk the device poses to the patient and/or user is a major factor is determining to which class it is assigned.

It is understood that because of the vast number and changing nature of variables involved, it is difficult to set a simple classification rule and examples for all cases. However, the general approach for device classification is as indicated in Annex II for Medical Devices other than IVD, and Annex III for IVD Medical Devices. The manufacturer generally assigns the class of the device; it is the responsibility of the Authority to accept the assigned allocation of the device based on its safety and performance characteristics. In cases where the manufacturer is unable to classify its device, consultation with the staff of the Authority is important.

The class to which the device is assigned determines, among other things, the type of pre-marketing submission/application required for registration, and the elements of safety and performance conformity assessments. Roman numerals I, II, III, and IV are used to classify medical devices other than IVDs, and the Alphabet (A, B, C, and D) is used to classify IVD medical devices for easy identification and alienation.

This Guideline consists of six sections, five annexes. All devices, including IVD medical devices, should meet the essential principles of safety and performance requirement described in Section I. Medical devices other than IVD medical devices should meet the device safety and performance conformity assessment requirements stated in Section II. The extent of the requirements depends on the risk and class of the device. Section III provides the requirements for the conformity assessment of an IVD medical device. Requirements for re-registration and variations of medical devices are provided in Section IV and Section V respectively. Section VI provides the requirement for registration of medical devices with SRA procedure.

Separate applications and dossiers are required for each device falling in Class III and above for medical devices other than IVDs, and for each device in Class C and above for IVD medical devices. Where applicable grouping of medical devices for lower class medical devices is acceptable, the Authority will handle them on a case-by-case basis.

Before making an application for registration, the manufacturer is required to classify his device and compile the data and information needed based on the requirement for that class of device. Thus, the applicant and the staff of the Authority should refer to the principles of device classification and the Guideline section on “Borderline Issues,” as well as with other international guidelines such as GHTF guideline on medical devices.

Devices that are in the market prior to the issuance of this guideline will be reclassified based on the nature of the device and the application for re-registration, as required and explained in Section IV of the Guideline.

DEFINITIONS

For the purposes of this Guideline, the following have the meanings hereby assigned to them. They may have different meanings in other contexts.

Active medical device

Any medical device, the 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. Medical devices intended to transmit energy, substances, or other elements between an active medical device and the patient, without any significant change, are not considered to be active medical devices.

Applicant

A person, manufacturer, or company who may submit an application for registration of a medical device to the Authority

Authority

The Food, Medicine and Healthcare Administration and Control Authority (FMHACA) of Ethiopia, established by Regulation No. 189/2010

Authorized local agent (representative)

Any company or legal person established within a country or jurisdiction who has received a mandate from the manufacturer to act on its behalf for specified tasks with regard to the manufacturer's obligations under the legislation of medical devices and other regulatory guidance's issued by the Authority.

Absorbable surgical ligatures and suture

Threads or strand of materials that are digested by body enzymes or hydrolyzed by tissue fluids, which may include the following:

- catgut (boilable, non-boilable)
- reconstituted collagen
- synthetic absorbable polymers
- kangaroo tendon
- ribbon gut and fascia lata

Central circulatory system

The following vessels are considered part of the central circulatory system: arteriaepulmonales, aorta ascendens, arcus aorta, aorta descendens to the bifurcatio aortae, arteriaecoronariae, arteriacarotiscommunis, arteriacarotisexterna, arteriacarotisinterna, arteriaecerebrales,

truncusbrachiocephalicus, venae cordis, venae pulmonales, vena cava superior, vena cava inferior.

Conformity assessment

The systematic examination of evidence generated and procedures undertaken by a manufacturer to determine that a medical device is safe and performs as intended by the manufacturer and, therefore, conforms to the essential principles of safety and performance of medical devices

Clinical evaluation

The review of relevant scientific literature and/or the review and assessment of data collected through clinical investigation

Clinical investigation

Any designed and planned systematic study in human subjects undertaken to verify the safety and/or performance of a specific device

Diagnostics

Biochemicals that are used to test organ function, determine blood volume and hemopoietic function, or reveal anatomic evidence of disease or other conditions by outlining various body structures and cavities, including all biochemical, such as reagents, antibiotic sensitivity discs, and test kits for diagnosis of disease and other conditions (e.g., pregnancy)

Harm

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

Hazard

Potential source of harm

Instrument

Equipment or apparatus intended by the manufacturer to be used as an IVD medical device

Implantable device

Any device, including those that are partially or wholly absorbed, that is intended to:

- be totally introduced into the human body, or
- replace an epithelial surface or the surface of the eye by surgical intervention, which is intended to remain in place after the procedure

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.

Intended use/purpose

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

Invasive device

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

Invitro diagnostics medical devices

Diagnostics that are used outside the body or do not achieve any of their principal intended purposes by chemical action in or on the body, or by being metabolized, including reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles.

Invivo diagnostics

Diagnostics that are administered or applied to human beings and achieve their principal intended purposes by chemical action in or on the body or by being metabolized. Diagnostics that work by such chemical or metabolic action are regulated as “Medicines” and are subject to Guideline for Registration of Medicines.

Labeling

Any legend, word, or mark attached to, included in, belonging to, or accompanying any medical device, including:(1) the immediate container label; (2) the carton, wrapper, or similar item; and (3) information materials about the medical device such as an instructional brochure or package insert.

Lay person

An individual who does not have formal training in a specific field or discipline

Life supporting or life sustaining

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

Manufacturer

A company that carries out at least one step of the manufacture of a medical device, which includes the responsible person and/or company that designs and/or manufactures a medical device with the intention of making the medical device available for use, under his/her/its name, whether or not such medical device is designed and/or manufactured by that person or on behalf of that person by another person(s).

Manufacture (manufacturing)

All operations of generating a medical device, including purchase of materials and components, production, quality control, packing, labeling, release, storage, and shipment

Medical device

Refers to an instrument, apparatus, implement, medical equipment, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part or accessory, that is:

- a) recognized in a pharmacopoeia or any supplement to it;
- 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 function of the body of a human being or other animal and which does not achieve any of its principal intended purposes through chemical action within the body of a human being or other animals and is not dependent upon being metabolized for the achievement of any of its principal intended purposes.

The term "medical device" includes a great number of instruments and appliances, such as thermometers, blood pressure apparatus, syringes and needles, catheters, gloves, tubes of all kinds, cardiac devices, kidney dialysis machines, microscopes, x-ray machines, and electronic devices, to name a few.

Instruments, apparatus, appliances, materials or other articles, including software, that are intended to be used for research purposes without any medical objective are not regarded as devices for performance evaluation.

Medical device group

A medical device comprising a collection of medical devices, such as a procedure pack or tray, which is sold under a single name

Performance evaluation

Review of the performance of a medical device based upon data already available, scientific literature, and, where appropriate, laboratory, animal, or clinical investigations

Non-absorbable sutures and ligature

Strand(s) of materials that are suitably resistant to the action of living mammalian tissue, including silk, linen, polyamides (nylon), polyester, polyolefins, and stainless steel wire

Quality system

A system that consists of the organizational structure, responsibilities, procedures, processes, and resources for implementing a quality management system

Quality management system

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

Reagent

Chemical, biological, or immunological components, solutions, or preparations intended by the manufacturer to be used as an IVD medical device

Recognized standards

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

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 that are intended by the manufacturer to be reused after appropriate procedures for cleaning and/or sterilization have been carried out

Reprocessing

All the steps performed to make a contaminated reusable device or a single-use device ready for use with a patient, which may include cleaning, functional testing, repackaging, relabeling, disinfection, or sterilization

Self-testing

Testing performed by lay persons

Specimen receptacle

A device, whether vacuum-type or not, specifically intended by the manufacturer for the primary containment of specimens derived from the human body

Subsidiary medical device manufacturer

A manufacturer of medical devices whose voting stock is more than 50% controlled by another company, usually referred to as the parent company or holding company; it is a manufacturer that is partly or completely owned by another company that holds a controlling interest in the subsidiary company.

Surgical dressings

A wide range of materials used for dressing of wounds, employed as coverings, adsorbents, protective or supports for injured or diseased parts, which can include bandages, cotton wools, gauzes, plasters, lint, and other wound-dressing materials

Surgically invasive device

A device that penetrates inside the body through the surface of the body with the aid of or during a surgical operation

Suture

A thread or a strand of material used to approximate, sew, or stitch together the edges of various tissues and hold them in a position until healing has taken place.

Technical Documentation

Recognized evidence of a quality management system that demonstrates compliance of a given device to the essential principles of safety and performance of medical devices

Transmissible agent

An agent capable of being transmitted to a person, as a communicable, infectious, or contagious disease

Verification

Confirmation, by examination and provision of objective evidence, that specified requirements have been fulfilled

GENERAL GUIDANCE AND PRINCIPLES

The content of this Guideline should be read in conjunction with relevant information described in other existing Global Harmonization Task Force (GHTF) reference documents and guidelines. The quality and performance of the intended product to be registered should not be inferior to the available options.

Alternate approaches to the principles and practices described in this Guideline may be acceptable provided they are supported by adequate scientific justification. It is important to note that the Authority may request information or material, or define conditions not specifically described in this guidance, in order to adequately assess the safety, performance, and quality of a medical device prior to and after approval.

General format and guidance for preparation of dossiers

There may be a number of instances where repeated sections can be considered appropriate. Whenever a section is repeated, it should be made clear what that section refers to by creating a distinguishing heading.

Well organized and compiled documents will facilitate the evaluation process and decrease the delay in the screening time. In contrast, poorly compiled documents may lead to unnecessary loss of time, both for the applicant and the Authority. Therefore, documents should have unambiguous contents: title, nature, and purpose should be clearly stated. They should be laid out in an orderly fashion and be easy to check.

Guidance on the compilation and follow-up of the product dossier is summarized below:

1. Paper size is A4; top, bottom, header, and footer margins are 12.5 mm; left and right margins are 25mm
2. Single-spaced paragraphs
3. Times New Roman font, 12-point; letter space 0%.
4. The weight of the font should be legible when copied.
5. The dossier should have a “hard cover,” labeled with the name of the device, device class, and name of the manufacturer.
6. The color of the dossier folder for a new normal application should be black; for a new medical device application by a Stringent Regulatory Authority (SRA) should be red; for re-registration should be blue; for a variation, reply to the previous further request, and amendment should be yellow or light yellow.
7. One hard copy of the Product Dossier (PD) should be submitted with an electronic copy.
8. The application form and the PD should always be in electronic Microsoft® Word format.
9. The attached data and documents should appear in the English language.
10. Any abbreviations should be clearly defined.

11. The compilation of the document should be outlined according to the flow of this e guideline and should be indexed or annotated as described in this Guideline.
12. Applications submitted for registration will be screened chronologically by the date of submission to the Authority, and the applicant will be notified of the evaluation results within 30 days of its submission to the Authority.
13. Rapid test kits for malaria, HIV, and tuberculosis, and devices used for emergent humanitarian aid shall have priority for evaluation and registration (Fast Track).
14. To request that a change be made in specifications, use of the product, or to add or reduce the authorized products, the applicant must follow the guideline for variation and/or amendment (Section V).
15. A request to add supplemental materials must be submitted within six months of being notified of missing elements and/or clarification. If the supplemental submission is not implemented within that time period, urge to be supplemented within 15 days shall follow. If the supplemental document is not submitted within the urge period, or the contents of the replenishment is inappropriate, the speculation shall be clarified and the document shall be returned and/or rejected. However, if the applicant calls for an extension, the submission period shall be determined based on the speculation.
16. Generally, the first and the last three letters of any trade name should not be identical to a registered product in Ethiopia.
17. The agent or the manufacturer should appoint a technical person who is able to understand this and related guidelines of the Authority, who is familiar with the registration process of the products, and who can freely communicate with the assessors should clarification be needed (product-related or administrative) on queries raised by the Authority.
18. The Authority will not accept applications for registration by different applicants or local agents for the same product manufactured by the same manufacturer and/or subsidiaries of one manufacturer.
19. If the manufacturer of a medical device has one or more subsidiaries, the applicant is responsible for submitting the technical documents of each specific product under registration from each of the subsidiaries and/or from the site where the file is kept.
20. If the medical device use accessory and/or consumable (such as reagents, controls, etc.) which is manufactured by a company's subsidiary, the free sale certificate should indicate the same and/or a separate free sale certificate should be a part of the document.
21. If the medical device use accessory and/or consumable (such as reagents, controls, etc.) which is manufactured by an independent manufacturer, information regarding the manufacturer and the technical documents should be submitted. The authority will review on a case-by-case basis.
22. A medical device that an applicant has registered with the USFDA, Health Canada, European Union, Ministry of Health, Labour and Welfare (Japan), Therapeutic Goods Administration (Australia), or WHO Prequalification Programme is considered to be registered with an SRA (Section VI).

BORDERLINE ISSUES RELATED TO MEDICAL DEVICES

1. Medical Device

The principal intended action of a medical device may be deduced from the scientific data regarding its mechanism of action and the manufacturer's labeling and claims. A medical device does not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but may be assisted in its function by such means. In general, the functions of medical devices are achieved by physical means (including mechanical action, physical barrier, or replacement of or support to organs or body functions).

2. Examples of Medical Devices

In view of their principal intended action, the following examples should generally be considered as medical devices subject to relevant criteria being met. The function of some of the devices indicated in these examples may be assisted by the presence of medicinal substances, where such substances have an ancillary action to that of the device.

- Bone cements
- Dental filling materials
- Materials for sealing, approximation, or adhesion of tissues (e.g., cyanoacrylates, fibrin-based adhesives not of human origin)
- Resorbable materials used in osteo-synthesis (e.g., pins or bone screws manufactured using polylactic acid)
- Sutures and absorbable sutures
- Soft and hard tissue scaffolds and fillers (e.g., calcium phosphate, bioglass)
- Bone void fillers intended for the repair of bone defects where the primary action of the device is a physical means or matrix, which provides a volume and a scaffold for osteoconduction
- Intrauterine devices, except products such as intrauterine contraceptives whose primary purpose is to release progestogens
- Blood bags
- Systems intended to preserve and treat blood
- Gases and liquids for ocular endotamponades
- Cell separators, including those incorporating fixed antibodies for cell binding
- Wound dressings, which may be in the form of liquids, gels and pastes, etc. (e.g., hydrocolloid, hydrogel)
- Hemostatic products, for example, patches, plugs and powders where the hemostatic effect results from the product's physical characteristics, or is due to the surface properties of the material; this includes products such as calcium alginate or oxidized cellulose where adhesion of platelets to the surface triggers platelet adhesion and aggregation.
- Concentrates for hemodialysis

- Pressure reducing valves and regulators
- Irrigation solutions intended for mechanical rinsing (e.g., bladder irrigation solution, ocular irrigation solution)
- Devices such as catheters, guide wires, and stents containing or incorporating radioisotopes where the radioactive isotope, as such, is not released into the body, used, for example, in cardiology for the prevention of restenosis

Note:

- Systems intended for the collection, storage, and preservation of blood or blood components and as an ancillary function, the treatment of blood or blood components where this effect is achieved outside the human body, are classified as devices provided that any residual material is not intended to achieve its effect when the blood or cells are reintroduced into the body, e.g., systems incorporating chemicals activated by light to reduce the viral load where the quantity of chemical remaining has no intended effect when transfused.
- If the solution contains a medicinal substance, such as chlorhexidine, where the principal intended purpose is to provide a local antimicrobial effect, it will be a medicinal product. Solutions incorporating substances for other purposes, e.g., antimicrobial agent for the preservation of the solution, remain a medical device.

3. Medical Device and Accessory

“Accessory” means an article that, while not being a (medical) device, is intended specifically by its manufacturer to be used together with a device to enable it to be used in accordance with the use of the device intended by the manufacturer of the device.

The following products fall under the definition of “accessory”:

- Contact lens care products (disinfecting, cleaning, rinsing, and hydrating solutions including those which aid the insertion and/or wearing of contact lenses without therapeutic claim)
- Disinfectants specifically intended for use with medical devices (e.g., endoscopes)
- Lubricants specifically intended for use together with medical devices (e.g., for gloves, endoscopes, condoms)
- Skin barrier powders and pastes or other skin care products specifically intended for use together with ostomy bags
- Gases used to drive cryoprobes and surgical tools.

4. Medical Device and Medicinal Product

Proclamation 661/2009 defines Medicines as “Any substances or mixtures of substances used in the diagnosis, treatment, mitigation or prevention of a disease in humans.”

