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HEALTH SCIENCES AUTHORITY

REGULATORY GUIDANCE

December 2017

MEDICAL DEVICE GUIDANCE

GN-14: Guidance on the Risk Classification of *In Vitro* Diagnostic Medical Devices

Revision 1.2

HSA Health Sciences Authority

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PREFACE

R1.1 ►This document is intended to provide general guidance. Although we have tried to ensure that the information contained here is accurate, we do not, however, warrant its accuracy or completeness. The Health Sciences Authority (HSA) accepts no liability for any errors or omissions in this document, or for any action/decision taken or not taken as a result of using this document. The information contained in this document should not be a substitute for professional advice from your own professional and healthcare advisors. ◄

REVISION HISTORY

Guidance Version (Publish Date)	Revision
GN-14: Revision 1 (October 2008)	R1
R1.1 ►GN-14: Revision 1.1 (May 2014)	R1.1
R1.2 ►GN-14: Revision 1.2 (01 December 2017)	R1.2

**Where applicable, changes and updates made in each document revision are annotated with or within the arrow symbol "►". Deletions may not be shown*

1. INTRODUCTION

1.1. Purpose

This document provides guidance to assist product owners in risk classification of *in vitro* diagnostic (IVD) medical devices using the appropriate risk classification rules.

1.2. Background

Regulatory controls should be proportional to the level of risk associated with an *in vitro* diagnostic (IVD) medical device. The level of regulatory control should increase with increasing degree of risk, taking account of the benefits offered by use of the IVD medical device. Therefore, there is a need to classify IVD medical devices based on their risk to patients, users and other persons.

The risk presented by a particular IVD medical device depends substantially on its intended purpose and the effectiveness of the risk management techniques applied during design, manufacture and use.

The risk presented by an IVD medical device also depends, in part, on its intended user(s), its mode of operation, and/or technologies. In general, the classification rules are intended to accommodate new technologies.

1.3. Scope

This document is applicable to IVD device products that fall within the definition of an IVD medical device as defined in First Schedule of the Health Products Act (*Act*).

1.4. Definitions

Definitions that do not indicate they are set out in the *Act* and Health Products (Medical Devices) Regulations (*Regulations*) are intended as guidance in this document. These definitions are not taken verbatim from the above legislation and should not be used in any legal context. These definitions are meant to provide guidance in layman terms.

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

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

NOTE Examination of an analyte in a biological sample is commonly referred to as a test, assay or analysis.

HAZARD: Potential source of harm.

INSTRUMENT: Equipment or apparatus intended by the product owner to be used as IVD medical device.

INTENDED PURPOSE/INTENDED USE *(as set out in the Regulations)*: in relation to a medical device or its process or service, means the objective intended use or purpose, as reflected in the specifications, instructions and information provided by the product owner of the medical device.

IN VITRO DIAGNOSTIC (IVD) PRODUCT (*as set out in the Regulations*): means any reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, whether used alone or in

combination with any other reagent, reagent product, calibrator, control material, kit, instrument, apparatus, equipment or system, that is intended by its product owner to be used in vitro for the examination of any specimen, including any blood or tissue donation, derived from the human body, solely or principally for the purpose of providing information —

- concerning a physiological or pathological state or a congenital abnormality;
- to determine the safety and compatibility of any blood or tissue donation with a potential recipient thereof; or
- to monitor therapeutic measures; and

includes a specimen receptacle;

IVD MEDICAL DEVICE FOR SELF-TESTING: Any IVD medical device intended by the product owner for use by lay persons.

LAY PERSON: Any individual who does not have formal training in a relevant field or discipline.

NEAR PATIENT TESTING: Any 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. Also known as Point-of-Care (POC).

PRODUCT OWNER (*as set out in the Regulations*): in relation to a health product, means a person who —

- supplies the health product under his own name, or under any trade mark, design, trade name or other name or mark owned or controlled by him; and
- is responsible for designing, manufacturing, assembling, processing, labelling, packaging, refurbishing or modifying the health product, or for assigning to it a purpose, whether those tasks are performed by him or on his behalf.

REAGENT: Any chemical, biological or immunological components, solutions or preparations intended by the product owner to be used as IVD medical devices.

RISK: The combination of the probability of occurrence of harm and the severity of that harm.

SELF-TESTING: Testing performed by lay persons.

SPECIMEN RECEPTACLE (*as set out in the Regulations*): An IVD medical device, whether vacuum-type or not, specifically intended by their product owner 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 conveyance of disease to a person.

2. GENERAL PRINCIPLES

The classification for an IVD medical device is determined based on a set of rules derived from those features that create risk. These include:

- the intended purpose and indications for use as specified by the product owner (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.

NOTE Regardless of the risk class, all medical devices including IVD medical devices must meet the Essential Principles of Safety and Performance of Medical Devices and labelling requirements.

3. CLASSIFICATION SYSTEM FOR IVD MEDICAL DEVICES

IVD medical devices are classified into four classes, based on the individual risk and public health risk level.

