EAST AFRICAN COMMUNITY

Requirements for Assessment and Market Authorization of In Vitro Diagnostic Medical Devices

JUNE 2020

REQUIREMENTS DEVELOPMENT HISTORY

STEP	DATE
Draft Model Framework Developed by EAC/WHO Consultants	June -September 2018
Draft Model Framework Presented to the EAC Experts for Review and Validation	27th to 30th November 2018
Incorporation of expert inputs into the framework by EAC/WHO consultants	December 2018 to January 2019
Final Draft Model Framework Adopted by the Heads of EAC NMRAs	30th June 2020

AUTHORS/CONTRIBUTORS

Jean Nestor BAHIZI
Directorate of Sanitary Infrastructures and Equipment National Laboratory for Quality Control of Medicines
Bujumbura, Burundi

Raphael BARAYANDEMA
Head of the Division, Department of Pharmaceuticals and Medical Laboratories (DPML)
Bujumbura, Burundi

Godeberthe NDIHOKUBWAYO
Head of the National Laboratory for Quality Control of Medicines
Bujumbura, Burundi

Pauline WAIRIMU
Head of Medical Devices Kenya Pharmacy & Poisons Board (PPB)
Nairobi, Kenya

Patrick Maleth KISABEI
Senior Laboratory Expert
Kenya Medical Laboratory and Technologist Board
Nairobi, Kenya

Axelle MUTEZINKWANO
Medical Devices Officer
Ministry of Health
Kigali, Rwanda

Peter BAAK
Regulatory Officer
Drug Food and Control Authority (DFCA)
Juba, South Sudan

Brenda KITIMBO
Principal Regulatory Officer
Medical Devices Directorate of Inspectorate and Enforcement National Drug Authority (NDA)
Entebbe Uganda

Wilberforce KWIRINGIRA
Ag Director, Quality Control Laboratory, National Drug Authority (NDA)
Kampala, Uganda

Abdul MUTAKA
Lead Engineering Section
Central Public Health Laboratory
Kampala,Uganda

Nyambura MOREMI
Director, National Public Health Laboratory
Dar Es Salaam Tanzania

Engerasiu MTUI
Regulatory Officer, Medical Devices
Tanzania Medicines and Medical Devices Authority (TMDA)
Dar Es Salaam Tanzania

Samuel XADAY
Medical Devices Officer
Tanzania Medicines and Medical Devices Authority (TMDA)
Dar Es Salaam Tanzania

Salma Hafidh ALI
Head of Medical Device and Diagnostics Unit, Zanzibar Food and Drugs Authority (ZFDA)
Zanzibar, Tanzania

Aki Rajab MAULID
Medical Devices Officer
Zanzibar Food and Drugs Authority (ZFDA)
Zanzibar, Tanzania

Nawal Jumbe MGAZA
Pharmaceutical Laboratory Analyst
Zanzibar Food and Drugs Authority (ZFDA)
Zanzibar, Tanzania

Paul TANUI
Senior Programme Officer

Africa Development Agency-NEPAD
Midrand South Africa

Jane MASHINGIA
Senior Health Officer
East African Community Secretariat
Arusha, Tanzania

Patrick MWESIGYE
Senior Health Officer
East African Community Secretariat
Arusha, Tanzania

Nancy CHEROTICH
Pharmaceutical Programme Assistant
East African Community Secretariat
Arusha, Tanzania

Samvel AZATYAN
Team Lead
Regulatory Convergence and Networks (RCN)
World Health Organization
Geneva, Switzerland

Stanislav KNIAZKOV
Technical Officer
Health Technologies & Innovations
Regional Office for Africa
World Health Organization
Brazzaville, Congo

Agnes KIJO
Technical Officer
World Health Organization
Geneva, Switzerland

Willy URASSA
Professor, Invitro Diagnostics (IVD) and Quality Management System (QMS)
World Health Organization
Geneva, Switzerland

Table of Contents

ABBREVIATIONS

AHWP	Asian Harmonization Working Party
CSDT	Common Submission Dossier Template
CSF	Cerebrospinal Fluid
DoC	Declaration of Conformity
EAC	EAC Food and Drugs Authority
EPSP	Essential Principles of Safety and Performance
GHTF	Global Harmonization Task Force
GMDN	Global Medical Devices Nomenclature
HSA	Health Sciences Authority
IFU	Instructions for use
IMDRF	International Medical Devices Regulator's Forum
ISO	International Organization for Standardization
IVD	In Vitro Diagnostic Device
LRP	Local Responsible Person
MSD	Medical Stores Department
NMRA	National Medicine Regulatory Authority
OEM	Original equipment manufacturer
QMS	Quality Management System
STED	Summary Technical Documentation
SOP	Standard operating procedure
UN	United Nations
WHO	World Health Organization

DEFINITION OF TERMS

Abridged assessment:
Assessment including performance evaluation, manufacturing site inspection of abridged scope and labelling review

Accessory
An article which is intended specifically by its manufacturer to be used together with a parent device to enable that device to be used in accordance with its intended use as an IVD or to augment or extend the capabilities of the parent device in fulfilment of its intended use as an IVD, and therefore should be considered an IVD.

Act
The relevant EAC NMRA Act.

Analytical performance
Ability of an IVD to detect or measure a particular analyte.

Applicant
Any person or institution or company that applies formally to get market authorization for IVD in EAC partner states.

Assay
Investigative (analytic) procedure in laboratory for qualitatively assessing or quantitatively measuring the presence, amount or functional activity of a target entity (the analyte).

Authority
The <Relevant EAC NMRA> or the acronym “NMRA” established under section 4(1) of the Act.

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

Certified Copy
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.

Clinical Performance
Ability of an IVD to yield results that are correlated with a particular clinical condition/ physiological state in accordance to target population and intended use.

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

Conformity Assessment Body
A body engaged in the performance of procedures for determining whether the relevant requirements in technical regulations or standards are fulfilled. A Conformity Assessment Body (CAB) is authorized to undertake specified conformity assessment activities by a Regulatory Authority (RA) that will ensure performance of the CAB is monitored and, if necessary, withdraw designation.

Dossier screening: Systematic process to ensure that all requisite sections of the product dossier are submitted

Dossier review:
Review and assessment of documentation including data, protocols, reports, procedures, etc., to support the quality, safety and performance of a product for the purpose of NMRA registration.

Full assessment:
Assessment including dossier review, performance evaluation, inspection of manufacturing site(s) and labelling review.

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

Intended use
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

Inspection of manufacturing site(s):
Inspection of the manufacturing site(s) of product undergoing assessment

In vitro diagnostic medical device (IVD):
A medical 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

Note: IVDs include reagents, calibrators, control materials, specimen receptacles, software, and related instruments or apparatus or other articles, and are used, for example, for the following test purposes: diagnosis, aid to diagnosis, screening, monitoring, predisposition, prognosis, prediction, determination of physiological status.

Label
Any written, printed or graphic representation that appears on or is attached to the IVD 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.

