ZAMBIA MEDICINES REGULATORY AUTHORITY

GUIDELINES ON APPLICATION FOR GRANT OF MARKETING AUTHORISATION OF IN-VITRO DIAGNOSTIC DEVICES FOR HUMAN USE

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FOREWORD

The Medicines and Allied Substances Act (No. 3) of 2013 requires that Allied Substances in this case in-vitro diagnostics intended to be marketed in Zambia meet acceptable standards of quality, safety and performance and at the same time be assessed to have been manufactured in facilities which comply with current Good Manufacturing Practices (cGMP).

One of the means of ensuring that in–vitro diagnostics meet the required standards of quality, safety and performance is by conducting product specific pre-marketing assessments to determine whether or not the product meets the minimum acceptable requirements for it to be granted marketing authorisation.

These guidelines have been prepared to provide information to applicants for grant of Marketing Authorisation of in – vitro diagnostics for human use in Zambia.

This document has been developed by the Zambia Medicines Regulatory Authority to provide guidance to applicants on the content and format of the dossier in respect of products submitted for Grant of Marketing Authorisation. The guidelines also provide for the order in which documents are to be submitted and the minimum requirements for product Marketing Authorisation.

Compliance to these guidelines will facilitate the timely processing and evaluation of the applications for in – vitro diagnostics and the subsequent grant of Marketing Authorisation thereof. This will enable the prospective marketing authorisation holders to market their products on time and make them available to the consumers in Zambia.

It is therefore, my sincere hope that these guidelines will provide the necessary information in preparing and submitting documents when applying for grant of Marketing Authorisation of in - vitro diagnostics for human use in Zambia.

Dr. Kennedy Malama
PERMANENT SECRETARY (Technical Services)
Ministry of Health

ACKNOWLEDGEMENTS

I wish to take this opportunity to thank all who in one way or another assisted in drafting of these guidelines.

Special thanks are extended to the European Union and The Ministry of Health for the logistical and technical assistance provided during the entire process leading to the development and finalisation of these guidelines.

I further extend my thanks to the Consultant and Technical Working Group who worked tirelessly in the development and finalisation of these guidelines.

Special thanks are further extended to all our esteemed stakeholders: the Ministry of Health, The European Union, Zambia Bureau of Standards (ZABS), The Pharmaceutical Society of Zambia, The Biomedical Society of Zambia, The Veterinary Association of Zambia (VAZ), The Zambia Pharmaceutical Business Forum, University of Zambia School of Veterinary and Representatives from Industry who discussed the guidelines and gave commendable inputs for improving the document.

I wish to also commend the Zambia Medicines Regulatory Authority team who worked tirelessly to ensure that these guidelines were finalised, a job well done.

The development of these Guidelines is a huge milestone in the regulation of medical devices in Zambia which will surely ensure that all in – vitro diagnostics for human use being imported in the country are safe, effective and of the acceptable quality.

Bernice C Mwale (Mrs)
Director - General
Zambia Medicines Regulatory Authority

INTERPRETATION

In these guidelines, unless the context otherwise requires -

“Accessory”

Means an article which, is intended specifically by its manufacturer to:

- be used together with an IVD device to enable that device to be used in accordance with its intended use as an IVD device.
- augment or extend the capabilities of that device in fulfilment of its intended use as an IVD device.

“ Act”

Means the Medicines and Allied Substances Act (No. 3) of 2013.

“Authority”

Means the Zambia Medicines Regulatory Authority.

“Conformity assessment”

Means the systematic examination of evidence generated and procedures undertaken by the manufacturer, under requirements established by the Authority, to determine that the IVD device is safe and performs as intended by the manufacturer and conforms to the Essential Principles of Safety and Performance of IVD devices.

“Fast Track process”

Means the authorised expedited evaluation or assessment of an application submitted for the purpose of grant of Marketing Authorisation.

“Good Manufacturing Practices”(check with WHO def)

Means a system for ensuring that products are consistently produced and controlled according to quality standards.

“Harm”

Means the physical injury or damage to the health of people; or damage to property or the environment.

“Hazard”

Means a potential source of harm.

“Instructions for use”

Means information provided by the manufacturer to inform the device user of the IVD device’s intended purpose and proper use and of any precautions to be taken.

“Instrument”

Means equipment or apparatus intended by the manufacturer to be used as an IVD device.

