IVD Classification & Conformity assessment in IMDRF

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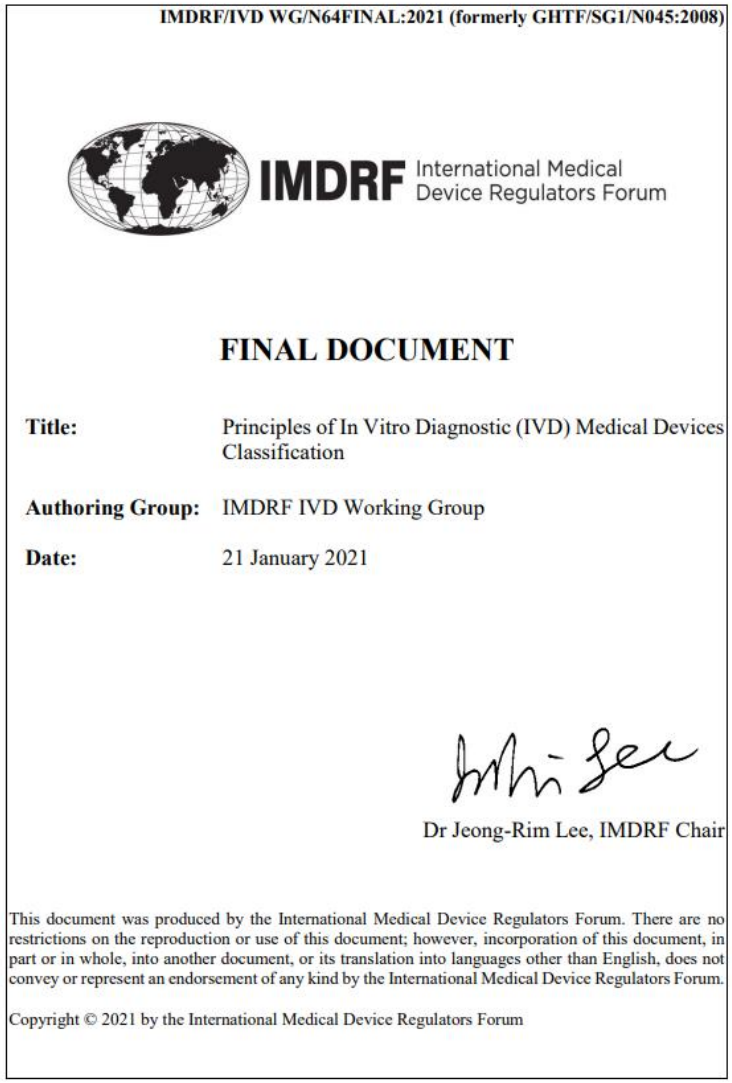
Contents

