Classification of IVD medical devices

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Abstract

Medical devices, including IVDs, are classified according to the level of regulatory control necessary to reasonably ensure safety and effectiveness. In particular, IVDs are classified based on their potential risk to individuals and public health.

Accurate classification of products is important because the level of comformity assessment procedure and pre- and post-marketing management differs depending on the classification level.

This lecture explains the principles and general rules of the classification criteria based on the IMDRF/IVD WG/N64 FINAL:2021 document (formerly GHTF/SG1/N045:2008). In addition, I introduce the IVD classification systems in the US, Europe, and Korea, and representative examples for each classification.

Ministry of Food and Drug Safety

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(based on IMDRF/IVD WG/N64 FINAL:2021 document)

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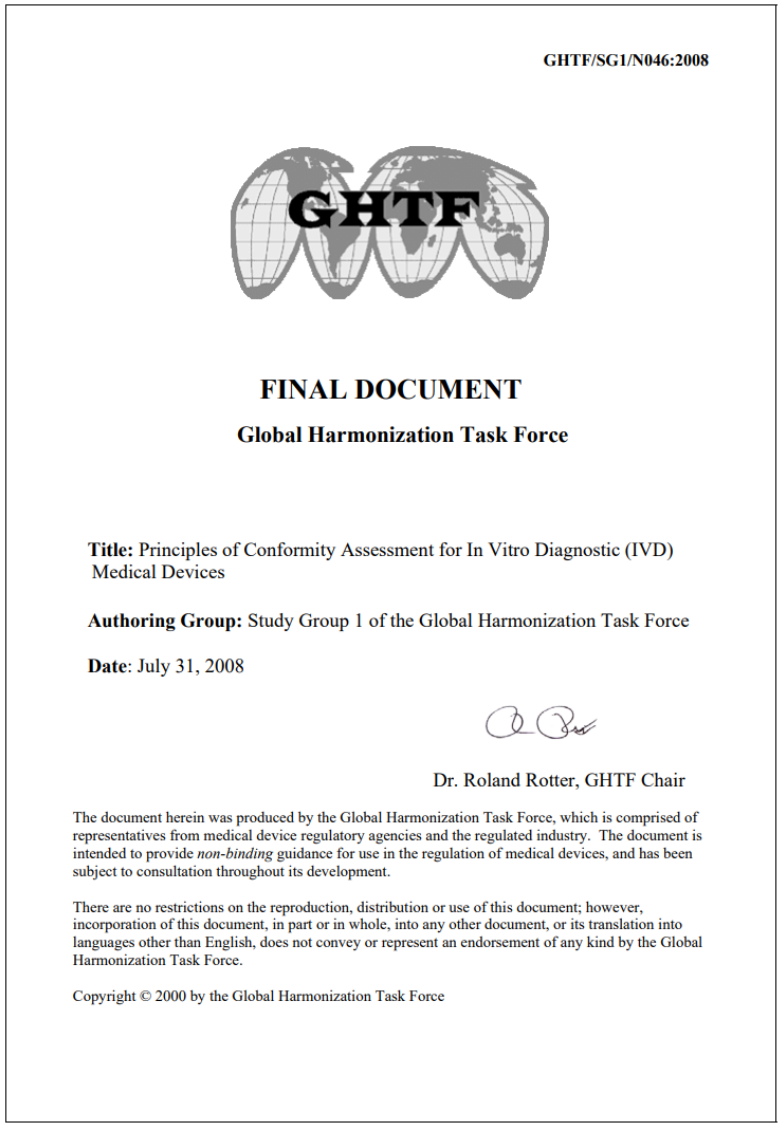
Ministry of Food and Drug Safety

I. Classification of IVD in IMDRF

About the Guideline

- **It provides guidance on the principles of classification of IVD Medical devices.**



GHTF/SG1/N046:2008

GHTF

FINAL DOCUMENT

Global Harmonization Task Force

Title: Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices

Authoring Group: Study Group 1 of the Global Harmonization Task Force

Date: July 31, 2008

Dr. Roland Rotter, GHTF Chair

The document herein was produced by the Global Harmonization Task Force, which is comprised of representatives from medical device regulatory agencies and the regulated industry. The document is intended to provide *non-binding* guidance for use in the regulation of medical devices, and has been subject to consultation throughout its development.