Due to the definition of a medicinal product, substances used in or administered to human beings to make a medical diagnosis, even if they fulfill their function by physical or chemical means and not by pharmacological, immunological, or metabolic means, are considered to be medicinal products. The following examples should generally be considered as medicinal products subject to relevant criteria being met:

- Spermicidal preparations
- Gases intended to be used in anesthesia and inhalation therapy (e.g., oxygen, medical air supplied in containers), including their primary containers
Note: These gases are also used in minimal access surgery; however, a product intended exclusively for minimal access surgery would be considered a medical device.
- Topical disinfectants (antiseptics) for use on patients
- Hemostatic and sealant products interacting with the coagulation cascade through a pharmacological process, i.e., where the primary mode of action is not mechanical (such as certain collagens that have a molecular structure capable of surface independent demonstrated interaction with platelet receptors and therefore achieve platelet adhesion through a pharmacological process).
- Water for injections, intravenous fluids, and other fluids for drug injection, and plasma volume expanders
- Non-medicinal ophthalmic solutions used for diagnosis, treatment, or mitigation purposes
- In vivo diagnostic agents, e.g., x-ray contrast media, nuclear magnetic resonance enhancing agents, fluorescent ophthalmic strips for diagnostic purposes
- Carrier solutions to stabilize microbubbles for ultrasound imaging, radiopharmaceuticals for diagnostic use
- Gases for invivo diagnostic purposes, including lung function, tests, e.g., carbon dioxide for vascular diagnostic purposes
- Antacids
- Fluoride dental preparations
Note: Dental preparations with a typical device mode of action, such as cements or varnishes incorporating fluoride, are medical devices, where the fluoride is of ancillary action to that of the device
- Solutions administered invivo to the local circulation for the cooling of organs during surgery.

5. Drug Delivery Products and Medical Devices Incorporating Medicinal Substances as an Integral Part or as Ancillary Human Blood Derivatives

5.1. Drug-delivery products regulated as medicinal products

This category involves a device that is intended to administer a medicinal product, where the device and the medicinal product form a single integral product, which is intended exclusively for use in the given combination and is not reusable. Examples are:

- Prefilled syringes
- Aerosols containing a medicinal product
- Nebulizers pre-charged with a specific medicinal product
- Patches for transdermal drug delivery
- Implants containing medicinal products in a polymer matrix whose primary purpose is to release the medicinal product, e.g., plastic beads
- Antibiotic for treating bone infections, or a matrix to release osteoinductive proteins into surrounding bone
- Intrauterine contraceptives whose primary purpose is to release progestogens
- Single-use disposable iontophoresis devices incorporating a medicinal product
- Wound treatment products comprising a matrix whose primary purpose is the administration of medicinal products, for example, wound dressings containing an—
 - Antimicrobial agent where the primary action of the dressing is to administer the agent to the wound for the purpose of controlling infection ,or,
 - Temporary root canal fillers incorporating medicinal products, whose primary purpose is to deliver the medicinal product.

5.2. Drug-delivery products regulated as medical devices

This category concerns a device that is intended to administer a medicinal product. Examples are:

- Drug delivery pump
- Implantable infusion pump
- Iontophoresis device
- Nebulizer
- Syringe, jet injector
- Spacer devices for use with metered dose inhalers
- Port systems.

5.3. Medical devices incorporating, as an integral part, an ancillary medicinal substance

This case relates to a device that incorporates, as an integral part, a substance which, if used separately, may be considered a medicinal product within the meaning of Proclamation 661/2009.

Note: The substance incorporated in the device must meet the three conditions:

- The substance, if used separately, may be considered to be a medicinal product;
- The substance is liable to act upon the human body; and,
- The action of the substance is ancillary to that of the device.

A medical device incorporates a medicinal substance *as an integral part*, if and only if the device and the substance are physically or chemically combined at the time of administration (i.e., use, implantation, application etc.) to the patient. Examples are:

- Catheters coated with heparin or an antibiotic agent
- Bone cements containing an antibiotic
- Root canal fillers that incorporate medicinal substances with ancillary action
- Soft tissue fillers incorporating local anesthetics
- Bone void fillers intended for the repair of bone defects where the primary action of the device is a physical means or matrix, which provides a volume and a scaffold for osteoconduction and where an additional medicinal substance is incorporated to assist and complement the action of the matrix by enhancing the growth of bone cells. In such cases, the ancillary nature would be determined by the performance of the matrix on its own and by the extent of the enhancement of growth due to the presence of the substance. With reference to the overall purpose of the product, where the medicinal substance has such an effect that its ancillary nature cannot be clearly established, then the product should be considered in accordance with the concept of a drug delivery system.
- Condoms coated with spermicides
- Electrodes with steroid-coated tips
- Wound dressings, or surgical or barrier drapes (including tulle dressings) with an antimicrobial agent
- Intrauterine contraceptives containing copper or silver
- Ophthalmic irrigation solutions principally intended for irrigation which contain components that support the metabolism of the endothelial cells of the cornea
- Drug-eluting coronary stents.

It should be noted that the mere coating of a product with a chemical does not imply that the chemical is a medicinal substance. For example, hydroxyapatite, frequently used as coating for orthopedic and dental implants, is not considered a medicinal substance. Other coatings in use that are not medicinal substances are hydromers and phosphorylcholines.

6. Medical Devices Incorporating as an Integral Part, an Ancillary Human Blood Derivative

The same rule applies when a medical device, or an active implantable medical device, incorporates as an integral part, a substance which, if used separately, may be considered to be a medicinal product constituent or a medicinal product derived from human blood or human plasma within the meaning of Proclamation No. 661/2009, and which is liable to act upon the human body with ancillary action to that of the device. Such a device shall be assessed and authorized in accordance with the Guideline for Registration of Medicines.

7. Essential Principles of IVD Medical Devices

The essential characteristics of an IVD, whether consisting of a single component or a combination of components, are that:

- Its principal intended purpose is to –
 - Provide information concerning a physiological or pathological state, or
 - Provide information concerning a congenital abnormality, or
 - Determine the safety and compatibility with potential recipients, or
 - Monitor therapeutic measures;
- The device is used *in vitro* for the examination of a specimen derived from the human body; and,
- The information thus obtained is to be used for one or more of the medical purposes. If no medical purpose is intended by the manufacturer then the product is not a medical device. Thus the intended purpose for a product will be key in determining whether or not the product is an IVD medical device.

Examples:

- Devices for detection of agents of biological or chemical warfare in the environment are not IVDs because such products have no medical purpose. On the other hand, a device intended to be used on human specimens in the detection of biological or chemical warfare agents with medical purpose would fall within the scope of the IVD medical devices section.
- Devices intended to be used only in the course of law enforcement or other non-medical purposes, for example, devices for detecting drugs of abuse or alcohol are outside the scope of IVD medical devices. If however, the *in vitro* examination of human specimens with a medical purpose is one of the intended uses of a specific product, the product is an IVD.
- A product for research use *only*, which has no medical purpose, cannot be a medical device and, therefore, cannot be an IVD medical device. By definition, these products fall outside the scope of IVD and other medical device requirements.

8. Sample Specimen Receptacle, Medical Devices, Accessory, and IVD Medical Devices

A sample specimen receptacle is defined as a specimen receptacle specifically intended by the manufacturer to be used for the primary containment and preservation of specimens derived from the human body for the purposes of *in vitro* diagnostic examination. This applies whether the product is a vacuum type or not. This includes receptacles into which the specimen is placed (by aliquoting or otherwise); they may be glass or plastic tubes, cups, cuvettes, or other receptacles.

Specimen receptacles that come into contact with a patient are considered to fall within the scope of the medical device and not the IVD.

Invasive sampling devices or those which are directly applied to the human body for the purpose of obtaining a specimen within are not to be considered as accessories to IVDs. Thus, for example, where a manufacturer's kit includes lancets or pricking devices to obtain a blood specimen, they are to be regarded as being devices within the scope of the medical devices and not accessories to the IVD.

9. Products for General Laboratory Use

Products for general laboratory use (non-IVD products) are not IVDs unless, on the basis of its specific characteristics, the manufacturer specifically intends such products to be used for in vitro diagnostic purposes. Thus, such a product must possess specific characteristics to make it suitable for in vitro diagnostic procedures in order to be classified as an IVD.

Products used in vitro in the preparation of samples that have been obtained for examination, but are not used directly in the actual test, can be considered to be IVD's if the manufacturer specifically states that the product can be used for in vitro diagnostic purposes; otherwise, they fall outside the scope of the medical device definition.

Examples:

General laboratory products that are not usually considered to fall within the scope of IVD and medical devices include: sterilizers, laboratory centrifuges, general purpose automatic pipettes, weighing machines, microtomes, multipurpose tubes, pipettes, and flasks, etc., where such items have no specifically intended in vitro diagnostic use. Other examples include items for general purpose use such as fetal calf serum, culture media, and stains, unless the manufacturer's intended purpose falls within the definition of an in vitro diagnostic medical device.

10. Products for Research Use Only

A product for research use only which has no medical purpose cannot be a medical device and, therefore, cannot be an IVD medical device. By definition, these products fall outside the scope of registration requirements for IVDs or other medical devices.

11. Devices for IVD Purposes with Invasive Body Contact

Some devices may incorporate both specimen collection and analytical functions. These devices may be considered "borderline" between a medical device and an IVD medical device. Borderline cases such as these should be approached with regard to the principal intended purpose of the product. Thus, if the principal intended purpose of the product is to be used in vitro for the examination of specimens derived from the human body for the purposes of providing information, the IVD medical device requirement would apply.

Devices which, during their measuring function, involve contact with the human system in order to obtain a continuous sample are not considered to be IVD medical devices.

Example 1:

The use of a device involving the vacuum suction of saliva into the integrated handle of a device which contains reagent material (e.g., for the detection of HIV) involves the penetration of the device into a body orifice for the collection of the specimen; this may appear to make it a medical device within the scope of the Medical Device requirement. However, its principal intended purpose is the provision of relevant information by the in vitro examination of the specimen derived from the patient. The device's brief contact with the patient or penetration into the patient's body to collect the specimen is subsidiary and incidental to its principal intended purpose.

Mouth and other swabs bearing integrated reagents or reagent areas are IVDs because their principal intended purpose is to provide information relevant to the medical purposes.

The intended purpose, invasiveness, and continuity of sampling are important criteria in deciding the correct regulatory route for border line IVD and other medical devices.

Example 2:

A "Holter" blood glucose monitoring system that includes a subcutaneous catheter to provide a continuous supply of the patient's specimen to an in vitro analyzing instrument is a medical device, not an IVD, because, during the in vitro measuring function, surgically invasive contact with the patient is necessary in order to obtain a continuous specimen flow. In this case, the analytical function is carried out at the same time as the continuous specimen collection process. There is no dissociation of the specimen from the patient; therefore, the analytical function cannot properly be regarded as being in vitro. Therefore, such a device would be a medical device.

Other examples are continuous pH measurements during hemodialysis and oxygen saturation devices.

12. Kits Containing IVDs and Medicinal Products

Medicinal products made available together with IVD medical devices (kits) are to be authorized for marketing by the normal process for medicinal products; and the primary and, if applicable, the secondary, packages of the medicinal products are to be labeled according to the rules for medicinal product requirements. The IVD components of the kits themselves fall within the scope of the IVD medical device and must therefore comply with its requirements.

Example:

A *Helicobacter pylori* breath test kit, which contains labeled urea (medicinal product) to be ingested prior to sampling for analysis, a straw (a medical device), and a sample container (an IVD).

Note: So far as the medicinal product is concerned, it must have been granted a marketing authorization covering the actual use for which it is being included in the IVD kit, and it must be labeled in accordance with the regulations relating to medicinal products. The IVD component of the kit must comply with all the applicable essential and other requirements of the IVD (including the labeling requirements).

13. Devices with No Specimen Involved

Some medical diagnostic devices function without a specimen being taken from the patient.

Example:

A non-invasive medical device for the detection of blood glucose by energy emission (e.g., near infrared energy) is not an IVD because no specimen derived from the human body is involved; but it would be a medical device and must comply with medical device registration requirement.

PRINCIPLES OF MEDICAL DEVICE CLASSIFICATION

It is not economically feasible or justifiable in practice to subject all medical devices to the most rigorous conformity assessment procedures available. A graduated system of control is more appropriate. In such a system, the level of control corresponds to the level of potential hazard inherent in the type of device concerned. A medical device classification system is therefore needed in order to apply to medical devices an appropriate conformity assessment procedure.

Appropriate medical device classification should always be linked with device safety conformity and performance assessment. The purpose of risk classification is to make sure that the registration and regulatory requirement applied to a medical device is proportionate to risk. In this Guideline, devices are categorized into four classes, namely Classes I, II, III, and IV for medical devices other than IVDs, and Classes A, B, C, and D for IVD medical devices to easily distinguish between the two types of devices. Any other alternative classification rules selected by the device manufacturer may be acceptable, with appropriate justification.

1. MEDICAL DEVICE CLASSIFICATIONS OTHER THAN IVD

In order to ensure that conformity assessment implementation is effective, manufacturers should be able to determine the classification of their product as early as possible in the device development. The manufacturer must use a systematic approach to applying the classification rules described within this Guideline.

The classification rules are based on various criteria, such as the duration of contact with the patient, the degree of invasiveness and the part of the body affected by the use of the device, intended purpose, and duration. Transient devices are normally intended to be used continuously for less than 60 minutes; short-term devices are normally not more than 30 days; and, long-term devices are normally devices to be used continuously for more than 30 days.

Any device which, in whole or in part, penetrates inside the body, either through a natural body orifice or through the surface of the body, is an invasive device. A surgically invasive device always implies that it enters through an artificially created opening. This can be a large opening, such as a surgical incision, or it can be a pinprick opening created by a needle. Therefore, surgical gloves and needles used with syringes are surgically invasive. The concept of surgically invasive should be understood as covering also liquids that are in invasive contact with organs, tissue, or other parts of the body if the access for such liquids is through a surgically created opening.

In the context of invasiveness, however, a surgically created stoma used in urostomy, colostomy, ileostomy, or permanent tracheostomy is considered to be a body orifice. Therefore devices

introduced into such a stoma are not surgically invasive. A surgically created opening to allow access to the circulatory system, in contrast, should not be considered to be such a "body orifice." Devices introduced into such an opening are surgically invasive. And also, a device that administers energy to the body should not be considered as invasive if only energy penetrates the body, and not the device itself. Energy, as such, is not a device and, therefore, it cannot be classified. Only the device generating the energy must be classified. However, if a device administers a substance, whether this substance is a medicine or a medical device, such a substance must be assessed in its own right (e.g., substances administered by a jet injector).

One of the key elements in defining an implantable device is the concept of "procedure." Thus an implantable device must remain in the patient after the procedure. A "procedure" must be understood in this context to include the surgical procedure during which the implant is placed into the body and the immediate post-operative care that is associated with the procedure. The "procedure" does not extend to the conclusion of the therapeutic treatment, e.g., the removal of an implant must be considered to be another "procedure." Thus a plate used to reduce a fracture of the bone is an implant even if it is taken out after the fracture has healed. In this case, the placing of the plate and its explanations are two different surgical procedures.

Some partially implanted devices are deemed to be implants. For instance, if an operation is carried out specifically to place an infusion port into the body, then such an infusion port would remain for at least 30 days after the procedure and, consequently, be an implant. However, a non-tunneled central venous catheter which is intended for use for temporary vascular access and intended to be removed after 7–10 days is not a long-term implantable device. Nor would a suture used for skin wound closure that is taken out prior to 30 days be considered an implant.

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."

The classification of medical devices is a "risk based" system based on the vulnerability of the human body, taking account of the potential risks associated with the devices. This approach allows the use of a set of criteria that can be combined in various ways in order to determine classification, e.g., duration of contact with the body, degree of invasiveness, and local vs. systemic effect.

It is recognized that although the existing rules will adequately classify the vast majority of existing devices, a small number of products may be more difficult to classify. Such cases may,

in particular, include devices which are borderline cases between two different classes of medical devices. In addition, there may be devices that cannot be classified by the existing rules because of their unusual nature or situations where the classification would result in the wrong level of conformity assessment in light of the hazard represented by the device.

Medical devices using pre-stored gases and/or vacuum as a power source are regarded as active devices, e.g., gas mixers with anesthesia machines and gas-powered suction pumps.

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.

Radioactive sources that are intended to deliver ionizing radiation are regarded as active medical devices, unless they are radiopharmaceuticals where they are considered as medicinal products and not medical devices.

For a procedure pack that is a device in its own right, the classification is normally determined by the intended use. In those cases where the intended use of the procedure pack is not specific enough to determine the classification, the classification of the pack is at the level of the highest classified device included in the pack.