About the Guidelines



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

IMDRF International Medical Device Regulators Forum

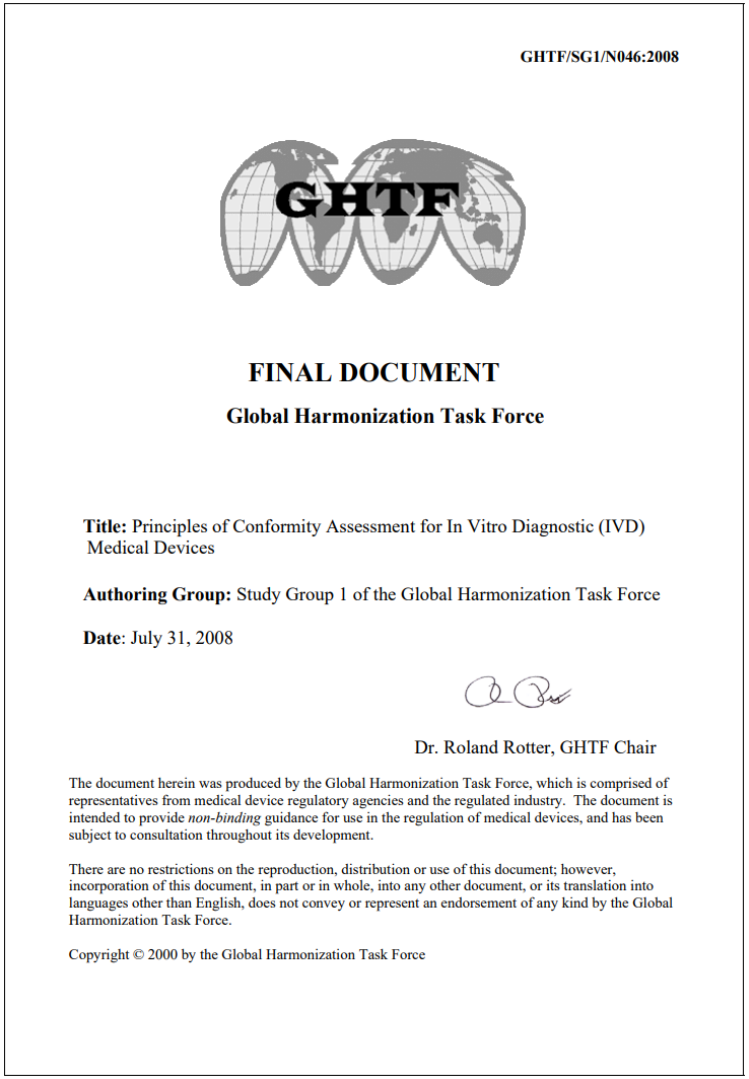
FINAL DOCUMENT

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



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

Purposes and Scope

- **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
- **Purposes**
  - To assist a manufacturer to **allocate its IVD medical devices to an appropriate risk class** (IMDRF/IVD WG/N64)
  - To describe **the conformity assessment elements for each class of devices** (GHTF/SG1:N046:2008)
- **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)

- Since the inter-relationship between device class and conformity assessment is critical in establishing a consistent approval across all countries, it is recommended to read both documents in conjunction with one and another

Definition of IVD medical device

- **IVD Medical Device** : a device, whether used alone or in combination, **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

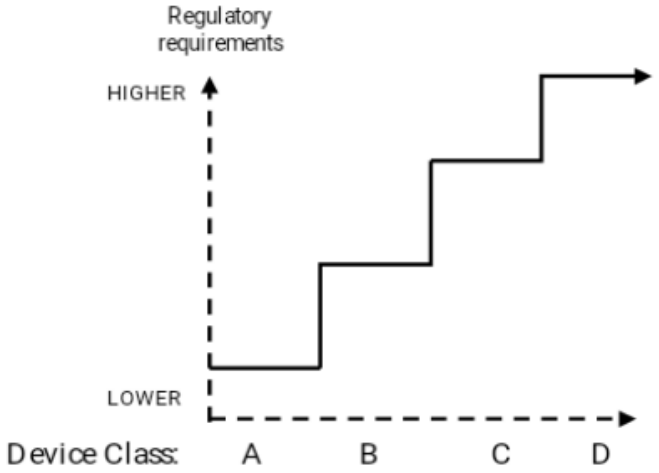
  - **NOTE 1**: IVD medical devices include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles and are used, for example, for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction, determination of physiological status.
  - **NOTE 2:** In some jurisdictions, **certain IVD medical devices may be covered by other national regulations.**

    * e.g. Specimen receptacles is an IVD medical device by IMDRF definition, but not an IVD medical device in Korea

General Principles

- The risk presented by a particular device depends substantially on **its intended use**, **indications for use** and **intended user**
- The **Classification of an IVD medical device** is based on the following criteria:
  - **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

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

The Determination of Device Class

- The manufacturer should:
  - 1. **Take into consideration all the rules as listed in section 9.0** in order to establish the adequate classification for the device. Where an IVD medical device has **multiple intended uses**, as specified by the manufacturer, which can place the device into more than one class, **it will be classified in the higher class**.
  - 2. **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-testing for HIV would be a class D under rule 1 and not a class C under rule 4.

  - **NOTE: Where special national rules are applied,** resulting in a device class other than that suggested by the present rules, then **a different conformity assessment procedure may be indicated.** This may have an effect on the acceptability of such devices for free movement in a global context unless other, or additional, conformity assessment procedures are carried out. For example, where such special national rules result in the lower classification of a particular IVD medical device than that indicated in the rules indicated below, and as a consequence, a less vigorous conformity assessment procedure is carried out, this may be unacceptable to other jurisdictions.

