Document number: ZFDA/ MCD/MD/GDL/003
Rev.No.00

THE REVOLUTIONARY GOVERMENT OF ZANZIBAR

MINISTRY OF HEALTH

ZANZIBAR FOOD AND DRUGS AGENCY

GUIDELINE FOR SUBMISSION OF DOCUMENTATION FOR REGISTRATION OF IN VITRO DIAGNOSTICS DEVICES

March, 2019

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ACKNOWLEDGEMENTS

These guidelines have been developed to define procedure and requirement of registration of In Vitro Diagnostic Devices.

The process to develop these guidelines started when members of Medicines, Cosmetics and other Medical product department produce first draft. Subsequently, other staff in ZFDA who produced the final document took the process forward.

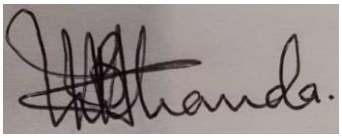
I would like to take this opportunity to thank all members who in one way or another assisted in organized of these Guidelines. Acknowledgement is particularly extended to Mr. Bora Lichanda, Mrs Salma H Ali, Mrs Amne Nassor Issa, Mr Mwadini A. Mwadini, Ms Nawwal J Mgaza, Mr Abrahman H. Mussa, Mr Ali R. Maulid, Mr. Nassir S. Buheti, Mr Hamid I. Haji, Omar H. Ussi, Mrs Kibibi S. Mohd

We would also like to thank the Tanzania Food and Drugs Authority (TFDA), Health Canada and Health Science Authority (HSA) of Singapore for making their guidelines available for reference.

I would also like to thank the Tanzania Food and Drugs Authority (TFDA) Global Harmonization Task Force (GHTF), World Health Organization (WHO), Asian Harmonization Working Party (AHWP) and Health Science Authority (HSA) of Singapore; for making their guidelines available for reference.

Special thanks are also owed to TFDA esteemed stakeholders; dealers in In vitro Diagnostics, Medical Stores Department (MSD), Private Health Laboratories Board (PHLB), Ministry of Health and Social Welfare (MoHSW) and the academia who discussed the draft guidelines and gave commendable inputs for improving the guidelines.

Last but not the least, ZFDA Management are acknowledged for constructive comments and inputs during deliberation and approval of the guidelines.



Bora Lichanda
Director of Medicine and Cosmetics
Zanzibar Food and Drug Agency

FOREWORD

The Zanzibar Food and Drugs Agency (ZFDA) was established under Section 3(1) of the Zanzibar Food, Drugs and Cosmetics Amendment Act No.3/2017 to regulate among other products, the quality, safety and performance of In vitro diagnostic devices.

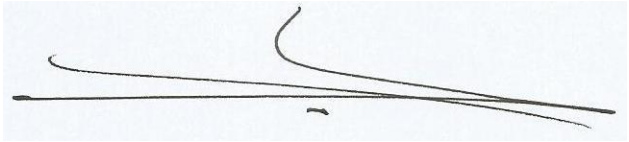
The regulation of In-vitro diagnostics (IVDs) involves amongst other things, registration which is an official authorization for the purpose of marketing or free distribution of products after their safety and performance have been confirmed. In order to address various concerns from stakeholders and the general public, the Agency has set up a framework for regulating In-vitro diagnostics in Zanzibar. To begin with, the Agency has developed these guidelines which define requirements for registration of In-vitro diagnostics.

The guidelines are first of its kind and together with other requirements; it provides guidance on classification of IVDs depending on their level of risk. The Agency will therefore take risk-based approach when regulating IVDs. The guidelines have also adapted key elements of the Summary Technical Documentation (STED) for Demonstrating Conformity to the Essential Principles of Safety and Performance of Medical Devices. This is in line with the need for global convergence of regulatory systems for medical devices.

Applicants are encouraged to familiarize with the guidelines and follow them when preparing and submitting applications for registration of IVDs. However, the requirements highlighted are minimum and whenever there will be additional information; these may be submitted to ZFDA.

Adherence to these guidelines will ensure that all relevant information is provided in the dossiers submitted for registration. This will facilitate efficient and effective evaluation as well as approval process. It will also help to avoid queries which results in unnecessary delays in giving approvals.

Since the world of science is always dynamic and due to the fact that the field of in-vitro diagnostics keeps changing over time, the Agency welcome inputs and comments that will help in improving these guidelines.



Dr. Burhani Othman Simai
Executive Director
Zanzibar Food and Drug Agency

ABBREVIATIONS

AHWP	-	Asian Harmonization Working Party
CSDT	-	Common Submission Dossier Template
DoC	-	Declaration of Conformity
EPSP	-	Essential Principles of Safety and Performance
GHTF	-	Global Harmonization Task Force
GMDN	-	Global Medical Devices Nomenclature
GMP	-	Good Manufacturing Practices
HSA	-	Health Sciences Authority
ISO	-	International Organization for Standardization
IVDs	-	In Vitro Diagnostics
LRP	-	Local Responsible Person
MoH	-	Ministry of Health
CMS	-	Central Medical Stores
PHL	-	Private Health Laboratories
QMS	-	Quality Management System
STED	-	Summary Technical Documentation
TBS	-	Tanzania Bureau of Standards
TFDA	-	Tanzania Food and Drugs Authority
ZFDCA	-	Zanzibar Food, Drugs and Cosmetics Act No,2/2006 and its Amendment Act No. 3/2017
ZFDA	-	Zanzibar Food, Drugs and Cosmetics Agency
ZBS	-	Zanzibar Bureau Standards

1. Introduction

These guidelines have been developed to provide guidance for submission of in -vitro diagnostic device information to demonstrate conformity to the Essential Principles of Safety and Performance. This is in accordance with the section 53(1) of the Zanzibar Food, Drugs and Cosmetic Act No. 2, 2006 which among other things prescribes conditions for registration of medical devices in Zanzibar.

Such conditions include; safety and efficacy of the IVDs, compliance of the manufacturer to Quality Management System requirements and any other requirements as may be prescribed by the Agency.

In developing the guidelines, reference was made from the following GHTF guidance documents:

a) Principles of In Vitro Diagnostic (IVD) Medical Devices Classification: GHTF/SG1/N045:2008.
b) Principles of Conformity Assessment for In Vitro Diagnostic (IVD) Medical Devices: BGHTF/SG1/N046:2008.
c) Summary Technical Documentation (STED) for Demonstrating Conformity to the Essential Principles of Safety and Performance of In Vitro Diagnostic Medical Devices: GHTF/SG1/N063:2011.
d) Essential Principles of Safety and Performance of Medical Devices: GHTF/SG1/N41R9:2005.

In addition, the Common Submission Dossier Template (CSDT) of the Asian Harmonization Working Party (AHWP) and the Medical Devices Regulations – Global Overview and Guiding Principles of WHO were also used. These guidelines apply to products that fall within the definition of in-vitro diagnostic devices. The guidelines are divided into the following sections:

a) General Requirements
b) Device Details
c) Summary Technical Documentation
d) Labeling Requirements
e) Annexes

It should be noted that the assessment of dossiers submitted will be based on these guidelines.

1.1 Definition of terms

In the context of this guideline, the following terms shall be defined as:

Applicant
Means any person or institution or company that applies formally to get market authorization for IVDs in Zanzibar.

Agency
Means the Zanzibar Food, Drugs and Cosmetics Regulatory Agency established under section 3 of ZFDC Amendment Act No.3/ 2017

Calibrator
Means any substance, material or article intended by its manufacturer / owner to be used in the calibration of a measuring instrument or measuring system.

Conformity Assessment
Means the systematic examination of evidence generated and procedures undertaken by the manufacturer, under requirements established by the Agency, to determine that an in vitro diagnostic device is safe and performs as intended by the manufacturer and, therefore, conforms to the Essential Principles of Safety and Performance of Medical Devices.

Certified Copy
Means a true copy of the original document certified by a person registered to practice law in the manufacturer's country of origin and endorsed with the legal practitioner's official stamp and signature.

High Dose Hook Effect
Means the wrong low measurement of analyte (s) which are present in the specimen in a very high concentration.

In Vitro Diagnostics (IVDs)
Means 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.

Products for general laboratory use are not in vitro diagnostics unless such products, in view of their characteristics, are specifically intended by their manufacturer to be used for in vitro diagnostic examination.

Label
Means any written, printed or graphic representation that appears on or is attached to the medical device or active ingredient or any part of its packaging, and includes any informational sheet or leaflet that accompanies the in vitro diagnostics or active ingredient when it is being supplied.

Labeling / information supplied by the manufacturer
Means a written, printed or graphic matter affixed to an in vitro diagnostic device or any of its containers or wrappers, or, accompanying a medical device, related to identification, technical description, and use of the device, but excluding shipping documents.

Lay Person
Means any individual who does not have formal training in a relevant field or discipline.

Local Responsible Person
Means a local responsible person is a natural person residing in Zanzibar or cooperate body registered in Zanzibar who has received a mandate from the applicant to act on his behalf with regard to matters pertaining to registration of devices in Zanzibar.

Manufacture
Means to make, fabricate, produce or process an in vitro diagnostic and includes:

a) any process carried out in the course of so making, fabricating, producing or processing the in vitro diagnostics; and
b) the packaging and labeling of the in vitro diagnostics before it is supplied;

Manufacturer
Means a person or a firm that is engaged in the manufacture of in vitro diagnostics.