Labelling review
Review and assessment of the instructions for use and product labels

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

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

Manufacturer
Any natural or legal person with responsibility for design and/or manufacture of a medical device with the intention of making the medical device available for use, under his name; whether or not such a medical device is designed and/or manufactured by that person himself or on his behalf by another person(s).

Medical Device(s)
Any instrument, apparatus, laboratory equipment and reagents, implement, machine, appliance, implant, in vitro reagent or calibrator, software, material or other similar or related article which is intended by manufacturer to be used, alone or in combination for human beings or other animals for one more of the specific purpose(s) of-

- diagnosis, prevention, monitoring, treatment or alleviation of diseases or compensation for an injury;
- investigation, replacement, modification or support or the anatomy or of a physiological process;
- supporting or sustaining life;
- control of conception;
- disinfection of medical devices;
- providing information for medical or diagnostic purposes by means of in vitro examination or specimens derived from the human body or other animal; and
- does not achieve its primary intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its intended function by such means.

National Standard
A standard as prescribed by the EAC Partner State's Bureau of Standards.

Near Patient Testing
Any testing performed outside the laboratory environment by qualified personnel, generally near to or at the side of the patient, also known as Point-of-Care Testing (POCT).

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

Performance Evaluation
Assessment and analysis of data to establish or verify the performance (analytical performance and where applicable, clinical performance) of an IVD.

Process Validation

Confirmation by objective evidence that a process consistently produces a result or product meeting its pre-determined requirements.

Risk assessment
Overall process comprising a risk analysis and a risk evaluation.

Quality Audit
The process of systematic examination of a quality system of IVDs manufacturing facilities carried out by the Authority to demonstrate conformity for regulatory purposes.

Quality Management System
Collection of business processes aim to direct and control an organization with regard to quality, from establishing quality policy, quality objectives and implementing and maintaining quality system.

Reagent
Any chemical, biological or immunological component, solution or preparation intended by the manufacturer to be used as IVD.

Re-brander A manufacturer of a rebranded IVD.

Rebranded product: A rebranded product is identical in every respect to the product manufactured by the original manufacturer, except that the product is labelled with the "rebranded" product name and product code, and bears the brander's name.

Recall
Any action taken by its manufacturer, importer, supplier or registrant to remove the medical device from the market or to retrieve the medical device from any person to whom it has been supplied, because the medical device may: be hazardous to health; fail to conform to any claim made by its manufacturer or importer relating to its quality, safety or performance.

Regulatory version: Relates to the information associated with a submission for approval by a regulatory authority. The submitted version is defined by all of the documentation related to development, manufacture and intended use, labelling and post-market surveillance of the product and all the documented evidence supporting the safety and performance claims associated with that submission. If any aspect of this documentation differs in any way between the submissions to different regulatory authorities or assessment bodies (United States Food and Drug Administration, Health Canada, a Notified Body for CE marking, etc.) it is considered to be a different regulatory version.

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

Market Authorization Holder OR Registrant
The person who applied for and obtained market authorization or registration of the medical devices including IVDs

Risk
Combination of the probability of occurrence of harm and the severity of that harm.

Specimen receptacles
Devices, whether vacuum-type or not, specifically intended by their manufacturers for the primary containment and preservation of specimens derived from the human body and other animals for the purpose of IVD examination.

Technical Documentation
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 an IVD.

Validation
Confirmation by examination and provision of objective evidence that the requirements for a specific intended use have been fulfilled.

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

FOREWORD

East Africa Community harmonized guidelines for In vitro diagnostic devices (IVDs) has been developed to assist National Medicines Regulatory Authorities of the Partner States to harmonize processes for issuance marketing authorization. Harmonized processes for gaining access to the EAC partner state's market will significantly improve access to safe, quality and affordable in vitro diagnostics.

This is a simplified guideline which provide details on requirements of applying for market authorization in EAC partner states including evidences of safety and performance, application procedures, classification rules and essential requirement checklist.

Oversight on market authorization is a pre-market condition which requires the manufacturer to provide evidence on quality and performance of the product's intended to be marketed in the EAC market. It is therefore important that the procedures are clear and are harmonized to reduce barrier of the manufacturers when compiling information required by NMRAs.

It is my expectation that individuals who are interested to sell their products in EAC Partner States will read and understand the requirements outlined in these guidelines to ensure smooth processing and assessment of the application and reduce timelines for granting market authorization.

Amb. Liberat Mfumukeko
EAC Secretary General

PREFACE

The EAC Requirements for In Vitro Diagnostic medical devices (IVDs) Assessment and Market Authorization is an EAC guideline which enumerates market authorization requirements and procedures for in vitro diagnostics for the purpose of ensuring transparency and quick access of IVDs within the EAC partner states. The document contains eighteen (18) chapters and five annexes including harmonized application form, classification rules, Summary of Technical Documentation (STED), essential requirements checklist, annual post market reporting form and variation form for reporting any change of an IVD which has been issued market authorization.

EAC Partner States have been facing a lot of challenges in assessing safety, efficacy and performance of IVDs. Some of the challenges include, lack of expertise considering complexity of IVDs, varying standards of regulations, long procedures to introduce new products in the market. The World Health Organization harmonized and transparent procedures to facilitate market authorization within the partner states which will in turn reduce timelines for issuance market authorization and improve access of IVDs.

Manufacturers are urged to read, understand and adherence to the guidelines to facilitate correct compilation of information/evidence, timely assessments and approvals of applications for IVDs by the NMRAs.

I wish to express my gratitude to all experts from EAC Partner States' NMRAs, regional and international organizations who actively participated in the development and review of the guidelines. I therefore urge all technical experts from the Partner States National Medicines Regulatory Authorities and EAC Secretariat to use these guidelines as a tool to effectively carry out IVDs assessment and authorization processes.

Hon. Christophe Bazivamo
EAC Deputy Secretary General
Productive and Social Sectors

RESPONSIBILITY FOR THE IMPLEMENTATION OF THE EAC REQUIREMENTS FOR MARKET AUTHORIZATION OF IN VITRO DIGNOSTIC MEDICAL DEVICES

The EAC Sectoral Council of Ministers of Health recognizes the work done by the EAC Secretariat in collaboration with the lead EAC Partner States National Medicines Regulatory Authorities (NMRAs), Tanzania Medicines and Medical Devices Authority (TMDA) for coordinating the development of harmonized requirements for market authorization of in vitro diagnostic medical devices. Implementation of the requirements for market authorization of in vitro diagnostic medical devices will facilitate uniformity in performance assessment of diagnostics and reduce duplication of efforts between National Medicines Regulatory Authorities in the region.

Harmonization of medical product and health technologies is an explicit policy priority under Chapter 21 (Article 118) of the EAC Treaty and vital in enabling the free movement of goods in line with the EAC Common Market Protocol. Streamlining safety and performance evaluation of diagnostics will have a positive impact to public health by increasing access to good quality and safe medical devices in the region.

The EAC Sectoral Council of Ministers of Health approves the use of harmonized requirements for market authorization of in vitro diagnostic medical devices in the East African Community Partner States' National Medicines Regulatory Authorities (NMRAs) in accordance with the existing regional legal instruments. Implementation of the harmonized requirements will facilitate mutual recognition of regulatory decisions and attestation of the quality and safety of in vitro diagnostic medical devices manufactured, produced, imported, exported or traded in East African Community.

