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Medical Device Administrative Control System (MDACS)

Classification of In Vitro Diagnostic Medical Devices (IVDMDs)

Technical Reference: TR-006

中華人民共和國
香港特別行政區政府衞生署

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The Government of the Hong Kong Special Administrative Region
The People's Republic of China

Revision History

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1	30 Sep 2021	• Update document name and format; and • Rename of Medical Device Control Office to Medical Device Division.	TR-006:2021(E)
2	22 Dec 2023	• Revision of TR-006 with reference to guidance document: *Principles of In Vitro Diagnostic (IVD) Medical Devices Classification. IMDRF/IVD WG/N64FINAL:2021* published by the International Medical Device Regulators Forum; • Revision of Clause 1 – Introduction; • Revision of Clause 2 – Rationale, Purpose and Scope; • Revision of Clause 3 – Definitions and Abbreviations; • Revision of Clause 4 – General Principle; • Revision of Clause 5.6; • Revision of Clause 6 – Classification System for IVDMDs; • Revision of Clause 7.1.3; • Revision of Clause 8 – Classification Rules; • Revision of Clause 9.1; and • Revision of Clause 10 – References	TR-006:2023(E)
3	16 Jul 2024	• Revision of Clause 8.3.11 and 8.6	TR-006:2024(E)
4	15 Nov 2024	• Revision of Clause 8.3.7; • Revision of Clause 8.3.8;	TR-006:2024-1(E)

		• Revision of Clause 8.6; and • Revision of Clause 10 – References	

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1. Introduction

1.1 This document describes the principles of IVDMD classification in accordance with the requirements of MDACS.

2. Rationale, Purpose and Scope

2.1 Rationale

2.1.1 This guidance document provides guidance on the principles of classification of IVDMDs.

2.2 Purpose

2.2.1 The purpose of this document is to

(a) assist a manufacturer to allocate its IVDMD to an appropriate risk class using a set of harmonised classification principles;

(b) base such classification principles on an IVDMD's intended use;

(c) allow MDD to rule upon matters of interpretation for a particular IVDMD, when appropriate.

2.3 Scope

2.3.1 This document applies to all products that fall within the definition of an IVDMD. An IVDMD is defined as a device which, whether used alone or in combination, is intended by the manufacturer for the in-vitro examination of specimens derived from the human body solely or principally to provide information for diagnostic, monitoring or compatibility purposes. This includes reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles. Note: International reference materials (e.g. WHO) and materials used for external quality assessment

schemes are excluded.

3. Definitions and Abbreviations

3.1 **Companion diagnostics (CDx) medical device** means an IVDMD which is essential for the safe and effective use of a corresponding medicinal product to:

3.1.1 identify, before and/or during treatment, patients who are most likely to benefit from the corresponding medicinal product; or

3.1.2 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.

Note 1: CDx are essential for defining patients' eligibility for specific treatment with a medicinal product through the quantitative or qualitative determination of specific markers identifying subjects at a higher risk of developing an adverse reaction to the medicinal product in question or identifying patients in the population for whom the therapeutic product has been adequately studied, and found safe and effective. Such biomarker or biomarkers can be present in healthy subjects and/or in patients.

Note 2: Devices that are used to monitor treatment with a medicinal product in order to ensure that the concentration of relevant substances in the human body is within the therapeutic window are not considered to be CDx, in which case they could be classified as Class C by the rule in Clause 8.3.10 of this document.