Medical Device or Devices
Means an instrument, apparatus, implement, medical equipment, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part or accessory, which is -

a) recognized in the Official National Formulary, or Pharmacopoeia or any supplement to them;
b) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease, in man or other animals or;
c) intended to affect the structure or any function of the body of man or other animals and which does not achieve any of its principal intended purposes through chemical action within the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its principle intended purposes.

National Standard
Means a standard as prescribed by the Zanzibar Bureau Standards and Tanzania Bureau of Standards for those standards not available in ZBS

Near Patient Testing
Means any testing performed outside a laboratory environment by qualified personnel, generally near to or at the side of, the patient. Also known as Point-of-Care (POC).

Objective Evidence
Means information that can be proved true, based on facts obtained through observation, measurement, testing or other means.

Process Validation
Means confirmation by objective evidence that a process consistently produces a result or product meeting its pre-determined requirements.

Quality System
Means a system which consists of the organizational structure, responsibilities, procedures, processes and resources for implementing quality management and achieving its objectives.

Quality Management System
Means the management system to direct and control an organization with regard to quality, from establishing quality policy, quality objectives and implementing and maintaining quality system.

Reagent
Means any chemical, biological or immunological components, solutions or preparation intended by the manufacturer to be used an IVD devices.

Recall
Means any action taken by the manufacturer, importer or distributor in respect of an in vitro diagnostic device that has been sold to recall or correct the device, or to notify its owners and users of its defectiveness or potential defectiveness, after being aware that the device may be hazardous to health, may fail to conform to any claim made by the manufacturer or importer relating to its effectiveness, benefits, performance characteristics or safety or may not meet the requirements of the Act or Regulations.

Recognized Standards
Means national or international standards deemed to offer the presumption of conformity to specific Essential Principles of Safety and Performance.

Registrant
Means the person who applied for and obtained the registration of the medical devices including IVDs device under the medical device regulations.

Risk
Means a combination of the probability of occurrence of harm and the severity of that harm.

Self-testing
Means testing performed by lay person.

Specimen receptacles
Means devices, whether vacuum-type or not, specifically intended by their manufacturers for the primary containment and preservation of specimens derived from the human body for the purpose of in vitro diagnostic examination.

Technical Documentation
Means documented evidence, normally an output of the Quality Management System that demonstrates compliance of a device to the Essential Principles of Safety and Performance of Medical Devices.

Verification
Means confirmation by examination and provision of objective evidence that the specified requirements have been fulfilled.

2. GENERAL REQUIREMENTS

All applications shall be made by submitting a duly filled in application form ***(Annex 1)*** accompanied with prescribed information as detailed in these guidelines.

2.1 Applicant

An application for registration of in vitro diagnostic (s) can be made by a manufacturer or by a person who orders the IVDs to be manufactured for sale in Zanzibar.

The applicant shall be responsible for the product, information supplied in support of the application for registration and variations thereof.

An applicant who is not a resident in Zanzibar shall nominate a Local Responsible Person (LRP). A certified copy of power of attorney, formal agreement or any other official authorization shall be submitted by an applicant as official proof of nomination of an LRP.

2.2 Local Responsible Person

The Local Responsible Person shall:

a) Monitor the device on the market and inform the Agency immediately after the detection of any problem relating to a registered device such as serious manufacturing defects which may endanger public health.
b) Facilitate communication between the Applicant and the Agency on matters relating to the product.
c) Handle device recalls.
d) Provide technical support and services to users of registered device(s).

2.3 First time application

A separate and complete product dossier in both hard copy and electronic form, in both PDF and MS WORD formats on a CD-ROM, is required for each in vitro diagnostic being sent for registration.

Applications shall be accompanied by the following:

a) A non-refundable application fee as provided for in the current ZFDA Fees and Charges document.
b) One sample of the device or artwork, where applicable, at the time of lodging an application for registration.

2.4 Documentation

a) Language

All applications and supporting documents shall be made in Kiswahili or English.

b) Requirements for class A

The submission requirements for class A IVD medical devices are stipulated in ***section 3.1*** of these guidelines.

c) Requirements for class B, C and D

Application for registration of Class B, C and D IVD medical devices shall be prepared in accordance to requirements prescribed in ***section 3, 4, 5*** of these guidelines.

d) Paper type and binding

Data shall be presented on A4 and 80g/m^2 paper with readily readable letters of at least 12 font sizes. Every page shall be numbered sequentially. Extension sheets, tables, diagrams and other supporting documents shall as far as possible be of the same size, well annotated, numbered and appropriately cross-referenced.

All parts must be bound separately and arranged sequentially in spring file covers with flexible seat. Lever arch files are not permissible. One or more spring file covers may be used depending on the number of pages contained in a part. The file cover should be made of hard, non-collapsible biodegradable material. The thickness should be expandable or reducible depending on the total thickness of the contents.

2.5 Classification of In-Vitro Diagnostic (IVD) devices

In vitro diagnostic should be classified into one of the four classes of devices A, B, C or D as described below.

General Classification System for IVDs

CLASS	RISK LEVEL	EXAMPLES
A	Low Individual Risk and Low Public Health Risk	Clinical Chemistry Analyzer prepared selective culture media.
B	Moderate Individual Risk and/or Low Public Health Risk	Vitamin B12 level test, Pregnancy self -testing, Anti-Nuclear Antibody, and Urine test strips.
C	High Individual Risk and/or Moderate Public Health Risk	Blood glucose self-testing, Human Leukocyte antigen (HLA), Prostate Specific Antigen (PSA) screening, Rubella Antibodies Test
D	High Individual Risk and High Public Health Risk	HIV Blood donor screening, HIV Blood diagnostic

Classification should be done based on classification rules appended in ***Annex 3*** of these guidelines.

If more than one classification rule is applicable to the device, the rules resulting to the highest risk classification shall be applicable to the device. However, the Agency reserves the right to decide on the class of the device.

Accessories and software for IVDs

a) Accessories

Where applicable, the following considerations should apply;

i. Calibrators intended to be used with an IVD reagent should be placed in the same class as the IVD reagent.
ii. Stand alone control materials with no assigned values intended for use with multiple or single analyte (s) should not be placed in the same class as the IVD reagent(s).
iii. Stand alone control materials with quantitative or qualitative assigned values intended for one specific analyte or multiple analyte (s) should be placed in the same class as the IVD reagent(s).

b) Software

While most soft-wares are incorporated into the IVDs itself, some are not. Provided that such standalone software falls within the scope of the definition for an IVD it should be classified as follows:

i. Where it controls or influences the intended output of a separate IVD medical device, it will have the same class as the device itself.
ii. Where it is not incorporated in an IVD device, it is classified in its own right using the classification rules.

2.6 Payment of fees

Every application shall be accompanied by appropriate fees as specified in the current ZFDA Fees and Charges document at the time of application. All fees are payable at the time of lodging an application. The fees may be paid directly to ZFDA or by bank transfer to:

The fees may be paid directly to ZFDA or by bank transfer to: -

Zanzibar Food, Drugs and Cosmetics Agency,
Account No. 021103000579 PBZ Bank Local Currency, and
Account No. 02210000015 PBZ Bank Foreign Currency,

When payment is made by bank transfer all bank charges shall be borne by the applicant who shall also make sure that advice note is submitted to ZFDA giving details of the payment in particular the name of the applicant, the device
or devices paid for and amount of fees paid.

Fees are non-refundable once paid to the Agency.

For each registered device an annual retention fees shall be paid on or before the end of January of each year for which the fees are due to maintain a medical device on the medical device register. The registration number of the device must be quoted at the time of payment.

The amount of retention fee to be paid shall be as prescribed in the current ZFDA Fees and Charges document at the time of application.

Note:

a) All bank charges shall be borne by the applicant.
b) For details of fee schedule, refer to the ZFDA current Fees and Charges Documents.

2.7 Processing of applications

Once an application has been accepted and evaluation fees paid the processing of application will take 270 calendar days. This will involve evaluation of applications, request for additional data/samples and clarification of some issues, where applicable.

Once a query or a request has been raised, the processing shall halt until after the response to the query has been received. If no response to the query or request has been received within six months the application will be rejected.

2.8 Registration of the device

When an IVD device is found to have complied with all the prescribed registration requirements, the applicant will be informed to that effect. A certificate of registration together with such conditions as the ZFDA may determine shall be issued.

a) Validity of registration

The registration of an IVD device shall be valid for five (5) years unless suspended or revoked by ZFDA or terminated by the registrant. The validity of registration shall be subject to:

i. Payment of annual retention fees as prescribed in the current ZFDA Fees and Charges document.
ii. Submission of biannual post-marketing surveillance report (s).
iii. Submission of adverse effects reports associated with the use of device.

b) Termination of registration

The ZFDA may, by giving reasons in writing, suspend or revoke the registration of a device, or amend the conditions of its registration. The registrant may, by giving 60 days written notice and reasons to the ZFDA, terminate the registration of a device.

2.9 Application for variation of a registered device

The Agency should be informed on any anticipated significant change(s) that could reasonably be expected to affect the safety or effectiveness of an IVD device. Significant change(s) will include any of the following:

a) The manufacturing process, facility or equipment;
b) The manufacturing quality control procedures, including the methods, tests or procedures used to control the quality, purity and sterility of the device or of the materials used in its manufacture;
c) The design of the device, including its performance characteristics, principles of operation and specifications of materials, energy source, software or accessories; and
d) The intended use of the device, including any new or extended use, any addition or deletion of a contraindication for the device and any change to the period used to establish its expiry date.

These changes will require ZFDA approval before they can be implemented. Any other change(s) should be notified immediately to the Agency and may be implemented without prior approval.