1.1 Application of Classification Rule

In terms of further interpretation of the classification rules, the following should be considered:

- It is the intended purpose that determines the class of the device and not the particular technical characteristics of the device, unless these have a direct bearing on the intended purpose, e.g., incorporation of an ancillary substance, tissue of animal origin, etc.
- It is the intended and not the accidental use of the device that determines the class of the device. For instance, a suture organizer that is intended to keep order of suture threads used in open heart surgery should not be considered as an invasive device if, in the normal use, it can be kept outside the patient. Similarly, if a medical practitioner uses the device in a manner not intended by the manufacturer, this does not change the class of the device for the purpose of conformity assessment. However, if the normal clinical use of the device changes in time with evolving clinical practice, such that the intended purpose and classification of the device changes, this should be addressed by the manufacturer and the conformity of the device assessed for the new intended purpose.
- It is the intended purpose assigned by the manufacturer to the device that determines the class of the device and not the class assigned to other similar products. For instance, two sutures that have the same composition may well have different intended purposes.

- As an alternative to classifying the system as a whole, the determination of the class of a particular device may be made with respect to the simplest configuration that can still be considered, in view of its proper functional features, as a device in its own right. A device that is part of a system, e.g., a tube in an extra corporeal circulation set, may be classed as a device in its own right rather than classifying the system as a whole. The device, however, must be assessed in its own right as a separate device in such instances.
- Combination devices with parts that have different functional purposes may be analyzed and assessed separately with respect to each of these parts. For instance, a drainage device will have an invasive tube and a non-invasive collection device. These components may be classified separately.
- Accessories are classified in their own right separately from the device with which they are used.
- If a given device can be classified according to several rules, then the highest possible class applies. For instance, a wound dressing incorporating collagen is covered by rules #4 (Class I, Class II, or Class III depending on intended use) and #17 (Class IV). All rules must be considered; for instance, if an active device is also surgically invasive, the relevant rules for surgically invasive devices must also be considered.
- If the device is not intended to be used solely or principally in a specific part of the body, it must be considered and classified on the basis of the most critical specified use. Classification of the 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 the intended purpose in the labeling 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.
- For a device to be "specifically intended" for the 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. Otherwise, it is deemed to have the intended use which is principally used and accepted in general medical practice.
- Multi-application equipment, such as laser printers and identification cameras, which may be used in combination with medical devices, are not medical devices unless their manufacturer places them on the market with a specific intended purpose as medical devices.

1.2 Medical Device Classification Example

A simple wound drainage device has three components that must be taken into consideration: the cannula, the tubing, and the collector unit. If the device is marketed without a cannula, then the classification of the cannula does not need to be taken into account. It is assumed here that the device is used for short term duration, i.e., that uninterrupted intended use is

more than 60 minutes and less than 30 days. It is furthermore assumed that the collected liquids are not intended to be re-infused into the body nor reprocessed for eventual re-infusion, and that the device is not intended to be connected to a powered suction system.

INTENDED USE	RULE	DEVICE CLASS
Surgically invasive cannula to reach a wound site in the pleural cavity to drain the cavity	7	II
Non-invasive tubing to evacuate body liquids towards the collector	1	I
Non-invasive collector to receive the body liquids	1	I

The manufacturer would have a choice of applying Class II to the whole device or carrying out separate conformity assessment procedures for the cannula on one hand, and the tubing and collector on the other hand.

The general approaches for medical device classification other than IVD medical devices are given in the following table:

CLASS	RISK LEVEL	DEVICE EXAMPLES
I	Low Risk	Surgical retractors / tongue depressors
II	Low–Moderate Risk	Hypodermic needles / suction equipment
III	Moderate–High Risk	Lung ventilator / bone fixation plate
IV	High Risk	Heart valves / implantable defibrillator

For further reference and explanations of individual classification approaches, please refer to Annex II of this Guideline, where any special terms used are explained and practical issues related to the rules are clarified. It must be emphasized that, even if a particular device type is given as an example, this does not mean that such devices are in all cases in the class indicated by the example. It is always possible that some manufacturer will assign to such a device an entirely different intended use than what was used in the context of the example.

2. IVD MEDICAL DEVICE CLASSIFICATIONS

2.1 Classification of an IVD Medical Device

The classification of an IVD Medical Device is based on the following criteria:

- Intended use and indications for use as specified by the manufacturer (including but not limited to specific disorder, populations, condition, or risk factor for which the test is intended);
- Technical/scientific/medical expertise of the intended user (lay person or healthcare professional);
- Importance of the information to the diagnosis (sole determinant or one of several factors), taking into consideration the natural history of the disease or disorder, including presenting signs and symptoms which may guide a physician; and,
- Impact of the result (true or false) to the individual and/or to public health.

2.2 Determination of Device Class

The manufacturer should:

- Decide if the product concerned is an IVD Medical Device based on the intended use and the indications for use using the principles described above.
- Take into consideration all the rules as listed in Annex IV in order to establish the proper classification for the device. Where an IVD Medical Device has multiple intended uses, as specified by the manufacturer, which place the device into more than one class, it will be classified in the higher class.
- Where more than one of the classification rules applies to the IVD medical device, it should be allocated to the highest class indicated, e.g., a self-test for HIV would be a Class D under rule 1 and not a Class C under rule 4 (see Annex IV).

The general principles of IVD Medical Device classification are listed in the following table:

CLASS	RISK LEVEL	EXAMPLES
A	Low Individual Risk and Low Public Health Risk	Clinical Chemistry Analyzer, prepared selective culture media
B	Moderate Individual Risk and/or Low Public Health Risk	Vitamin B12, Pregnancy self-testing, Anti-Nuclear Antibody, Urine test strips
C	High Individual Risk and/or Moderate Public Health Risk	Blood glucose self-testing, HLA typing, PSA screening, Rubella
D	High Individual Risk and High Public Health Risk	HIV Blood donor screening, HIV Blood diagnostic

For further IVD Medical Device classification approaches and examples, please refer to Annex IV of this Guideline.

SECTION I: GENERAL REGISTRATION REQUIREMENTS OF ALL MEDICAL DEVICES

1. APPLICATION FORM

The application form for registration of a Medical Device is provided in Annex I of this Guideline. The date of application should correspond to the date of submission of the registration dossier to the Authority.

2. AGENCY AGREEMENT

- a) An agency agreement should be made between the manufacturer of the medical device for registration and the agent responsible for the import, distribution, and sale of the product in Ethiopia. Where the manufacturer manufactures a product at two or more places, the agreement and responsibility of each party made between the manufacturers should be submitted. In such a case, the agency agreement between the local agent and the manufacturer should be the site where the file is kept and the applicant for registration.
- b) The agreement should be signed by both parties and such is what is to be presented. The seal/stamp of both parties should also be affixed to the document for agency agreement.
- c) The agreement should specify the first agent to handle the medical device registration process. In case the manufacturer wishes to have more than one distributor, this must be mentioned in the agreement; but the maximum number of distributors is limited to three. The appointed agent(s) is responsible for correspondence and complete compliance with regulatory requirements pertaining to the product's distribution life cycle in the country.
- d) The agreement should state that if any fraud or unsuspected and unacceptable adverse event occurs to the consumer under normal utilization, both parties will be responsible for collecting the product from the market and are responsible for substantiating any event.
- e) The agreement for higher class devices should specify that the applicant and local representative shall collect and submit to the Authority device safety and performance evidence within one year of its marketing in Ethiopia.
- f) The agreement should specify that both parties are responsible for pharmacovigilance and post-marketing reporting of the device.
- g) For the purpose of administration, the agreement should remain valid at least for the period of one year from the date of submission to the Authority, unless it is found to be satisfactory for the termination of the agreement.
- h) The agent representing the manufacturer for importation should hold a license issued by the ministry of trade and certificate of competence issued by the Authority at the time of importation of the product.

3. DECLARATION OF CONFORMITY

The manufacturer should attest that its medical device complies fully with all applicable *Essential Principles for Safety and Performance* as documented in a written “Declaration of Conformity” (DOC). At a minimum, this declaration should contain the following information:

- A statement that each device that is the subject of the declaration–
 - complies with the applicable *Essential Principles for Safety and Performance*,
 - has been classified according to the classification rules, and,
 - has met all the applicable conformity assessment elements;
- A Global Medical Device code and term for the device(s);
- The risk class allocated to the device(s) after following the guidance described in *Principles of In Vitro Diagnostic (IVD) Medical Devices Classification*;
- Conformity assessment procedures applied;
- Date from which the Declaration of Conformity is valid;
- Name and address of the device manufacturer; and,
- The name, position, and signature of the responsible person who has been authorized to complete the Declaration of Conformity on behalf of the manufacturer.

4. CERTIFICATE OF COMPLIANCE WITH RECOGNIZED STANDARDS

The applicant should submit the applicable certificate of GMP, product certificate, TSE/BSE risk free attestation letter, and certificate of conformity in line with the DOC declared under item 3 above.

4.1 Good manufacturing certificate

A valid Good Manufacturing Practice Certificate issued by the competent national regulatory authority should, at least, bear the name of manufacturer, address, medical device name, device category, and class. The copy of this GMP Certificate should be authenticated by the Ethiopian embassy.

4.2 Certificate of conformity to recognized standard

Valid quality system and conformity certificates issued by a recognized certifying authority, in line with the device Declaration of Conformity described under item 3 above, should be provided with the dossier. The certificate should be valid.

4.3 Free sale certificate

A confirmatory letter issued by the competent national regulatory authority, which indicates the name(s) of the device(s) (with model if applicable) and explains whether the products are freely sold in the country of origin should be provided; if not, the reasons thereof should be clearly stated with appropriate justification.

If the manufacturer of the medical device has subsidiaries, a free sale certificate should indicate the name and address of the subsidiaries with the name of the device they manufacture, and/or a separate free sale certificate should be submitted for each subsidiary. The certificate should be original, valid, and authenticated by the Ethiopian embassy. If the certificate comes from a country where there is no Ethiopian embassy, the Authority will contact directly the responsible body that provides the free sale certificate.

4.4 Product certificate

Product specific certificates, where applicable (e.g., for surgical ligatures and sutures, etc.), issued by a competent national regulatory authority should be provided with the dossier. The product certificate should indicate the type and origin of the components of the device, and should be valid and authenticated by the Ethiopian embassy.

4.5 Risk-free TSE/BSE attestation

The applicant should provide an attestation letter and/or declaration that the materials used for the manufacture of the device are free of any TSE/BSE-risk origin materials.

5. MANUFACTURER NAME AND QUALITY MANAGEMENT

The following information should be provided about the manufacturer of the product:

- Name of the manufacturer;
- Complete address, including the street name, telephone number, e-mail, and website;
- Background information, including year of establishment, development since establishment, capital, total work force, organogram, and subsidiaries (if any); and,
- Quality control and quality management system, including quality control and general quality management system of source and authorization of raw materials, component handling, packaging, release, recall procedures, and handling of compliance and out of specifications.

6. MEDICAL DEVICE ESSENTIAL SAFETY AND PERFORMANCE REQUIREMENTS

All medical devices, irrespective of their class, should meet the essential requirements of medical device safety and performance principles as described in this Guideline.

The manufacturer should have an appropriate procedure in place to manufacture a device which meets consistent identification, selection and safety, and performance principles through proper design and manufacturing procedure to demonstrate the device suitability for its intended use.

Essential requirements for the safety and performance of medical devices that should be provided with the registration dossier are:

6.1 Chemical, physical, and biological characteristics

- Choice of materials used, particularly as regards toxicity and, where appropriate, flammability;
- Compatibility between the materials used and the biological tissues, cells, body fluids, and specimens, taking into account the intended purpose of the device;
- Choice of materials used should reflect, where appropriate, matters such as hardness, wear, and fatigue strength;
- Procedure for removal and minimization of contaminants and residues to the persons involved in the transport, storage, and use of the devices, and to patients;
- Compatibility with substances and gases with which they enter into contact during their normal use or during routine procedures; if the devices are intended to administer medicinal products, compatibility evidence with the medicinal products concerned should be provided. Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product, this should be applied and registered separately as per the guideline for medicinal product registration;
- Evidence for the absence and/or risk minimization from a substance that may leach or leak from the devices; and,
- Procedures and evidence for reduction of unintentional ingress or egress of substances into or from the device, taking into account the device and the nature of the environment in which it is intended to be used.

6.2 Microbial contamination and infection control

The device manufacturing processes should be designed in such a way as to eliminate or reduce as much as is reasonably practicable and appropriate the risk of infection to patients, users, and, where applicable, other persons.

- Device drawing and design should reflect the easy handling of the medical device for risk minimization from infection during use.
- Reduce as far as reasonably practicable and appropriate any microbial leakage from the device and/or microbial exposure during use.
- Prevent microbial contamination of the device, or specimen where applicable, by the patient, user, or other person.
- Where a device incorporates substances of biological origin, the risk of infection must be reduced as far as reasonably practicable and appropriate by selecting appropriate sources, donors and substances and by using, as appropriate, validated inactivation, conservation, test, and control procedures.
- Devices delivered in a sterile state should be designed, manufactured, and packed in a non-reusable pack, and/or according to appropriate procedures, to ensure that they are sterile when placed on the market and remain sterile, under the transport and storage

conditions indicated by the manufacturer, until the protective packaging is damaged or opened.

- Devices labeled either as sterile or as having a special microbiological state should have been processed, manufactured, and, if applicable, sterilized by appropriate, validated, methods.
- Devices intended to be sterilized should be manufactured in appropriately controlled (e.g., environmental) conditions; and,
- Packaging systems for non-sterile devices should keep the device without deterioration at the level of cleanliness stipulated and, if the devices are to be sterilized prior to use, minimize the risk of microbial contamination. The packaging system should be suitable taking into account the method of sterilization.

6.3 Manufacturing design and environmental properties of medical device

- From the device design, drawing, manufacturing, and labeling, if the device is intended to be used in combination with other devices or equipment, an evidence for the safety of the whole system, including the connection system, should be provided. Any restrictions on use applying to such combinations should be indicated on the label and/or in the instructions for use.
- The device manufacturer should provide a justification that the selected design of the medical device reduces and/or removes any risks of injury by providing–
 - Physical features, including the volume/pressure ratio, dimensional and, where appropriate, ergonomic features should not cause any injury to the user;
 - Risks connected with external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, pressure, humidity, temperature, or variations in pressure and acceleration;
 - Risks connected to their use in conjunction with materials, substances, and gases with which they may come into contact during normal conditions of use;
 - Risks of accidental penetration of substances into the device;
 - Risk of incorrect identification of specimens;
 - Risks of reciprocal interference with other devices normally used in the investigations or for the treatment given;
 - Risks arising where maintenance or calibration are not possible (as with implants), from aging of materials used or loss of accuracy of any measuring or control mechanism; and,
 - Risks of fire or explosion during normal use and in single fault condition. Particular attention should be paid to devices whose intended use includes exposure to or use in association with flammable substances or substances which could cause combustion.
- Safe disposal of the device and/or any other waste substances.

6.4 Particulars of device with diagnostic or measuring functions

- Devices with a measuring function, where inaccuracy could have a significant adverse effect on the patient, should be designed and manufactured in such a way as to provide sufficient accuracy, precision, and stability for their intended purpose. The limits of accuracy should be indicated by the manufacturer.
- Diagnostic devices should be designed and manufactured in such a way as to provide sufficient accuracy, precision, and stability for their intended use, based on appropriate scientific and technical methods. In particular, the design should address sensitivity, specificity, trueness, repeatability, reproducibility, control of known relevant interference, and limits of detection, as appropriate.
- Where the performance of devices depends on the use of calibrators and/or control materials, the traceability of values assigned to such calibrators and/or control materials should be assured through a quality management system.
- Any measurement, monitoring, or display scale should be designed in line with ergonomic principles, taking into account the intended purpose of the device. Values expressed numerically should be given in standardized units.

6.5 Particulars of medical devices emitting radiation

- Medical devices should be designed, manufactured, and packaged in such a way that exposure of patients, users, and other persons to any emitted radiation should be reduced as far as practicable and appropriate, compatible with the intended purpose, while not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes.
- Where devices are designed to emit hazardous, or potentially hazardous, levels of visible and/or invisible radiation necessary for a specific medical purpose, the benefit of which is considered to outweigh the risks inherent in the emission, it should be possible for the user to control the emissions. Such devices should be designed and manufactured to ensure reproducibility of relevant variable parameters within an acceptable tolerance.
- Where devices are intended to emit potentially hazardous, visible, and/or invisible radiation, they should be fitted, where practicable, with visual displays and/or audible warnings of such emissions.
- Unintended exposure of patients, users, and other persons to the emission, stray, or scattered radiation should be reduced as far as practicable and appropriate.
- The operating instructions for devices emitting radiation should give detailed information as to the nature of the emitted radiation, means of protecting the patient and the user, and on ways of avoiding misuse and eliminating the risks inherent in installation.