“Intended use / purpose”

Means the objective intent of the manufacturer regarding the use of a product, process or service as reflected in the specifications, instructions and information provided by the manufacturer.

“In-vitro diagnostic device / IVD device”

Means a medical device, whether used alone or in combination with one or more accessories, 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 and includes reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles as may be determined or classified or identified as such by the Authority excluding in-vitro diagnostics for veterinary use.

“Label”

Means written, printed, or graphic information either appearing on the IVD device itself, or on the packaging of each unit, or on the packaging of multiple devices.

“Labelling”

Means the label, instructions for use, and any other information that is related to identification, technical description, intended purpose and proper use of the IVD device, but excluding shipping documents.

“Laboratory”

Means the National Drug Quality Control Laboratory; or an appropriate laboratory recognised by the Authority.

“Lay person”

Means an individual that does not have formal training in a relevant field or discipline.

“Local Responsible person”

Means a person, resident in Zambia, appointed by a foreign-based Marketing Authorisation Holder to be responsible for all regulatory matters in respect of products granted marketing authorisation with Power of Attorney.

“Manufacture”

Means all operations involved in the production, preparation, processing compounding, formulating, filling, refining, transformation, packing, packaging, repackaging and labelling of IVD devices.

“Manufacturer”

Means any person and/or institution with the responsibility to design and/or manufacture IVD devices with the intention of making the IVD device available for use, under their name.

“Marketing Authorisation”

Means the authorisation granted under section *thirty-nine* of the Medicines and Allied Substances Act (No. 3) of 2013 for the placement of a medicine or allied substance on the Zambian market.

“Measurand”

Means a quantity intended to be measured.

“Nominee”

Means a distributor, wholesaler or manufacturers’ representative.

“Notified Body”

Means a third party independent certification organisation which a competent authority designates to carry out certain tasks in respect of the conformity assessment procedures.

“Quality Management System”

Means a set of policies, processes and procedures required for planning and execution (production/development/service) in the core business area of an organization.

“Reagent”

Means a chemical, biological or immunological components, solutions or preparations intended by the manufacturer to be used as/in IVD devices.

“Recognised standards”

Means national or international standards accepted to offer conformity to specific essential principles of safety and performance.

“Risk”

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

“Shelf Life”

Means the period of time during which an IVD device, if handled and stored correctly, is expected to comply with the specification as determined by the Essential Principles of Quality, Safety and Performance.

“Single use”

Means one use of an IVD device during a single procedure after which the IVD device is disposed.

“Specimen receptacle”

Means a device, whether vacuum-type or not, specifically intended by its manufacturer for the primary containment of specimens derived from the human body.

“Technical Committee”

Means a committee appointed by the Authority comprising of experts drawn from relevant fields.

“Technical Documentation”

Means the documented evidence, normally an output of the quality management system, which demonstrates conformity of a device to the Essential Principles of Safety and Performance of Medical Devices.

“Transmissible agent”

Means an agent capable of being transmitted to a person, as a communicable, infectious or contagious disease.

“User”

Means the person(s) who uses an in-vitro-diagnostic device.

ABBREVIATIONS AND ACRONYMS

cGMP	Current Good Manufacturing Practices
GMDN	Global Medical Device Nomenclature
GMP	Good Manufacturing Practices
GHTF	Global Harmonisation Task Force
IMDRF	International Medical Devices Regulators Forum
IVD	In-Vitro Diagnostic
NDQCL	National Drug Quality Control Laboratory
QMS	Quality Management System
STED	Summary Technical Documentation
WHO	World Health Organisation
ZAMRA	Zambia Medicines Regulatory Authority

1.0 GENERAL REQUIREMENTS

An application for grant of Marketing Authorisation of In-Vitro Diagnostics (IVDs) for human use shall be made by submitting completed Form 1 and payment of the prescribed fee.

1.1 Application

The application for grant of Marketing Authorisation of In-Vitro Diagnostics for human use shall be made as set out in Form I by:

1.1.1 A manufacturer or a person who orders/procures the IVD devices for use or sale in Zambia.

1.1.2 A nominee of the applicant, who must submit a copy of the Power of Attorney.

1.1.3 An applicant who is not resident in Zambia shall nominate a Local Responsible person who must submit a copy of the Power of Attorney and shall be responsible for compliance to regulatory requirements with respect to their IVD devices.