The EAC Partner States Ministries responsible for Health shall be responsible for the enforcement of this requirement for market authorization of in vitro diagnostic medical devices in the East African Community through the respective National Medicines Regulatory Authorities (NMRAs).

SIGNED by the Leaders of Delegation

Hon. Dr. Daniel Ngamije	**Hon. Mutahi Kagwe,EGH**		**Hon. Ummy Ally Mwalimu**	**Hon.Elizabeth Achuei Yol Kuol**	**Hon.Sarah Aceng Opendi**
Minister of Health	Cabinet Secretary	Minister of Public Health and Fight against HIV/AIDS	Minister of Health	Minister of Health	Minister of Health
Ministry of Health	Ministry of Health	Ministry of Public Health and	Ministry of Health, Community	Ministry of Health	Ministry of Health

		Fight against HIV/AIDS	Development, Gender, Elderly and Children		
REPUBLIC OF RWANDA	**REPUBLIC OF KENYA**	**REPUBLIC OF BURUNDI**	**THE UNITED REPUBLIC OF TANZANIA**	**REPUBLIC OF SOUTH SUDAN**	**REPUBLIC OF UGANDA**

1 INTENDED AUDIENCE

This document is intended to provide manufacturers with an overview of the harmonized processes and requirements for market authorization of in vitro diagnostic medical devices (IVD) applicable in East African community (EAC) partner states. Manufacturers wishing to apply for NMRA assessment of their product(s) should read this document before submitting applications.

2 INTRODUCTION

East African Community is a Regional Inter-Governmental Organization of the six Partner States, namely the Republic of Burundi, the Republic of Kenya, the Republic of South Sudan, the Republic of Rwanda, the United Republic of Tanzania and the Republic of Uganda. The Treaty for establishment of the East African Community, Article 118, prioritized harmonization of medical products and health technologies to ensure their safety, quality and effectiveness. It is therefore important that requirements for issuance of marketing authorization (Registration) are harmonized throughout the region to enable timely availability and access of IVDs when required.

Registration of IVDs is a legal requirement pursuant to regulation of EAC NMRA. Such process allows for assessment of data to ascertain the quality, safety and performance of IVDs. IVDs are universally used in all health settings for diagnosis, management, prevention of infectious and non-infectious diseases. Availability of IVDs of acceptable quality, safety and performance will improve public health taking into account the fact that some tests are used in laboratory or other health professional settings and others are used by consumers at home.

This is the first edition of harmonized requirements for market authorization of In-Vitro Diagnostic Medical Devices that provides an overview of risk classification of IVDs, associated assessment requirements, processes and strategies applicable within the EAC partner states. All applicants are therefore expected to conduct studies, tests evaluations and investigations, which will provide adequate evidence to allow registration of their products in EAC countries. It is henceforth utterly pivotal that applicants read and comprehend the requirements as set-out in these requirements to accelerate approval process and increase access to IVDs in EAC partner states.

As part of registration process, the EAC partner states will assess IVDs to verify compliance to EAC partner states requirements. The assessment will be based on requirements provided in this document which has been prepared based on requirements of ISO standards, CLSI guidelines, WHO guidelines and other guidance documents. Therefore, in the course of assessment of applications, reference can be made to ISO standards and other internationally accepted guidelines to include those published by Word Health Organization (WHO) and International Medical Device Regulatory Forum (IMDRF) to ensure that IVDs of good quality, safe and performance are authorized for marketing. A risk based abridged assessment procedure can be adopted for IVDs which have been prequalified by WHO to avoid duplications and hasten registration of such products.

Applicants should also note that they will be required to conduct post marketing surveillance (PMS) of IVDs to accrue information on their quality, safety and performance to testify whether they still meet registration requirements post approval.

2.1 GUIDING PRINCIPLES FOR MEDICAL DEVICES REGULATION IN EAC PARTNER STATES

Regulation of medical devices including IVDs in the EAC partner states is in infancy compared to many developed countries. As the capacity to regulate medical devices including in vitro diagnostics in EAC countries grows, the process will be guided by three main principles:

i. The WHO Global Framework Model Regulation of medical devices including IVDs which is based on the GHTF/IMDRFT principles.
ii. Harmonized requirements for submission, assessment and registration of medical devices including IVDs
iii. Risk-based joint assessment, recognition and reliance within or outside EAC will be implemented to accelerate registration and reduce duplication.

2.2 CLASSIFICATION OF IVDs

Risk classification during the assessment of IVD in EAC partner states will be based on GHTF recommendations based on the following criteria:

i. The intended use and indications for use as specified by the manufacturer (specific disorder, condition or risk factor for which the test is intended),
ii. The technical/scientific/medical expertise of the intended user (lay person or professional),
iii. The importance of the information to the diagnosis (sole determinant or one of several), taking into consideration the natural history of the disease or disorder including presenting signs and symptoms which may guide a physician/veterinarian,
iv. The impact of the result (true or false) to the individual and/or to public health.

Therefore, applicants aiming to submit the IVD for assessment in EAC partner states shall classify IVD into four (4) risk classes A, B, C or D using classification rules appended as **Annex I** of these requirements. 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 Authority reserves the right to decide on the class of the device. Examples of IVD is shown in Table 1.

CLA	RISK LEVEL	EXAMPLES
A	Low Individual Risk and Low Public Health Risk	Specimen receptacles, Selective/differential microbiological media, identification kits for cultured microorganisms, wash solutions, instruments and plain urine cup.

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 Test, Human Leukocyte Antigen (HLA) Test, Prostate Specific Antigen (PSA) Screening, Rubella Antibodies Test.
D	High Individual Risk and High Public Health Risk	Screening and confirmatory tests for HIV, HIV NAT assays, Hepatitis B, Hepatitis C, , Malaria, CD4 technologies

Table 1 Examples of IVDs in different risk classes

Table 2 summarizes the conformity assessment approaches of the different risk classes which will be implemented by EAC Partner States.

Conformity assessment element	**Class A**	**Class B**	**Class C**	**Class D**
Quality management system (QMS)	Regulatory audit normally not required, except where assurance of sterility or accuracy of the measuring function is required.	The regulatory authority should have confidence that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.	The regulatory authority should have confidence that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.	The regulatory authority should have confidence that a current and appropriate QMS is in place or otherwise conduct a QMS audit prior to marketing authorization.
Technical documentation	Premarket submission normally not requested.	Not normally reviewed premarket. The regulatory authority may request and conduct a premarket or post-marketing review sufficient to determine conformity with Essential Principles.	The regulatory authority will undertake a review sufficient to determine conformity with Essential Principles prior to the device being placed on the market.	The regulatory authority will undertake an in-depth review to determine conformity with Essential Principles, prior to the device being placed on the market.
Declaration of conformity	Submission normally not requested.	Review and verify compliance with requirements by the regulatory authority (see footnote to Table A4.1).	Review and verify compliance with requirements by the regulatory authority (see footnote to Table A4.1).	Review and verify compliance with requirements by the regulatory authority (see footnote to Table A4.1).