All applications for variation to a registered device shall be made in writing and shall be accompanied by variation fee as prescribed in the current ZFDA Fees and Charges document at the time of application.

2.10 Application for renewal of registration

Applications for renewal of registration shall be made at least 90 days prior to the expiry date of registration of the device. The application shall include submission of filled in application form ***(Annex 1)*** and information pertaining to changes that were made to a registered device (if any).

2.11 Compilation of the dossier (Class B, C and D)

Applicants are required to arrange the application dossier in the format described below:

a) The application form (Annex 1)
b) Device Details (**Item 3.2 of these guidelines**)
c) Summary technical documentation (**Item 4 of the guideline**)
d) Labeling information (**Item 5 of the guideline**)
e) Essential requirement checklist (**Annex 3 of the dossier**)

Failure to arrange the application dossier accordingly will lead to rejection of the application.

NB: *Compilation of the dossier for Class A requires an application for class A and items described under section 3.1.*

2.12 Evidence of Compliance to Quality Management System

For the IVD medical devices with higher risks the pre-registration quality audit will be conducted to verify their compliance with requirements. The audit will be conducted on risk basis. However, in most cases evidence of compliance to Quality Management System for IVD provided by manufacturer will be considered.

For IVDs that require evidence of compliance to Quality Management System, a CE certificate issued by a Notified Body designated in Europe for the purposes of the In Vitro Diagnostic Medical Devices Directive (98/79/EC) (IVDD) and issued under Annex IV Section 3 or Annex VII of the Directive will be accepted (may also be referred to as an EU Certificate, an EC certificate or an EEC Certificate). ISO 13485 certificates issued by Notified Bodies designated in Europe for the purposes of the IVDD will also be accepted.

2.13 Appeals

Any person aggrieved by a decision of the Agency in relation to any application for registration of an IVD device may make representations in writing to ZFDA.

If after consideration of the representations, the Agency is satisfied it may approve registration of an IVD device and if not satisfied it shall reject the application. In case the

applicant is not satisfied with the decision, may appeal to the Minister responsible for Health. The Ministers decision shall be final. If the Registrant would not be satisfied by the Minister's decision, he may appeal to the Court of Law.

3. SUBMISSION REQUIREMENTS FOR IN VITRO DIAGNOSTICS

3.1 Submission requirements for Class A IVDs

Applicants are required to submit the following information for Class A IVDs

a) Dully filled in application form as appended in **Annex 1** of these guidelines.

b) Copies (in English and in original colour) of the labels on the IVD medical device and its packaging are to be provided for the primary and secondary levels of packaging. Labels must be provided for all the components of IVD medical device system, members of IVD medical device family and accessories submitted for registration. Alternatively, a representative label may be submitted for variants, provided the variable fields on the artwork are annotated, and the range of values for the variable fields are indicated;

c) The instructions for use.

d) The patient information leaflet.

e) The promotional material (including brochures and catalogues.

f) For sterile IVD medical devices: the sterilization validation report

g) IVDs with measuring function: certification on IVDs metrology or equivalent.

h) For active IVD medical devices: certification to electrical safety standards e.g. **IEC 60601.**

i) For class A In vitro diagnostics containing materials of animal, human, microbial and/or recombinant origin, the following information must be submitted in addition to the information above:

   i. A list of all materials of animal, human, microbial and/or recombinant origin used in the IVDs medical device and in the manufacturing process of the IVDs medical device. This includes, but not limited to animal or human cells, tissues and/or derivatives, and cells, tissues and/or derivatives of microbial or recombinant origin; and

   ii. Identity of immediate sources of the above.

j) Review of application for class A IVDs medical devices the risk associated with the use of the IVDs medical devices has been determined to be low. The Authority does not conduct a premarket evaluation of the safety, quality and performance for such IVDs medical devices. The Agency's role in the review of the application is to determine that:

   i. The class A IVDs medical device is correctly classified. In the event that the IVDs medical device is incorrectly classified or the product claims are questionable, the Agency may request for the full technical documentation of the IVD medical device

ii. The intended purpose/indications for use for the class A IVDs medical device is appropriate for the design of the IVDs and no exaggerated claims are made.

3.2 Submission requirements for Class B, C and D IVDs

Applicants are required to submit the following information for Class B, C & D IVDs

i. A dully filled in application form as provided in annex 1 of this guideline

ii. Device details as described below

a) Name(s)

State the generic and brand name of the IVD medical device.

b) Description

Provide a general description on design, characteristics and performance of the IVD medical device. The description should also include information on device packaging.

c) Category

State the class of the IVD medical device and the applicable classification rule as appended in ***Annex 3*** of these guidelines.

d) Intended Use/Indication

State the intended use of the IVD medical device and/or provide a general description of the disease or condition that the device will diagnose, treat, prevent, or mitigate. The description of the target patient population for which the device is intended should also be included, whether it is automated or not, whether it is qualitative or quantitative; type of specimen it requires (serum, plasma, urine) and what the assay type is e.g. immunoassay, chemistry, cyto-chemistry, image analysis should be stated.

e) Instructions of Use

Give a concise summary of information for safe use of the device including procedures, methods, frequency, duration, quantity and preparation to be followed.

f) Contraindications

State conditions under which the IVD medical device should not be used. For example, a limitation of an assay using specimens from patients who have received preparations of mouse monoclonal antibodies for therapy when tested with assay kits which employed mouse monoclonal antibodies. It may show either false elevated or depressed values.

g) Warnings

State the specific hazard alert information that a user needs to know before using the IVD medical device. E.g. for products containing biological material, radioactive material, explosive material and any other hazardous material, safety warnings must be included.

h) Precautions

State briefly precautions to be taken and any special care necessary for the safe and effective use of the IVD medical device.

i) Adverse Effects

Describe all adverse and side effects associated with the IVD medical device under normal conditions of use.

j) Alternative Use

Describe any alternative practices or procedures for diagnosing, treating, or mitigating the disease or condition for which the IVD medical device is intended.

k) Storage conditions

State the storage conditions for the IVD medical device.

l) Recommended shelf-life (where applicable)

State the recommended shelf-life of the IVD medical device.

4. SUMMARY TECHNICAL DOCUMENTATION

4.1 Device description and features

Provide a detailed description of the device attributes that are necessary to explain how the device functions. These details should include:

a) Intended use of the diagnostic. This may include:

i. What is detected;
ii. The function of the IVD medical device (e.g. screening, monitoring, diagnostic or aid to diagnosis, staging or aid to staging of disease);
iii. The specific disorder, condition or risk factor of interest that is intended to detect, define or differentiate;
iv. Whether the product is automated or not;
v. Whether the test is qualitative or quantitative;
vi. The type of specimen(s) required (e.g. serum, plasma, whole blood, sputum, urine);
vii. The intended testing population (e.g. neonates, antenatal women);

b) The intended user (laboratory professional and/or at point-of-care);

c) A general description of the principle of the assay method or instrument principles of operation.

d) A description of the components of the assay (e.g. reagents, assay controls and calibrators), and where appropriate, a description of the reactive ingredients of relevant components (such as antibodies, antigens and nucleic acid primers).

e) A description of the specimen collection and transport materials provided with the product or description of specifications recommended for use.

f) For instruments of automated assays: a description of the appropriate assay characteristics or dedicated assays.

g) For automated assays: a description of the appropriate instrumentation characteristics or dedicated instrumentation.

h) If applicable, a description of any software to be used with the device.

i) If applicable, a description or complete list of the various configurations/variants of devices that will be made available. For example, a family of pregnancy rapid test can consist of device available in different configurations, such as test strip or in a cassette.

j) If applicable, a description of the accessories, and other non IVD products that are intended to be used in combination with the diagnostic.

k) Risk class and the applicable classification rule for the IVD medical device according to IMDRF guidelines.

The instruction for use may be used to provide some of this information on the condition that a cross-reference to the different requirements is supplied in conjunction with the instructions-for-use.

4.2 Evidence of Conformity to Essential Principles

Provide evidence of conformity to Essential Principles of Safety and Performance (EPSP) by completing the checklist appended as **Annex II**.

Note:

a) Manufacturer should identify the essential principles of safety and performance that are applicable to the device and the general methods used to demonstrate conformity to each applicable Essential Principle. The methods that may be used include:

i. Conformity with a recognized or other standard(s)
ii. Conformity with a commonly accepted industry test method (reference method)
iii. Conformity with appropriate in-house test methods that have been validated and verified;
iv. Comparison to a diagnostic already available on the market.

b) When the manufacturer uses national, international or other standards to demonstrate conformity with the Essential Principles, full title of the standard, identifying numbers, date of the standard and the organization that created the standard should be provided.

The IVD device, to which the Essential Principles (EP) conformity checklist is applicable, should be identified by the brand name, common name and risk class on the checklist itself. The columns of the checklist (**Annex III**) should be completed as follows:

a) Applicable to the IVD device?

Either a "Yes" or "No" answer is required. If the answer is "No" there should be a brief explanation.

b) Method of conformity

State the title and reference of the standard(s), industry or in-house test method(s), comparison study (ies) or other methods to demonstrate compliance. For standards, this should include the date of the standard and where a standard is referred to more than once in the checklist, the reference number and date can be repeated.

c) Identity of specific documents

The column should contain the reference to the actual technical documentation that demonstrates compliance to the essential principle, i.e. the certificate number(s), test reports, study reports or other documents that resulted from the method used to demonstrate compliance, and its location within the technical documentation or dossier.

