ETHIOPIAN FOOD AND DRUG AUTHORITY

Guideline for Classification of In Vitro Diagnostic Medical Devices

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Acronyms

CMV	Cytomegalovirus
HBV	Hepatitis B virus
HCV	Hepatitis C Virus
HIV	Human Immunodeficiency Virus
HLA	Human Leukocyte Antigen
HLV	Herpes Like Virus
HSV	Herpes Simplex Virus
HTLV	Human T-Lymphotropic Virus
IgE	Immunoglobulin E
IVD	In Vitro Diagnostic
PSA	Prostate-Specific Antigen
RH4	Rhodopsin 4

1. Introduction

Regulatory controls are intended to safeguard the health and safety of patients, users and other persons by ensuring that manufacturers of IVD devices follow specified procedures during design, manufacture and marketing. The risk presented by a particular device depends substantially on its intended use. The Essential Principles of Safety and Performance of medical devices also applies to IVD devices.

Regulatory controls shall be proportional to the level of risk associated with a medical device. The level of regulatory control shall increase with increasing degree of risk, taking account of the benefits offered by use of the device. The imposition of regulatory controls should not place an unnecessary burden on regulators or manufacturers.

Article 19 (1) of Food and Medicine Administration proclamation No. 1112/2019 of the Authority is also indicate that the rigor of regulatory assessment of medicine and medical device will be commensurate with the product's type, nature, and potential risk to human health.

It is also not feasible economically nor justifiable in practice to subject all IVD 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. An IVD medical device classification system is therefore needed, in order to apply to the devices an appropriate conformity assessment procedure.

In order to ensure that the conformity assessment described in the General Guidelines for medical device Marketing Authorization functions effectively, manufacturers should be able to determine the classification of their product as early as possible in device development. It is therefore important to set up a system of classification rules, so that each manufacturer could classify its own devices.

This guideline provides the principles of In vitro diagnostic medical device classification and their classification rules.

2. Terms and Definition

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

In Vitro Diagnostic Medical devices: - Means reagents, instruments, and systems intended for use in diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body.

Companion diagnostic:- Means a device which is essential for the safe and effective use of a corresponding medicinal product to: (a) identify, before and/or during treatment, patients who are most likely to benefit from the corresponding medicinal product; or (b) identify, before and/or during treatment, patients likely to be at increased risk of serious adverse reactions as a result of treatment with the corresponding medicinal product;

IVD medical device for self-testing

Any IVD medical device intended by the manufacturer for use by laypersons.

Layperson

Individual that does not have formal training in a relevant field or discipline.

Near patient / point of care testing (testing)

Testing performed outside a laboratory environment by a healthcare professional not necessarily a laboratory professional, generally near to, or at the side of, the patient.

Examination

Set of operations having the object of determining the value of a property.

Note: In the IVD medical device industry and in many laboratories that use IVD medical devices, examination of an analyte in a biological sample is commonly referred to as a test, assay or analysis.

Harm

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

Hazard

Potential source of harm.

Risk

Combination of the probability of occurrence of harm and the severity of that harm.

Intended use / purpose

The objective intent of the manufacturer regarding the use of an IVD medical device as reflected in the specifications, instructions and information provided by the manufacturer.

Instrument

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

Reagent

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

Specimen receptacle

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

Transmissible agent

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

Transmission

The spread of disease to a person.

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).

3. Objectives

The objectives of this guideline is to describe the principles of In vitro diagnostic medical devices classification and their classification rules which will help the applicants and assessors classify the devices appropriately.

4. Purpose

The purpose of this guideline is to

1) provide guidance for application assessors on how to determine the classification of IVD medical devices.
2) assist IVD medical device manufacturers to allocate their devices into appropriate risk class according to the authority's classification system, based on IVD medical device intended use and classification principles.

5. Scope

This guideline is applicable to risk-based classification of all medical devices that fulfil the definition of In vitro diagnostic medical devices.

6. General Principles

The IVD medical device classification system is based on the following criteria-

- the 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);
- the technical / scientific / medical expertise of the intended user (lay person or healthcare professional);
- the importance of the information to the diagnosis (sole determinant or one of several), taking into consideration the natural history of the disease or disorder including presenting signs and symptoms which may guide a physician;
- the impact of the result (true or false) to the individual and/or to public health.