3.2 Abbreviations of the analytes appeared in this document are provided below:

3.2.1 **ALK** stands for Anaplastic Lymphoma Kinase

3.2.2 **ALP** stands for Alkaline Phosphatase

3.2.3 **AST** stands for Aspartate Aminotransferase

3.2.4 **BUN** stands for Blood Urea Nitrogen

3.2.5 **CA 125** stands for Carbohydrate Antigen 125

3.2.6 **CEA** stands for Carcinoembryonic Antigen

3.2.7 **HbA1c** stands for Glycated Heamoglobin

3.2.8 **HLA** stands for Human Leukocyte Antigen

3.2.9 **PD-L1** stands for Programmed Death Ligand 1

3.2.10 **PSA** stands for Prostate Specific Antigen

3.2.11 **SHBG** stands for Sex Hormone-Binding Globulin

3.3 Abbreviations of the diseases appeared in this document are provided below:

3.3.1 **ELF** stands for Enhanced Liver Fibrosis

3.3.2 **NSCLC** stands for Non-Small Cell Lung Carcinoma

3.4 Abbreviations of the pathogens appeared in this document are provided below:

3.4.1 **CMV** stands for Cytomegalovirus

3.4.2 **HBV** stands for Hepatitis B Virus

3.4.3 **HCV** stands for Hepatitis C Virus

3.4.4 **HIV** stands for Human Immunodeficiency Virus

3.4.5 **HSV** stands for Herpes Simplex Virus

3.4.6 **HTLV** stands for Human T Lymphotrophic Virus

3.5 **EGFR** stands for Epidermal Growth Factor Receptor

3.6 **FFPE** stands for Formalin-Fixed, Paraffin-Embedded

3.7 **WHO** stands for World Health Organization

3.8 Please refer to Guidance Notes GN-00 (Guidance Notes for Definitions and Abbreviations for Medical Device Administrative Control System) for other definitions and abbreviations of the terms that appear in this document.

4. General Principles

4.1 The risk presented by a particular device depends substantially on its intended use, indications for use and intended user.

4.2 The Classification of an IVDMD is based on the following criteria:

4.2.1 the intended use and indications for use as specified by the manufacturer

4.2.2 the technical/scientific/medical expertise of the intended user

4.2.3 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

4.2.4 the impact of the result (true or false) to the individual and/or to public health

5. Recommendations in IVDMD Classification

5.1 The manufacturer should document its justification for placing its product into a particular risk class, including the resolution of any matters of interpretation where it has asked a Conformity Assessment Body and/or MDD for a ruling.

5.2 Where more than one of the classification rules applies to the IVDMD, the device should be allocated to the highest class indicated.

5.3 Accessories should be classified separately using this guidance document.

5.4 Calibrators intended to be used with an IVD reagent should be placed in the same class as the IVD reagent.

5.5 Stand alone control materials with quantitative or qualitative assigned values intended for one specific analyte or multiple analytes should be placed in the same class as the IVD reagent(s).

5.6 Stand alone control materials with no assigned values intended for use with multiple or single analytes could be placed in the same or lower class as it is for corresponding IVD reagent(s).

5.7 While most software is incorporated into the IVDMD itself, some is not. Provided such standalone software falls within the scope of the definition for an ‘IVDMD’, it should be classified as follows:

5.7.1 Where it controls or influences the intended output of a separate IVDMD, it will

have the same class as the device itself.

5.7.2 Where it is not incorporated in an IVDMD, it is classified in its own right using the rules in Clause 8 of this document.

Note 1: Performance of software or instrument that is specifically required to perform a particular test will be assessed at the same time as the test kit.

Note 2: The interdependence of the instrument and test methodology prevents the instrument from being assessed separately, even though the instrument itself is still classified as Class A.

6. Classification System for IVDMDs

6.1 **Figure 1** indicates the four risk classes of devices. The examples given are for illustration only; the manufacturer must apply the classification rules to each IVDMD according to its intended use.

Figure 1: Classification system for IVDMDs.

CLASS	RISK LEVEL	EXAMPLES
A	Low Individual Risk and Low Public Health Risk	Clinical chemistry analyser, Plain urine cup
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

6.2 **Figure 2** shows a conceptual illustration of increasing levels of regulatory requirements as the device risk class increases. These may include, for example:

6.2.1 operation of a quality system (recommended for all devices);

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

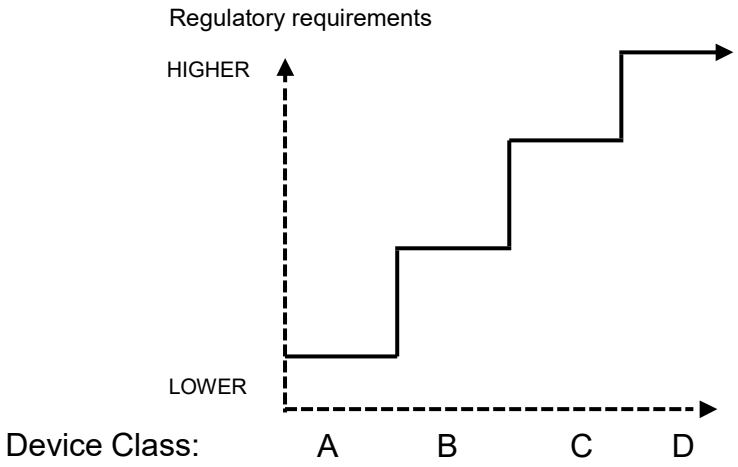
6.2.3 the need for technical data;

6.2.4 product testing using in-house or independent resources;

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

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

Figure 2: Conceptual illustration of regulatory requirements increasing with device risk class.