6.5.1 Ionizing Radiation

- Devices intended to emit ionizing radiation should be designed and manufactured in such a way as to ensure that, where practicable, the quantity, geometry, and energy

distribution (or quality) of radiation emitted can be varied and controlled taking into account the intended use.

- Devices emitting ionizing radiation intended for diagnostic radiology should be designed and manufactured in such a way as to achieve appropriate image and/or output quality for the intended medical purpose while minimizing radiation exposure of the patient and user.
- Devices emitting ionizing radiation, intended for therapeutic radiology, should be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam type and energy, and, where appropriate, the energy distribution of the radiation beam.

6.6 Particulars of medical devices connected to or equipped with an energy source

- Medical devices incorporating electronic programmable systems, including software, should be designed to ensure the repeatability, reliability, and performance of these systems according to the intended use. In the event of a single fault condition in the system, appropriate means should be adopted to eliminate or reduce, as far as practicable and appropriate, consequent risks.
- For medical devices where the safety of the patient depends on an internal power supply, it should be equipped with a means of determining the state of the power supply.
- For medical devices where the safety of the patients depends on an external power supply, it should include an alarm system to signal any power failure.
- 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 that could lead to death or severe deterioration of the patient's state of health.
- Devices should be designed and manufactured in such a way as to reduce as far as practicable and appropriate the risks of creating electromagnetic interference which could impair the operation of this or other devices or equipment in the usual environment.
- Devices should be designed and manufactured in such a way as to provide an adequate level of intrinsic immunity to electromagnetic disturbance to enable them to operate as intended.
- Devices should be designed and manufactured in such a way as to avoid, as far as possible, the risk of accidental electric shocks during normal use and in single fault condition, provided the devices are installed and maintained as indicated by the manufacturer.

6.7 Protection against mechanical risks

- Devices should be designed and manufactured in such a way as to:
 - Protect the patient and user against mechanical risks connected with, for example, resistance to movement, instability, and moving parts.

- Reduce to the lowest practicable level the risks arising from vibration generated by the devices, taking into account technical progress and the means available for limiting vibrations, particularly at the source, unless the vibrations are part of the specified performance.
- Reduce to the lowest practicable level the risks arising from the noise emitted, taking into account technical progress and the means available to reduce noise, particularly at the source, unless the noise emitted is part of the specified performance.
- Accessible parts of the 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.

6.8 Protection against supplied energy or substances

- Devices for supplying the patient with energy or substances should be designed and constructed in such a way that the delivered amount can be set and maintained accurately enough to guarantee the safety of the patient and of the user.
- Devices should be fitted with the means of preventing and/or indicating any inadequacies in the delivered amount that could pose a danger. Devices should incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy from an energy and/or substance source.
- The function of the controls and indicators should be clearly specified on the devices. Where a 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.

6.9 Particulars of devices for self-testing or self-administration

- Such devices should be designed and manufactured in such a way—
 - that they perform appropriately for their intended purpose taking into account the skills and the means available to users and the influence resulting from variation that can reasonably be anticipated in the user's technique and environment. The information and instructions provided by the manufacturer should be easy for the user to understand and apply.
 - as to reduce as far as practicable the risk of use error in the handling of the device and, if applicable, the specimen, and also in the interpretation of results.
 - as to include a procedure by which the user can verify that, at the time of use, that the product will perform as intended by the manufacturer.

6.10 Performance evaluation including, where appropriate clinical evaluation

- Clinical investigations on human subjects should be carried out in accordance with the spirit of the Helsinki Declaration. This includes every step in the clinical investigation from first consideration of the need and justification of the study to publication of the result.

Note: Please refer to the device conformity and performance requirements section of this Guideline.

7. MANUFACTURING AND PRODUCTION

The manufacturer should provide a narrative of the manufacturing procedure and schematic manufacturing flow chart by including an in-process standard control mechanism. 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, labeling, and storage of the device.

Where the device is manufactured and packed as a sterile device (e.g., disposable syringes, etc.), the process of sterilization, suitability of the sterilization method, and effectiveness and evidence of the sterilization process should be sufficiently described in the manufacturing process of the device. Where ethylene oxide is used as a means of sterilization, an evidence for the control of the ethylene oxide residue after evaporation to the minimum acceptable level should be provided.

The standards followed during manufacturing and the conformity of the finished medical device to the claimed standard should be adequately discussed with relevant supporting data in this section or in other parts of the dossier.

8. LABELING OF MEDICAL DEVICES

8.1 General labeling requirements

All classes of medical devices should be properly labeled based on the justification and information provided with the registration dossier. Labeling serves to communicate safety- and performance-related information to users of medical devices and/or to patients, as well as to identify individual devices. Such information may appear on the device itself, on packaging (or as a packaging insert), or as instructions for use:

- a) All label statements required by regulation are in Amharic and/or English.
- b) The label should not be described or presented in a manner that is false, misleading, or deceptive or that is likely to create an erroneous impression regarding its use in any respect, either pictorially or in words.
- c) The medium, format, content, readability, and location of labeling 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.

- d) Instructions may not be needed or may be abbreviated for devices of low or moderate risk if they can be used safely and as intended by the manufacturer without any such instructions.
- e) Labeling 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, downloaded from the manufacturer's website using the Internet, magnetic, or optical media. However, at the time of submission, a copy or print out and/or electronic version should be provided with the dossier for registration.
- f) Any residual risks identified in the risk analysis should be reflected as contraindications or warnings within the labeling.
- g) The information needed to identify and use the device safely should be provided on the device itself, and /or on the packaging for each unit, and/or on the packaging of multiple devices. If individual packaging of each unit is not practicable, the information should be set out in the leaflet, packaging insert, or other media supplied with, or applicable to, one or multiple devices.
- h) The use of internationally recognized (i.e., standardized) symbols should have high priority, provided that 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 device user, e.g., for a lay-user or for a newly introduced symbol, an explanation should be provided.

8.2 Content of medical device labeling

Irrespective of the class of the device, the labeling of any medical device should bear the following information:

- a) Name or trade name of the device;
- b) Name and complete address of the actual manufacturer of the device (street name, number, telephone, fax, e-mail, website);
- c) Date of issue or latest revision of the instructions for use and, where appropriate, an identification number;
- d) Sufficient details for the user to identify the device and, where these are not obvious, its intended purpose, user, and patient population of the device, and, where relevant, the contents of any packaging;
- e) An indication of either the batch code/lot number (e.g., on single-use disposable devices or reagents) or model, or the serial number (e.g., on electrically-powered medical devices), where relevant, to allow appropriate actions to trace and recall the devices.
- f) An unambiguous indication of the 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. 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.

- g) For devices other than those covered by (f) above, and as appropriate to the type of device, an indication of the dates of manufacture and expiration. This indication may be included in the batch code/lot number or serial number;
- h) The information needed to verify whether the device is properly installed and can operate correctly and safely, plus details of the nature and frequency of preventative and regular maintenance and, where relevant, any quality control, replacement of consumable components, and calibration needed to ensure that the device operates properly and safely during its intended life;
- i) Any warnings, precautions, limitations, or contra-indications;
- j) The performance intended by the manufacturer and, where relevant, any undesirable side effects;
- k) An indication on the external packaging of any special storage and /or handling conditions that apply;
- l) Details of any further treatment or handling needed before the device can be used (e.g., sterilization, final assembly, calibration, preparation of reagents and/or control materials, etc.) where relevant;
- m) If the device is sterile, an indication of that condition and necessary instructions in the event of damage to the sterile packaging and, where appropriate, description of methods for re-sterilization;
- n) If the device has been specified by the manufacturer as intended for single-use only, an indication of that state;
- o) If the device is intended for premarket clinical investigation, or for in vitro diagnostic medical devices, or for performance evaluation only, an indication of that situation;
- p) If the device is intended for presentation or demonstration purposes only, an indication of that situation;
- q) If the device is to be installed with or connected to other medical devices or equipment, or with dedicated software in order to operate as required for its intended use, sufficient details of its characteristics to identify the correct devices or equipment to use in order to obtain a safe combination;
- r) If the device is implantable, information regarding any particular risks in connection with its implantation;
- s) Information regarding the risks of reciprocal interference posed by the reasonably foreseeable presence of the device during specific investigations, evaluations, treatment, or use (e.g., electromagnetic interference from other equipment);
- t) 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, and any restriction on the number of reuses. Where a device is supplied with

the intention that it is sterilized before use, the instructions for cleaning and sterilization should be such that, if correctly followed, the device will still perform as intended by the manufacturer and comply with the *Essential Principles of Safety and Performance of Medical Devices*;

- u) If the device emits radiation for medical purposes, details of the nature, type, and where appropriate, the intensity and distribution of this radiation,
- v) Precautions and/or measures to be taken in the event of changes in the performance, or malfunction, of the device including a contact telephone number, if appropriate;
- w) Precautions and/or measures to be taken as regards exposure, in reasonably foreseeable environmental conditions, to magnetic fields, external electrical influences, electrostatic discharge, pressure or variations in pressure, temperature, humidity, acceleration, thermal ignition sources, proximity to other devices, etc.;
- x) If the device administers medicinal products, adequate information regarding any medicinal product(s) that the device in question is designed to administer, including any limitations in the choice of substances to be delivered;
- y) Any medicinal substances or biological material incorporated into the device as an integral part of the device;
- z) Any requirement for special facilities, or special training, or particular qualifications of the device user and/or third parties;
- aa) Any precautions to be taken related to the disposal of the device and/or its accessories (e.g., lancets), to any consumables used with it (e.g., batteries or reagents), or to any potentially infectious substances of human or animal origin;
- bb) Where relevant, for devices intended for lay persons, a statement clearly directing the user not to make any decision of medical relevance without first consulting his or her health care provider; and,
- cc) For in vitro diagnostic medical devices, in addition to the information required above, directions/instructions for the proper use should include:
 - i. Intended use/purpose (e.g., monitoring, screening, or diagnostic) including an indication that it is for *in vitro* diagnostic use;
 - ii. Test principles;
 - iii. Specimen type;
 - iv. Condition for collection, handling, and preparation of the specimen;
 - v. Reagent description and any limitation (e.g.. use with a dedicated instrument only);
 - vi. 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;
 - vii. Assay procedure, including calculations and interpretation of results;
 - viii. Information on interfering substances that may affect the performance of the assay;
 - ix. Analytical performance characteristics, such as sensitivity, specificity, and accuracy (which is a combination of trueness and precision);

- x. Diagnostic performance characteristics, such as sensitivity and specificity; and,
- xi. Reference intervals.

9. SAMPLE OF ACTUAL PRODUCT

Where applicable, a sample of actual products may be requested for the purpose of visual confirmation and/or for the purpose of laboratory testing or analytical performance evaluation of the device. Also, as ample specimen of the packaging materials may be requested, when applicable.

SECTION II: MEDICAL DEVICE CONFORMITY ASSESSMENT OTHER THAN IVD

1. RATIONALE

The Authority is responsible for ensuring a high level of protection of public health and safety. Public trust and confidence in medical devices, and in the administrative systems by which they are regulated, are based on the safety and performance of such products throughout their life cycle. Conformity assessments, conducted before and after a medical device is placed on the market, and post-market surveillance of devices in actual use are complementary elements of the medical device global regulatory system. Medical device conformity assessments are intended to provide the objective evidence of safety, performance, and benefits and risks to maintain public confidence in the product.

Conformity assessment is primarily the responsibility of the medical device manufacturer; however, it is done in the context of the established requirements stated in this Guideline, and both the process and conclusions are subject to further review and approval by the Authority prior to its implementation. In general, the degree of requirement of conformity assessment is proportional to the risks associated with a particular category of devices. The conformity assessment elements indicated in this Guideline reflect the need to make conformity assessment more rigorous as the risk class of a medical device increases.

2. ELEMENTS OF CONFORMITY ASSESSMENT FOR ALL CLASSES OF MEDICAL DEVICE

The conformity assessment elements that should be provided with the registration dossier and/or after marketing of the device when requested by the Authority should include: a quality management system, a system for post-market surveillance, summary technical documentation, a declaration of conformity, and the registration of manufacturers and their medical devices. Requirements on a declaration of conformity and registration of medical devices and their manufacturers are described in Section I of this Guideline. All five conformity assessment elements are required for each of the device classes. Where there are alternatives within a conformity assessment element, the manufacturer may choose the one that it believes to be the most suitable and provide justification for its suitability.

2.1 Conformity assessment of the quality management system (QMS)

A manufacturer needs to demonstrate its ability to provide medical devices that consistently meet both customer and regulatory requirements. Manufacturers of medical devices should demonstrate compliance through an established and effectively implemented quality management system that it meets the regulatory requirements of the medical devices. Processes required by the quality management system but carried out on the manufacturer's

behalf by third parties remain the responsibility of the manufacturer and are subject to control under the manufacturer's quality management system, and its adequacy should be assessed.

Conformity assessment of the manufacturer's quality management system is influenced by the class of the medical device.

The manufacturer should always provide certification of conformity against internationally recognized standards for all class devices. The adequacy of the standards in relation to safety and performance of the device should be discussed with relevant supporting data for Class II and higher devices. In case the provided certification is found to be unsatisfactory, the Authority may conduct an onsite audit and inspection of the facilities of Class III and IV device manufacturers. Unless it is deemed to be necessary, the QMS of Class I medical device manufacturers' facilities are normally not subjected to onsite inspection.

Manufacturers of Class III and above devices should have a full quality management system that includes design and development, and this should be provided with the registration dossier at the time of submission. Manufacturers of Class II devices should have a quality management system also; however, the procedures incorporated within it may not include design and development activities. Manufacturers of Class I devices are expected to have the basic elements of a QMS in place but it need not include design and development activities.

2.2 System for post-marketing surveillance

Prior to and after placing the product on the market, the manufacturer should put a process in place, as part of its quality management system, to assess the continued conformity of the device to the essential principles of safety and performance through the post-marketing phase. This process will include complaint handling, post-market vigilance reporting, and corrective and preventive actions. The manufacturer and/or local representative should provide annual post-marketing vigilance and post-marketing reports of Class II and higher devices.

2.3 Summary of Technical Documentation (STED)

Manufacturers of all classes of devices are expected to demonstrate conformity of the device to the essential principles of safety and performance through the preparation of technical documentation that shows how each medical device was developed, designed, and manufactured, together with the descriptions and explanations necessary to understand the manufacturer's determination with respect to such conformity. The technical documentation should always be updated as necessary to reflect the current status, specifications, and configuration of the device. The extent of evidence in the STED is likely to increase with the risk class of the medical device, its complexity, and the extent to which it incorporates new technology.

The STED should always be provided at the time of dossier submission at pre-market level for Class III and higher devices. The STED for Class I and II devices shall be subject to the device type and this may not necessarily be submitted by the applicant at the time of initial dossier submission. However, when deemed necessary, the Authority may request the STED prior to marketing authorization and after marketing of Class I and II medical devices.

The manufacturer should create the STED from existing technical documentation to provide evidence to the Authority that the medical device is in conformity with the essential principles of device safety and performance. The STED reflects the status of the medical device at a particular moment in time (e.g., at the moment of pre-market submission or when requested by the Authority for post-market purposes) and is prepared in order to meet regulatory requirements.

The depth and detail of the information contained in the STED will depend on:

- The classification of the device;
- The complexity of the device;
- The device's particular characteristics, such as—
 - If the device incorporates novel technology,
 - If the marketed device is now being marketed for an intended use different from the original one,
 - It is a new device to the manufacturer,
 - The device type has been associated with a significant number of adverse events, including use errors,
 - It incorporates novel or potentially hazardous materials, or,
 - The device type raises specific public health concerns.

The STED should contain summary information on selected topics, detailed information on certain specific topics, and an essential principles checklist (as indicated below).

2.3.1. Contents of Summary Technical Documentation (STED)

a) Device description and specification

(i) Device description

- (1) General description including its intended use/purpose;
- (2) The intended patient population and medical condition to be diagnosed and/or treated and other considerations, such as patient selection criteria;
- (3) Principles of operation;
- (4) Risk class and the applicable classification rule according to the principles of medical devices classification;
- (5) An explanation of any novel feature;

- (6) A general description of accessories, various configurations, and the key functional elements, e.g., its parts/components (including software, if appropriate), its formulation, its composition, and its functionality. Where appropriate, this will include labelled pictorial representations (e.g., diagrams, photographs, and drawings), clearly indicating key parts/components, including sufficient explanation to understand the drawings and diagrams; and,
- (7) A description of the materials incorporated into key functional elements and those making either direct contact with the human body or indirect contact with the body.