7. Determination of IVD Medical devices Class

A four class system is adopted. There are four classes of IVD medical devices namely CLASS A, B, C and D as indicated in table 1.

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 the table below (table 1) 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 table 2).The general principles of IVD Medical Devices classification are listed in the following table.

Table 1: General classification system for IVD medical devices

CLASS	RISK LEVEL	DEVICE EXAMPLE
A	Low Individual Risk and Low Public Health Risk	Clinical Chemistry Analyser, 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

The regulatory requirements increases as the device class levels increases as shown in the conceptual illustration below figure-1. These may include, for example-

a. operation of a quality system, for all devices;

b. documentation of clinical evidence to support the manufacturer's specified intended use;

c. the need for technical data;

d. product testing using in-house or independent resources;

e. the need for and frequency of independent external audit of the manufacturer's quality system; and

f. independent external review of the manufacturer's technical data.

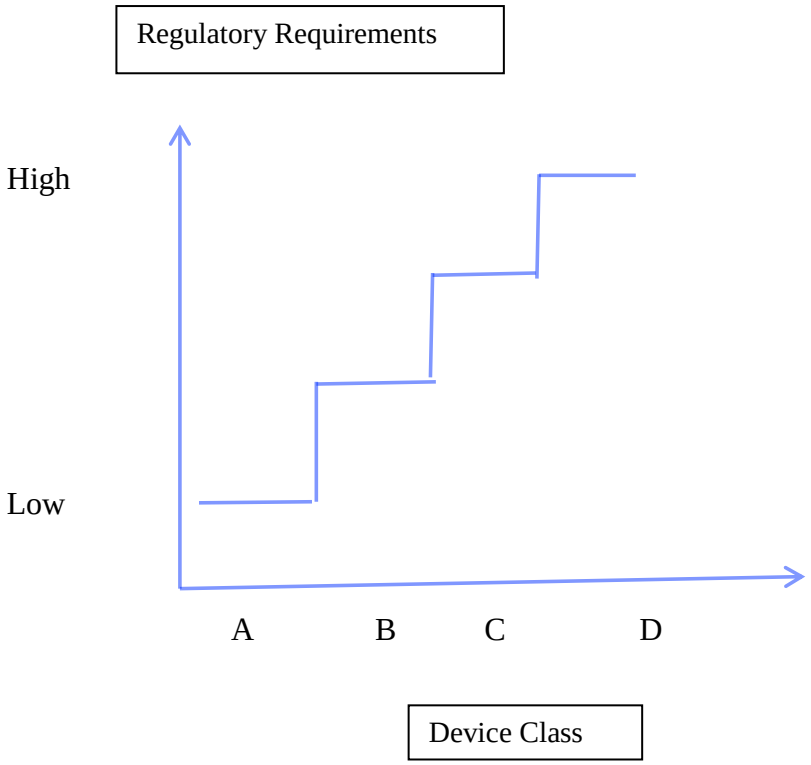

Figure 1. Conceptual illustration of regulatory requirements increasing with device risk class

8. IVD Medical Devices Classification Rules

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.

Table 2: Rules for classification medical device with their explanation and examples of IVD medical devices

<table>
<tr><th>Rule</th><th>Explanation</th><th>Examples</th></tr>
<tr><td>Rule 1</td><td>IVD medical devices intended for the following purposes are classified as Class D</td><td rowspan="3">Tests to detect infection by HIV, HCV, HBV, HTLV. Pyrogenicity tests (Endotoxin Activity Assay) marketed for detection of bacterial contamination of blood components. This Rule applies to all types of assays, such as first-line assays, confirmatory assays and supplemental assays.</td></tr>
<tr><td></td><td>a) Devices intended to be used to detect the presence of, or exposure to, a transmissible agent in blood, blood components, blood derivatives, cells, tissues or organs in order to assess their suitability for transfusion or transplantation; or</td></tr>
<tr><td></td><td>b) Devices intended to be used to detect the presence of, or exposure to, a transmissible agent that causes a life-threatening often incurable disease with a high risk of propagation.</td></tr>
<tr><td colspan="3">Rationale:
Devices in this Class are intended to be used to ensure the safety of blood and blood components for transfusion and / or cells, tissues and organs for transplantation. In most cases, the result of the test is the major determinant as to whether the donation/product will be used. Serious diseases are those that result in death or long-term disability, that are often incurable or require major therapeutic interventions and where an accurate diagnosis is vital to mitigate the public health impact of the condition.</td></tr>
<tr><td>Rule 2</td><td>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</td><td>HLA, Duffy system (other Duffy systems except those listed in the rule as Class D are in Class C).</td></tr>
</table>

	(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.	