Table 2 Conformity assessment processes as determined by device class

2.3 RESPONSIBILITIES

2.3.1 Applicant

Application for registration of an IVD can be made by the manufacturer of the device or their representatives or by a person who orders the IVD to be manufactured for sale in EAC. The applicant shall be responsible for:

i. quality and safety of the product,

ii. information supplied in support of the application for registration
iii. variations that may occur
iv. nomination of a local Responsible Person (LRP).
v. submission of formal agreement or any other official authorization by an applicant as official proof of nomination of a LRP

An applicant who is not a resident in EAC 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 a LRP.

2.3.2 Local responsible person

The Local responsible person (LRP) shall:

i. Monitor the device on the market and inform the Authority immediately after the detection of any problem relating to a registered device such as serious manufacturing defects which may endanger public health.
ii. Facilitate communication between the Applicant and the Authority on matters relating to the product.
iii. Handle device recalls implementation.
iv. Provide technical support and service maintenance of registered device(s).
v. Collect and submit PMS data on behalf of the manufacturer

3 COMPONENTS OF THE ASSESSMENT

3.1 Application

A completed application form **(Annex II)** provides summary information about the product, its regulatory version and the manufacturer. The details provided in this form will inform NMRA in its decision on whether or not the product submitted is eligible for assessment and, if so, whether or not the assessment can be abridged. It is also used to determine the plan for each of the components of the assessment process. It is therefore important for the manufacturer to ensure that the information supplied in the application form is accurate and complete.

For all IVD risk classes the Applicant will submit the application form together with dossier (technical file) which has been compiled according to the summary of technical documentation (STED) format **(Annex III)** and a sample of the IVD (where applicable). All documents will be in English and must be submitted, preferably electronically. The manufacturer will pay an application fees according to fee payment structure of individual NMRA and bank details and payment procedures must also be clearly indicated.

If the documents are physically submitted, then NMRA will have to define the type of paper, size, colour and binding requirements for the purpose of uniformity.

The Application form, supporting documentation including proof of payment will be reviewed by NMRA against the established eligibility criteria to determine the product's eligibility for assessment. If necessary, the manufacturer may receive a communication from NMRA requesting additional information and/or clarifications to assist it in the

eligibility decision. The manufacturer must provide NMRA with the information and/or clarifications so requested within the dead- lines prescribed by NMRA. NMRA will inform the manufacturer in writing of its decision concerning whether or not the product is eligible for assessment.

3.2 Conformity assessment

National Medicines Regulatory Authority (NMRA) will determine the appropriate type of assessment at the time of review of the pre-submission form. Full and abridged assessments can take place, depending on the regulatory version submitted and evidence from a previous stringent review by WHO prequalification team. A full assessment process includes; review of a product dossier; performance evaluation including operational characteristics; inspection of manufacturing site(s); and labelling review. On the other hand an abridged assessment includes: performance evaluation including operational characteristics; manufacturing site inspection of abridged scope; and labelling review. The aim of abridged assessment is to avoid duplication of effort and reduce the time taken to assess and issue market authorization by focusing on aspects where NMRA assessment brings added value. NMRA will review the pre-submission form and supporting documentation to determine whether the product qualifies for an abridged assessment. The rationale for abridged assessment is that a prior regulatory approval provides a level of assurance relating to the product's quality, safety and performance in countries where it is approved but it cannot always provide the same assurance when the product is used in other jurisdictions, including resource-limited settings. Products that do not qualify for abridged assessment will require a full assessment.

3.3 Product Dossier Submission and Screening

Manufacturers must ensure that the contents of the product dossier are consistent with the information submitted in the application form and that any changes in the information submitted in or as part of the application form are promptly notified in writing to NMRA. When submitting similar product (same regulatory version) that has been assessed by either WHO PQ team or more matured NMRA is submitted, the manufacturer will be encouraged to submit a complete copy of the dossier and other relevant documentation, the dossier assessment and manufacturing site inspection reports for possible recognition/reliance.

Once the product dossier has been received by NMRA, it will be screened for completeness before being reviewed. This screening is aimed at ensuring that all requisite sections of the product dossier have been submitted and as such does not take into consideration the technical appropriateness of all the information provided in the product dossier. If the product dossier is incomplete, the manufacturer will be informed in writing that an incomplete dossier has been received and will be requested to provide supplemental information to complete the dossier within a specified deadline. The manufacturer will be given two opportunities to submit the required additional information within the deadlines set by NMRA. In the event of non-compliance, the product dossier will be rejected on grounds of incompleteness and the application will be rejected without reimbursement of the paid fees. Dossiers that are considered complete following the screening will proceed for dossier review. NMRA will inform the manufacturer in writing on the outcome of screening and review processes as soon as its completed.

3.3.1 Product dossier review

NMRA reviews the product dossier with the purpose of

i. assessing evidence in support of safety and performance of the product; and
ii. assessing the product design and manufacture.

The information submitted in the product dossier will be assessed by experts (assessors) appointed by NMRA after submission of proof of payment of the applicable assessment fee. Assessors involved in the product dossier review must have appropriate qualifications and expertise in the relevant fields. The assessment of product dossiers will be conducted in accordance with standard operating procedures (SOPs) established by NMRA for that purpose so as to ensure uniformity in evaluation and timeliness of assessment activities. Any deficiencies in the documentation submitted and/or in the data that are identified in the product dossier review will be communicated in writing to the manufacturer by NMRA.

A corrective action plan that details the amendments needed to correct the deficiencies (i.e. responses to comments; documentation and/or data that is missing) and deadlines for their submission must be provided by the manufacturer to NMRA. The manufacturer will have the opportunity to submit up to two corrective action plans and, provided that the corrective action plan is accepted by NMRA, only one amendment to the original product dossier will be permitted. The assessment procedure is usually suspended (i.e. NMRA will not undertake any further action) until a corrective action plan has been submitted by the manufacturer and accepted by NMRA. In certain cases, NMRA may agree, in its sole discretion, to permit the manufacturer to correct specific nonconformities after registration provided that the manufacturer commits in writing to correct them by an agreed upon deadline. Such a “commitment to registration” will be reflected in the NMRA registration report and will be verified during the re-inspection. Failure to comply with registration commitments within agreed deadlines will result in the delisting from the NMRA list of registered IVDs.

The manufacturer may request a hearing or meeting with NMRA to clarify issues identified during dossier review. NMRA may provide technical guidance and specifications to manufacturers to facilitate compliance with NMRA requirements.

If the product successfully meets the NMRA registration requirements, a summary of the product dossier review will be included in the NMRA registration report. In the case of abridged assessment, the NMRA registration report may also include manufacturer’s commitments to registration to resolve findings from the manufacturing site inspection relating to the technical documentation. If the product dossier does not meet NMRA requirements or if any of the other conditions outlined under rejection of the application section, the application will be rejected.