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Update

IMDRF/IVD WG/N64FINAL:2021 (formerly GHTF/SG1/N045:2008)

IMDRF International Medical Device Regulators Forum

FINAL DOCUMENT

Title: Principles of In Vitro Diagnostic (IVD) Medical Devices Classification

Authoring Group: IMDRF IVD Working Group

Date: 21 January 2021

Dr Jeong-Rim Lee, IMDRF Chair

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About the Guideline

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About the Guideline

- **(Section 1.0) It is all about "Harmonization"**
  - To encourage **convergence at the global level in evolution of regulatory system for IVD medical devices**
  - To provide **harmonized guidance documents** suitable for implementation or adaptation by member Regulatory Authorities
- **(Section 2.2) Purpose**
  - To assist a manufacturer to **allocate its IVD medical devices to an appropriate risk class** (IMDRF/IVD WG/N64)
    - Such classification will determine **the conformity assessment route as described in the GHTF document on Principles of Conformity Assessment for IVD Medical devices** (GHTF/SG1:N046:2008)
- **(Section 2.3) Scope**
  - To all products that fall within **the definition of an IVD medical device**
    - **Note** : International reference materials (e.g. WHO) and materials used for external quality assessment schemes are excluded (IMDRF/IVD WG/N64)

General Principles of Classification for IVD

- The IMDRF recommends that each IVD medical device be allocated to one of four **risk classes**, using a set of rules as defined in this document.
- Class A devices are the lowest risk devices, Class B are moderate to low risk, Class C are moderate to high risk and Class D devices present the highest risk.

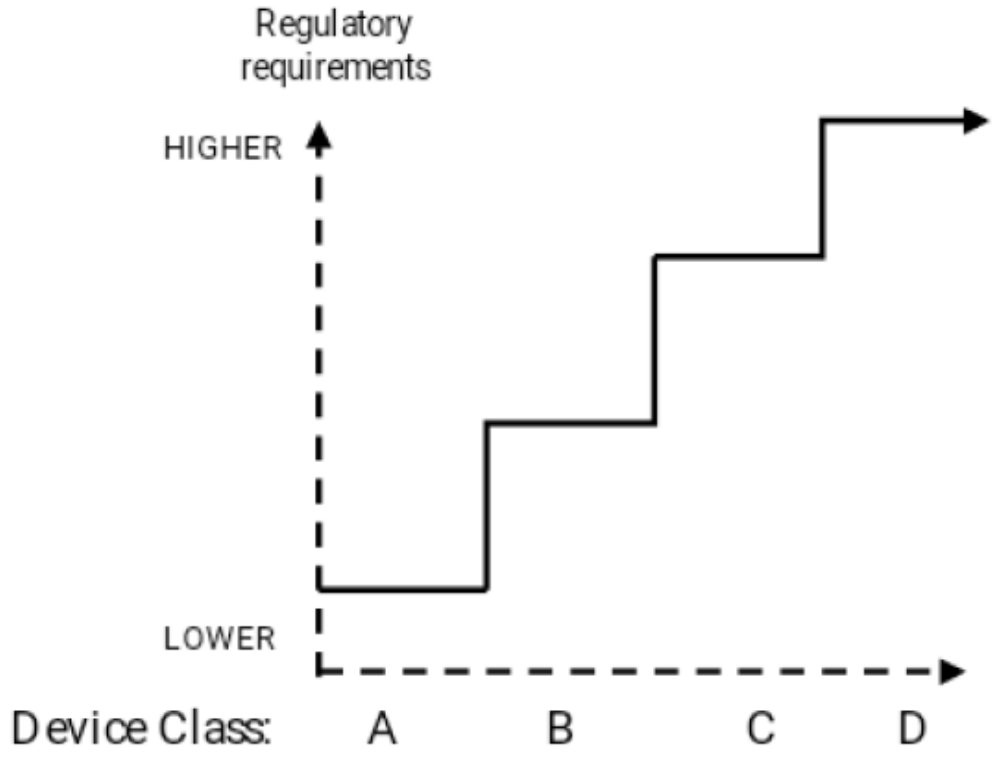
Figure 1: Proposed general classification system for IVD medical devices.