(ii) Product specification

The STED should contain a list of the features, dimensions, and performance attributes of the medical device, its variants, and accessories (if such are within the scope of the STED) that would typically appear in the product specification made available to the end user, e.g., in brochures, catalogues, and the like.

(iii) Reference to similar and previous generations of the device

Where relevant to demonstrating conformity to the essential principles, and to the provision of general background information, the STED should contain an overview of:

- (1) The manufacturer's previous generation(s) of the device, if such exist; and/or,
- (2) Similar devices available on the local and international markets.

b) Design and Manufacturing Information

(i) Device design

The STED should contain information to obtain a general understanding of the design stages applied to the device. It is not intended to take the place of the more detailed information required for a QMS audit or other conformity assessment activity. The information may take the form of a flow chart.

(ii) Manufacturing process

The STED should contain information on a general understanding of the manufacturing processes. It is not intended to take the place of the more detailed information required for a QMS audit or other conformity assessment activity. The information may take the form of a process flow chart showing, for example, an overview of production, assembly, any final product testing, and packaging of the finished medical device.

(iii) Design and manufacturing site

For the activities in (i) and (ii), the STED should identify the sites where these activities are performed. If QMS certificates or the equivalent exist for these sites, they should be annexed to the STED.

c) *Essential Principles (EP) Checklist for Conformity Assessment*

The manufacturer of the medical device should provide evidence for the conformance of the device to essential principles of the safety and performance by completing the checklist provided in Annex III of this Guideline.

The EP checklist should incorporate a cross-reference to the location of such evidence both within the full technical documentation held by the manufacturer and within the STED.

The STED should contain an EP checklist that identifies:

- The essential principles;
- Whether each essential principle applies to the device and, if not, why not;
- The method(s) used to demonstrate conformity with each essential principle that applies;
- A reference for the method(s) employed (e.g., standard); and,
- The precise identity of the controlled document(s) that offers evidence of conformity with each method used.

Methods used to demonstrate conformity may include one or more of the following:

- Conformity with recognized or other standards;
- Conformity with a commonly accepted industry test method(s);
- Conformity with an in-house test method(s);
- Evaluation of pre-clinical and clinical evidence; or,
- Comparison to a similar device already available on the market.

d) *Risk Analysis and Control Summary*

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

e) ***Product Verification and Validation***

The STED should summarize the results of verification and validation studies undertaken to demonstrate conformity of the device with the essential principles that apply to it. Such information would typically cover:

- Engineering tests;
- Laboratory tests;
- Simulated use testing;
- Any animal tests for demonstrating feasibility or proof of concept of the finished device; and,
- Any published literature regarding the device or substantially similar devices.

Such summary information may include:

- Declaration/Certificate of conformity to a recognized standard(s) and summary of the data, if no acceptance criteria are specified in the standard;
- Declaration/Certificate of conformity to a published standard(s) that has not been recognized, supported by a rationale for its use, and summary of the data, if no acceptance criteria are specified in the standard;
- Declaration/Certificate of conformity to a professional guideline(s), industry method(s), or in-house test method(s), supported by a rationale for its use, a description of the method used, and summary of the data in sufficient detail to allow assessment of its adequacy; or,
- A review of published literature regarding the device or substantially similar devices.

In addition, where applicable to the device, the STED should contain detailed information on:

(i) **Biocompatibility**

The STED should contain a list of all materials in direct or indirect contact with the patient or user.

Where biocompatibility testing has been undertaken to characterize the physical, chemical, toxicological, and biological response of a material, detailed information should be included on the tests conducted, standards applied, test protocols, the analysis of data, and the summary of results. At a minimum, tests should be conducted on samples from the finished, sterilized (when supplied sterile) device.

(ii) **Medicinal substances**

Where the medical device incorporates a medicinal substance(s), the STED should provide detailed information concerning that medicinal substance, its identity and

source, the intended reason for its presence, and its safety and performance in the intended application.

(iii) Biological safety

The STED should contain a list of all materials of animal or human origin used in the device. For these materials, detailed information should be provided concerning the selection of sources/donors; the harvesting, processing, preservation, testing, and handling of tissues, cells and substances of such origin should also be provided.

Process validation results should be included to substantiate that manufacturing procedures are in place to minimize biological risks, in particular, with regard to viruses and other transmissible agents. The system for record-keeping to allow traceability from sources to the finished device should be fully described.

(iv) Sterilization

Where the device is supplied sterile, the STED should contain the detailed information of the initial sterilization validation including bioburden testing, pyrogen testing, testing for sterilant residues (if applicable), and packaging validation.

Typically, the 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.

Evidence of the ongoing revalidation of the process should also be provided. Typically, this would consist of arrangements for, or evidence of, revalidation of the packaging and sterilization processes.

(v) Software verification and validation

The STED should contain 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, 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 labeling.

(vi) Animal studies

Where studies in an animal model have been undertaken to provide evidence of conformity with the essential principles related to functional safety and performance, detailed information should be contained in the STED.

The STED should describe the study objectives, methodology, results, analysis, and conclusions and should document conformity with Good Laboratory Practices. The rationale (and limitations) of selecting the particular animal model should be discussed.

(vii) Clinical studies

Where studies in human subjects have been undertaken to provide evidence of conformity with the essential principles related to functional safety and performance, detailed information should be contained in the STED.

The STED should describe the study objectives, methodology, results, analysis, and conclusions and document conformity with Good Clinical Practices. The rationale (and limitations) of selecting the particular study design should be discussed.

f) Stability and Use-by Date

This section should describe claimed shelf life, in-use stability, and shipping studies where applicable. When a stability study is not applicable, the applicant should provide a “Use-by Date” of the device.

(i) Claimed shelf life

This section should provide information on stability testing studies to support the claimed shelf life. Testing should be performed on at least three different lots manufactured under conditions that are essentially equivalent to routine production conditions (these do not need to be consecutive lots). Accelerated studies or extrapolated data from real time data are acceptable for initial shelf life claim but need to be followed up with real time stability studies.

Such detailed information should describe:

- The study report (including the protocol, number of lots, acceptance criteria, and testing intervals);
- When accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies; and,
- Conclusions and claimed shelf life.

(ii) In-use stability

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

In the case of automated instrumentation if calibration stability is claimed, supporting data should be included. Such detailed information should describe:

- The study report (including the protocol, acceptance criteria, and testing intervals); and,
- Conclusions and claimed in-use stability.

(iii) Shipping stability

This section should provide information on shipping stability studies for one lot to evaluate the tolerance of products to the anticipated 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.

Such information should describe:

- The study report (including the protocol, acceptance criteria);
- Method used for simulated conditions; and,
- Conclusion and recommended shipping conditions.

(iv) “Use-by” date

A “Use-by” date is required where a safety-related characteristic or claimed performance is likely to deteriorate over time. It is not a lifetime determination, as described above.

In deciding whether there is such a safety-related deterioration, the manufacturer must provide proper risk analysis and measures taken to manage risk:

- The risk analysis will identify those performances and characteristics necessary for the safe use of the particular device. For example, the risk analysis may indicate that sterility is necessary for safe use. Equally, the risk analysis would not cover the color of the device if this is purely aesthetic, but it might cover the color of the device if that color has a purpose related to safe use of the device (e. g., the color signifies the size of the device).
- The risk analysis and measures taken to manage risk will also identify the level or extent of performance or characteristic but only in so far as they are relevant to safe use of the device. For example, the level of resistance to gas flow or rate of leakage from a breathing system, or the probability of non-sterility.
- The risk analysis and measures taken to manage risk will also identify the period over which the relevant performance or characteristic would be expected to be maintained for safe use, including the shelf life and intended period of use. For example, the period over which a pacemaker battery maintains sufficient energy to function after implantation as long as intended by the manufacturer.

The information that must provide to justify the decision;

- **Information required when the Use-by date is given**

The manufacturer must demonstrate that the relevant performances and characteristics of the device are maintained over the claimed shelf life which the Use-by date reflects. This may be achieved by—

- Prospective studies using accelerated aging, validated with real time degradation correlation; or,
- Retrospective studies using real time experience, involving, e.g., testing of stored samples, review of the complaints history, or published literature, etc.;
- or,
- A combination of the two methods.

- **Information required when Use-by date is not given**

As the absence of a Use-by date constitutes an implicit claim of an infinite shelf life, the manufacturer must demonstrate through appropriate risk analysis and risk management either:

- That there are no safety-related performances or characteristics which are likely to deteriorate over time; or,
- That the extent of any likely deterioration does not represent an unacceptable risk.

Examples of the Use-by date determination approach

(1) Cardiac catheter with latex balloon

The only aspect considered in this example is the time-related deterioration of the balloon. A cardiac catheter incorporates a latex balloon to locate the catheter tip within and temporarily occlude a blood vessel. The ability of the balloon to withstand certain pressure is necessary for safe use. The latex of the balloon, however, deteriorates over time. The packaging and the storage instructions to protect the device from light reduce the rate of deterioration, but do not prevent it. It is therefore necessary to give a Use-by date.

The manufacturer must demonstrate that the latex balloon remains able to withstand the relevant pressure over the claimed shelf life, when the device is stored in accordance with the manufacturer's instructions.

(2) Orthopedic hip joint (supplied sterile)

The only aspect considered in this example is the time-related deterioration of the sterile packaging. A metal and ceramic orthopedic implant is supplied sterile in a composite plastic/paper unit container. The ability of the packaging to maintain

sterility is necessary for safe use. While the maintenance of sterility is, in part, event-related (i.e., a function of the actual storage and handling conditions), it is also a function of time, due to, e.g., the reduction in flexibility and seal strength of the package material over a period, rendering it more susceptible to the events which may compromise sterility.

Moreover, as such implants are available in a variety of sizes to suit different clinical applications; a particular device may remain in the store over a long time until needed for implantation.

It is therefore necessary to give a Use-by date. In the case of maintenance of sterility, the Use-by date will reflect a combination of:

- The time-related deterioration in the performance of the pack, e.g., seal strength, seal integrity, and resistance to penetration of particles carrying micro-organisms; and,
- The probability of events occurring during transport and storage which compromise sterility, but are not evident, and therefore, where the warning not to use the device when the package is opened or damaged, will not assist.

The manufacturer must demonstrate that the packaging material is able to maintain device sterility over the claimed shelf life, when stored in accordance with the storage instructions.

(3) Implantable cardiac pacemaker

The only aspect considered in this example is battery lifetime. An implantable cardiac pacemaker is supplied with a battery fitted and sealed into the device. Due to self-discharge, all batteries have a limited life, even if not used. The period for which the battery maintains sufficient energy for the device to function as intended by the manufacturer following implantation is important to avoid the need for a surgical operation to explant and replace the device unnecessarily soon. It is therefore necessary to give a Use-by date. The manufacturer must demonstrate that the battery retains sufficient energy to function for the manufacturer's claimed operating time even if implanted at the end of the claimed shelf life.

SECTION III: CONFORMITY ASSESSMENT FOR IVD MEDICAL DEVICES

1. ELEMENTS OF IVD DEVICE CONFORMITY ASSESSMENT

The conformity assessment elements that should be provided with the registration dossier and/or after marketing of the device when requested by the Authority should include: a quality management system, a system for post-market surveillance, summary technical documentation, a declaration of conformity, and the registration of manufacturers and their medical devices. Requirements on a declaration of conformity and registration of medical devices and their manufacturers are described in Section I of this Guideline. All five conformity assessment elements are required for each of the device classes. Where there are alternatives within a conformity assessment element, the manufacturer may choose the one that it believes to be the most suitable and provide justification for its suitability.

1.1 Conformity assessment of quality management system

A manufacturer needs to demonstrate its ability to provide IVD medical devices that consistently meet both customer and regulatory requirements. Manufacturers of IVD medical devices should demonstrate compliance through an established and effectively implemented quality management system that it meets the regulatory requirements of the IVD medical devices. Processes required by the quality management system but carried out on the manufacturer's behalf by third parties remain the responsibility of the manufacturer (applicant) and are subject to control under the manufacturer's quality management system and thus its adequacy should be assessed and discussed.

Conformity assessment of the manufacturer's quality management system is influenced by the class of the IVD medical device.

The manufacturer should always provide certification of conformity against internationally recognized standards for all class of IVD devices.

The adequacy of the standards in relation to safety and performance of the IVD device should be discussed with relevant supporting data for Class B and higher devices. In case the provided certification found to be not satisfactory, the Authority may conduct an onsite audit and inspection of Class B and higher IVD device manufacturer facilities before issuance of marketing authorization. Unless it is deemed to be necessary, the QMS of a Class A IVD medical device manufacturer's facilities are normally not subjected to onsite inspection at the time of marketing authorization.

Manufacturers of Class C and higher IVD devices should have a full quality management system that includes design and development, and this should be provided with the registration dossier at the time of submission. Manufacturers of Class B IVD devices should have a quality management system, also; however, the procedures incorporated within it may not include design and development activities. Manufacturers of Class A IVD devices are expected to have the basic elements of a QMS in place but need not include design and development activities.

1.2 System for post-marketing surveillance

Prior to and after placing the product on the market, the manufacturer should put a system in place, as part of its quality management system, a process to assess the continued conformity of the device to the Essential Principles of Safety and Performance through the post-marketing phase. This process will include complaint handling, post-market vigilance reporting and corrective and preventive actions. The manufacturer and/or local representative should provide annual post market vigilance and post-marketing report of class B and higher devices.

1.3 Summary technical documentation (STED) of IVD devices

The technical documentation provides the evidence that the IVD medical device meets the essential principles of safety and performance of the device.

The manufacturer should create the STED from existing technical documentation to provide evidence to the Authority that the medical device is in conformity with the essential principles of device safety and performance. The STED reflects the status of the IVD medical device at a particular moment in time (e.g., at the moment of pre-market submission or when requested by the Authority for post-market purposes).

The depth and detail of the information contained in the STED will depend upon:

- The classification of the IVD device;
- The complexity of the IVD device; and,
- The particular characteristics of the device, such as—
 - If the IVD device incorporates novel technology,
 - Marketed IVD device but now being marketed for an intended use different from the original one,
 - New IVD device to the manufacturer,
 - The IVD device type has been associated with a significant number of adverse events, including use errors,

- Incorporates novel or potentially hazardous materials, or,
- The IVD device type raises specific public health concerns (e.g., virulent influenza pandemic).

The STED should be prepared and submitted to the Authority for Class C and D IVD medical devices. For Class A and B IVD medical devices, the STED will be prepared and submitted only at the request of the Authority.

The STED should contain summary information on selected topics, detailed information on certain specific topics and an essential principles checklist (as indicated below).

1.3.1 Contents of IVD device summary technical documentation

a) *Device description including accessories*

(i) Device Description

- (a) The intended use of the IVD medical device. This may include:
 - i.* what is detected;
 - ii.* its function (e.g., screening, monitoring, diagnosis or aid to diagnosis);
 - iii.* the specific disorder, condition or risk factor of interest that it is intended to detect, define, or differentiate;
 - iv.* whether it is automated or not;
 - v.* whether it is qualitative or quantitative;
 - vi.* the type of specimen(s) required (e.g. serum, plasma, whole blood, tissue biopsy, urine); and,
 - vii.* testing population;
- (b) Intended user (lay person or professional),
- (c) General description of the principle of the assay method or instrument principles of operation,
- (d) The class of the device and the applicable classification rule according to *Principles of In Vitro Diagnostic Medical Devices Classification*,
- (e) Description of the components (e.g., reagents, assay controls and calibrators) and, where appropriate, a description of the reactive ingredients of relevant components (such as antibodies, antigens, or nucleic acid primers),
- (f) Description of the specimen collection and transport materials provided with the IVD medical device or descriptions of specifications recommended for use,
- (g) For instruments of automated assays: a description of the appropriate assay characteristics or dedicated assays,
- (h) For automated assays: a description of the appropriate instrumentation characteristics or dedicated instrumentation,
- (i) Description of any software to be used with the IVD medical device;
- (j) Description or complete list of the various configurations/variants of the IVD medical device that will be made available, and,

- (k) Description of the accessories, other IVD medical devices, and other products that are not IVD medical devices, which are intended to be used in combination with the IVD medical device.