3.4 Inspection of manufacturing site(s)

The inspection of the manufacturing site(s) is conducted to assess compliance of the manufacturer’s quality management system and manufacturing practices with

international standards, such as the most current ISO 13485 Medical devices — Quality Management Systems — requirements for regulatory purposes and other relevant standards and guidelines. However, the NMRAs inspection of the manufacturing site will focus on the suitability of the implemented processes and procedures for the reliable supply of IVDs to EAC Partner states. Therefore, customer-related issues that may be covered only in general terms in ISO 13485 shall be inspected in detail. Importantly, the inspection shall also verify the content of the product dossier (or, in the case of an abridged assessment, the technical documentation) through review of reports and raw data onsite, and interviews with the personnel involved.

If serious or critical nonconformities of public health concern are identified in connection with an inspection, NMRA reserves the right to use, publish, issue, share with relevant authorities of EAC Partner states. The manufacturer should carefully read the information set out in the NMRA guidance document on the requirements of inspection process reports and nonconformities.

3.4.1 Inspection of manufacturing site(s) under the full assessment

Under the full assessment, the initial inspection of the manufacturing site will be performed in two stages:

i. The stage 1 Desk audit (desk review) shall evaluate the documentation related to the quality management system to ensure readiness for the stage 2 inspection. General information about the documented quality management system (including the quality manual and manufacturing processes, organigram, workflows, critical suppliers and floor plan) will be reviewed during the stage 1 inspection to establish the readiness of the manufacturer's quality management system and to prepare for an on-site visit. Any issues of concern will be communicated to the manufacturer. A satisfactory stage 1 inspection is a precondition for proceeding to stage 2 inspection.

ii. The stage 2 inspection shall comprehensively evaluate the effective implementation of the quality management system and production processes through an onsite(s) inspection. The inspection team is composed of NMRA staff, external experts (inspectors) appointed by NMRA as well as, potentially, interpreters and observers. The inspectors involved in the onsite(s) inspection should have appropriate qualifications and expertise in the relevant fields.

3.4.2 Inspection of manufacturing site(s) under the abridged assessment

Under the abridged assessment, a manufacturing site inspection of abridged scope will take place. Upon request by NMRA, the manufacturer must submit an information package that will assist NMRA in preparing for the inspection of the manufacturing site(s). The on-site inspection time will be calculated and limited to those product- and user-specific processes that are a major focus of NMRA inspections (e.g. risk management, in-use stability under poorly controlled conditions, impact on stability of transportation, information gathered from the market etc., user training and training material). The inspection scope will not include an in-depth review of all QMS procedures

and processes usually inspected, but instead will take into consideration the findings of the most recent regulatory audit report. There will be limited sampling of some of the general quality management processes and associated records and a follow-up on, or clarification of individual findings identified during the previous inspection.

3.4.3 Report on the inspection of the manufacturing site(s)

A preliminary conformance or non-conformance report detailing outcome of concern (if any) shall be provided to the manufacturer on the final day of the inspection. A final inspection report, including the graded nonconformities will be issued to the manufacturer after the inspection of the manufacturing site(s) at least one month after the inspection.

All nonconformities must be corrected by the manufacturer through suitable corrective actions addressing the root cause of each nonconformity. The manufacturer will have the opportunity to submit up to two corrective action plans. Depending on the nature and number of nonconformities objective evidence of the effective implementation of proposed corrective actions may be required. NMRA will assess the information provided and decide whether the corrective action plan can be accepted. Conformity with NMRA requirements will be established based on assessment of such information. In some instances, the number and criticality of nonconformities may require that the effective implementation of proposed corrective actions needs to be verified in a follow up inspection, before the nonconformities can be closed off.

A summary of the findings of the inspection of the manufacturing site(s) will be included in the NMRA public report, if the product successfully meets the NMRA requirements. In certain cases, NMRA may agree, in its sole discretion, to permit the manufacturer to correct specific nonconformities after registration, provided that the manufacturer commits in writing to address them by an agreed upon deadline. Such a “commitment to registration” will be reflected in the NMRA public report and will be verified during the re-inspection. Failure to comply with market authorization commitments within agreed deadlines will result in the removal from the NMRA list of authorized IVDs. If the manufacturer does not meet NMRA requirements the application will be rejected.

3.5 Performance evaluation of the product

The performance evaluation is essential for independent verification of the performance claims and operational characteristics of IVDs submitted for registration. It also allows NMRA to verify performance and operational characteristics that are considered essential for use in resource-limited settings. The data obtained complement the verification and validation data submitted by the manufacturer in the product dossier. The performance evaluation is a component of both the full assessment and the abridged assessment. The performance evaluation of the product is carried out by specified NMRA appointed laboratory.

NMRA will coordinate the performance evaluation. The performance evaluation must be carried out in accordance with publicly available NMRA protocol developed based on

global best practices. The manufacturer will be requested to send sufficient quantities from at least three different lots of the product. Detailed shipping instructions (e.g. number of test kits and/or instruments, number of lots etc.) will be communicated in due time to the manufacturer by the evaluating site(s). The manufacturer should not send tests to the evaluating site(s) unless explicitly invited to do so.

The manufacturer must send to the evaluating site(s) the requisite quantities and lots of the product (test kits and/or instruments) “free domicile”, in accordance with the aforementioned detailed shipping instructions, free-of-charge, and delivered with all customs declarations, customs duties, and transport and other charges paid for by the manufacturer. If necessary, special equipment needed to perform the assay must be made available by the manufacturer at no charge (i.e. customs declaration and payment of customs duties, transport, installation, training, etc., will be made by the manufacturer) to the evaluating site for the duration of the assessment process. NMRA will have absolute, exclusive, unfettered control over the manner in which the assessment process is carried out (including the performance evaluation and/or the publication of results of the assessment, regardless of the outcome).

Without prejudice to the foregoing and in agreement with NMRA, the manufacturer may wish to visit the specified evaluating site (s) to observe the operator performing the test procedure on the manufacturer’s product(s) before commencing the performance evaluation. There should not, however, be any changes made to the test procedure as outlined in the instructions for use. If so, the manufacturer must notify NMRA in writing, and the performance evaluation will be suspended.

NMRA will send the draft performance evaluation report including the data to the manufacturer, who will have the opportunity to review and comment on the report and results. NMRA will reasonably consider any comments by the manufacturer to the draft performance evaluation report, provided that such comments are submitted by the manufacturer in writing to NMRA within one month after the manufacturer’s receipt of the draft performance evaluation report. For the avoidance of doubt, NMRA will maintain full and exclusive control over the data analysis, the reporting of the performance evaluation results and the form and content of any publication thereof. After such one-month period, the performance evaluation report will be considered as final.

For the purposes of NMRA performance evaluation, a lot is defined as “The amount of material that is uniform in its properties and has been produced in one process or series of processes. The material can be either starting material, intermediate material or finished product.” Furthermore, the two lots must be sourced from a representative production run and not produced especially for the purpose of the NMRA performance evaluation. A summary of the performance evaluation report will be included in the NMRA public report if the product successfully meets the NMRA requirements.

3.6 Labelling review

Product labelling is considered a critical element of the evidence submitted for assessment. Only clear and comprehensive labelling will effectively communicate the product information to the intended user and ensure the safe use of the registered IVD. The version of the instructions for use (IFU) of the product which is submitted with the pre-submission form will be considered during the assessment. The manufacturer must

obtain NMRA's written agreement prior to implementing any changes to this version of the instructions for use; otherwise, the application may be cancelled.