CLASS	RISK LEVEL	EXAMPLES
A	Low Individual Risk and Low Public Health Risk	Clinical Chemistry Analyser, general 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

General Principles of Classification for IVD

- The level of scrutiny and evidence needed to demonstrate that the IVD medical device meets the Essential Principles of Safety and Performance and conformity assessment procedures should be proportional to the risk class of the IVD medical device.

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



General Principles of Classification for IVD

- **GHTF/SG1/N046:2008 Principle of Conformity assessment for IVD**

CLASS "A" DEVICE

Conformity Assessment Element	Manufacturer Responsibility	RA / CAB Responsibility
Quality Management System (QMS)	Establish and maintain a full QMS or a QMS without design and development controls.	Premarket regulatory audit not required.
Post Market Surveillance	Establish and maintain an adverse event reporting procedure according to GHTF SG2 guidance.	May audit post-market to investigate specific safety or regulatory concerns.
Technical Documentation	Upon request prepare STED.	Premarket submission of STED not required. May be requested to investigate specific safety or regulatory concerns.
Declaration of Conformity	Prepare, sign and maintain.	On file with the manufacturer; available upon request.
Registration of manufacturers and their devices	Perform according to regulatory requirements.	Maintain and verify as appropriate.

CLASS "D" DEVICE

Conformity Assessment Element	Manufacturer Responsibility	RA / CAB Responsibility
Quality Management System (QMS)	Establish and maintain a full QMS.	Be satisfied that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.
Post Market Surveillance	Establish and maintain an adverse event reporting procedure according to GHTF SG2 guidance.	Be satisfied that a current and appropriate adverse event reporting procedure is in place as part of the QMS.
Technical Documentation	Prepare and submit STED for review. A STED for this class should contain more extended information such as full performance evaluation reports.	Receive and conduct a premarket review of the STED to determine conformity to Essential Principles.
Declaration of Conformity	Prepare, sign and submit.	Review and verify compliance with requirements.
Registration of manufacturers and their devices	Perform according to regulatory requirements.	Maintain and verify as appropriate.

General Principles of Classification for IVD

- **Considerations for determination of Risk Level(Section 5.0)**

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

✓ 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

⇒ **The intended purpose of product ultimately also determines the classification, depending on the risk.**

General Principles of Classification for IVD

- **Intended purpose (IVDR Annex II. Technical Documentation)**

(c) the intended purpose of the device which may include information on:

(i) what is to be detected and/or measured;

(ii) its function such as screening, monitoring, diagnosis or aid to diagnosis, prognosis, prediction, companion diagnostic;

(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, semi-quantitative or quantitative;

(vi) the type of specimen(s) required;

(vii) where applicable, the testing population;

(viii) the intended user;

(ix) in addition, for companion diagnostics, the relevant target population and the associated medicinal product(s).

Classification Rules

- **2 parts**

✓ 1st part : General rules (section 6.0 & 8.0)

✓ 2nd part : Seven rules derived from those features that create risk (section 9.0)

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Classification Rules – (1) General rules

- **Take into consideration all the rules in order to establish the adequate classification for the device**.
- The rules should be capable of accommodating generally acknowledged state of the art.
- Where more than one of the classification rules applies to the IVD medical device, the device should be allocated to the highest class indicated.
- Calibrators intended to be used with an IVD reagent should be placed in the same class as the IVD reagent.
- 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).
- 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).

Classification Rules – (2) 7 Rules related risks

- IMDRF recommends the seven rules derived from those features that create risk.

Rule 1	IVD medical devices intended for the following purposes are classified as **Class D**.
Rule 2	IVD medical devices 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 grouping for cell administration, blood components, cells, tissue, or organs** that are intended **for transfusion or transplantation,** 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)]; or Duffy system [FY1(Fya), FY2(Fyb)], in which case they are classified as Class D.
Rule 3	IVD medical devices are classified as **Class C** if they are intended for use.
Rule 4	IVD medical devices intended for use by lay users (such as 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, and those devices which are classified under Class D by Rule 1 and/or Rule 2.
Rule 5	The following IVD medical devices are classified as **Class A**.
Rule 6	IVD medical devices not covered in Rules 1 through 5 are classified as **Class B**.
Rule 7	IVD medical devices that are **Controls without a quantitative or qualitative assigned value** will be classified as Class B.