4.3 Risk Analysis

Provide a summary of the risks identified during the risk analysis process and how such risks have been controlled to an acceptable level. Preferably, the risk analysis should be based on recognized standards and be part of the manufacturer's risk management plan.

The summary should address possible hazards for the IVD medical device such as the risk from false positive or false negative results, indirect risks which may lead to erroneous results, or from user-related hazards, such as reagents containing infectious agents. The results of the risk analysis should provide a conclusion with evidence that remaining risks are acceptable when compared to the benefits.

4.4 Design and Manufacturing Information

a) Product design

Provide information such as to give a general understanding of the design applied to the IVD medical device. It should include a description of the critical ingredients of an assay such as antibodies, antigens, enzymes and nucleic acid primers provided or recommended for use with the IVD medical device.

i. For instruments include a description of major subsystems, analytical technology (e.g. operating principles, control mechanisms), dedicated computer hardware and software.
ii. For instruments and software, give an overview of the entire system, including an Architecture Design Chart which is typically a flowchart of the relationships among the major functional units in the software, including relationships to hardware and to data flows such as networking.
iii. For standalone software, include a description of the data interpretation methodology (i.e. algorithms).
iv. For self-testing devices the design should include a description of the design aspects that make it suitable for lay person use.
v. If design takes place at multiple sites, a controlling site must be identified.

Formulation and composition

Provide formulation/composition for each of the ingredients;

Materials

Provide complete details of material specifications, including raw materials;

i. All components of the IVD medical device should be listed and chemically and biologically characterized, including antibodies, antigens, and assay controls, substrates used to detect antigen-antibody complexes, and test reagents. Appropriate references should be cited.
ii. If synthetic peptides are used, the peptide sequence should be provided.
iii. If components are of biological origin or recombinant, the source must be indicated and details on production must be provided. These details would include the strain of the virus, the cell line for cultivation of the virus, sequences of relevant nucleic acids and amino acids, etc., used in the manufacturing process of viral lysate, purified proteins, recombinant and synthetic proteins.
iv. If applicable, process validation results to be provided to substantiate that manufacturing procedures are in place to minimize biological risks, in particular, with regard to viruses and other transmissible agents. This also includes inactivation of infectious organisms in reagents and the production of reagents.
v. If applicable, information to be provided on irradiating components, non-ionizing or ionizing (e.g. Iodide- 131 in the Radioimmunoassay kit, radio-labelled Phosphorus-32 DNA probes in Southern blots).
vi. If applicable, information should be provided on the poison or controlled substance (e.g. Buprenorphine in drug assay kit).
vii. Given the nature and specification of the packaging material(s) including complete chemical and physical characterization of the packaging material making either direct or indirect contact with the IVD medical device.
viii. Identify the sources of the materials from which the components are constructed.

Biological Safety

List all biological components included in the IVD device to include material of bacterial, viral, parasitic, animal, or human origin or their derivatives where applicable. Indicate the name of the biological component, details of its use in the product and description of steps taken for the reduction of transmission or infection risk.

Documentation of design change

Provide records of each design change, if any, with reasons for these changes along with associated validation/verification data. Include evidence that the change achieves the desired effect, and that the product continues to comply with the Essential Principles of Safety and Performance.

b) Manufacturing Processes

Overview of Manufacturing Process

Provide information on the manufacturing process, which may be in form of a process flow chart, showing an overview of production including technologies used, assembly and packaging of the finished IVD device. Include details of any in-process and final product

testing (e.g. the manufacturer's QC release program).

Sites of Manufacture

Provide the following information;

i. Name of site,
ii. Physical address of the site,
iii. Description of the component manufacture/stage of manufacturing process carried out at the site,
iv. A simple sight plan highlighting production areas and number of employees at the site,
v. A description of any other manufacturing that occurs at the site;

For all the critical manufacturing sites that are involved in the manufacture of this product (i.e. including design, warehousing and quality control stages of manufacture)

Key Suppliers

Provide a list of key suppliers of ingredients/products/services for the manufacture of the IVD device, indicating the;

i. Name of the supplier,
ii. Supplier's manufacturing site physical address
iii. A description of the ingredient/product/service supplied
iv. Evidence of purchasing and verification procedures for the ingredients/products/services sourced from these suppliers.

4.5 Device Specifications

Describe functional characteristics and technical performance specifications for the device including as relevant, accuracy, sensitivity, specificity of measuring and other specifications including chemical, physical, mechanical, electrical and biological.

A list of the features, dimensions and performance characteristics of the IVD medical device its variants and accessories should be provided in the dossier and also made available to the end user.

a) Device Verification and Validation

Summarize the results of verification and validation studies undertaken to demonstrate compliance of the IVD medical device with Essential Principles that apply to it. Whenever applicable the information should cover:

i. The complete study protocol,
ii. The method of data analysis,
iii. Complete study report,
iv. The study conclusion,
v. Any published literature regarding the device or substantially similar devices.
vi. Summaries or reports of tests and evaluations based on other standards, manufacturer methods and tests or alternative ways of demonstrating compliance.

Declarations/certificate of compliance to a recognized standard as applied by the manufacturer should be provided.

When a recognized standard exists that contains the protocol and the method of data analysis, this information can be substituted by a declaration/certificate of conformity to the recognized standard. However, a summary of the data and conclusions should be provided. Where appropriate actual test result summaries with their acceptance criteria should be provided and not just pass/fail statements.

b) Specimen type

This section should describe the different specimen types that can be used, including their stability (and storage) conditions and is typically applicable to all systems and assay types.

i. Stability includes storage and where applicable transport conditions. Storage includes elements such as duration, temperature limits and freeze/thaw cycles.

ii. Summary information for each matrix and anticoagulant when applicable, including a description of the measurement procedure for comparison or determination of measurement accuracy. This includes information such as specimen type tested, number of samples, sample range (using spiked samples as appropriate) or target concentrations tested, calculations and statistical methods, results and conclusions.

4.6 Analytical performance characteristics

a) Accuracy of measurement

Provide information to describe both trueness and precision studies.

b) Trueness of measurement

Provide information on the trueness of the measurement procedure and summarize the data used to establish the trueness measures for both quantitative and qualitative assays.

i. Precision of measurement

Provide information to describe repeatability and reproducibility studies.

ii. Repeatability

Provide detail on repeatability estimation and information about the studies used to estimate, as appropriate, within-run variability. Repeatability data is obtained for instrumentation in conjunction with an appropriate assay.

iii. Reproducibility

Provide information on reproducibility estimates and information about the studies used to estimate, as appropriate, variability between days, runs, sites, lots, operators and instruments. Such variability is also known as “Intermediate Precision”.

c) Analytical sensitivity

Provide information about the study design and results. Give a detailed description of specimen type and preparation including matrix, analyte (measured) levels, and how levels were established. The number of replicates tested at each concentration should also be provided as well as a description of the calculation used to determine assay sensitivity. For example:

i. Number of standard deviations above the mean value of the sample without analyte (measurand), commonly referred to as 'limit of blank' (LoB).
ii. Lowest concentration distinguishable from zero, based on measurements of samples containing analyte (measurand), commonly referred to as 'limit of detection, (LoD).
iii. Lowest concentration at which precision and/or trueness are within specified criteria, commonly referred to as 'limit of quantitation' (LoQ).

d) Analytical specificity

i. Give information to describe interference and cross reactivity studies to determine the analytical specificity, defined as the ability of a measurement procedure to detect or measure only the analyte (measurand) to be detected, in the presence of other substances/agents in the sample.
ii. Provide information on the evaluation of potentially interfering and cross reacting substances/agents on the assay. Information should be provided on the substance/agent type and concentration tested, sample type, analyte (measurand) test concentration, and results.
iii. Interferents and cross reacting substances/agents, which vary greatly depending on the assay type and design, could derive from exogenous or endogenous sources such as:
iv. Substances used for patient treatment (e.g. therapeutic drugs, alcohol, vitamins, foods, etc.), substances added during sample preparation (e.g. preservatives, stabilizers), substances encountered in specific specimen types (e.g. haemoglobin, lipids, bilirubin, proteins), and; analytes of similar structure (e.g. precursors, metabolites) or medical conditions unrelated to the test condition including specimens negative for the assay but positive for a condition that may mimic the test condition (e.g. for a hepatitis A assay: test specimens negative for hepatitis A virus, but positive for hepatitis B virus)

e) Metrological traceability of calibrator and control material values

Where applicable, summarize the information about metrological traceability of values assigned to calibrators and trueness control materials. Include, for reference materials and/or reference measurement procedures and a description of value assignment and validation.

Measuring range of the assay

Provide a summary of studies which define the measuring range (linear and non-linear measuring systems) including the limit of detection and describe information on how these were established. The summary should include a description of specimen type, number of samples, number of replicates, and preparation including information on matrix, analyte (measurand) levels and how levels were established. If applicable, add a description of high dose hook effect and the data supporting the mitigation (e.g. dilution) steps.

Validation of assay cut-off

Provide a summary of analytical data with a description of the study design including methods for determining the assay cut-off, including: the population (s) studied, method or mode of characterization of specimens and statistical methods e.g. Receiver Operator Characteristic (ROC) to generate results and if applicable, define gray-zone/equivocal zone.

4.7 Stability (excluding specimen stability)

Describe claimed shelf life, in use stability and shipping studies.

a) Claimed shelf life

Provide information on stability testing studies, to support the claimed shelf life, performed on at least three different lots manufactured under conditions that are essentially equivalent to routine production conditions (these lots do not need to be consecutive lots). The summary should include:

i. The study report (i.e. protocol, number of lots, acceptance criteria and testing intervals),
ii. When accelerated studies have been performed in anticipation of the real time studies, the method used for accelerated studies;
iii. Conclusion and claimed shelf life.