The product labelling will be reviewed as part of the pre-submission form, product dossier, performance evaluation and inspection of manufacturing site(s). The IFU is reviewed for clarity, correctness, consistency with the information submitted in the product dossier and in the technical documentation. The overall feedback on the labelling review will be provided to the manufacturer after all assessment components have been completed. If requested by NMRA, the manufacturer shall amend the labelling before the product can be registered. The agreed product labelling will be included in the public report.

3.7 Outcome of the assessment

Each dossier review report, manufacturing site(s) inspection report, performance evaluation report and labelling review report will be finalized according to the relevant SOPs and format established by NMRA, describing the findings and including requests and recommendations to the manufacturer. The assessment reports will be communicated in writing to the manufacturer.

If any additional information is required, or if corrective action has to be taken by the manufacturer, NMRA will postpone its decision on the acceptability of the product and/or manufacturing site(s) concerned until, as applicable:

i. such information has been provided by the manufacturer, assessed and found satisfactory by NMRA, and/or
ii. such corrective action has been taken by the manufacturer and found satisfactory by NMRA, in light of the specified standards.

As NMRA is responsible for the assessment process, the ownership of the reports arising from or relating to the assessment process lies with NMRA. Thus, NMRA shall be entitled to use and publish such reports while ensuring the protection of any commercially sensitive confidential information of the manufacturer. Confidential information in this context means:

i. confidential intellectual property, know-how, and trade secrets (including, e.g. formulas, processes or information contained or embodied in a product, unpublished aspects of trademarks, patents, etc.); and
ii. commercial confidences (e.g. structures and development plans of a company).

Subject to the protection of commercially sensitive confidential information, NMRA may publish on the NMRA website and make publicly available the following information in connection with the assessment process:

iii. the names of products and of manufacturers that have applied for registration, the product code(s) submitted for registration and the registration status of each application;
iv. NMRA public report summarizing the findings of the assessment; and

v. any negative outcomes of the assessment, including product alerts such as NMRA information any notices for users, NMRA notices of suspension and/or NMRA.

3.8 Notices of Concern.

Not withstanding any of the aforementioned, NMRA reserves the right to use, publish, issue, share with relevant authorities of EAC partner states and other relevant international or intergovernmental organizations, and/or make publicly available (in each case, in accordance with the provisions of this document, including provisions regarding the protection of any commercially sensitive information of the manufacturer) any outcomes, reports, notices and/or results— whether in draft or final form, and whether positive or negative— of the assessment process including, but not limited to, the dossier review, performance evaluation and/or manufacturing site inspection, and including any confidential information to which NMRA may gain access in the course of the assessment process.

4 SUCCESSFUL ASSESSMENT

Once the NMRA is satisfied that the assessment process is complete for the relevant product, and that the product meets the NMRA requirements, the product bearing a specific product name, product code(s) and regulatory version, as manufactured at the specific manufacturing site(s) inspected, will be included in the NMRA list of IVDs which have been issued market authorization. The NMRA list of registered IVDs will be compiled in accordance with an SOP established by NMRA for final decision-making on inclusion in that list. The list will be published on the NMRA website and will specify product name, the respective product code(s), regulatory version, the manufacturer's name, the manufacturing site(s), the product packaging and the year in which the product was issued market authorization.

The manufacturer will receive market authorization letter from NMRA informing it of the outcome of the overall assessment of the product. Once the product is included in the NMRA list of registered IVDs, the manufacturer will be responsible for:

i. fulfilling market authorization commitments;
ii. annual reporting;
iii. reporting of changes;
iv. post-market surveillance obligations;
v. receiving re-inspections; and
vi. continued compliance with NMRA technical specifications.
vii. adverse event reporting

The decision to include the product in the NMRA list of registered IVDs is made based upon information available to NMRA at the time of the assessment, including information obtained as a result of the product dossier review, performance evaluation, the inspection of manufacturing site(s) and/or the labelling review conducted by NMRA. This decision is subject to change on the basis of new information that may become available to NMRA.

NOTE:
If serious or critical non-conformities or concerns (including with respect to quality, safety and/or performance) are identified in connection with the registration assessment of a product and/or a registered product, NMRA reserves the right to use, publish, issue, share with relevant authorities of EAC partner states, and/or make publicly available (in each case, pursuant to the provisions of this document, including provisions regarding the protection of any commercially sensitive information of the manufacturer) any outcomes, reports, notices and/or results—whether in draft or final form, and whether positive or negative—arising from or relating to the assessment process and/or registered product, including without limitation any NMRA Notices of Concern, NMRA Notices of Suspension, NMRA information notice to end users and/or manufacturer-issued field safety notices. Consequently, NMRA may de-register the product after evaluation of the evidence and risk–benefit assessment or may suspend the product until results of further investigations become available and are assessed by NMRA. NMRA may re-register the product only after the aforementioned evidence, risk–benefit and other assessments, and investigation results are considered acceptable by NMRA.

4.1 Correcting nonconformities identified during assessment and registration commitments

Nonconformities identified as part of any component of the assessment must be corrected by the manufacturer within the deadlines agreed with NMRA. All critical nonconformities must be corrected before the product is registered. In certain cases, NMRA may agree, in its sole discretion, to permit the manufacturer to correct specific nonconformities after registration occurs, provided that the manufacturer commits in writing to correct them by an agreed upon deadline. Such commitments to registration must be fulfilled by the manufacturer within the agreed deadlines in order to keep the registration status of the product. Failure to fulfil all registration commitments within the agreed deadlines will lead to delisting of the product from the NMRA list of registered IVDs.

5 REJECTION OF APPLICATION

NMRA reserves the right to cancel an application for a specific product at any time or stage of the assessment procedure if:

i. the product dossier or, in the case of an abridged assessment the technical documentation, does not contain all of the required information or does not meet NMRA requirements; and/or
ii. the manufacturer is not able to, or fails to, provide the required or requested information within a specified deadline; and/or
iii. the product does not meet the acceptance criteria for the performance evaluation; and/or
iv. the manufacturer is not able to, or fails to, implement any corrective actions which NMRA may require within a specified deadline; and/or
v. the information supplied is inadequate to complete the assessment in a timely manner.

In this case, the manufacturer will be allowed to re-apply for NMRA assessment. In case of any falsification discovered during the assessment, the manufacturer will not be allowed to reapply for market authorization unless otherwise agreed by NMRA.

6 WITHDRAWAL FROM THE ASSESSMENT

NMRA provides the manufacturer with the right to withdraw its application for assessment at any time or stage. To exercise this right of withdrawal, the manufacturer must provide NMRA with written notice specifying the product(s) to be withdrawn. In this case, the manufacturer will not be allowed to re-apply for NMRA assessment for the products withdrawn for a period of time determined by NMRA, usually one year from date of notification of withdrawal, unless otherwise agreed by NMRA.