7. The Determination of Device Class

7.1 The manufacturer should:

7.1.1 Decide if the product concerned is an IVDMD based on the intended use and the indications for use using the definition in Guidance Notes GN-00.

7.1.2 Take into consideration all the rules as listed in Clause 8 in order to establish the proper classification for the device. Where an IVDMD 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.

7.1.3 Where more than one of the classification rules applies to the IVDMD, it should be allocated to the highest class indicated, e.g. a self-testing for HIV would be a Class D under Rule 1 and not a Class C under Rule 4.

8. Classification Rules

8.1 **Rule 1:** IVDMDs intended for the following purposes are classified as Class D:

8.1.1 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 or any of their derivatives, in order to assess their suitability for transfusion or transplantation or cell administration.

8.1.2 Devices intended to be used to detect the presence of, or exposure to, a transmissible agent that causes a life-threatening, disease with a high or suspected high risk of propagation.

Note 1: Several factors contribute to the risk of propagation of a pathogen within a population, namely: the direct or in-direct transmissibility (i.e. the probability of infection when there is contact between a susceptible and an infected individual), which includes for example consideration of the infectious dose and route of transmission (e.g. aerosol, zoonosis, vector-mediated), the contact rate of infected and susceptible individuals (i.e.

the number of contacts per time), and the duration of infectiousness.

Note 2: The list of high-risk agents may be updated based on quantitative analysis of new scientific evidence on the incidence, pathogenicity, burden of mortality and morbidity, and transmission dynamics of infectious agents in the population.

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

Examples: Tests to detect infection by HIV, HCV, HBV, HTLV, HIV blood donor screening and HIV blood diagnostics. This rule applies to first-line assays, confirmatory assays and supplemental assays.

8.2 **Rule 2:** IVDMDs intended to be used for blood grouping, or to determine foeto-maternal blood group incompatibility, or tissue typing to ensure the immunological compatibility of blood, blood components, cells, tissue or organs that are intended for transfusion or transplantation or cell administration, are classified as Class C, except when intended to determine the presence of the antigen or antibody for any of the following markers: ABO system [A (ABO1), B (ABO2), AB (ABO3)], Rhesus system [RH1 (D), RH2 (C), RH3 (E), RH4 (c), RH5 (e), and weak or partial Rh (D)], Kell system [Kel1 (K)], Kidd system [JK1 (Jka), JK2 (Jkb)] and Duffy system [FY1 (Fya), FY2 (Fyb)], in which case they 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 IVDMD is designed to detect,

and its importance in a transfusion setting.

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

8.3 **Rule 3:** IVDMDs are classified as Class C if they are intended for use:

8.3.1 in detecting the presence of, or exposure to, a sexually transmitted agent. Examples: Sexually transmitted diseases, such as *Chlamydia trachomatis*, *Neisseria gonorrhoeae*.

8.3.2 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.*

8.3.3 in detecting the presence of an infectious agent, if there is a significant risk that an erroneous result would cause death or severe disability to the individual, foetus or embryo being tested or to the individual's offspring. Examples: diagnostic assay for CMV, *Chlamydia pneumoniae,* Methycillin Resistant *Staphylococcus aureus*, Zika.

8.3.4 in pre-natal screening of women in order to determine their immune status towards transmissible agents. Examples: Immune status tests for Rubella or Toxoplasmosis.

8.3.5 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 or severe disability for the patient or for the patient's offspring. Examples: Enteroviruses, CMV and HSV in transplant patients.

8.3.6 in screening for selection of patients for selective therapy and management as CDx. Examples: Devices intended to detect antibodies against a specific medicinal product during the course of treatment, Devices intended for the qualitative detection of ALK protein in FFPE NSCLC tissue, intended as an aid

in identifying patients eligible for treatment with crizotinib or ceritinib, and Devices intended to identify defined EGFR mutations in order to administer the tyrosine-kinase inhibitor dacomitinib for the treatment of adult patients with locally advanced or metastatic NSCLC and EGFR-activating mutations.

8.3.7 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. Examples: Brain type natriuretic peptide, Devices intended for staging of ELF for detecting the following markers: hyaluronic acid, procollagen III amino terminal peptide, tissue inhibitor or metalloproteinase, and Software medical devices intended to generate an ELF score which correlates to the level of fibrosis.

8.3.8 in screening, diagnosis or staging of cancer. Examples: Tests for PSA, CEA, CA 125, and Image analysis software medical devices intended to aid in the detection and semi-quantitative measurement of PD-L1 protein in FFPE lung tissue using deep learning/machine learning algorithms.