Note: Shelf life can be derived from the lot with the longest real time stability data as long as accelerated or extrapolated data from all three lots are comparable.

b) In use stability

Provide information on in use stability studies for one lot reflecting actual routine use of the device (real or simulated). This may include open vial stability and/or, for automated instruments, on board stability.

In case of automated instrumentation if calibration stability is claimed, supporting data should be included sufficient to describe: the study protocol (i.e. protocol, acceptance criteria and testing intervals), conclusions and claimed in use stability.

c) Shipping stability

Provide information on shipping stability studies for one lot to evaluate the tolerance of products to the anticipated shipping conditions, describing the study report (i.e. protocol, acceptance criteria), method used for simulated conditions, conclusion and recommended shipping conditions.

Shipping studies can be done under real and/or simulated conditions and should include variable shipping conditions such as extreme heat and/or cold.

4.8 Software Verification and Validation (if applicable)

Provide information on the software design and development process and evidence of the validation of the software, as used in the finished device. This information should typically

include the summary results of all verification, validation protocol and report and testing performed both in-house and in a simulated or actual user environment prior to final release. It should also address all of the different hardware configurations and, where applicable, operating systems identified in the labeling.

4.9 Clinical Performance

Provide evidence of assessment and analysis of data generated from the clinical use of the product sufficient enough to verify the clinical safety of the IVD device. Include claims for clinical/diagnostic sensitivity and specificity. All claims should be supported by well-designed performance evaluations which should include:

d) A detailed written plan and protocol of the evaluation study

e) Dates on which the study was performed and by which site

f) A written report on the outcome of the study; all anomalous results should be explained and justified. The report outline should contain,

   i. The technology on which the medical device is based, the intended use of the device and any claims made about the device's clinical performance or safety.
   ii. The nature and extent of the clinical data that has been evaluated; and,
   iii. How the referenced information (recognized standards and/or clinical data) demonstrate the clinical performance and safety of the device in question.

g) Details of the IVD device lots/batches used for the evaluation including lot number date of expiry, and the storage conditions of the product prior to and during study.

h) The clinical evaluation report should be signed and dated by evaluator(s) and accompanied by manufacturer's justification of the choice of evaluator.

i) The clinical evaluation report should be summarized as per required information elaborated above.

5. LABELLING REQUIREMENTS

Labeling information shall be in English and/or Kiswahili and shall be expressed in a legible, indelible, permanent and prominent manner that can be easily understood by the intended user.

Provide a complete set of labeling information associated with the IVD medical device including immediate and outer container labels on the IVD medical device and instructions for use.
The labeling should contain the final content as determined by the manufacturer.

Depending on the type of device, the following minimum information should be provided on the label:

a) the name of the IVD medical device. If the name does not uniquely identify the IVD medical device, an additional means of identification shall also be provided. Examples: Catalogue number and commodity number.

b) manufacturing site name and physical address.

c) the identifier of the device, including the identifier of a device that is part of a system, test kit, or IVD medical device class.

d) batch or lot number.

e) if the contents are not readily apparent, an indication of what the package contains, expressed in terms appropriate to the device, such as size, net weight, length, volume or number of units, volume after reconstitution shall be indicated.

f) the words "Sterile" if the manufacturer intends to sell the IVD medical device in a sterile condition.

g) the word "For Single Use Only" shall be included if the IVD medical device is intended for single use.

h) in vitro diagnostics use: The In vitro diagnostics use of the device shall be indicated e.g. "For In vitro diagnostics use" or graphical symbol: "In vitro diagnostic medical device".

i) the Expiry date: An expiry date based upon the storage instructions shall be indicated and shall follow the requirements of ISO 8601. Expiry dates shall be expressed as the year, the month and where relevant, the day. E.g. "YYYY-MM-DD" or "YYYY-MM".

j) unless self-evident to the intended user, the medical conditions, purposes and uses for which the device is manufactured, sold or represented, including the performance specifications of the device if those specifications are necessary for proper use.

k) the directions for use, unless directions are not required for the device to be used safely and effectively.

l) warning and precautions: If an IVD device is considered hazardous, the outer container label shall include the appropriate danger wording or symbol(s) e.g. chemical, radioactive and biological hazards.

m) storage and handling conditions: The storage conditions necessary to maintain the stability of the reagents, calibrators, control materials in the unopened state and other IVDs shall be indicated. If there are any other conditions that may affect the handling or storage of the reagents, calibrators, control materials and other IVDs shall be specified e.g. Fragile.

n) intended use: If the intended use is not indicated by the name of the IVD medical device, then an abbreviated intended use statement shall be given or included in the instruction for use e.g. For measurement of plasma glucose concentration.

In case the device is intended to be sold to the general public, labeling information:

a) Shall be set out on the outside of the package that contains the device; and be visible under normal conditions of sale.

b) where a package that contains a device is too small to display all the information in

accordance with (a-k) above, the directions for use shall accompany the device but need not be set out on the outside of the package or be visible under normal conditions of sale.

c) Specimen label(s), promotional material(s) and user manual(s) should be provided.

Note:
Requirements that have been described in a respective standard should also be followed when labeling a device.

ANNEX 1: APPLICATION FORM FOR REGISTRATION OF IN VITRO DIAGNOSTIC DEVICES

APPLICATION FORM FOR REGISTRATION OF IN VITRO DIAGNOSTIC DEVICES

Under Section No.53 (1) of the Zanzibar Food, Drug and Cosmetic Act, 2/2006

Please read this section carefully before completing the form

1. Please check the corresponding boxes in the "Encl." column if any document is enclosed and indicate the respective indexes in the submission folder
2. Please check the boxes as appropriate

Note	Part A: Particulars of Applicant		Encl.
A1	Applicant's name		
	Address of Head Office		
	Post Code:	Country:	
	Contact Person:	Telephone:	
	Fax:	E-mail:	
	Website:		
	Part B: Particulars of Manufacturer		
B1	Manufacturer's name		
	Address of Head Office		
	Physical address of the site		
	Post Code:	Country:	
	Contact Person:	Telephone:	
	Fax:	E-mail:	
	Website		
	Quality Management System Established by the Manufacturer		

B2	Mention current Standards with which the system complies: ☐ _____ ☐ _____ ☐ _____ ☐ System certified by _____ and a certified copy of the certificate is enclosed. Indicate areas covered by Quality Management System ☐ Device design, ☐ Production ☐ Post-production processes ☐ Others (***please specify***) _____		☐
C1	**Part C: Particulars of Local Responsible Person (LRP)**		
	LRP's name		☐
	Address of the registered business premise		
	Contact person:	Telephone:	
	Fax:	E-mail:	
	Contact telephone for public enquiries **(*if different from the number given above*):**		
C2	☐ Certified copy of business registration certificate with business registration number: _____ is enclosed		
C3	☐ Certified copy of Power of attorney or formal agreement or any other official authorization of the LRP is enclosed		
C4	☐ The LRP is also an importer of the device named in Part D		
	Part D: Particulars of the Device		
D1	Generic name of the Device		
D2	Brand name of the Device		
D3	Model /Series/System (***if applicable***)		
D4	Family (***if applicable***)		

D5	Country of origin		
D6	Select GMDN (Global Medical Device Nomenclature) Categories: 01 - Active implantable device 02 - Anaesthetic and respiratory devices 03 - Dental devices 04 - Electro mechanical devices 05 - Hospital hardware 06 - In vitro diagnostic devices 07 - Non-active implantable devices 08 - Ophthalmic and optical devices 09 - Reusable instruments 10 - Single use devices 11 - Technical aids for disabled persons 12 - Diagnostic and therapeutic radiation devices 13 - Complimentary therapy devices 14 - Biologically -derived devices 15 - Healthcare facility products and adaptations 16 - Laboratory equipment 17 - Others _____		
D7	Description of the device ***(Please enter appropriate GMDN description. If none of the descriptions in GMDN appear appropriate, enter a short description of the device)*** _____ _____		
D8	GMDN Code: _____ ***(Please enter if known)***		
D9	Other common descriptions of the device: _____ _____ _____		
D10	Intended use of device		
D11	Class of the medical device: ☐ Class A ☐ Class B ☐ Class C ☐ Class D Reasons for classifying the device as Class A, B, C or D device: _____ _____		
	<u>History</u>		

D12	☐ No previous recalls, reportable adverse incidents, banning in other countries or post-market surveillance studies ☐ Yes ***(Please tick the appropriate boxes and provide details):*** ☐ Recalls completed or in progress ☐ Any reportable adverse incidents bearing implications to the device ☐ The device banned previously in other countries ☐ Pro-active post-market surveillance studies	
D13	Performance and Safety International or national standards with which the device complies _____ _____ (Please enclose copy of the standard)	☐
	Part E: Marketing Approvals in Foreign countries	
E1	Mention the countries where the device has obtained marketing approvals _____ _____ (Please enclose certified copy of valid marketing authorization)	☐
E2	Mention the countries where the device approval is still pending _____ _____	☐
	Part F: Declaration of conformity (DoC)	
F1	Submit a written declaration of conformity. The DoC should contain the following:- a) An attestation that a device complies with the applicable EPSP, has been classified accordingly and has met applicable conformity assessment elements. b) Information sufficient to identify the device including its nomenclature. c) The risk class allocated to the device. d) Which of the conformity assessment elements have been applied. e) The date from which the DoC is valid. f) The name and address of the device manufacturer. g) The name, position and signature of the responsible person who has been authorized to complete the DoC.	☐

Declaration by applicant
I, the undersigned certify that all the information in this form and accompanying documentation is correct and true to the best of my knowledge.