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Classification Rules – (2) 7 Rules relate to risks

Class	Risk Level	Rules to be considered	Examples
D	**High Individual risk and High Public helth risk**	• 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.	HIV Blood donor screening, high-risk Blood typing devices 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)]; or Duffy system [FY1 (Fya), FY2 (Fyb)]
		• Diagnosis or therapeutic intervention of Serious diseases or disease with significant public health implication.	HIV, HBV, HCV, HTLV diagnostic
		• Self-test or POC devices which are classified under Class D by Rule 1 and/or Rule 2.	HIV self-testing

Classification Rules – (2) 7 Rules relate to risks

Class	Risk Level	Rules to be considered	Examples
C	High Individual risk and/or Moderate Public helth risk	* The devices provide the critical, or sole, determinant for the correct diagnosis and monitoring.	
		• in detecting the presence of an infectious agent, if there is a significant risk that an erroneous result would cause death or severe disability.	CMV, HSV, Chlamydia trachomatis, Neisseria gonorrhoeae
		• in screening, diagnosis or staging of cancer	PSA, CEA, CA125 screening
		• in screening for selection of patients for selective therapy and management as companion diagnostics	CDx
		• monitoring of endogenous/exogenous substances in life-threatening diseases	troponin, Cyclosporin, Prothrombin time testing
		• in the management of patients suffering from a life-threatening disease or condition.	HBV monitoring marker, HIV/HCV viral load, HIV/HCV geno- and subtyping, Blood glucose monitoring
		• in human genetic testing	Huntington's Disease, Cystic Fibrosis
		• in screening for congenital disorders in the new-born babies, foetus or embryo.	Spina Bifida, Down Syndrome
		• intended for use by lay users - Self-test or POC	Blood glucose self-testing

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Classification Rules – (2) 7 Rules relate to risks

Class	Risk Level	Rules to be considered	Examples
B	Moderate Individual risk and/or Low Public helth risk	• 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.	Blood gases, physiological markers such as hormones, vitamins, and enzymes, metabolic markers
		• 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.	AST, ALP, BUN, Creatinine, HbA1c, C-reactive protein
		• also includes those devices that present a low public health risk because they detect infectious agents that are not easily propagated in a population.	H. pylori, Candida albicans
		• Self-test or POC devices from which the result is not determining a critical situation.	Pregnancy self-test, Urine test strips.
		• Controls without a quantitative or qualitative assigned value - The qualitative or quantitative value is assigned by the user and not the manufacturer.	Urinalysis controls, Chemistry controls

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Classification Rules – (2) 7 Rules relate to risks

Class	Risk Level	고려되는 rules	Examples
A	Low Individual risk and Low Public health risk	• Reagents or other articles, which possess no critical characteristics intended by the manufacturer to make them suitable for in vitro diagnostic procedures related to a specific examination;	General culture media (excluding the dehydrated powders which are considered not to be a finished IVD medical device), Wash solutions, Microbiological specimen collection devices
		• Instruments intended by the manufacturer specifically to be used for in vitro diagnostic procedures.	Instrument (ELISA reader, clinical chemistry analyzer)
		• Specimen receptacles.	Specimen containers for the diagnosis (Plain urine cup etc)

II. IVD Classification systems In the US, EU, and Korea

Comparison of US/EU/KOR Regulatory system

	US	EU	KOR
Laws/Acts	FD&C Act	IVDD 98/79/EC IVDR 2017/746	The In vitro Diagnostic Devices Act
Quality system	cGMP (QSR)	ISO 13485	KGMP
Classification	Class I, II, III	Class A, B, C, D	Class 1, 2, 3, 4
Licensing system	Class I : Registration Class II : 510(k) Class III : PMA	Class A : DoC Class B, C, D : NB approval	Class 1 : permission Class 2 : certification or approval Class 3,4 : approval
RA	FDA *reviewed by CDRH	Notified Body	MFDS *reviewed by NIFDS or NIDS

1. US Classification system

- In the US, the Food and Drug Administration (FDA) regulates IVDs based on their risk level and the classification is based on the level of control necessary to ensure the safety and effectiveness of the device.
- The FDA classifies IVDs into three classes: Class I, Class II, and Class III.
- The Code of Federal Regulations lists the classification of existing IVDs in 21 CFR 862, 21 CFR 864, and 21 CFR 866.