Classification Rules 1/4

- **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, cells, tissues or organs or any of their derivatives, in order to assess their suitability for transfusion, transplantation or cell administration
  - 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 risk of propagation**
  - **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**
  - **High Individual risk/High Public health risk**
- **Rule 2 :** IVD medical devices are classified as **Class C**
  - 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
  - **Except for 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**.
  - **High Individual risk/ Moderate Public health risk**

Classification Rules 2/4

- **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**.
  - in detecting the presence in **cerebrospinal fluid or blood of an infectious agent** with a risk of limited propagation.
  - 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.
  - ~ ~ ~
  - in screening for selection of patients for selective therapy and management as **companion diagnostics**
  - in **screening, diagnosis or staging of cancer**;
  - in **human genetic testing**
  - ~ ~ ~
  - 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
  - **High Individual risk/Moderate Public health risk**

Classification Rules 3/4

- **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
  - Example for self-testing class C : Blood glucose monitoring, self-testing class B : Pregnancy self-test, etc
- **Rule 5:** The following IVD medical devices are classified as **Class A**
  - **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
  - **Instruments** intended by the manufacturer specifically to be used for in vitro diagnostic procedures
  - **Specimen receptacles**
  - **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 IVD medical device, as defined in this document.
  - **NOTE 2:** In certain jurisdictions there may be differences as to whether a device classified in this rule is considered an IVD medical device.
  - **NOTE 3:** 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).

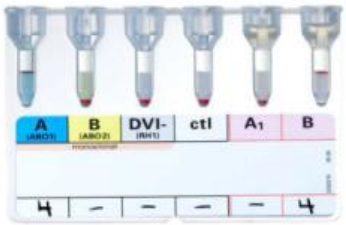
Classification Rules 4/4

- **Rule 6**: IVD medical devices not covered in Rules 1 through 5 are classified as **Class B**
  - Moderate Individual risk/Low Public health risk
  - No major impact on patient
  - **Examples :** Blood gases, H.pylori, physiological markers
- **Rule 7:** IVD medical devices that are controls without a quantitative or qualitative assigned value will be classified as **Class B**
  - **Examples :** Urinalysis controls and chemistry controls

Summary for classification of IVD

High Risk in both
Indiv. & public health

Class D
HIV, HBV, HCV, HTLV, ABO, Rh(D) test f
Blood Screening & Diagnostic



High Indiv. Risk &
Moderate Pub. Risk

Class C
High risk infection agent(SDT, Influe, CoV-19, etc.), Cancer marker, Cardiac marker, etc.

Moderate Indiv. Risk.
& Low Pub. Risk

Class B
Low risk infection agent(helico bactor, c. difficile, etc), GOT, GPT, g-protein, creatinine, pregnant test, etc.

Low Risk in both
Indiv. & public health

Class A
Nucleic acid extraction, H&E, Media, etc.

Conformity Assessment

- **Conformity :** Compliance with standards, rules, or laws
- **Conformity Assessment**
  - **the systematic examination of evidence** generated and procedures **undertaken by the manufacturer**, under requirements established by the Regulatory Authority, 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 (SG1/N041)**
- **Conformity Assessment Elements**
  - a quality management system (QMS)
  - a system for post-market surveillance (PMS)
  - summary technical documentation (STED)
  - a declaration of conformity
  - the registration of manufacturers and their IVD medical devices by the RA

Conformity Assessment Elements 1/4

- **Quality management system (QMS)**
  - The requirements for a quality management system that is **accepted by RAs for regulatory purposes and based on international recognised standards for medical devices(e.g. ISO13485),** combined with the other conformity assessment elements are intended to ensure that IVD Medical Devices will be safe and perform as intended by the manufacturer.
  - **A manufacturer needs to demonstrate its ability to provide IVD Medical Devices that consistently meet both customer and regulatory requirements**. Manufacturers demonstrate compliance through an established and effectively implemented quality management system that meets the regulatory requirements.
  - **The scope and complexity of the quality management system that a manufacturer needs to establish is influenced by varying needs,** objectives, the products provided, processes employed, the size and structure of the organisation, and the specific regulatory requirements.
  - **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. The RA/CAB should assess the adequacy of this control as part of the conformity assessment process.
  - **The extent of the RA/CAB assessment of the manufacturer's quality management system is influenced by the class of the IVD Medical Device.**

Conformity Assessment Elements 2/4

- **System for post market surveillance (PMS)**
  - Prior to placing the product on the market, the manufacturer will put 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* throughout the IVD Medical Device lifecycle.** This process will include complaint handling, vigilance reporting, and corrective and preventive action.
  - **The RA or CAB will confirm** that such a process is in place, usually at the time of the quality management system audit.