Name: _____
Position: _____
Signature: _____
Official stamp:
Date: _____

ANNEX 2: CLASSIFICATION RULES FOR IN VITRO DIAGNOSTIC DEVICES

CLASSIFICATION RULES FOR *IN VITRO* DIAGNOSTIC DEVICES

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: 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. 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)] 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.

Examples:

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

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. Examples: 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. Examples: *Neisseria meningitis* 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. Examples: 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. Examples: 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. Examples: Enteroviruses, CMV and HSV in transplant patients.
- in screening for selection of patients for selective therapy and management, or for or for disease staging, or in the diagnosis of cancer. Example: personalized medicine.
  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.
- in human genetic testing. Examples: 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. 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 sub-typing.
- In screening for congenital disorders in the fetus. Examples: 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: 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.

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 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-strips.

Rule 5

The following IVD medical devices are classified as Class A:

- Reagents or other articles that possess specific 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: 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.

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.

Note 1: In certain jurisdictions there may be differences as to whether a device classified in this rule is considered an IVD medical device.

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 test kit.

Note 3: The interdependence of the instrument and the test methodology prevents the instrument from being assessed separately, even though the instrument itself is still classified as Class A.

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 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.

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 qualitative or quantitative value is assigned by the user and not the manufacturer.

ESSENTIAL REQUIREMENTS CHECK LIST

ESSENTIAL REQUIREMENTS CHECK LIST		
Brand name : _____	**Generic name: _____**	**RISK CLASS: _____**

Clause	Essential Principal	Applicable to the device?	Method of Conformity	Identity of specific Documents
1.	**GENERAL REQUIREMENTS** Medical devices should be designed and manufactured in such a way that, when used under the conditions and for the purposes intended and, where applicable, by virtue of the technical knowledge, experience, education or training, and the medical and physical conditions of intended users, they will perform as intended by the manufacturer and not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons, provided that any risks which may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.			
2.	The solutions adopted by the manufacturer for the design and manufacture of the devices should conform to safety principles, taking account of the generally acknowledged state of the art. When risk reduction is required, the manufacturer should control the risk(s) so that the residual risk(s) associated with each hazard is judged acceptable. The manufacturer should apply the following principles in the priority order listed: • identify known or foreseeable hazards and estimate the associated risks arising from the intended use and foreseeable misuse; • eliminate risks as far as reasonably practicable through inherently safe design and manufacture; • reduce as far as is reasonably practicable the remaining risks by taking adequate protection measures, including alarms; and • inform users of any residual risks.			
3.	Medical devices should achieve the performance intended by the manufacturer and be designed and manufactured in such a way that they are suitable for their intended purpose.			
4.	The characteristics and performances referred to in Clauses 1, 2 and 3 should not be adversely affected to such a degree that the health or safety of the patient or the user and, where applicable, of other persons are compromised during the lifetime of the device, as indicated by the manufacturer, when the device is subjected to the			

	stresses which can occur during normal conditions of use and has been properly maintained in accordance with the manufacturer's instructions.			
5.	Medical devices should be designed, manufactured and packaged in such a way that their characteristics and performances during their intended use will not be adversely affected by transport and storage conditions (for example, fluctuations of temperature and humidity) taking account of the instructions and information provided by the manufacturer.			
6.	Medical devices should achieve their intended performance during normal conditions of use. All known, and foreseeable risks, and any undesirable effects, should be minimized and be acceptable when weighed against the benefits of the intended performance.			
7. 7.1	**ESSENTIAL PRINCIPLES APPLICABLE TO MEDICAL DEVICES OTHER THAN IVD MEDICAL DEVICES** **<u>DESIGN AND MANUFACTURING REQUIREMENTS</u>** <u>Chemical, physical & biological properties</u> The devices should be designed and manufactured in such a way as to ensure the characteristics and performance referred to in clause 6. Particular attention should be paid to: the choice of materials used, particularly as regards toxicity and, where appropriate, flammability, the compatibility between the materials used and biological tissues, cells, and body fluids taking account of the intended purpose of the device. the choice of materials used should reflect, where appropriate, matters such as hardness, wear and fatigue strength.;			
7.2	The devices should be designed, manufactured and packaged in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to patients, taking account of the intended purpose of the product. Particular attention should be paid to tissues exposed and to the duration and frequency of exposure.			
7.3	The devices should be designed and manufactured in such a way that they can be used safely with the materials, substances and gases with which they enter into contact during their normal use or during routine procedures; if the devices are intended to administer medicinal products they should be designed and manufactured in such a way as to be compatible with the medicinal products concerned according to the provisions and restrictions governing these products and that their			

	performance is maintained in accordance with the intended use.			
7.4	The devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate the risks posed by substances that may leach or leak from the device. Special attention shall be given to substances which are carcinogenic, mutagenic or toxic to reproduction.			
7.5	Devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate risks posed by the unintentional ingress or egress of substances into or from the device taking into account the device and the nature of the environment in which it is intended to be used.			
8. 8.1	**<u>Infection & microbial contamination</u>** The devices and manufacturing processes should be designed in such a way as to eliminate or to reduce as far as reasonably practicable and appropriate the risk of infection to patients, users and, where applicable, other persons. The design should: • allow easy handling, and, where necessary: • reduce as far as reasonably practicable and appropriate any microbial leakage from the device and/or microbial exposure during use, • prevent microbial contamination of the device or specimen, where applicable, by the patient, user or other person.			
8.2	Devices labelled as having a special microbiological state should be designed, manufactured and packaged to ensure they remain so when placed on the market and remain so under the transport and storage conditions specified by the manufacturer.			
8.3	Devices delivered in a sterile state should be designed, manufactured and packaged in a non-reusable pack, and/or according to appropriate procedures, to ensure that they are sterile when placed on the market and remain sterile, under the transport and storage conditions indicated by the manufacturer, until the protective packaging is damaged or opened.			
8.4	Devices labelled either as sterile or as having a special microbiological state should have been processed, manufactured and, if applicable, sterilized by appropriate, validated methods.			
8.5	Devices intended to be sterilized should be manufactured in			

	appropriately controlled (e.g. environmental) conditions.			
8.6	Packaging systems for non-sterile devices should maintain the integrity and cleanliness of the product and, if the devices are to be sterilized prior to use, minimize the risk of microbial contamination; the packaging system should be suitable taking account of the method of sterilization indicated by the manufacturer.			
8.7	The labelling of the device should distinguish between identical or similar products placed on the market in both sterile and non-sterile condition.			
9. 9.1	**B5.1 <u>Medical devices incorporating a substance considered to be a medicinal product/drug</u>** Where a device incorporates, as an integral part, a substance which, if used separately, may be considered to be a medicinal product/drug as defined in the relevant legislation that applies within that jurisdiction and which is liable to act upon the body with action ancillary to that of the device, the safety, quality and performance of the device as a whole should be verified, as well as the safety, quality and efficacy of the substance in the specific application,			
10. 10.1	**<u>Medical devices incorporating materials of biological origin</u>** In some jurisdictions products incorporating tissues, cells and substances of animal origin may be considered medical devices. In this case, such tissues, cells and substances should originate from animals that have been subjected to veterinary controls and surveillance adapted to the intended use of the tissues. National regulations may require that the manufacturer and/or the Regulatory Authority retain information on the geographical origin of the animals. Processing, preservation, testing and handling of tissues, cells and substances of animal origin should be carried out so as to provide optimal safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.			
10.2	In some jurisdictions products incorporating human tissues, cells and substances may be considered medical devices. In this case, the selection of sources, donors and/or substances of human origin, the processing, preservation, testing and handling of tissues, cells and substances of such origin should be carried out so as to provide optimal safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents should be addressed by implementation of			

	validated methods of elimination or inactivation in the course of the manufacturing process.			
10.3	In some jurisdictions products incorporating cells and substances of microbial origin may be considered medical devices. In this case, processing, preservation, testing and handling of cells and substances should be carried out so as to provide optimal safety for patients, users and, where applicable, other persons. In particular, safety with regard to viruses and other transmissible agents should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process.			
11. 11.1	**<u>Manufacturing and environmental properties</u>** If the device is intended for use in combination with other devices or equipment, the whole combination, including the connection system should be safe and should not impair the specified performance of the devices. Any restrictions on use applying to such combinations should be indicated on the labelling and/or in the instructions for use. Connections which the user has to handle, such as fluid, gas transfer or mechanical coupling, should be designed and constructed in such a way as to minimize all possible risks from incorrect connection.			
11.2	Devices should be designed and manufactured in such a way as to remove or reduce as far as reasonably practicable and appropriate: • the risk of injury to the patient, user or other persons in connection with their physical and ergonomic features, • the risk of use error due to the ergonomic features, human factors and the environment in which the device is intended to be used; • risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, radiation associated with diagnostic or therapeutic procedures, pressure, humidity, temperature or variations in pressure and acceleration; • the risks associated with the use of the device when it comes into contact with materials, liquids, and gases to which it is exposed during normal conditions of use; • the risk associated with the possible negative interaction between software and the environment within which it operates and interacts; • the risks of accidental penetration of substances into the device; • the risk of incorrect identification of specimens; • the risks of reciprocal interference with other devices normally used in the investigations or for the treatment given; • risks arising where maintenance or calibration are not possible (as with implants), from ageing of materials used or loss of accuracy of any measuring or control mechanism.			