1.1.4 Completed Application forms shall be accompanied with:

(a) A complete product dossier file, one hard copy and one soft copy for each single IVD device.

(b) Evidence of payment of the prescribed fee for marketing authorisation application.

(c) Samples of the IVD device and artworks supplied with the intended consumer packaging labelled primarily in English.*(Translations should be in English)*

(d) Checklist indicating that all sections of the application have been completed and the pages thereof.

1.2 Documentation format

1.2.1 Language

All applications and supporting documentation shall be in English.

1.2.2 Paper Type and Binding

Organising documents

Each section of the dossier is to be marked by use of clearly annotated tabs and the documentation should be filed in accessible files. Lever arch files are not acceptable. Documents can be combined in volumes as long as appropriately named tab identifiers separate them. For example, the Package insert should be separated from the other documents by a tab identifier.

Paper size

Standard A4 paper should be used for all submissions. Text and tables should be prepared using margins that allow the document to be printed on A4 paper. The left-hand margin should be sufficiently large that information is not obscured through binding. All parts must be bound separately and arranged sequentially in accessible files.

Fonts

Font sizes for text and tables should be of a style and size that are large enough to be easily legible, even after photocopying or when provided electronically**.** *Arial / Times New Roman 12* point font is preferred for narrative text, but printing in a font size with a legibility equivalent to at least Arial 10 point black on white could be used. The copies, including figures, tables and photos should be clearly legible. Shading and/or coloured filling/background and/or print, e.g. in tables and headers, or across pages, is unacceptable and should be avoided.

1.3 Payment for the application

1.3.1 The application fees applicable to each type of application should be paid as required. An application not accompanied by the appropriate fee will not be accepted.1.3.2 Applicants may remit payment of fees in, telegraphic transfers and/or by direct deposits into the Authority's account. When a payment is made by direct transfer, all bank charges shall be paid for by the

applicant who shall also ensure that proof of payment is submitted to the Authority.

1.3.3 Application fees for grant of Marketing Authorisation for IVD devices cover the costs of evaluating the initial submission and exclude laboratory testing and current Good Manufacturing Practices (cGMP) inspection fees which may be charged separately for site inspection.

1.3.4 A holder of a Marketing Authorisation shall pay such annual retention fees as may be determined from time to time by the Authority.

1.4 Receipt of applications

1.4.1 All applications shall be physically delivered to the Authority.

1.4.2 Applications shall be entered into the Authority's' record systems upon confirmation of payment of the application fees.

1.5 Screening of applications

1.5.1 All applications shall be screened for completeness by the Authority before being accepted for evaluation to ensure that there are no deficiencies that would delay and hinder the evaluation process **Reference should be made to the New Dossier Submission Checklist.*

1.5.2 If any deficiencies are identified during screening, a request for additional information or material shall be made to the applicant. The applicant shall be required to submit all the requested information and material identified in the input request within twenty-one (21) working days from the date of receipt of request. Any deficiencies indicated must be addressed before the application can be accepted for evaluation. If the applicant anticipates difficulty in responding in full or within the specified timeframe, the applicant shall inform the Authority in writing within fourteen (14) working days of receipt of the input request for information/clarification.

1.5.3 Reasons for non-acceptance of applications

1.5.3.1 If the applicant fails to provide the required information, the application shall not be accepted.

1.5.3.2 Applications not submitted in the prescribed format shall not be accepted at the screening stage.

1.6 Evaluation of applications

1.6.1 Applications shall be evaluated in the order of submission unless expedited evaluation has been authorised by the Authority.

1.6.2 Applications are evaluated against this guideline for completeness, adequacy and acceptability of the Technical Data submitted.

1.7 Laboratory testing of sample IVD devices

Sample IVD devices may be tested by the Authority's' National Drug Quality Control Laboratory (NDQCL) or an appropriate laboratory recognised by the Authority. The number of samples required to be tested shall be determined and requested for by the NDQCL. The Laboratory shall generate a test report that shall form part of the evaluation process.

1.8 GMP inspection of the facility

1.8.1 The Authority may carry out a GMP inspection of a manufacturing site/facility of IVD devices established on a risk based approach using cGMP guidelines. An inspection fee, separate from Marketing Authorisation application fee shall be payable to the Authority. The Authority shall inspect the manufacturing facility and prepare an inspection report.