Rationale:

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

Rule 3	IVD medical devices are classified as Class C if they are intended for use:	
	a) in detecting the presence of, or exposure to, a sexually transmitted agent. Examples: Sexually transmitted diseases, such as Chlamydia trachomatis, Neisseria gonorrhoeae;	
	b) in detecting the presence in cerebrospinal fluid or blood of an infectious agent with a risk of limited propagation. Examples: Neisseria meningitidis or Cryptococcus neoformans;	
	c) in detecting the presence of an infectious agent where there is a significant risk that an erroneous result would cause death or severe disability to the individual or fetus being tested. Examples: diagnostic assay for CMV, Chlamydia pneumoniae, Methycillin Resistant Staphylococcus aureus;	
	d) in pre-natal screening of women in order to determine their immune status towards transmissible agents. Examples: Immune status tests for Rubella or Toxoplasmosis;	
	e) in determining infective disease status or immune status, and where there is a risk that an erroneous result will lead to a patient management decision	

	resulting in an imminent life-threatening situation for the patient. Examples: Enteroviruses, CMV and HSV in transplant patients;	
	f) to be used as companion diagnostics,	
	g) to be used for disease staging, where there is a risk that an erroneous result would lead to a patient management decision resulting in a life-threatening situation for the patient or for the patient's offspring. **NOTE:** *those IVD medical devices where the therapy decision would usually be made only after further investigation and those used for monitoring would fall into class B under rule 6.*	
	h) to be used in screening, diagnosis, or staging of cancer;	
	i) in human genetic testing. Examples: Huntington's Disease, Cystic Fibrosis;	
	j) to monitor levels of medicines, substances or biological components, when there is a risk that an erroneous result will lead to a patient management decision resulting in an immediate life-threatening situation for the patient. Examples: Cardiac markers, Cyclosporin, Prothrombin time testing;	
	In the management of patients suffering from a life-threatening infectious disease. Examples: HCV viral load, HIV Viral Load and HIV and HCV geno- and subtyping;	
	k) for screening for congenital disorders in the embryo or foetus; Examples: Spina Bifida or Down Syndrome.	
	l) for screening of congenital disorders in new-born babies where failure to detect and treat such	

	disorders could lead to life-threatening situations or severe disabilities.	
Rationale: The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: 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.		
Rule 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; **Example for self-testing class B**: Pregnancy self-test, Fertility testing, Urine test-strips.
	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.	
Rationale: The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: In general, these devices are used by individuals with no technical expertise and thus the labeling and instructions for use are critical to the proper outcome of the test.		
Rule 5	The following IVD medical devices are classified as Class A	Examples: 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.
	a) reagents or other articles which possess specific characteristics, intended by the manufacturer to make them suitable for in vitro diagnostic procedures related to a specific examination;	
	b) b) instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures;	
	c) specimen receptacles.	

	Note:*Any product for general laboratory use not manufactured, sold or represented for use in specified in vitro diagnostic applications are not deemed to be IVD medical devices, as defined in this document. However, in certain jurisdictions products for general laboratory use are considered to be IVD medical devices.*	
Rationale: The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: These devices present a low individual risk and no or minimal public health risk.		
Rule 6	IVD medical devices not covered in Rules 1 through 5 are classified as Class B.	Blood gases, H. pylori and physiological markers such ashormones, vitamins, enzymes, metabolic markers, specific IgE assays and celiac disease markers.
Rationale: The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: These devices present a moderate individual risk as they are not likely to lead to an erroneous result that would cause death or severe disability, have a major negative impact on patient outcome or put the individual in immediate danger. The devices give results that are usually one of several determinants. If the test result is the sole determinant however other information is available, such as presenting signs and symptoms or other clinical information which may guide a physician, such that classification into Class B may be justified. Other appropriate controls may also be in place to validate the results. This Class also includes those devices that present a low public health risk because they detect infectious agents that are not easily propagated in a population.		
Rule 7	IVD medical devices that are controls without a quantitative or qualitative assigned value will be classified as Class B.	
Rationale: For such controls, the qualitative or quantitative value is assigned by the user and not the manufacturer.		