11.3	Devices should be designed and manufactured in such a way as to minimize the risks of fire or explosion during normal use and in single fault condition. Particular attention should be paid to devices whose intended use includes exposure to or use in association with flammable substances or substances which could cause combustion.			
11.4	Devices must be designed and manufactured in such a way as to facilitate the safe disposal of any waste substances.			
12. 12.1	**<u>Devices with a diagnostic or measuring function.</u>** Devices with a measuring function, should be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended purpose of the device, based on appropriate scientific and technical methods. The limits of accuracy should be indicated by the manufacturer.			
12.2	Diagnostic devices should be designed and manufactured in such a way as to provide sufficient accuracy, precision and stability for their intended use, based on appropriate scientific and technical methods.			
12.3	Any measurement, monitoring or display scale should be designed in line with ergonomic principles, taking account of the intended purpose of the device.			
12.4	Wherever possible values expressed numerically should be in commonly accepted, standardized units, and understood by the users of the device.			
13. 13.1 13.1.1	**<u>Protection against radiation</u>** General Devices should be designed and manufactured and packaged in such a way that exposure of patients, users and other persons to any emitted radiation should be reduced as far as practicable and appropriate, compatible with the intended purpose, whilst not restricting the application of appropriate specified levels for therapeutic and diagnostic purposes.			
13.2 13.2.1	**<u>Intended radiation</u>** Where devices are designed to emit hazardous, or potentially hazardous, levels of visible and/or invisible radiation necessary for a specific medical purpose the benefit of which is considered to outweigh			

	the risks inherent in the emission, it should be possible for the user to control the emissions. Such devices should be designed and manufactured to ensure reproducibility of relevant variable parameters within an acceptable tolerance.			
13.2.2	Where devices are intended to emit potentially hazardous, visible and/or invisible radiation, they should be fitted, where practicable, with visual displays and/or audible warnings of such emissions.			
13.3 13.3.1	**<u>Unintended radiation</u>** Devices should be designed and manufactured in such a way that exposure of patients, users and other persons to the emission of unintended, stray or scattered radiation is reduced as far as practicable and appropriate.			
13.4 13.4.1	**<u>Instructions</u>** The operating instructions for devices emitting radiation must give detailed information as to the nature of the emitted radiation, means of protecting the patient and the user and on ways of avoiding misuse & of eliminating the risks inherent in installation.			
13.5 13.5.1	**<u>Ionising radiation</u>** Devices intended to emit ionizing radiation should be designed and manufactured in such a way as to ensure that, where practicable, the quantity, geometry and energy distribution (or quality) of radiation emitted can be varied and controlled taking into account the intended use.			
13.5.2	Devices emitting ionizing radiation intended for diagnostic radiology should be designed and manufactured in such a way as to achieve appropriate image and/or output quality for the intended medical purpose whilst minimizing radiation exposure of the patient and user. .			
13.5.3	Devices emitting ionizing radiation, intended for therapeutic radiology should be designed and manufactured in such a way as to enable reliable monitoring and control of the delivered dose, the beam type and energy and where appropriate the energy distribution of the radiation beam.			
14. 14.1	**B5.2 <u>Medical devices that incorporate software and standalone medical device software</u>** Devices incorporating electronic programmable systems, including software, or standalone software that are devices in themselves, should be designed to ensure repeatability, reliability and performance			

	according to the intended use. In the event of a single fault condition, appropriate means should be adopted to eliminate or reduce as far as practicable and appropriate consequent risks.			
14.2	For devices which incorporate software or for standalone software that are devices in themselves, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, validation and verification.			
15.	**B5.3 Active medical devices and devices connected to them**			
15.1	For active medical devices, in the event of a single fault condition, appropriate means should be adopted to eliminate or reduce as far as practicable and appropriate consequent risks.			
15.2	Devices where the safety of the patients depends on an internal power supply should be equipped with a means of determining the state of the power supply.			
15.3	Devices where the safety of the patients depends on an external power supply should include an alarm system to signal any power failure.			
15.4	Devices intended to monitor one or more clinical parameters of a patient should be equipped with appropriate alarm systems to alert the user of situations which could lead to death or severe deterioration of the patient's state of health			
15.5	Devices should be designed and manufactured in such a way as to reduce as far as practicable and appropriate the risks of creating electromagnetic interference which could impair the operation of this or other devices or equipment in the usual environment.			
15.6	Devices should be designed and manufactured in such a way as to provide an adequate level of intrinsic immunity to electromagnetic disturbance to enable them to operate as intended.			
15.7	Devices should be designed and manufactured in such a way as to avoid, as far as reasonably practicable, the risk of accidental electric shocks to the patient, user or any other person, both during normal use of the device and in the event of a single fault condition in the device, provided the device is installed and maintained as indicated by the manufacturer			
16.0 16.1	**B5.4 Protection against mechanical risks** Devices should be designed and manufactured in such a way as to protect the patient and user against mechanical risks connected with,			

	for example, resistance to movement, instability and moving parts.			
16.2	Devices should be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.			
16.3	Devices should be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source, unless the noise emitted is part of the specified performance			
16.4	Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user has to handle should be designed and constructed in such a way as to minimize all possible risks.			
16.5	Accessible parts of the devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings should not attain potentially dangerous temperatures under normal use.			
17.0 17.1	**B5.5 Protection against the risks posed to the patient or user by supplied energy or substances** Devices for supplying the patient with energy or substances should be designed and constructed in such a way that the delivered amount can be set and maintained accurately enough to guarantee the safety of the patient and of the user			
17.2	Devices should be fitted with the means of preventing and/or indicating any inadequacies in the delivered amount which could pose a danger. Devices should incorporate suitable means to prevent, as far as possible, the accidental release of dangerous levels of energy or substances from an energy and/or substance source.			
17.3	The function of the controls and indicators should be clearly specified on the devices. Where a device bears instructions required for its operation or indicates operating or adjustment parameters by means of a visual system, such information should be understandable to the user and, as appropriate, the patient.			
18.0 18.1	**B5.6 Protection against the risks posed by medical devices intended by the manufacturer for use by lay persons** Devices for use by lay persons should be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to lay persons and the influence resulting from variation that can reasonably be anticipated in the lay person's technique and environment. The information and instructions provided by the manufacturer should be			

	easy for the lay person to understand and apply.			
18.2	Devices for use by lay persons should be designed and manufactured in such a way as to reduce as far as practicable the risk of error during use by the lay person in the handling of the device and also in the interpretation of results.			
18.3	Devices for use by lay persons should, where reasonably possible, include a procedure by which the lay person can verify that, at the time of use, the product will perform as intended by the manufacturer.			
19.0 19.1	**B5.7 Label and Instructions for Use** Users should be provided with the information needed to identify the manufacturer, to use the device safely and to ensure the intended performance, taking account of their training and knowledge. This information should be easily understood			
20.0 20.1	**Clinical evaluation** For all medical devices, the demonstration of conformity with essential principles includes a clinical evaluation in accordance with GHTF guidance. The clinical evaluation should review clinical data in the form of any: • clinical investigation reports, • literature reports/reviews, and • clinical experience to establish that a favourable benefit-risk ratio exists for the device. **Note:** Further information is provided in GHTF/SG5/N2R8:2007 *Clinical Evaluation.*			
20.2	Clinical investigations[1] on human subjects should be carried out in accordance with the spirit of the Helsinki Declaration. This includes every step in the clinical investigation from first consideration of the need and justification of the study to publication of the results. In addition, some countries may have specific regulatory requirements for pre-study protocol review or informed consent.			
  21.0 21.1	Essential Principles applicable to IVD Medical Devices **Chemical, physical and biological properties** The IVD medical devices should be designed and manufactured in such a way as to ensure the characteristics and performance referred to in Section 6. Particular attention should be paid to the possibility			

[1] See GHTF/SG5/N3:2010 *Clinical Investigations*

	of impairment of analytical performance due to incompatibility between the materials used and the specimens and/or analyte (measurand) to be detected (such as biological tissues, cells, body fluids and micro-organisms) intended to be used with the device, taking account of its intended purpose.			
21.2	The IVD medical devices should be designed, manufactured and packaged in such a way as to minimize the risk posed by contaminants and residues to the persons involved in the transport, storage and use of the devices and to patients, taking account of the intended purpose of the product.			
21.3	The IVD medical devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate the risks posed by substances that may leach or leak from the IVD medical device. Special attention should be given to substances which are carcinogenic, mutagenic or toxic to reproduction.			
21.4	IVD medical devices should be designed and manufactured in such a way as to reduce as far as reasonably practicable and appropriate risks posed by the unintentional ingress or egress of substances into or from the IVD medical device taking into account the device and the nature of the environment in which it is intended to be used.			
22.0 22.1	**Infection and microbial contamination** The IVD medical devices and manufacturing processes should be designed in such a way as to eliminate or to reduce as far as reasonably practicable and appropriate the risk of infection to user, professional or lay, or, where applicable, other person. The design should: • allow easy and safe handling; and, where necessary: • reduce as far as reasonably practicable and appropriate any microbial leakage from the IVD medical device and/or microbial exposure during use; and prevent microbial contamination of the IVD medical device or specimen where applicable, by the user, professional or lay, or other person.			
22.2	IVD medical devices labeled either as sterile or as having a special microbiological state should be designed, manufactured and packaged to ensure they remain so when placed on the market and remain so under the transport and storage conditions specified by the manufacturer, until the protective packaging is damaged or opened.			
22.3	IVD medical devices labeled either as sterile or as having a special microbiological state should have been processed, manufactured and, if applicable, sterilized by appropriate, validated methods.			
22.4	IVD medical devices intended to be sterilized should be manufactured in appropriately controlled (e.g. environmental) conditions.			
22.5	Packaging systems for non-sterile IVD medical devices should maintain the integrity and cleanliness of the product.			