7 FEES

The cost of the activities required to assess IVDs for registration will be covered by the manufacturer. The non-refundable coordination fee will contribute to the costs associated with joint review of the application for determining eligibility for assessment, product dossier screening and review, performance evaluation, inspection of manufacturing site(s), labelling review and dissemination of assessment information. The coordination fee schedule is summarized in table below

Stage of assessment	Full assessment (USD)	Abridged assessment (USD)
Pre-submission form	250	150
Dossier	1500	1000
Performance evaluation	800	500
Changes	350	250
Annual maintenance	300	150

Once a regional recommendation is issued, manufacturer will notify the EAC NMRA for marketing authorization and pay relevant fee based on EAC Partner States fee structure. Manufacturers should note that NMRA reserves the right to decide, based on the assessment findings, whether a product meets the requirements to become registered. If the assessment of a change to a registered IVD or to the quality management system is required, the manufacturer may need to pay an additional fee.

DURATION OF THE VALIDITY OF THE STATUS

NMRA will reassess products included in the NMRA list of registered IVDs and their associated manufacturing sites at intervals determined by NMRA using a risk-based approach. If as a result of this reassessment, it is found that a product and/or specified manufacturing site(s) no longer meets NMRA requirements, such products will be removed from the list. Failure of a manufacturer to participate in the reassessment procedure will also lead to delisting of the product from the NMRA list of registered IVDs.

8 FULFILMENT OF REGISTRATION COMMITMENTS

Commitments to registration must be fulfilled by the manufacturer within the agreed deadlines in order to keep the registration status of the product. Failure to meet registration commitments within the agreed deadlines will lead to delisting of the product(s) from the list of registered IVDs.

9 ANNUAL REPORTING

For all registered products, the manufacturer must submit to NMRA an annual report that details sales data and all categories of complaints in a summarized form. The annual report, in the format prescribed by NMRA, must be submitted by the manufacturer to NMRA every year following market authorization. The manufacturer will receive a letter from NMRA requesting submission of the annual report together with the prescribed report format. The report for the previous calendar year must be submitted no later than 28 February. The information provided in the annual report will inform NMRA's decision on the frequency of re-inspections. Format of the report is attached as **Annex IV.**

10 SUBMISSION OF CHANGES FOR A REGISTERED IVDS

NMRA registers an IVD as it is submitted to and assessed by NMRA at a particular point in time. To meet the NMRA requirements, the manufacturer must establish, maintain and implement a procedure for categorizing and documenting any changes to the product and/or the quality management system. This procedure must be available as part of the product dossier and during the inspection of the manufacturing site(s). The manufacturer of product(s) included in the NMRA list of registered IVDs must comply with the duties and responsibilities set out in NMRA – reportable changes to a NMRA registered IVD including, without limitation, the obligation to report to NMRA:

i. changes to the registered product or its design, labelling or manufacture;
ii. changes to the quality management system under which the product was designed and manufactured; and/or
iii. other reportable administrative changes.

To determine whether a change to the product, including its design, labelling and manufacture, or to the quality management system, requires reporting to NMRA, the manufacturer should evaluate the potential effect this change may have on the safety, quality or performance of the product. For all reportable changes to a registered product, the manufacturer must submit to the NMRA variation form **(Annex V)** for a NMRA registered IVD and supporting documentation and, in some cases, a new application. The manufacturer must communicate to NMRA its intent to introduce a change well in advance (i.e. early in the process of designing and validating the change), in order to allow sufficient time for NMRA to assess the change before its implementation. NMRA will not approve any changes without due assessment. Depending on the type of change, the assessment may also include an inspection of the manufacturing site(s) and/or performance evaluation.

Once the change report form and supporting documentation are received by NMRA, they will be screened for completeness and, provided all the required information has been supplied, they will undergo assessment by NMRA. If any aspect of the change report

form or the supporting documentation is incomplete, the manufacturer will be informed in writing and requested to complete it within a specified deadline set by NMRA. If the manufacturer fails to complete the aspect within the specified deadline, the product may be removed from the list of registered IVDs.

NMRA will inform the manufacturer in writing of the outcome of its assessment of the change. The manufacturer will also be notified if NMRA deems (based on the nature of the change and its potential impact on the quality, safety and/or performance of the product), that an inspection of the manufacturing site(s) and/ or performance evaluation is also required. Once NMRA is satisfied that the change assessment of a product is complete and provided that the overall findings demonstrate as determined by NMRA, that the product continues to meet all requirements, then the NMRA list of registered IVDs will be updated, as necessary, to reflect the relevant change accepted by NMRA

In some cases, changes affect the safety and performance of the product to such a magnitude that a new application for NMRA assessment is required. This will occur where it is deemed that the changes have resulted in a product or application information of substantial difference to that which was registered. In these cases, NMRA will notify the manufacturer that a new application to NMRA assessment is required.

If the submitted documentation supporting the change does not meet NMRA requirements or if all the requested information is not provided by the manufacturer within the specified deadline, NMRA will reject the change. The impact of such a decision on the registration status of the registered IVD will be communicated to the manufacturer in writing by NMRA.

11 APPEALS

NMRAs shall provide provisions for appeals by applicant (s) who is not satisfied with the decision of the NMRA.

12 POST-MARKET SURVEILLANCE OF NMRA REGISTERED IVDS

Post-market surveillance monitors the continued compliance of NMRA registered products with NMRA requirements. The NMRA post-market surveillance system includes proactive collection of information on quality, safety and performance of the IVD after it has been registered, as well as reactive reporting for the notification and evaluation of complaints, enabling appropriate action to be taken. As soon as an IVD is accepted into the NMRA assessment process, and as long as that IVD is included in NMRA list of registered IVDs, the manufacturer must comply with the manufacturer's obligations to undertake the following post-market surveillance activities:

i. To notify NMRA of any events relating to the IVD that have affected (or could have affected) the performance of the IVD, safety of the person being tested, safety of users of the IVD or safety of any person associated with the IVD, including:
    - any serious adverse effect, which should be reported to NMRA immediately
    - any moderate adverse event or any change in the trend of mild adverse events, which should be reported to NMRA within 30 calendar days; and

- all complaints (as well as all serious, moderate and mild adverse events), which must be reported to NMRA annually in the periodic summary report.

In the case of a complaint, NMRA will request the manufacturer to provide (and, upon such a request, the manufacturer must promptly provide to NMRA) further information relating to the complaint, including details regarding the investigation undertaken, and any corrections and corrective actions taken:

i. to activate the manufacturer's complaint-handling system, to inform NMRA of reportable adverse events, and to encourage end users to report on problems experienced with the use of the IVD;
ii. to notify NMRA of all events that require field-safety corrective actions, such as withdrawal of products from sale or distribution, physical return of the IVD to the manufacturer or destruction of the product (e.g. recall), product exchange, product modification(s) or provision of additional advice to customers to ensure that the product continues to function as intended; and
iii. if required, to supply sufficient quantities of the registered product to NMRA, or to laboratories designated by NMRA, free-of-charge and delivered duty paid, for post-market surveillance lot verification testing.