8.3.9 in human genetic testing. Examples: Huntington’s Disease, Cystic Fibrosis.

8.3.10 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 or for the patient’s offspring. Examples: Troponin, Cyclosporin, Prothrombin time testing.

8.3.11 in the management of patients suffering from a life-threatening disease or condition. Examples: HBV monitoring marker, HCV viral load, HIV Viral Load and HIV and HCV geno- and subtyping.

8.3.12 in screening for congenital disorders in the foetus or embryo. Examples: Spina Bifida or Down Syndrome, Glucose-6-Phosphate Dehydrogenase Deficiency, and Tay-Sachs Disease.

8.3.13 in screening for congenital disorders in new-born babies where failure to detect and treat such disorders could lead to life-threatening situations or severe disabilities. Examples: Beta-thalassaemia, Biotinidase Deficiency.

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 and monitoring. 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.

8.4 **Rule 4:** IVDMDs intended for self-testing or near patient testing are classified as Class C, except those devices from which the result is not determining a critical situation, in which case they are classified under Class B by Rule 6, and those devices which are classified under Class D by Rule 1 and/or Rule 2.

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

Example for self-testing Class C: Blood glucose monitoring.

Example for near patient testing Class C: Blood glucose monitoring.

Example for self-testing or near patient testing Class D: Rapid test for detection of HIV.

Example for near patient testing Class D: Pre-transfusion ABO compatibility test card intended to be used at the recipients' bedside as precaution against ABO-incompatible transfusion.

Examples for self-testing Class B: Pregnancy self-test, Fertility testing, Urine test strips.

Example for near patient testing Class B: Quantitative test for haemoglobin as an aid in diagnosing iron deficiency.

8.5 **Rule 5:** The following IVDMDs are classified as Class A:

8.5.1 Products for general laboratory use, or accessories which possess no critical characteristics, intended by the manufacturer to make them suitable for in vitro diagnostic procedures related to a specific examination. Examples: Buffer solutions, Washing solutions, Histological stains.

8.5.2 Instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures. Examples: Clinical chemistry analyser, Enzyme immunoassay analyser.

8.5.3 Specimen receptacles. Examples: Plain urine cup, Microbiological specimen collection devices.

Note 1: Any product for general laboratory use which is not specifically intended by the manufacturer to be used in in vitro diagnostic applications is not deemed to be an IVDMD, as defined in this document.

Note 2: The performance of software or an instrument that is specifically required to perform a particular test will be assessed at the same time as the respective reagent(s).

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.

8.6 **Rule 6:** IVDMDs not covered in Rules 1 through 5 are classified as Class B.

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

Examples: Blood gases, *Helicobacter pylori* test, Physiological markers such as hormones, vitamins, enzymes, metabolic markers, Specific IgE assays, Coeliac disease markers, Tests for Anti-Nuclear Antibody, SHBG, BUN, AST, ALP, Creatinine and HbA1c, and Software medical devices intended to aid in identification of possible disease associated with the result from the test for Anti-Nuclear Antibody by Artificial Intelligence (AI) algorithms. (If those devices are intended for use in the management of patients suffering from a life-threatening disease or condition, they are classified under Class C by the rule in Clause 8.3.11.)

8.7 **Rule 7:** IVDMDs 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.

Examples: Urinalysis controls and Chemistry controls.

9. Enquiries

9.1 Enquiries concerning this document and MDACS should be directed to:

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Email address: mdd@dh.gov.hk
Website: www.mdd.gov.hk/

9.2 All latest versions of published documents and application forms for MDACS are available at MDD website.

10. References

10.1 International Medical Device Regulators Forum. Principles of In Vitro Diagnostic (IVD) Medical Devices Classification. IMDRF/IVD WG/N64FINAL:2021. https://www.imdrf.org.

10.2 Medical Device Coordination Group. Guidance on Classification Rules for *in vitro* Diagnostic Medical Devices under Regulation (EU) 2017/746. MDCG 2020-16 rev.3. https://health.ec.europa.eu.

10.3 Health Science Authority. Guidance on the Risk Classification of *In Vitro* Diagnostic Medical Devices. GN-14: Revision 3. https://www.hsa.gov.sg.

10.4 Department of Health. Guidance Notes for Definitions and Abbreviations for the Medical Device Administrative Control System. Guidance Notes GN-00.

10.5 Department of Health. Overview of the Medical Device Administrative Control System. Guidance Notes GN-01.