23.0 23.1	**<u>IVD medical devices incorporating materials of biological origin</u>** Where IVD medical devices include tissues, cells and substances originating from animals, processing, preservation, testing and handling of tissues, cells and substances of animal origin should be carried out so as to provide optimal safety for user, professional or lay, or other person. In particular safety with regard to viruses and other transmissible agents should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process. This may not apply to certain IVD medical devices if the activity of the virus and other transmissible agent are integral to the intended purpose of the IVD medical device or when such elimination or inactivation process would compromise the performance of the IVD medical device. National regulations may require that the manufacturer and/or the Regulatory Authority retain information on the geographical origin of the animals.			
23.2	Where IVD medical devices include human tissues, cells and substances, the selection of sources, donors and/or substances of human origin, the processing, preservation, testing and handling of tissues, cells and substances of such origin should be carried out so as to provide optimal safety for user, professional or lay, or other person. In particular safety with regard to viruses and other transmissible agents should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process. This may not apply to certain IVD medical devices if the activity of the virus and other transmissible agent are integral to the intended purpose of the IVD medical device or when such elimination or inactivation process would compromise the performance of the IVD medical device.			
23.3	Where IVD medical devices include cells and substances of microbial origin, processing, preservation, testing and handling of cells and substances should be carried out so as to provide optimal safety for user, professional or lay, or other person. In particular, safety with regard to viruses and other transmissible agents should be addressed by implementation of validated methods of elimination or inactivation in the course of the manufacturing process. This may not apply to certain IVD medical devices if the activity of the virus and other transmissible agent are integral to the intended purpose of the IVD medical device or when such elimination or inactivation process would compromise the performance of the IVD medical device.			
24.0 24.1	**<u>Manufacturing and environmental properties</u>** If the IVD medical device is intended for use in combination with other devices or equipment, the whole combination,			

	including the connection system should not impair the specified performance of the devices. Any restrictions on use applying to such combinations should be indicated on the label and/or in the instructions for use.			
24.2	IVD medical devices should be designed and manufactured in such a way as to remove or reduce as far as reasonably practicable and appropriate: • the risk of injury to user, professional or lay, or other person in connection with their physical and ergonomic features, • the risk of use error due to the ergonomic features, human factors and the environment in which the IVD medical device is intended to be used; • risks connected with reasonably foreseeable external influences or environmental conditions, such as magnetic fields, external electrical and electromagnetic effects, electrostatic discharge, pressure, humidity, temperature or variations thereof; • the risks associated with the use of the IVD medical device when it comes into contact with materials, liquids, and gases to which it is exposed during normal conditions of use; • the risk associated with the possible negative interaction between software and the environment within which it operates and interacts; • the risks of accidental penetration of substances into the IVD medical device; • the risk of incorrect identification of specimens; and the risks of reasonably foreseeable interference with other devices such as carry over between IVD medical devices			
24.3	IVD medical devices should be designed and manufactured in such a way as to minimize the risks of fire or explosion during normal use and in single fault condition. Particular attention should be paid to IVD medical devices whose intended use includes exposure to or use in association with flammable substances or substances which could cause combustion.			
24.4	IVD medical devices must be designed and manufactured in such a way as to facilitate the safe disposal of any waste substances.			
25.0 25.1	**Performance characteristics** IVD medical devices should be designed and manufactured in such a way that the performance characteristics support the intended use, based on appropriate scientific and technical methods. In particular, where appropriate, the design should address sensitivity, specificity,			

	accuracy which is trueness and precision (repeatability and reproducibility), control of known relevant interference and limits of detection. These performance characteristics need to be maintained during the lifetime of the IVD medical device as indicated by the manufacturer.			
25.2	Where the performance of devices depends on the use of calibrators and/or control materials, the traceability of values assigned to such calibrators and/or control materials should be assured through available reference measurement procedures and/or available reference materials of a higher order.			
25.3	Wherever possible values expressed numerically should be in commonly accepted, standardized units, and understood by the users of the device. **Note:** While SG1 generally supports convergence on the global use of internationally standardized measurement units, considerations of safety, user familiarity, and established clinical practice may justify the use of other recognized measurement units.			
26.0 26.1	**Protection against radiation** IVD medical devices should be designed, manufactured and packaged in such a way that exposure of user, professional or lay, or other person to the emitted radiation (intended, unintended, stray or scattered) is reduced as far as practicable and appropriate			
26.2	When IVD medical devices are intended to emit potentially hazardous, visible and/or invisible radiation, they should as far as practicable and appropriate be: designed and manufactured in such a way as to ensure that the characteristics and the quantity of radiation emitted can be controlled and/or adjusted; and fitted with visual displays and/or audible warnings of such emissions			
27.0 27.1	**IVD medical devices that incorporate software and standalone IVD medical device software** For IVD medical devices which incorporate software or for standalone software that are IVD medical devices in themselves, the software must be validated according to the state of the art taking into account the principles of development lifecycle, risk management, verification and validation.			
28.0 28.1	**IVD medical devices connected to, or equipped with, an energy source** IVD medical devices where the safety of the patient depends on an internal power supply in the IVD medical device, should be equipped with a means of determining the state of the power supply.			
28.2	IVD medical devices should be designed and manufactured in such a way as to reduce as far as practicable and appropriate the risks of			

	creating electromagnetic interference which could impair the operation of this or other devices or equipment in the usual environment.			
28.3	IVD medical devices should be designed and manufactured in such a way as to provide an adequate level of intrinsic immunity to electromagnetic disturbance to enable them to operate as intended.			
28.4	IVD medical devices should be designed and manufactured in such a way as to avoid, as far as reasonably practicable, the risk of accidental electric shocks to the user, professional or lay, or other person both during normal use of the device and in the event of a single fault condition in the device, provided the IVD medical device is installed and maintained as indicated by the manufacturer.			
29.0 29.1	**Protection against mechanical and thermal risks** IVD medical devices should be designed and manufactured in such a way as to protect the user, professional or lay, or other person against mechanical risks connected with, for example, resistance to movement, instability and moving parts. Where there are risks due to the presence of moving parts, risks due to break-up or detachment, or leakage of substances, then appropriate protection means must be incorporated.			
29.2	IVD medical devices should be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from vibration generated by the devices, taking account of technical progress and of the means available for limiting vibrations, particularly at source, unless the vibrations are part of the specified performance.			
29.3	IVD medical devices should be designed and manufactured in such a way as to reduce to the lowest practicable level the risks arising from the noise emitted, taking account of technical progress and of the means available to reduce noise, particularly at source.			
29.4	Terminals and connectors to the electricity, gas or hydraulic and pneumatic energy supplies which the user, professional or lay, or other person has to handle should be designed and constructed in such a way as to minimize all possible risks.			
29.5	Accessible parts of the IVD medical devices (excluding the parts or areas intended to supply heat or reach given temperatures) and their surroundings should not attain potentially dangerous temperatures under normal use.			
30.0 30.1	**Protection against the risks posed by IVD medical devices intended by the manufacturer for self-testing** IVD medical devices intended for self-testing should be designed and manufactured in such a way that they perform appropriately for their intended purpose taking into account the skills and the means available to lay persons and the influence resulting from variation that can reasonably be anticipated in the lay person's technique and			

	environment. The information and instructions provided by the manufacturer should be easy for the lay person to understand and apply.			
30.2	IVD medical devices intended for self-testing should be designed and manufactured in such a way as to reduce as far as practicable the risk of error by the lay person in the handling of the device and, if applicable, the specimen, and also in the interpretation of results.			
30.3	IVD medical devices intended for self-testing should, where reasonably possible, include a procedure by which the lay person can verify that, at the time of use, the product will perform as intended by the manufacturer.			
31.0 31.1	**Label and Instructions for Use** Users should be provided with the information needed to identify the manufacturer, to use the device safely and to ensure the intended performance, taking account of their training and knowledge. This information should be easily understood. **Note:** Further information is provided in GHTF/SG1/N43:2005 *Labelling for Medical Devices*			
32.0 32.1	**Performance evaluation including analytical performance and, where appropriate, clinical performance** For an IVD medical device a performance evaluation should be conducted in accordance with GHTF guidance. The performance evaluation should review analytical performance data and, where appropriate, clinical performance data in the form of any: • literature; • performance study reports; and • experience gained by routine diagnostic testing. to establish that the IVD medical device achieves its intended performance during normal conditions of use and that the known, and foreseeable risks, and any undesirable effects, are minimized and acceptable when weighed against the benefits of the intended performance. The depth and extent of a performance evaluation should be appropriate to the nature, intended use and risks of the IVD medical device, and in accordance with GHTF guidance. **Note:** Further information is provided in GHTF/SG1/N46:2008 *Principles of Conformity Assessment for IVD Medical Devices*.			
32.2	Clinical performance studies using specimens from human subjects should be carried out in accordance with the spirit of the Declaration of Helsinki. This includes every step in the clinical performance study from first consideration of the need and justification of the study to publication of the results.			

I declare that the information provided in this form is accurate and correct and the device conforms to all applicable requirements stipulated above.

Name: ____

Signature: ____

Position: ____

Date: ____