- (ii) Reference to Manufacturer's previous Device Generation (s) and/or Similar Device or Device History
 - (a) For an IVD medical device not yet available in market

Where relevant to demonstrating conformity to the essential principles, and to provide general background information, the STED may provide a summary of:

 - i. The manufacturer's previous generation(s) of the IVD medical device, if such exists; and/or,
 - ii. The manufacturer's similar IVD medical devices available on the market.
 - (b) For an IVD medical device available in market

This information may include a summary of the number of adverse event reports related to the safety and performance of this IVD medical device in relation to the number of IVD medical devices placed on the market.

External certificates and documents that give written evidence of conformity with the essential principles may be annexed to the STED.

b) Design and Manufacturing Information

(i) Device Design

The STED should contain information to obtain a general understanding of the design stages applied to the IVD medical device.

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 IVD medical device.

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

For instruments and software, an overview of the entire system would be required, 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.

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

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

Typically for Class C and D IVD medical devices, detailed information on material specifications should be provided.

This section is not intended to take the place of the more detailed information required for a QMS audit or other conformity assessment activity. If design takes place at multiple sites, a controlling site must be identified.

(ii) Manufacturing Process

For Classes C and D medical devices only, the STED should contain manufacturing information to allow an assessor to obtain a general understanding of the manufacturing processes. It is not intended to take the place of the more detailed information required for a QMS audit or other conformity assessment activity.

This information may take the form of a process flow chart showing, for example, an overview of production including the technologies used, assembly, and packaging of the finished IVD medical device. It should also include details of any in-process and final product testing (e.g., the manufacturer's quality control release program).

(iii) Design and Manufacturing Site

For the activities in (i) and (ii), the STED should identify the sites where these activities are performed. If QMS certificates or the equivalent exist for the sites, they should be annexed to the STED.

c) Essential Principle (EP) checklist for conformity assessment of IVD medical device

The manufacturer of an IVD medical device should provide evidence for the conformance of the device to essential principles of safety and performance by completing the checklist provided in Annex VI of this Guideline.

The EP checklist should incorporate a cross-reference to the location of such evidence both within the full technical documentation held by the manufacturer, and within the STED.

The STED should contain an EP checklist that identifies:

- a. The essential principles;
- b. Whether each essential principle applies to the IVD device and, if not, why not;
- c. The method(s) used to demonstrate conformity with each essential principle that applies;
- d. Reference for the method(s) employed (e.g., standard); and,

- e. The precise identity of the controlled document(s) that offers evidence of conformity with each method used.

Methods used to demonstrate conformity may include one or more of the following:

- (i) Conformity with recognized or other standards;
- (ii) Conformity with a commonly accepted industry test method(s);
- (iii) Conformity with an in-house test method(s);
- (iv) Evaluation of pre-clinical and clinical evidence; or,
- (v) Comparison to a similar IVD device already available on the market.

d) Risk Analysis and Control Summary

The STED should contain a summary of the risks identified during the risk analysis process and a description of how these risks have been controlled to an acceptable level. Preferably, this 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 IVD medical device, such as the risk from false positive or false negative results; indirect risks which may result from IVD medical device-associated hazards, such as instability, which could 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.

Typically, for a Class D IVD medical device, detailed data and a report should be provided.

e) Product Verification and Validation

The STED should summarize the results of verification and validation studies undertaken to demonstrate conformity of the IVD medical device with the essential principles that apply.

The information provided in the product verification and validation section of the STED will vary in the level of detail as determined by the classification of the device. Where appropriate, such information might come from the literature.

For the purpose of the IVD STED, document summary and detailed information may be provided as described below:

- (i) Summary Information

A summary should provide enough information to allow the Authority to assess the validity of that information. This summary should contain a brief description of:

- (a) The study protocol;

- (b) The study results; and,
- (c) The study conclusion.

Such summary information may include:

- (a) Where a recognized standard exists, a declaration/certificate of conformity to a recognized standard can be provided with a summary of the data if no acceptance criteria are specified in the standard;
- (b) In the absence of a recognized standard, a declaration/certificate of conformity to a published standard that has not been recognized might be provided if it is supported by a rationale for its use, summary of the data, and a conclusion, if no acceptance criteria are specified in the standard;
- (c) In the absence of a recognized standard and non-recognized published standards, a professional guideline, industry method, or in-house standard may be referred to in the summarized information. However, it should be supported by a rationale for its use, a description of the method used, a summary of the data in sufficient detail and a conclusion to allow assessment of its adequacy;
- (d) A review of relevant published literature regarding the device/analyte (measurand) or substantially similar IVD medical devices.

(ii) Detailed Information

Detailed information should include:

- (a) The complete study protocol,
- (b) The method of data analysis,
- (c) The complete study report, and,
- (d) The study conclusion.

For detailed information, 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.

For clinical performance (which is part of the clinical evidence), the detailed information will typically include individual data points (formatted raw data) for a Class D IVD medical device.

Where appropriate, actual test result summaries with their acceptance criteria should be provided and not just pass/fail statements.

f) Analytical Performance

The statements and descriptions in the following sections refer to all IVD medical devices. It must be noted, however, that there are applicability differences between instrumentation and reagent-based assays, and that the assays themselves may be quantitative, semi-quantitative, or qualitative in nature. There may be limited applicability of some of the following subsections for qualitative or semi-quantitative assays:

(i) Specimen type

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

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

This section should include 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.

(ii) Analytical Performance Characteristics

(a) Accuracy of measurement

This section should provide information on the trueness of the measurement procedure and summarize the data in sufficient detail to allow assessment of the adequacy of the means selected to establish the trueness. Trueness measures apply to both quantitative and qualitative assays only when a reference standard or method is available. Typically for Class C and D IVD medical devices, detailed information should always be provided.

(b) Precision of measurement

The analytical performance in this section should describe repeatability and reproducibility studies.

i. Repeatability

This section should include repeatability estimates 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. Typically for Class C and D IVD medical devices, detailed information should be provided.

Note 1: Such studies should include the use of samples that represent the full range of expected analyte (measurand) concentrations that can be measured by the test as claimed by the manufacturer.

Note 2: If a recognized standard is used, a declaration/certificate of conformity to the recognized standard along with a summary of the data and conclusions should be provided.

ii. Reproducibility

This section should include 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.” Reproducibility data is obtained for instrumentation in conjunction with an appropriate assay. Typically for Class C and D IVD medical devices, detailed information should be provided.

Note 1: Such studies should include the use of samples that represent the full range of expected analyte (measurand) that can be measured by the test as claimed by the manufacturer.

Note 2: If a recognized standard is used, a declaration/certificate of conformity to the recognized standard, along with a summary of the data and conclusions, should be provided.

(c) Analytical sensitivity

The analytical sensitivity should provide a 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. Typically for Class C and D IVD medical devices, detailed information should be provided.

For example:

- i.* Number of standard deviations above the mean value of the sample without analyte (measurand), commonly referred to as “limit of blank” (LoB).
- ii.* Lowest concentration distinguishable from zero, based on measurements of samples containing analyte (measurand), commonly referred to as “limit of detection” (LoD).
- iii.* Lowest concentration at which precision and/or trueness are within specified criteria, commonly referred to as the “limit of quantitation” (LoQ).

(d) Analytical specificity

This section should 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.

The applicant should 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.

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:

- i.* Substances used for patient treatment (e.g., therapeutic drugs, anticoagulants, etc.)
- ii.* Substances ingested by the patient (e.g., over-the-counter medications, alcohol, vitamins, foods, etc.);
- iii.* Substances added during sample preparation (e.g., preservatives, stabilizers);
- iv.* Substances encountered in specific specimens types (e.g., hemoglobin, lipids, bilirubin, proteins);
- v.* 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).

Typically, interference studies involve adding the potential interferent to the sample and determining any bias of the test parameter relative to the control sample to which no interferent has been added. Typically for Class C and D IVD medical devices, detailed information should be provided.

(e) Metrological traceability of calibrator and control material

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

Precision control materials, used when establishing the reproducibility of a measurement procedure, do not require the assessment of metrological traceability to a reference material or a reference method.

Typically for a Class D IVD medical device, detailed information should be provided.

(f) Measuring range of assay

This section should include 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. This 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.

Typically for Class C and D IVD medical devices, detailed information should be provided.

(g) Assay cut of Definition

This section should provide a summary of analytical data with a description of the study design including methods for determining the assay cut-off, including:

- i.* The population(s) studied (demographics/selection/inclusion and exclusion criteria/number of individuals included);
- ii.* Method or mode of characterization of specimens; and,
- iii.* Statistical methods, e.g., Receiver Operator Characteristic (ROC), to generate results and, if applicable, define gray-zone/equivocal zone.

Typically, for Class C and D IVD medical devices, detailed information should be provided.

g) Clinical Performance

Where relevant, the STED should contain data on the clinical performance of the IVD medical device.

This clinical performance data is one of the elements of clinical evidence that demonstrates the conformity of the IVD medical device to the essential principles that apply to it. Analytical performance and clinical performance are elements of clinical evidence.

h) Stability (Excluding Specimen Stability)

This section should describe claimed shelf life, in- use stability, and shipping studies.

(i) Claimed shelf life

This section should provide information on stability testing studies to support the claimed shelf life. Testing should be 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). Accelerated studies or extrapolated data from real time data are acceptable for initial shelf life claim but need to be followed up with real time stability studies.

Typically for Class C and D IVD medical devices, detailed information should be provided.

Such detailed information should describe:

- (a) The study report (including the protocol, number of lots, acceptance criteria, and testing intervals);
- (b) When accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies; and,
- (c) Conclusions and claimed shelf life.

(ii) In-use stability

Information on in-use stability studies for one lot reflecting actual routine use of the device (real or simulated) should be provided. This may include open vial stability and/or, for automated instruments, onboard stability.

In the case of automated instrumentation, if calibration stability is claimed, supporting data should be included.

Such detailed information should describe:

- (a) The study report (including protocol, acceptance criteria, and testing intervals); and,
- (b) Conclusions and claimed in-use stability.

Typically for Class C and D IVD medical devices, detailed information should be provided.

(iii) Shipping stability

This section should provide information on shipping stability studies for one lot to evaluate the tolerance of products to the anticipated 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.

Such information should describe:

- (a) The study report (including the protocol, acceptance criteria);
- (b) Method used for simulated conditions; and,
- (c) Conclusion and recommended shipping conditions.

Typically for Class C and D IVD medical devices, detailed information should be provided.

i) Software Verification and Validation

The STED should contain 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, 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 labeling. Typically, for a Class D IVD medical device, detailed information would be provided.

(i) Animal studies

Where studies in an animal model have been undertaken to provide evidence of conformity with the essential principles related to functional safety and performance, detailed information should be contained in the STED.

The STED should describe the study objectives, methodology, results, analysis, and conclusions and should document conformity with Good Laboratory Practices. The rationale (and limitations) of selecting the particular animal model should be discussed.

(ii) Clinical studies

Where studies in human subjects have been undertaken to provide evidence of conformity with the essential principles related to functional safety and performance, detailed information should be contained in the STED.

The STED should describe the study objectives, methodology, results, analysis, and conclusions and should document conformity with Good Clinical Practices. The rationale (and limitations) of selecting the particular study design should be discussed.

SECTION IV: RE-REGISTRATION OF MEDICAL DEVICES

Once a device is registered, it is required to be re-registered in order to market the product. Re-registration is required after four years from the date of issue of the authorization. Therefore, an applicant is required to apply for re-registration within 120 days before the due date. With the applicable registration fee, the following data should be submitted for re-registration of the device:

1. Application form (as indicated in Annex I);
2. Certificate of compliance with international standards and/or Free Sale Certificate, as described in Section I of this Guideline;
3. Statements confirming that there is no change in general safety and performance of the device;
4. Pharmacovigilance and post-marketing report, including any adverse reaction report;
5. Updated Summary Technical Documentation (STED);
6. Updated Essential Principle Checklist for device safety and performance conformity assessment with due consideration of pharmacovigilance and post-marketing report; and,
7. Analytical performance evaluation data for the IVD medical device, particularly for Class C and D medical devices.

SECTION V: APPLICATION FOR VARIATION AND AMENDMENT TO A REGISTERED DEVICE

1. VARIATION

The Authority should be informed of any significant change(s) that could reasonably be expected to affect the safety or effectiveness of a medical device. Significant change(s) may include any of the following:

- a) The manufacturing process, facility, or equipment;
- b) The manufacturing quality control procedures, including the methods, tests, or procedures used to control the quality, purity, and sterility of the device or of the materials used in its manufacture;
- c) The design of the device, including its performance characteristics, principles of operation and specifications of materials, energy source, software or accessories; and
- d) The intended use of the device, including any new or extended use, any addition or deletion of a contraindication for the device, and any change to the period used to establish its expiry date.

These changes will require Authority approval before they can be implemented. Any other change(s) should be notified immediately to the Authority and may be implemented without prior approval.

2. AMENDMENT APPLICATION

Application for amendment (addition of product(s)) to an existing registered product, in terms of documentation, would normally be considered as a new application, except some administrative documents (such as agency agreement and company profile) may not be necessary. Therefore, based on the proposed product category, the applicant should follow the respective section of this Guideline for compilation of documents.

All applications for variation and amendment to a registered device shall be made in writing and shall be accompanied by a variation fee.

SECTION VI: REQUIREMENTS FOR APPLICATION OF A MEDICAL DEVICE WITH SRA PROCEDURE

An applicant claiming to have a registration certificate issued by a Stringent Regulatory Authority (SRA) as defined above should submit complete dossiers in soft copy, as required in this Guideline, respective of the device categories and/or classes. At the time of registration by the Authority, however, the information that must be submitted in hard copy and assessed is:

1. Full information under Section I (general registration requirement of all medical devices) of this Guideline;
2. A QA-certified copy of the Marketing Authorization and/or Free Sale Certificate issued by the relevant SRA;
3. A CE certificate for a product marketed in the European member states can be used as evidence for a marketing authorization in an SRA;
4. In the case of WHO PQP-accepted products, a final acceptance letter and a copy of the WHOPARs;
5. A written commitment letter to notify the Authority that whenever there is a pending variation, notice of concern, withdrawal, or recall initiated it shall be communicated to the Authority;
6. Evidence of a minimum of five (5) years of current and continuous manufacturing experience; and,
7. If applicable, a certificate of analysis from the manufacturer and/or accredited laboratory and samples of actual products for laboratory analysis by the Authority may be exempted.

Annex I: Application Form for Registration of Medical Devices

The applicant for registration of a medical device is required to provide the completed templates below by summarizing the registration dossiers. Information that is not provided in the dossier should not appear in the formats in the application form. Annexes and addendum in the registration dossier should always be cross-referenced in the application form.

Application Form for Registration of a Medical Device Health Product Registration and Licensing Directorate Food, Medicine and Health Care Administration and Control Authority of Ethiopia			
S/N	Title	To be completed by the applicant	Page number and/or annexes
1	Applicant		
	1.1.Name		
	1.2.Physical address including street number, telephone, e-mail, etc.		
	1.3.Contact person in the company		
2	Type of Application New <input type="checkbox"/> Re-Registration <input type="checkbox"/> Variation <input type="checkbox"/>		
3	Representative in Ethiopia		
	3.1. Name		
	3.2. Physical address including street number, telephone, e-mail, etc.		
	3.3. Contact person in the company		
4	Manufacturer of the Product		
	4.1. Name		
	4.2. Physical address including street number, telephone, e-mail, etc.		
	4.3. Contact person in the company		
5	Details of the Product		
	5.1. Name of the Product (common name, brand name, trade name)		
	5.2. Model/Serial number		
	5.3. Device intended use		
	5.2. Device description		
	5.3. Device classification	Circle: I, II, III, IV	
	5.4. Other classification, if applicable		

	5.5. Reason for classification		
	5.6. Shelf life and use period		
6	Device Safety and Performance Conformity Assessment		
	6.1. Declaration of conformity		
	6.2. Standards to which the device complies		
	6.3. Summary Technical Documentation		
7	Essential Principle Checklist (for Device Safety and Conformity Assessment)		
9	Regulatory Situation in Other Countries		
	List of countries in which this product has been registered, restrictions on sale or distribution, withdrawn from the market, etc.		
10	List of Documents Attached with This Application (Indicate page number, location in the dossier, and annexes, as applicable)		
	10.1. Agency agreement		
	10.2. Certificate of compliance with international standards		
	10.3. GMP Certificate/Free Sale Certificate		
	10.4. Summary Technical Documentation		
	10.5. Device design and manufacturing		
	10.6. Finished product specification		
	10.7. Analytical performance for IVD		
	10.8. Stability study, where applicable		
	10.9. Labeling		
	10.10. Essential Principle Checklist for device conformity to safety and performance		
	10.11. Others (please indicate type of document other than those mentioned above)		
11	Declaration by Applicant		
	<p>I, the undersigned, certify that all the information in the accompanying documentation concerning an application for registration of the medical device listed below is correct and true, and reflects the total information available.</p> <p>Name of the Device(trade name, common name)- _____</p>		

	<p>Device Category _____</p> <p>Duly authorized to represent (applicant company name) _____</p> <p>I further confirm that the information referred to in my application file is available for verification. I also agree that I am obliged to comply with the requirements of the Authority related to the Medical Device Registration at any time in future.</p> <p>Name _____</p> <p>Signature _____</p> <p>Position in company _____</p> <p>Date: _____</p>
10	To be completed by Authority designated person
	Date of Application:
	Remarks:

Annex II: General Approach for Classification of Medical Devices Other than IVD

The explanations of individual classification rules are given in the following table. Any special terms used are explained, and practical issues related to the rule are clarified. It must be emphasized that even if a particular device type is given as an example, this does not mean that such devices are in all cases in the class indicated by the example. It is always possible that some manufacturer will assign to a device an entirely different intended use than what was used in the context of the example.