Table 1: Classification system for IVD Medical Devices

CLASS	RISK LEVEL	DEVICE EXAMPLES
A	Low Individual Risk and Low Public Health Risk	Specimen receptacle
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 IgM
D	High Individual Risk and High Public Health Risk	HIV blood donor screening, HIV diagnostic kit

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

4. THE DETERMINATION OF DEVICE RISK CLASS BY THE PRODUCT OWNER USING THE RULES-BASED SYSTEM

The product owner should:

- decide if the product concerned is an IVD medical device based on the intended purpose and the indications for use using the definition of IVD;
- take into consideration all the rules in order to establish the proper classification for the device. Apply the classification rules to each IVD medical device according to its intended purpose. Where an IVD medical device has multiple intended purposes as specified by the product owner, which places the device into more than one class, it should be classified to 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;
- the justification for placing a product into a particular risk class should be documented.

Other factors influencing device classification include:

- calibrators intended to be used with an IVD reagent should be treated in the same class as the IVD reagent.
- standalone control materials with quantitative or qualitative assigned values intended for one specific analyte or multiple analyte should be placed in the same class as the IVD reagent(s).
- standalone control materials with no assigned values intended for use with multiple or single analytes should not be placed in the same class as the IVD reagent(s).
- most software is incorporated into the IVD medical device itself, for example, embedded software to operate an analyser. There is some software that is not incorporated (embedded) into the medical device itself, such as software to provide an analysis based on the results from the analyser. Such software is deemed to be standalone software. Standalone software that fall within the scope of the definition for a 'IVD medical device' should be classified as follows:
  - where it controls or influences the intended output of a separate IVD medical device, it will have the same class as the IVD medical device itself.
  - where it is not incorporated in an IVD medical device, it is classified in its own right using the classification rules in this document.

5. CLASSIFICATION RULES

RULE 1: IVD medical devices intended for the following purposes are classified as Class D:

- devices intended to be used to detect the presence of, or exposure to, a transmissible agent in blood, blood components, blood derivatives, cells, tissues or organs in order to assess their suitability for transfusion or transplantation, 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.

Rationale: The application of this rule as defined above should be in accordance with the rationale that follows: IVD medical 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, which are often incurable or require major therapeutic interventions and where an accurate diagnosis is vital to mitigate the public health impact of the condition.

Examples: Tests to detect infection by HIV, HCV, HBV, HTLV. This Rule applies to first-line assays, confirmatory assays and supplemental assays.

RULE 2: 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)] determination which are classified as Class D.

Rationale: The application of this rule as defined above should be in accordance with the following rationale: 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 IVD medical 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.

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

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RULE 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 (e.g. Sexually transmitted diseases, such as *Chlamydia trachomatis*, *Neisseria gonorrhoeae*).
- in detecting the presence in cerebrospinal fluid or blood of an infectious agent with a risk of limited propagation (e.g. *Neisseria meningitidis* or *Cryptococcus neoformans*).
- in detecting the presence of an infectious agent where there is a significant risk that an erroneous result would cause death or severe disability to the individual or fetus being tested (e.g. diagnostic assay for CMV, *Chlamydia pneumoniae,* Methycillin Resistant *Staphylococcus aureus*).
- in pre-natal screening of women in order to determine their immune status towards transmissible agents (e.g. 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 (e.g. 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 (e.g. personalised medicine). *NOTE: Those IVD medical devices where the therapy decision would usually be made only after further investigation (e.g. other IVD tests, markers) and those used for monitoring would fall into class B under rule 6. Due consideration should be given to the clinical use of the test when determining the risk class.*
- in human genetic testing (e.g. 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 (e.g. Cardiac markers, cyclosporin, prothrombin time testing).
- in the management of patients suffering from a life-threatening infectious disease (e.g. HCV viral load, HIV Viral Load and HIV and HCV geno- and subtyping).
- in screening for congenital disorders in the fetus (e.g. Spina Bifida or Down Syndrome). ◄

Rationale: The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: IVD medical 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 IVD medical 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.

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 IVD medical devices are used by individuals with no technical expertise and thus the labelling and instructions for use are critical to the proper outcome of the test.

Example for Self-testing Class C: Blood glucose monitoring,
Example for Self-testing Class B: Pregnancy self test, Fertility testing, Urine test strip.

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RULE 5: The following IVD medical devices are classified as Class A:

- reagents or other articles that possess specific characteristics, intended by the product owner to make them suitable for in vitro diagnostic procedures related to a specific examination.
- standalone instruments (inclusive of software) intended by the product owner specifically to be used for in vitro diagnostic procedures, not intended for use in specific medical diagnostic purposes.
- specimen receptacles.

Examples: Sample-preparation instruments, wash solutions, plain urine cup. ◄

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.

Rationale: The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: These IVD medical 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.

Rationale: The application of this rule as defined above should be in accordance with the rationale for this rule which is as follows: These IVD medical 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 IVD medical 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 that 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 IVD medical devices that present a low public health risk because they detect infectious agents that are not easily propagated in a population.

[for avoidance of doubt - IVD medical devices that are controls with a quantitative or qualitative assigned value will be covered under this rule]

Examples: Blood gases, *H. pylori* and physiological markers such as hormones, vitamins, enzymes, metabolic markers, specific IgE assays and celiac disease markers.

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 user, not the product owner, assigns the qualitative or quantitative value.

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Health Products Regulation Group
Blood Services Group
Applied Sciences Group

www.hsa.gov.sg

Contact Information:

Medical Devices Branch
Pre-marketing Cluster
Health Products Regulation Group
Health Sciences Authority

11 Biopolis Way, #11-03 Helios
Singapore 138667
www.hsa.gov.sg
Email: hsa_md_info@hsa.gov.sg

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