Regulations	
21CFR, Part 862	Clnical Chemistry and Clinical Toxicology devices
21CFR, Part 864	Hematology and Pathology Devices
21CFR, Part 866	Immunology and Microbiology Devices

21 CFR Part 864 (up to date as of 10/11/2023)
Hematology and Pathology Devices

21 CFR 864.7525

§ 864.7525 Heparin assay.

(a) *Identification.* A heparin assay is a device used to determine the level of the anticoagulant heparin in the patient's circulation. These assays are quantitative clotting time procedures using the effect of heparin on activated coagulation factor X (Stuart factor) or procedures based on the neutralization of heparin by protamine sulfate (a protein that neutralizes heparin).

(b) *Classification.* Class II (performance standards).

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1. US Classification system

	Medical devices		
Class	**Class I**	**Class II**	**Class III**
Risk	**Lowest**	**Moderate**	**Highest**
Potential Harm	Present minimal potential for harm	HIgher risk than Class I devices	Sustain or support life, are implated, or present potential unreasonable risk of illness or injury
Regulatory controls	General	General + Special (if available)	General+PMA
Submision type or Exemption	510(k) (mostly) 510(k) Exempt (some)	510(k) (mostly) 510(k) Exempt (some)	PMA

Trade/Device Name: cobas® Influenza A/B & RSV Nucleic Acid Test for Use on the cobas® Liat System (cobas® Liat Influenza A/B & RSV);
cobas® Influenza A/B & RSV Quality Control Kit
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay
Regulatory Class: II
Product Code: OCC, OZE, OOI, JJX
Dated: May 31, 2016

2. EU Classification system

- In Europe, the classification of IVDs is governed by Regulation (EU) 2017/746 on in vitro diagnostic medical devices (IVDR).

✓ Article 47 and Annex VIII

- The IVDR classifies IVDs into four classes: Class A, Class B, Class C, and Class D.

✓ The IVDR employs a classification structure for IVD consistent with that of the IMDRF.

	IVD devices			
Class	**Class A**	**Class B**	**Class C**	**Class D**
Risk	**Low**	**Medium-Low**	**Medium-High**	**High**
Process	TCF + DoC	TCF + CoC + QMS (ISO 13485)	TCF + CoC + QMS (ISO 13485)	TCF + CoC + QMS (ISO 13485) + Design dossier
Submision type or Exemption		NB review	NB review	NB review

2. EU Classification system

Article 47

Classification of devices

1. Devices shall be divided into classes A, B, C and D, taking into account the intended purpose of the devices and their inherent risks. Classification shall be carried out in accordance with Annex VIII.

2. Any dispute between the manufacturer and the notified body concerned, arising from the application of Annex VIII, shall be referred for a decision to the competent authority of the Member State in which the manufacturer has its registered place of business. In cases where the manufacturer has no registered place of business in the Union and has not yet designated an authorised representative, the matter shall be referred to the competent authority of the Member State in which the authorised representative referred to in the last indent of point (b) of the second paragraph of Section 2.2. of Annex IX has its registered place of business. Where the notified body concerned is established in a Member State other than that of the manufacturer, the competent authority shall adopt its decision after consultation with the competent authority of the Member State that designated the notified body.

ANNEX VIII

CLASSIFICATION RULES

istered place of business shall notify upon request.

the MDCG, decide, by means of

1. IMPLEMENTING RULES

1.1. Application of the classification rules shall be governed by the intended purpose of the devices.

1.2. If the device in question is intended to be used in combination with another device, the classification rules shall apply separately to each of the devices.

1.3. Accessories for an *in vitro* diagnostic medical device shall be classified in their own right separately from the device with which they are used.

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

If the software is independent of any other device, it shall be classified in its own right.