1.8.2 Where the Authority cannot conduct a GMP inspection it shall consider previous satisfactory inspection reports of the site/facility conducted by ZAMRA or other recognised competent Authorities, provided that the inspection was conducted within twenty four (24) months preceding receipt of the application.

1.9 Approval for Grant of Marketing Authorisation

1.9.1 Final evaluations of IVD devices application for Marketing Authorisation report(s) shall be tabled before the Technical Committee for approval.

1.9.2 The Technical Committee shall also determine the conditions of approval of Marketing Authorisation.

1.9.3 If there are unresolved safety or quality issues the Committee shall defer recommendation pending resolution of the issues. Should the applicant fail to provide the required data within 90 days, the Committee shall refuse to approve Marketing Authorisation of the IVD device.

1.9.4 The Committee may reject approval of an application based on the following reasons amongst others:

(a) The product contains a substance considered undesirable for use
(b) Failed cGMP by the manufacturer
(c) Failed laboratory analytical tests
(d) When the product Marketing Authorisation is not in the interest of the public as the Authority may determine.

1.10 Time frames

1.10.1 Evaluation of new application

All applications shall be evaluated within one hundred and eighty (180) working days from the date of receipt in the order of submission. The applicant shall be requested to provide additional data when required within ninety (90) working days of such a request.

Should more time be required to provide additional data, a formal request must be made by the applicant in writing within fourteen days (14) from the receipt of the request and approved by the Authority.

1.10.2 Closure of open files when the applicant has failed to submit additional information

Where the applicant fails to submit additional information within the stipulated time, the Authority shall close the application. Should the applicant wish to resubmit the application, the application shall be processed as a new application.

1.11 Grant of Marketing Authorisation of an IVD device

The Authority shall grant Marketing Authorisation if it is satisfied -

(a) that the product conforms with the Essential Principles of Safety and Performance.

(b) with labelling and packaging of the in-vitro diagnostics devices.

(c) with the findings of the laboratory analysis where applicable.

(d) that the product is manufactured in compliance with requirements of cGMP.

1.11.1 Validity of Marketing Authorisation

A Marketing Authorisation shall be valid for five (5) years subject to terms and conditions as may be specified by the Authority. The period of validity is from the date of grant of Marketing Authorisation.

1.11.2 Termination of Marketing Authorisation

(a) The Authority may suspend or revoke the Marketing Authorisation of an IVD device and remove it from the IVD device register through a written notice to the Marketing Authorisation holder or agent for any of the following reasons:

(i) Non-payment of the prescribed annual retention fee.

(ii) An unforeseen high public or personal health risk associated with using the device.

(iii) Inaccurate, false or misleading information given by the applicant during the application stage.

(iv) Suspension of a conformity assessment certificate.

(v) Non-compliance with the terms and conditions under which the Marketing Authorisation was granted.

(vi) Any other reason as the Authority may determine.

1.12 Application for amendment of an IVD device with Marketing Authorisation

The Authority shall be informed in writing with evidence of any change(s) to an IVD device that has been grant Marketing Authorisation that could may affect its safety or performance.

All applications for an amendment to an IVD device with Marketing Authorisation shall be made in writing and shall be accompanied by a prescribed fee.

1.13 Application for renewal of Marketing Authorisation

Application for renewal of a Marketing Authorisation shall be made one hundred and eighty days prior to the expiry of Marketing Authorisation.

The Applicant shall submit an application with supporting documentation with payment of the prescribed fees as prescribed by the Authority

1.14 Classification of In-vitro diagnostic devices

In-Vitro diagnostic devices may be classified in a four (4) class system, depending on the level of risk to the public as well as the individual *(Table 1).*

The class shall be determined by the manufacturer using a set of classification rules that takes the following into consideration:

(a) The manufacturers intended use and indication for use of the IVD device.

(b) Where an IVD device has multiple intended uses as specified by the manufacturer, which place the device into more than one class, then it shall be classified in the higher class.

(c) Where more than one of the classification rules applies to the IVD device, it shall be allocated to the highest class indicated.