Rule	Explanation	Example
1	All non-invasive devices are in Class I, unless one of the rules set out hereinafter applies.	<ul style="list-style-type: none"> - Body liquid collection devices intended to be used in such a way that a return flow is unlikely (e.g., to collect body wastes such as urine collection bottles, ostomy pouches, incontinence pads or collectors used with wound drainage devices). They may be connected to the patient by means of catheters and tubing - 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, plaster of Paris, cervical collars, gravity traction devices, compression hosiery) - Devices intended in general for external patient support (e.g., hospital beds, patient hoists, walking aids, wheelchairs, stretchers, dental patient chairs) - Corrective glasses and frames - Stethoscopes for diagnosis. - Eye occlusion plasters - Incision drapes - Conductive gels - Non-invasive electrodes (electrodes for EEG or ECG) - Image intensifying screens - Permanent magnets for removal of ocular debris
<p>Practical Issues of Classification</p> <p>Some non-invasive devices are indirectly in contact with the body and can influence internal physiological processes by storing, channeling, or treating blood, other body liquids, or liquids which are returned or infused into the body or by generating energy that is delivered to the body.</p>		
2	- All non-invasive devices intended for channeling or storing blood, body liquids or tissues, liquids or gases for the purpose of eventual infusion,	<ul style="list-style-type: none"> - Devices intended to be used as channels in active drug delivery systems, e.g., tubing intended for use with an infusion pump - Devices used for channeling, e.g., antistatic tubing for anesthesia, anesthesia breathing circuits, pressure indicator,

	administration or introduction into the body are in Class II - If they may be connected to an active medical device in Class II or a higher class,	pressure limiting devices - Syringes for infusion pumps
	- If they are intended for use for storing or channeling blood or other body liquids or for storing organs, parts of organs or body tissues	- Devices intended to channel blood (e.g., in transfusion, extracorporeal circulation) - Devices intended for temporary storage and transport of organs for transplantation (i.e. containers, bags and similar products) - Devices intended for long term storage of biological substances and tissues such as corneas, sperm, human embryos, etc. (i.e. containers, bags and similar products) - Fridges specifically intended for storing blood , tissues, etc.
	- In all other cases, they are in Class I.	- Devices that provide a simple channeling function, with gravity providing the force to transport the liquid, e.g., administration sets for infusion - Devices intended to be used for a temporary containment or storage function, e.g., cups and spoons specifically intended for administering medicines - Syringes without needles

Practical Issues of Classification

Blood bags are covered as an exception under a separate rule (see rule 18).

3	All non-invasive 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 III.	- Devices intended to remove undesirable substances out of the blood by exchange of solutes such as hemodialysers - Devices intended to separate cells by physical means, e.g., gradient medium for sperm separation - Hemodialysis concentrates
	Unless the treatment consists of filtration, centrifugation or exchange of gas or heat, in which case they are in Class II.	- Particulate filtration of blood in an extracorporeal circulation system. These are used to remove particles and emboli from the blood - Centrifugation of blood to prepare it for transfusion or autotransfusion - Removal of carbon dioxide from the blood and/or adding oxygen - Warming or cooling the blood in an extracorporeal circulation system

Practical Issues of Classification

These devices are normally used in conjunction with an active medical device covered under Rule 9 or Rule 11. Filtration and centrifugation should be understood in the context of this rule as exclusively mechanical methods.

4	All non-invasive devices which come into contact with injured skin:	- Wound dressings, such as: absorbent pads, island dressings, cotton wool, wound strips, adhesive bandages (sticking plasters, bandaid) and gauze dressings which act as a barrier, maintain wound position or absorb exudates from the wound
	- are in Class I if they are intended to be used as a mechanical barrier, for compression or for absorption of exudates.	
	- are in Class III if they are intended to be used principally with wounds which have breached the dermis and can only heal by secondary intent.	- Are principally intended to be used with severe wounds that have substantially and extensively breached the dermis, and where the healing process can only be by secondary intent such as: <ul style="list-style-type: none"> o dressings for chronic extensive ulcerated wounds o dressings for severe burns having breached the dermis and covering an extensive area o dressings for severe decubitus wounds o dressings incorporating means of augmenting tissue and providing a temporary skin substitute
	- are in Class II in all other cases, including devices principally intended to manage the micro-environment of a wound.	- Have specific properties intended to assist the healing process by controlling the level of moisture at the wound during the healing process and to generally regulate the environment in terms of humidity and temperature, levels of oxygen and other gases and pH values or by influencing the process by other physical means <ul style="list-style-type: none"> - These devices may specify particular additional healing properties whilst not being intended for extensive wounds requiring healing by secondary intent. - Adhesives for topical use - Polymer film dressings - Hydrogel dressings - Non-medicated impregnated gauze dressings

Practical Issues of Classification

Products covered under this rule are extremely claim sensitive, e.g., a polymeric film dressing would be in Class II if the intended use is to manage the micro-environment of the wound or in Class I if its intended use is limited to retaining an invasive cannula at the wound site. Consequently it is impossible to say a priori that a particular type of dressing is in a given class without knowing its intended use as defined by the manufacturer. However, a claim that the device is interactive or active with respect to the wound healing process usually implies that the device is in Class III.

Most dressings that are intended for a use that is in Class II or III, also perform functions that are in Class I, e.g., that of a mechanical barrier. Such devices are nevertheless classed according to the intended use in the higher class. For such devices incorporating a

medicinal product or a human blood derivative see Rule 13 or animal tissues or derivatives rendered non-viable see Rule 17.

5	All invasive devices with respect to body orifices, other than surgically invasive devices and which are not intended for connection to an active medical device or which are intended for connection to an active medical device in Class I:	
	- are in Class I if they are intended for transient use,	<ul style="list-style-type: none"> - Handheld mirrors used in dentistry to aid in dental diagnosis and surgery - Dental impression materials - Tubes used for pumping the stomach - Impression trays - Enema devices - Examination gloves - Urinary catheters intended for transient use - Prostatic balloon dilation catheters
	- are in Class II if they are intended for short term use,	<ul style="list-style-type: none"> - Short term corrective contact lenses - Tracheal tubes - Stents - Vaginal pessaries - Indwelling urinary catheters intended for short term use
	- except if they are used 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 I,	<ul style="list-style-type: none"> - Dressings for nose bleeds - Materials for manufacturing dentures
	- are in Class III if they are intended for long term use,	<ul style="list-style-type: none"> - Urethral stents - Long term corrective contact lenses - Tracheal cannula - Urinary catheters intended for long term use
	- except if they are used 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 II.	<ul style="list-style-type: none"> - Orthodontic wires - Fixed dental prostheses - Fissures sealants
	All invasive devices with respect to body orifices, other than surgically invasive devices, intended for connection to an active medical	<ul style="list-style-type: none"> - Tracheostomy or tracheal tubes connected to a ventilator - Blood oxygen analyzers placed under the eye-lid - Powered nasal irrigators - Nasopharyngeal airways

	device in Class II or a higher class, are in Class II.	<ul style="list-style-type: none"> - Some enteral feeding tubes - Fiber optics in endoscopes connected to surgical lasers - Suction catheters or tubes for stomach drainage - Dental aspirator tips
6	All surgically invasive ¹ devices intended for transient use are in Class II unless they are:	<ul style="list-style-type: none"> - Needles used for suturing - Needles or syringes - Lancets - Suckers - Single use scalpels and single use scalpel blades - Support devices in ophthalmic surgery - Staplers - Surgical swabs - Drill bits connected to active devices - Surgical gloves - Etchants - Tester of artificial heart valves - Heart valve occluders, sizers, and holders - Swabs to sample exudates - Single use aortic punches
	- intended specifically to control, diagnose, monitor or correct a defect ² of the heart or of the central circulatory system ¹ through direct contact with these parts of the body, in which case they are in Class III.	<ul style="list-style-type: none"> - Cardiovascular catheters (e.g., angioplasty balloon catheters, stent delivery catheters/systems), including related guidewires, related introducers and dedicated disposable cardiovascular surgical instruments e.g., electrophysiological catheters, electrodes for electrophysiological diagnosis and ablation - Catheters containing or incorporating sealed radioisotopes, where the radioactive isotope is not intended to be released into the body, if used in the central circulatory system - Distal protection devices
	- reusable surgical instruments ¹ , in which case they are in Class I..	<ul style="list-style-type: none"> - Scalpels and scalpel handles - Reamers - Drill bits - Saws, that are not intended for connection to an active device - Retractors forceps, excavators and chisels - Sternum retractors for transient use
	- intended specifically for use in direct contact with the central nervous system, in which case they are in Class IV.	<ul style="list-style-type: none"> - Neuro-endoscopes - Brain spatulas - Direct stimulation cannula - Spinal cord retractors - spinal needles
	- intended to supply energy in the form of ionizing radiation in	<ul style="list-style-type: none"> - Catheters containing or incorporating sealed radioisotopes, where the radioactive isotope as such is not

	which case they are in Class III.	intended to be released into the body, if used in the circulatory system, excluding the central circulatory system
	- intended to have a biological effect or to be wholly or mainly absorbed ⁶ in which case they are in Class III.	
	- intended to administer medicines by means of a delivery system, if this is done in a manner that is potentially hazardous, taking account the mode of application, in which case they are Class III.	- Devices for repeated self-application where dosage levels and the nature of the medicinal product are critical, e.g., insulin pens
7	All surgically invasive devices intended for short term use are in Class II unless they are intended:	- Clamps - Infusion cannula - Skin closure devices - Temporary filling materials - Tissue stabilisers ² used in cardiac surgery
	- either specifically to control, 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 IV,	- Cardiovascular catheters - Cardiac output probes - Temporary pacemaker leads - Thoracic catheters intended to drain the heart, including the pericardium - Carotid artery shunts - Ablation catheter
	- or specifically for use in direct contact with the central nervous system, in which case they are in Class IV,	- Neurological catheters - Cortical electrodes
	- or to supply energy in the form of ionizing radiation in which case they are in Class III.	- Brachytherapy devices
	- intended to have a biological effect or to be wholly or mainly absorbed in which case they are in Class IV,	- Absorbable sutures - Biological adhesives
	- or to undergo chemical change in the body, except if the devices are placed in the teeth, or to administer medicines ¹ , in which case they are Class III.	- Adhesives
Practical Issues of Classification		
Note 1: Administration of medicines is more than just channeling; it implies also		

storage and/or influencing the volume and rate of the medicine delivered. Implanted capsules for the slow release of medicines are medicines and not medical devices.

Note 2: The expression “correct a defect” does not cover devices that are used accessorially in heart surgery, e.g., tissue stabilizers.

8	All implantable devices and long-term surgically invasive devices are in Class III unless they are intended:	<ul style="list-style-type: none"> - Prosthetic joint replacements not covered by Directive 2005/50/EC - Ligaments - Shunts - Stents and valves (e.g., pulmonary) - Nails and plates - Intra-ocular lenses - Internal closure devices.(including vascular closure devices²) - Tissue augmentation implants - Peripheral vascular catheters - Peripheral vascular grafts and stents - Penile implants - Non-absorbable sutures, bone cements and maxillo-facial implants, visco-elastic surgical devices intended specifically for ophthalmic anterior segment surgery
	- to be placed in the teeth, in which case they are in Class II,	<ul style="list-style-type: none"> - Bridges and crowns - Dental filling materials and pins - Dental alloys, ceramics and polymers
	- to be used in direct contact with the heart, the central circulatory system or the central nervous system, in which case they are Class IV,	<ul style="list-style-type: none"> - Prosthetic heart valves - Aneurysm clips - Vascular prosthesis and stents - Central vascular catheters - Spinal stents - CNS electrodes - Cardiovascular sutures - Permanent and retrievable vena cava filters - Septal occlusion devices - Intra-aortic balloon pumps - External left ventricular assisting devices
	- to have a biological effect or to be wholly or mainly absorbed, in which case they are in Class IV,	<ul style="list-style-type: none"> - Absorbable sutures - Adhesives and implantable devices claimed to be bioactive through the attachment of surface coatings such as phosphorylcholine
	- or to undergo chemical change in the body, except if the devices are placed in the teeth, or to administer medicines, in which case they are in Class IV.	<ul style="list-style-type: none"> - Rechargeable non-active drug delivery systems

9	All active therapeutic devices intended to administer or exchange energy are in Class II	<p><u>Electrical and/or magnetic and electromagnetic energy</u></p> <ul style="list-style-type: none"> - Muscle stimulators - External bone growth stimulators - TENS devices - Eye electromagnets - Electrical acupuncture <p><u>Thermal energy</u></p> <ul style="list-style-type: none"> - Cryosurgery equipment. - Heat exchangers, except the types described below <p><u>Mechanical energy</u></p> <ul style="list-style-type: none"> - Powered dermatomes - Powered drills - Dental hand pieces. <p><u>Light</u></p> <ul style="list-style-type: none"> - Phototherapy for skin treatment and for neonatal care <p><u>Sound</u></p> <ul style="list-style-type: none"> - Hearing aids <p><u>Ultrasound</u></p> <ul style="list-style-type: none"> - Equipment for physiotherapy
	- Unless their characteristics are such that they may administer or exchange energy to and from the human body in a potentially hazardous way, taking account of the nature, the density and the site of application of the energy, in which case they are in Class II.	<p><u>Kinetic energy</u></p> <ul style="list-style-type: none"> - Lung ventilators <p><u>Thermal energy</u></p> <ul style="list-style-type: none"> - Incubators for babies - Warming blankets - Blood warmers - Electrically powered heat exchangers (for example, those used with patients incapable of reacting, communicating and/or who are without a sense of feeling) <p><u>Electrical energy</u></p> <ul style="list-style-type: none"> - High-frequency electrosurgical generators, and electrocautery equipment, including their electrodes - External pacemakers and defibrillators - Electroconvulsive therapy equipment. <p><u>Coherent light</u></p> <ul style="list-style-type: none"> - Surgical lasers <p><u>Ultrasound</u></p> <ul style="list-style-type: none"> - Lithotriptors, surgical ultrasound devices <p><u>Ionizing radiation</u></p> <ul style="list-style-type: none"> - Radioactive sources for after loading therapy - Therapeutic cyclotrons and linear accelerators - Therapeutic X-ray sources
	- All active devices intended to	- External feedback systems for active therapeutic devices

	control or monitor the performance of active therapeutic devices in Class III or intended to influence directly the performance of such devices are in Class III.	- After loading control devices
10	Active devices intended for diagnosis are in Class II: - if they are intended to supply energy which will be absorbed by the human body, except for devices used to illuminate the patient's body, in the visible spectrum,	- Magnetic resonance equipment. - Pulp testers. - Evoked response stimulators - Diagnostic ultrasound
	- if they are intended to image in vivo distribution of radiopharmaceuticals,	- Gamma cameras - Positron emission tomography and single photon emission computer tomography
	- if they are intended to allow direct diagnosis or monitoring of vital physiological processes,	- Electrocardiographs - Electroencephalographs - Cardioscopes with or without pacing pulse indicators ² - Electronic thermometers - Electronic stethoscopes - Electronic blood pressure measuring equipment.
	- Unless they are specifically intended for 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 CNS in which case they are in Class III.	- Intensive care monitoring and alarm devices (e.g. blood pressure, temperature, oxygen saturation) - Biological sensors - Blood gas analyzers used in open heart surgery - Cardioscopes - Apnea monitors, including apnea monitors in home care
	- Active devices intended to emit ionizing radiation and intended for diagnostic and therapeutic interventional radiology ³ including devices which control or monitor ⁴ such devices, or which directly influence their performance, are in Class III.	- Diagnostic X-ray sources
<p>Practical Issues of Classification</p> <p>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</p>		

	anesthesia, intensive care or emergency care are in Class III, whilst medical devices intended to be used to obtain readings of vital physiological signals in routine checkups and in self-monitoring are in Class II.	
11	All active devices intended to administer and/or remove medicines, body liquids or other substances to or from the body are in Class II, 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 of application, in which case they are in Class III.	<ul style="list-style-type: none"> - Suction equipment - Feeding pumps - Jet injectors for vaccination - Nebulizers to be used on conscious and spontaneously breathing patients where failure to deliver the appropriate dosage characteristics is not potentially hazardous <ul style="list-style-type: none"> - Infusion pumps - Ventilators - Anesthesia machines - Anesthetic vaporizers - Dialysis equipment - Blood pumps for heart-lung machines - Hyperbaric chambers - Pressure regulators for medical gases - Medical gas mixers - Moisture exchangers in breathing circuits if used on unconscious or non-spontaneously breathing patients - Nebulizers where the failure to deliver the appropriate dosage characteristics could be hazardous
12	All other active devices are in Class I.	<ul style="list-style-type: none"> - Active diagnostic devices intended to illuminate the patient's body in the visible spectrum such as examination lights or to optically view the body such as surgical microscopes - Devices intended in general for external patient support (e.g. hospital beds, patient hoists, wheelchairs, dental patient chairs) - Active diagnostic devices intended for thermography - Dental curing lights
13	All 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 IV.	<ul style="list-style-type: none"> - Antibiotic bone cements - Condoms with spermicide - Heparin coated catheters - Endodontic materials with antibiotics - Ophthalmic irrigation solutions principally intended for irrigation, which contain components which support the metabolism of the endothelial cells of the cornea - Dressings incorporating an antimicrobial agent where the purpose of such an agent is to provide ancillary action on the wound - Contraceptive intrauterine devices (IUDs) containing copper or silver - Drug eluting stents, e.g., coronary, pulmonary