2. EU Classification system

- **Regulation about Common Specification for Certain Class D devices**

COMMISSION IMPLEMENTING REGULATION (EU) 2022/1107

of 4 July 2022

laying down common specifications for certain class D *in vitro* diagnostic medical devices in accordance with Regulation (EU) 2017/746 of the European Parliament and of the Council

- ✓ For certain class D in vitro diagnostic medical devices falling within the scope of Regulation (EU) 2017/746, harmonised standards do not exist as regards certain requirements of Annex I to that Regulation, and there is a need to address public health concerns as the risk associated with the use of those devices is significant for public health and patient safety. It is therefore appropriate to adopt common specifications for those devices in respect of those requirements.
- ✓ ABO,Rh,Kell,Duffy,Kidd blood group systems / HIV / HTLV / HCV / HBV / HDV / vCJD / CMV / EBV / Treponema pallidum / Trypanosoma cruzi / **SARS-CoV-2**
  - CMV : first-line assays for total anti-CMV and anti-CMV IgG, qualitative and quantitative NAT
  - EBV : first-line assays for anti-EBV VCA IgG, qualitative and quantitative NAT
  - Treponema Pallidum : fist-line assays for anti-T.pallidum, confirmatory & supplimental anti-T.pallidum assays.

2. EU Classification system

- **Guidance documents by MDCG**

✓ MDCG 2020-16 Guidance on Classification Rules for in vitro Diagnostic Medical devices

✓ MDCG 2019-11 Qualification and classification of software

3. KOR Classification system

- In Korea, the classification of IVDs is governed by relevant regulation.

✓ Regulation on classification of In vitro diagnostic medical device

- classifies into four classes: Class 1, Class 2, Class 3, and Class 4.

✓ The regulation employs a classification structure for IVD consistent with that of the IMDRF.

	IVD devices			
Class	**Class 1**	**Class 2**	**Class 3**	**Class 4**
Risk	**Low**	**Medium-Low**	**Medium-High**	**High**
Process	TCF	TCF + QMS (KGMP)	TCF + QMS (KGMP)	TCF + QMS (KGMP)
Submision type or Exemption	MFDS permission	NIDS certification	MFDS approval	MFDS approval
		reviewed by NIDS (mostly), reviewed by NIFDS (some)	reviewed by NIFDS	reviewed by NIFDS

4. Differences observed in some products system

- **SARS-CoV-2 test product : EU/Class D vs. Korea/Class 3(Class C)**

- **Blood test product : IMDRF/Class D vs. Korea/Class 3(Class C)**

IMDRF	MFDS (KOR)
Rule 2	**L02000 IVD reagent for blood typing test**
<Class D> ABO system [A (ABO1), B (ABO2), AB (ABO3)], Rhesus system [RH1 (D)]	L02010.01 **[Class 4]** IVD reagents for ABO · RhD blood typing, RBC agglutination ABO typing test, RhD typing test
<Class D> Rhesus system [RH2 (C), RH3 (E), RH4 (c), RH5 (e), and weak or partial Rh(D)], Kell system [Kel1 (K)], Kidd system [JK1 (Jka), JK2 (Jkb)]; or Duffy system [FY1 (Fya), FY2 (Fyb)],	L02020.01 **[Class 3]** IVD reagents for blood typing other than ABO·RhD, red cell agglutination : ABO subtype, Rh subtype(C, c, E, e), Duffy, Kell, Kidd, MNS etc.

III. Summary

- The general principle of product classification is based on the level of individual and public health risk, with the Intended purpose of use being specifically considered when evaluating the risk level.
- A rule-based classification system is applied when grading developed products.

  IMDRF proposes general rules and seven types of risk-related rules.

  All proposed rules must be taken into account.
- The classification of an IVD medical device determines regulatory requirements, including conformity assessment procedure and pre- and post-marketing management, which in turn influence market introduction.
- Higher risk levels require more stringent conformity assessments, which, if not appropriately rated, will hamper the ability of regulatory authority to carry out their responsibilities to protect public health. Additionally, setting unnecessarily high classe will place unnecessary burden on the industry. Therefore, accurate classification of product is important.

- Finally, I would like to reiterate that the examples provided in the guideline are provided for illustrative purposes only and should not be considered all-inclusive. The practical application of classification rules must be evaluated on a case-by-case basis.

Thank you for your attention

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Government Innovation for a better (healthy)life
Better MFDS

청렴韓세상