Table 1: General classification system for IVD devices

CLASS	RISK LEVEL
A	Low Individual Risk and Low Public Health Risk
B	Moderate Individual Risk and/or Low Public Health Risk
C	High Individual Risk and/or Moderate Public Health Risk
D	High Individual Risk and High Public Health Risk

***Refer to ZAMRA Guidelines on the Classification of Medical Devices*

1.15 Compilation of the product application

Applicants shall be required to compile the product application in the format as per ZAMRA Guidelines for In-Vitro Diagnostic Medical Device Marketing Authorisation Table of Contents. The applicant shall also include:-

(a) Completed application form and Product/IVD device details

(b) Summary technical documentation (STED) *(Refer to ZAMRA STED)*

(c) Original documentation or notarized copies of the original documents regarding the issuance of any mark/s of quality (e.g. “CE” Mark) with respect to the respective Notified Body must be included in the submission.

(d) Labelling information (*Refer to ZAMRA Guidelines on Label and Instructions For Use for Medical Devices)*)

(e) Essential Principles of Safety and Performance (Refer *to ZAMRA Guidelines on Essential Principles of Safety and Performance of Medical Devices)*

(f) Any additional information that the Authority may require

REFERENCES

1. GHTF/SG1/N045:2008: Principles of In-vitro Diagnostic (IVD) Medical Devices Classification
2. GHTF/SG1/N063:2011: Summary Technical Documentation (STED) for Demonstrating Conformity to the Essential Principles of Safety and Performance of In-vitro Diagnostic Medical Devices
3. GHTF/SG1/N70:2011 Label and Instructions for Use for Medical Devices (revision of GHTF/SG1/N43:2005 Labelling for Medical Devices)
4. GHTF/SG1/N68:2012 Essential Principles of Safety and Performance of Medical Devices (revision of GHTF/SG1/N41:2005 Essential Principles of Safety and Performance of Medical Devices)
5. IMDRF/RPS WG/N13 FINAL: 2014 In-vitro Diagnostic Medical Device Market Authorisation Table of Contents

ANNEXES

ANNEX I: Application form

Form I

The Medicines and Allied Substances Act, 2013(Act No.3 of 2013)

The Medicines and Allied Substances (Marketing Authorisation of In-vitro Diagnostic Devices for Human Use) Guidelines, 2018

APPLICATION FOR GRANT OF MARKETING AUTHORISATION OF IN-VITRO DIAGNOSTIC (IVD) DEVICES FOR HUMAN USE IN ZAMBIA

For Official Use	
Date	Application number

The Guidelines on grant of Marketing Authorisation of an In-vitro diagnostic device to be consulted in completing this form and preparing of dossiers for submission to ZAMRA

PART I: PARTICULARS OF THE APPLICANT

Applicant name and address	Name: Physical and Postal Address: Phone: Fax: Email:
Contact Person[1]	Name: Designation: Phone: Fax: Email:
Local Responsible Person[2]	Name: Designation: Phone: Fax: Email:

1 *Contact person will be responsible for communicating with the Authority and a letter of Authorisation to communicate on behalf of the applicant should be submitted.*

2 *Should be a person, resident in Zambia, appointed by a foreign-based applicant to be responsible for all regulatory matters in respect of products granted marketing authorisation with Power of Attorney or a letter of acting as an agent.*

PART II: PARTICULARS OF THE IVD DEVICE

Manufacturers name and address	Name: Physical and Postal Address: Phone: Fax: Email:
Number of samples IVD devices submitted	
Generic name of the IVD device *(Where applicable)*	
Brand name of the IVD device	
Model/Series/System of the IVD device *(Where applicable)*	
GMDN description of the IVD device	
Short description if none of the GMDN descriptions seem appropriate	
GMDN code of the IVD device (if known)	
Intended use of the IVD device	
IVD device Classification	☐ Class A ☐ Class B ☐ Class C ☐ Class D
Have there been any of the following:	☐ Previous recalls ☐ Reportable adverse incidents ☐ Banning in other countries ☐ Post-market surveillance studies

Please provide details on each item you have ticked (attach any relevant documentation)	_____ _____ _____ _____ _____ _____ _____ _____ _____ _____
International or national standards with which the IVD device complies (enclose a copy)	
List the SADC states where the IVD device has obtained marketing approval (Attach documentation)	

PART III: DECLARATION AND SIGNATURE

I declare that all the information I have stated is correct and truthful to the best of my knowledge and belief.

Particulars of the Person Signing on Behalf of the Applicant

a) Name: ……

b) Designation: ……..

c) Signature: …… d) Date: …/…/…….*(dd/mm/yyyy)*