	All devices incorporating as an integral part, a human blood derivative are in Class IV.	- Surgical sealants containing human serum albumin
14	All devices used for contraception or the prevention of the transmission of sexually transmitted diseases are in Class III,	- Condoms - Contraceptive diaphragms
	- Unless they are implantable or long term invasive devices, in which case they are in Class IV.	- Contraceptive intrauterine devices (IUDs)
Note: Intrauterine contraceptives whose primary purpose is to release progestogens are not medical devices.		
15	- All devices intended specifically to be used for disinfecting, cleaning, rinsing or, when appropriate hydrating contact lenses are in Class III.	- Contact lens solutions - Comfort solutions
	- All devices intended specifically to be used for disinfecting medical devices are in Class II	- 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
	- Unless they are specifically to be used for disinfecting invasive devices in which case they are in Class III.	- Denture disinfecting products - Washers-disinfectors for endoscopes - Disinfectants for the fluid pathways of hemodialysis equipment - Disinfectants for ocular prosthesis, intraosseous transcutaneous amputation prosthesis, surgical equipment and invasive dental equipment
Practical Issues of Classification This rule does not apply to mechanical means of cleaning of devices, such as brushes and ultrasound. Such products will only fall under this rule if they are specifically intended for use with medical devices.		
16	- Devices specifically intended for recording of X-ray diagnostic images are in Class II.	- X-ray films - Photostimulable phosphor plates
17	All devices manufactured utilizing animal tissues or derivatives, rendered non-viable are Class IV except where such devices are intended to come into contact with intact skin only.	- Biological heart valves - Porcine xenograft dressings - Implants and dressings made from collagen - Devices utilizing hyaluronic acid of animal origin

Practical Issues of Classification

Devices made of non-viable animal tissue that comes into contact with intact skin only (e.g. leather components of orthopedic appliances) are in Class I in accordance to Rule 1.

Note 1: Derivatives are products that are processed from animal tissues and exclude substances such as milk, silk, beeswax, hair, lanolin

Note 2: Intact skin includes the skin around an established stoma unless the skin is breached.

18	By derogation from other rules, blood bags are in Class IIb.	- Blood bags (including those containing or coated with an anticoagulant). Where blood bags have a function greater than for storing purposes and include systems for preservation other than anti-coagulants, then other rules (e.g., rule 13) may apply .
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Note: Blood bags are described in the European Pharmacopoeia in the monograph on "Containers for Blood and Blood Components."

Annex III: Essential Principles Checklist for Medical Device other than IVD

Essential Principle Checklist for Medical Device Conformity Assessment Other than IVD Medical Device				
Medical Device Serial Number/Identity:				
Medical Device Name:				
Essential Principle	Applicable to the Device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
General Requirements				
1. Medical devices should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training of intended users, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.				

Essential Principle Checklist for Medical Device Conformity Assessment Other than IVD Medical Device

Medical Device Serial Number/Identity:
 Medical Device Name:

Essential Principle	Applicable to the Device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
<p>2. The solutions adopted by the manufacturer for the design and manufacture of the devices should conform to safety principles, taking account of the generally acknowledged state of the art. When risk reduction is required, the manufacturer should control the risk(s) so that the residual risk(s) associated with each hazard is judged acceptable. The manufacturer should apply the following principles in the priority order listed:</p> <ul style="list-style-type: none"> ▪ identify known or foreseeable hazards and estimate the associated risks arising from the intended use and foreseeable misuse, ▪ eliminate risks as far as reasonably practicable through inherently safe design and manufacture, ▪ reduce as far as is reasonably practicable the remaining risks by taking adequate protection measures, including alarms, ▪ inform users of any residual risks. 				
<p>3. Devices should achieve the performance intended by the manufacturer and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions within the scope of the definition of a medical device applicable in each jurisdiction.</p>				

Essential Principle Checklist for Medical Device Conformity Assessment Other than IVD Medical Device

Medical Device Serial Number/Identity:

Medical Device Name:

Essential Principle	Applicable to the Device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
4. The characteristics and performances referred to in Clauses 1, 2 and 3 should not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.				
5. The devices should be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected under transport and storage conditions (for example, fluctuations of temperature and humidity) taking account of the instructions and information provided by the manufacturer.				
6. The benefits must be determined to outweigh any undesirable side effects for the performances intended.				
Design and Manufacturing Requirements				
7. Chemical, physical and biological properties				

Essential Principle Checklist for Medical Device Conformity Assessment Other than IVD Medical Device

Medical Device Serial Number/Identity:
 Medical Device Name:

Essential Principle	Applicable to the Device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
<p>The devices should be designed and manufactured in such a way as to ensure the characteristics and performance referred to in Clauses 1 to 6 of the 'General Requirements'. Particular attention should be paid to:</p> <ul style="list-style-type: none"> ▪ the choice of materials used, particularly as regards toxicity and, where appropriate, flammability, ▪ the compatibility between the materials used and biological tissues, cells, body fluids, and specimens, taking account of the intended purpose of the device, ▪ the choice of materials used should reflect, where appropriate, matters such as hardness, wear and fatigue strength. 				
<p>The devices should be designed, manufactured and packed in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to patients, taking account of the intended purpose of the product. Particular attention should be paid to tissues exposed and to the duration and frequency of exposure.</p>				
<p>8. -----etc.----- -----</p>				
<p>9. -----etc.----- -----</p>				

Essential Principle Checklist for Medical Device Conformity Assessment Other than IVD Medical Device				
Medical Device Serial Number/Identity:				
Medical Device Name:				
Essential Principle	Applicable to the Device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
<p>I declare that the information provided in this EP format is accurate and correct and the device conforms to all applicable requirements stipulated in this Guideline and other international standards.</p> <p>Name: _____</p> <p>Signature: _____</p> <p>Position: _____</p> <p>Date: _____</p>				

Annex IV: Classification Approaches for IVD Medical Devices

The explanations of individual classification approaches are given in the following table. Any special terms used are explained and rationales related to the approaches are clarified at the bottom of each rule. It must be emphasized that even if a particular device type is given as an example, this does not mean that such devices are in all cases in the class indicated by the example. It is always possible that some manufacturer will assign to such a device an entirely different intended use than what was used in the context of the example.

Rule	Explanation	Example
1	<p>IVD medical devices intended for the following purposes are classified as Class D</p> <ul style="list-style-type: none"> - 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 - 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 	<p>Tests to detect infection by HIV, HCV, HBV, HTLV.</p> <p>This Rule applies to first-line assays, confirmatory assays and supplemental assays</p>
<p>Rationale for Classification</p> <p>Device 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.</p>		
2	<p>IVD medical devices intended to be used for blood grouping, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation, are classified as Class C, except for ABO system [A (ABO1), B (ABO2), AB (ABO3)], rhesus system [RH1 (D), RH2 (C), RH3 (E), RH4 (c), RH5 (e)], Kell system [Kel1 (K)], Kidd system [JK1 (Jka), JK2 (Jkb)] and Duffy system [FY1 (Fya), FY2 (Fyb)] determinations which are classified as Class D.</p>	<p>HLA, Duffy system (other Duffy systems except those listed in the rule as Class D are in Class C).</p>

Rationale for Classification

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 IVD medical device is designed to detect, and its importance in a transfusion setting.

3	IVD medical devices are classified as Class C if they are intended for use:	
	- In detecting the presence of, or exposure to, a sexually transmitted agent. Examples: Sexually transmitted diseases, such as <i>Chlamydia trachomatis</i> , <i>Neisseria gonorrhoeae</i> .	
	- In detecting the presence in cerebrospinal fluid or blood of an infectious agent with a risk of limited propagation. Examples: <i>Neisseria meningitidis</i> or <i>Cryptococcus neoformans</i> .	
	- In detecting the presence of an infectious agent where there is a significant risk that an erroneous result would cause death or severe disability to the individual or fetus being tested. Examples: diagnostic assay for CMV, <i>Chlamydia pneumoniae</i> , Methycillin Resistant <i>Staphylococcus aureus</i> .	
	- In pre-natal screening of women in order to determine their immune status towards transmissible agents. Examples: Immune status tests for Rubella or Toxoplasmosis.	
	- In determining infective disease status or immune status, and where there is a risk that an erroneous result will lead to a patient management decision resulting in an imminent life-threatening situation for the patient. Examples: Enteroviruses, CMV and HSV in transplant patients.	
	- In screening for selection of patients for selective therapy and management, or for disease staging, or in the diagnosis of cancer. Example: personalized medicine.	
	- In human genetic testing. Examples: Huntington's Disease, Cystic Fibrosis.	
	- To monitor levels of medicines, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in an immediate life-threatening situation for the patient. Examples: Cardiac markers, Cyclosporin, Prothrombin time testing.	
- In the management of patients suffering from a life-threatening infectious disease. Examples: HCV viral load, HIV Viral Load		

	and HIV and HCV geno- and sub-typing.	
	- In screening for congenital disorders in the fetus. Examples: Spina Bifida or Down Syndrome.	
<p>Rationale for Classification</p> <p>Devices in this Class present a moderate public health risk, or a high individual risk, where an erroneous result would put the patient in an imminent life-threatening situation, or would have a major negative impact on outcome. The devices provide the critical, or sole, determinant for the correct diagnosis. They may also present a high individual risk because of the stress and anxiety resulting from the information and the nature of the possible follow-up measures.</p>		
4	IVD medical devices 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.	Example for self-testing class C: - Blood glucose monitoring
	IVD medical devices intended for blood gases and blood glucose determinations for near-patient testing would be Class C. Other IVD medical devices that are intended for near-patient should be classified in their own right using the classification rules.	Example for self-testing class B: - Pregnancy self-test, fertility testing, urine test-strips
<p>Rationale of Classification</p> <p>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.</p>		
5	The following IVD medical devices are classified as Class A:	- Selective/differential microbiological media (excluding the dehydrated powders which are considered not to be a finished IVD medical device), identification kits for cultured microorganisms, wash solutions, instruments and plain urine cup.
	- Reagents or other articles which possess specific characteristics, intended by the manufacturer to make them suitable for in vitro diagnostic procedures related to a specific examination.	
	- Instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures.	
	- Specimen receptacles	

Rationale for Classification

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 low individual risk and no or minimal public health risk.

Any product for general laboratory use not manufactured, sold or represented for use for medical purpose are not deemed to be IVD medical devices. However, if the applicant wished to register as an IVD products for general laboratory use appropriate conformance assessment should be provide in line with this Guideline.

6	IVD medical devices not covered in Rules 1 through 5 are classified as Class B.	Blood gases, <i>H. pylori</i> and physiological markers such as hormones, vitamins, enzymes, metabolic markers, specific IgE assays and celiac disease markers.
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Rationale for Classification

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.

7	IVD medical devices that are controls without a quantitative or qualitative assigned value will be classified as Class B.	
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Rationale for Classification

For such controls, the qualitative or quantitative value is assigned by the user and not the manufacturer.

Annex V: Essential Principle Checklist for IVD Medical Devices

Essential Principles Checklist for IVD Medical Devices				
Identity/Serial Number of IVD:				
IVD medical Device Name:				
Essential Principle	Applicable to the device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
General Requirements				
1. Medical devices should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training of intended users, they will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.				

Essential Principles Checklist for IVD Medical Devices

Identity/Serial Number of IVD:

IVD medical Device Name:

Essential Principle	Applicable to the device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
<p>2. The solutions adopted by the manufacturer for the design and manufacture of the devices should conform to safety principles, taking account of the generally acknowledged state of the art. When risk reduction is required, the manufacturer should control the risk(s) so that the residual risk(s) associated with each hazard is judged acceptable. The manufacturer should apply the following principles in the priority order listed:</p> <ul style="list-style-type: none"> ▪ identify known or foreseeable hazards and estimate the associated risks arising from the intended use and foreseeable misuse, ▪ eliminate risks as far as reasonably practicable through inherently safe design and manufacture, ▪ reduce as far as is reasonably practicable the remaining risks by taking adequate protection measures, including alarms, ▪ inform users of any residual risks. 				

Essential Principles Checklist for IVD Medical Devices

Identity/Serial Number of IVD:

IVD medical Device Name:

Essential Principle	Applicable to the device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
<p>3. Devices should achieve the performance intended by the manufacturer and be designed, manufactured and packaged in such a way that they are suitable for one or more of the functions within the scope of the definition of a medical device applicable in each jurisdiction.</p>				
<p>4. The characteristics and performances referred to in Clauses 1, 2 and 3 should not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.</p>				

Essential Principles Checklist for IVD Medical Devices

Identity/Serial Number of IVD:

IVD medical Device Name:

Essential Principle	Applicable to the device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
5. The devices should be designed, manufactured and packed in such a way that their characteristics and performances during their intended use will not be adversely affected under transport and storage conditions (for example, fluctuations of temperature and humidity) taking account of the instructions and information provided by the manufacturer.				
6. All known and foreseeable risks, and any undesirable effects, should be minimized and be acceptable when weighed against the benefits of the intended performance of medical devices during normal condition of use.				
Design and Manufacturing Requirements				
7. Chemical, physical and biological properties				

Essential Principles Checklist for IVD Medical Devices

Identity/Serial Number of IVD:

IVD medical Device Name:

Essential Principle	Applicable to the device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
<p>- The devices should be designed and manufactured in such a way as to ensure the characteristics and performance referred to in Clauses 1 to 6 of the “General Requirements.” Particular attention should be paid to the:</p> <ul style="list-style-type: none"> ▪ choice of materials used, particularly as regards toxicity and, where appropriate, flammability, ▪ compatibility between the materials used and biological tissues, cells, body fluids, and specimens, taking account of the intended purpose of the device, ▪ choice of materials used should reflect, where appropriate, matters such as hardness, wear and fatigue strength. 				

Essential Principles Checklist for IVD Medical Devices				
Identity/Serial Number of IVD:				
IVD medical Device Name:				
Essential Principle	Applicable to the device?	Method Used to Demonstrate Conformity	Method Reference	Reference to Supporting Controlled Documents
- The devices should be designed, manufactured and packed in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to patients, taking account of the intended purpose of the product. Particular attention should be paid to tissues exposed and to the duration and frequency of exposure.				
8. ----- etc. ----- -----				
9. ----- etc. ----- -----				
<p>I declare that the information provided in this EP format is accurate and correct and the device conforms to all applicable requirements stipulated in this Guideline and other international standards.</p> <p>Name: _____</p> <p>Signature: _____</p> <p>Position: _____</p> <p>Date: _____</p>				