    * See GHTF/SG2 guidance documents
- **Technical documentation (STED)**
  - The technical documentation **provides the evidence that the IVD Medical Device meets the Essential Principles.**
  - For the purposes of conformity assessment, **the manufacturer will establish a subset of technical documentation (Summary Technical Documentation (STED)) to be held or submitted, as required by the class of the device.** The extent of evidence in that STED is likely to increase with the class of the IVD Medical Device and its complexity.

    * See GHTF guidance documents
  - **The RA or CAB determines** the adequacy of the documented evidence in support of the manufacturer's Declaration of Conformity to the Essential Principles through a review of the STED. The depth and the point in time of the review is likely to be influenced by the risk class of the IVD Medical Device and its complexity.

Conformity Assessment Elements 3/4

- **Declaration of conformity**
  - One element of the GHTF regulatory model for IVD Medical Devices requires that **the manufacturer attest that its IVD 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.
    - Information sufficient to identify the device(s) to which the Declaration of Conformity applies.
    - A Global Medical Device code and term for the device.
    - The risk class allocated to the device/s after following the guidance found in *Principles of IVD Medical Devices Classification*.
    - Which of the conformity assessment procedures described in Section 6.2 have been applied.
    - The date from which the Declaration of Conformity is valid.
    - The name and address of the device manufacturer.
    - The name, position and signature of the responsible person who has been authorised to complete the Declaration of Conformity upon the manufacturer's behalf.
  - **The RA or CAB may review and confirm** the adequacy of the Declaration of Conformity, if required, by examining the supporting documents or other evidence

Conformity Assessment Elements 4/4

- **Registration of manufacturers and their IVD Medical Devices by the Regulatory Authority**
  - considered to be the most **basic level of regulatory control of devices** in the market. This registration system will identify the IVD Medical Device/s and the party responsible for the IVD Medical Device/s within the particular jurisdiction, thereby facilitating any regulatory activity.
  - Prior to placing an IVD Medical Device on the market, the manufacturer, its local distributor or its Authorized Representative should provide the Regulatory Authority with the required information.
  - **The RA will maintain** the register.

Harmonized Conformity Assessment System

Conformity Assessment Element	Class A		Class B		Class C and D	
	Manufacturer	RA/CAB	Manufacturer	RA/CAB	Manufacturer	RA/CAB
Quality Management System	**a full QMS** or **a QMS w/o design and development controls**	Premarket regulatory **audit not required**	**a full QMS** or **a QMS w/o design and development controls**	**a current and appropriate QMS** is in place or conduct a QMS audit prior to MA	Establish and maintain **a full QMS**.	**a current and appropriate QMS** is in place or conduct a QMS audit prior to MA
Post Market Surveillance	**an adverse event reporting procedure**	**May audit post-market to investigate specific safety or regulatory concerns**	**an adverse event reporting procedure**	**a current and appropriate adverse event reporting procedure**	**an adverse event reporting procedure**	**a current and appropriate adverse event reporting procedure**
Technical Documentation	**Prepare STED and have available** for review upon request	Premarket submission of STED **not required**.	**Prepare STED and have available** for review upon request.	Premarket submission **normally not required**	**Prepare and submit STED for review**	**a premarket review of the STED**.
Declaration of Conformity	**Prepare, sign and maintain**	**On file with the manufacturer; available upon request**	**Prepare, sign and submit**	**Review and verify compliance with requirements**	**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	Perform according to regulatory requirements	Maintain and verify as appropriate	Perform according to regulatory requirements	Maintain and verify as appropriate

Conformity Assessment consideration

1. Relaxed Conformity Assessment

- RA/CAB may **defer the review of the STED** for Class C devices **until a subsequent regulatory audit.**
- RA/CAB may **exempt a complete premarket submission** or **mitigate audit** when ~
  - The device incorporates **well-established technology.**
  - RA/CAB is **familiar with the manufacturer**'s capability and its products.
  - **Updated version of device** from the same manufacturer **w/o substantive change.**
  - RA/CAB has **particular experience** with a **comparable device.**
  - The device has Internationally recognized standards

2. Tight Conformity Assessment

- RA/CAB may require a **more detailed premarket submission** and/or require a **more rigorous audit** and/or the provision of **more performance evaluation data** for risk class when ~
  - The device incorporates **Innovative technology**.
  - An **existing compliant device** is being proposed for **a new intended use**.
  - The **manufacturer's experience level** w/ the type of IVD Device is **limited**.
  - The device type trends to be associated with **an excessive number of adverse events**, including use errors.
  - The device incorporates innovative or potentially **hazardous materials**.
  - **The device type** raises specific **public health concerns.**

Thanks for your attention