NMRA will investigate any complaint concerning a registered IVD that is communicated to NMRA by end users or by manufacturers. First, NMRA will notify the manufacturer and, depending on the nature of the complaint, may also notify any interested EAC partner state and/or interested UN agencies of the complaint.

NMRA reserves the right to use, publish, issue, share with relevant authorities of EAC partner states as well as with UN agencies and other relevant intergovernmental organizations, and/or make publicly available (in each case, pursuant to the provisions of this document, including provisions regarding the protection of any commercially sensitive information of the manufacturer) any outcomes, reports and/or results—whether in draft or final form, and whether positive or negative of:

i. any investigation relating to a complaint concerning any registered product;
ii. any field safety corrective action;
iii. any NMRA Notices of Concern, NMRA Notices of Suspension or NMRA information notices for users;
iv. any manufacturer-issued field safety notices; and
v. any confidential information to which NMRA may gain access in the course of any of the foregoing.

NMRA will review the investigation conducted by the manufacturer to ensure that it complies with scientific principles and is in accordance with international guidance and standards. NMRA reserves the right to request a special inspection to verify that correction and corrective actions have been implemented.

13 ROUTINE RE-INSPECTION

Routine re-inspections which is risk based will be conducted to ensure continued compliance with registration requirements. Routine re-inspections will typically take place every three and up to five years after issuance of market authorization of a product, unless an earlier re-inspection is deemed necessary by NMRA.

14 CONFIDENTIALITY

NMRA assessors, inspectors and the designated evaluating Bodies will treat all information to which they will gain access during the assessments, inspections and evaluations, or otherwise in connection with the dis-charge of their responsibilities in regard to this assessment procedure, as confidential and proprietary to NMRA or parties collaborating with NMRA in accordance with the terms set forth below. NMRA assessors, inspectors and the designated evaluating Bodies will take all reasonable measures to ensure that confidential information:

i. is not used for any purpose other than the assessment, inspection and evaluation activities described in this document; and
ii. is not disclosed or provided to any person who is not bound by similar obligations of confidentiality and non-use as contained herein.

iii. NMRA assessors, inspectors and laboratories will not, however, be bound by any obligations of confidentiality and non-use to the extent they are clearly able to demonstrate that any part of the confidential information:
iv. was known to them prior to any disclosure by or on behalf of NMRA (including by the manufacturers); or
v. was in the public domain at the time of disclosure by or on behalf of NMRA (including by the manufacturers); or
vi. has become part of the public domain through no fault of theirs; or
vii. has become available to them from a third party not in breach of any legal obligations of confidentiality; or
i. was subsequently and independently developed by or on behalf of NMRA, as shown by written records, by persons who had no knowledge of such confidential information; or
ii. is required to be disclosed by law, provided that NMRA shall in such case immediately notify the manufacturer in writing of such obligation and shall provide adequate opportunity to the manufacturer to object to such disclosure or request confidential treatment thereof (provided always, however, that nothing contained herein shall be construed as a waiver of the privileges and immunities enjoyed by NMRA and/or to submit NMRA to any national court jurisdiction).

15 CONFLICT OF INTEREST

Before undertaking the work, each external inspector, assessor and the representative of the evaluating site will also (in addition to the above-mentioned confidentiality undertaking) be required to complete and sign the NMRA declaration of interest form. If, based on the above-mentioned declaration of interests, it is felt that there is no risk of a real or perceived conflict of interest (or it is felt that there is only an insignificant and/or irrelevant conflict of interest), and it is thus deemed appropriate for the assessor or inspector in question to undertake the work, then he/she will discharge his/her functions exclusively as adviser to NMRA. In this connection, each assessor and inspector is required to confirm that the information disclosed by him/her in the declaration of interest is correct and complete, and that he/she will immediately notify NMRA of any change in this information.

All inspectors furthermore agree that, at the manufacturer's request, NMRA will advise the manufacturer, in advance, of the identity of each inspector and the composition of the team performing the manufacturing site inspection and provide curricula vitae of the inspectors. The manufacturer then has the opportunity to express possible concerns regarding any of the inspectors to NMRA before the inspection visit. If such concerns cannot be resolved in consultation with NMRA, the manufacturer may object to a team member's participation in the manufacturing site visit. Such an objection must be made known in writing by the manufacturer to NMRA within 10 working days of receipt of the proposed team composition. In the event of such an objection, NMRA reserves the right to cancel all or part of its agreement with, and the activities to be undertaken by, that inspector.

16 DISPUTES – PRIVILEGES AND IMMUNITIES OF NMRA

In the event of any dispute or disagreement between the manufacturer and NMRA arising from or relating to the assessment process, an SOP established by NMRA for the handling of such disputes and disagreements will be followed to discuss and resolve the issue.

17 Contact Information for EAC Partner States NMRAs and EAC Secretariat;

Dr. Remy Habonimana
Regional Technical Officer for EAC-MRH Programme
Burundi National Medicines Regulatory Authority
(ABREMA)Bujumbura, Burundi
Tel:+257 61 90 19 52/76501438
Email: habrey2000@gmail.com

Dr. Felistas Chepwogen
Regional Technical Officer for EAC-MRH Programme
Pharmacy and Poisons Board (PPB)
P.O.BOX 27663-00506
Nairobi, Kenya
Tel: +254 722 644 527/ +254 737 667 944
Email:fchepwogen@pahrmacyboardkenya.org/ fellyano@gmail.com

Patrick Rugambya
Regional Technical Officer for EAC-MRH Programme
Rwanda Food and Drugs Authority (Rwanda FDA)
P.O.BOX 84, Kigali, Rwanda
Tel: +250 788 418 863

Dr.Peter Baak
Regional Technical Officer for EAC-MRH Programme
South Sudan Drug and Food Control Authority (DFCA)
Ministries Complex 88
Juba, South Sudan

Email:prugambya@rwandafda.gov.rw

Tel: +211 918 263 484
Email: p_baak@yahoo.com / baak211@gmail.com

Mujtaba M. Ratansi
Regional Technical Officer for EAC-MRH Programme
Tanzania Medicines and Medical Devices Authority
(TMDA)
Off Mandela Road, Mabibo External
P.O.BOX 77150, Dar Es Salaam, Tanzania
Tel: +255 713 039 394/+255 787 672 277
Email: mujtaba.ratansi@tmda.go.tz / mujtabar@gmail.com

Hidaya Juma Hamad
Regional Technical Officer for EAC-MRH Programme
Zanzibar Food and Drug Agency (ZFDA)
Ministry of Health
P.O.BOX 358, Zanzibar, Tanzania
Tel: +255 774 396 108
Email: hidaya@zfda.go.tz /hiddaya@gmail.com

Dr. Noel Aineplan
Regional Technical Officer for EAC-MRH Programme
Uganda National Drug Authority (NDA)
P.O.BOX 23096, Kampala, Uganda
Tel: +256 772 609 790
Email: amnoel@nda.or.ug

Jane Mashingia
Technical Advisor
EAC Medicines Regulatory Harmonization Programme
P.O.BOX 1096
EAC Close, Arusha, Tanzania
Tel: +255 754 775 335
Email:mashingiaj@eachq.org/ jmashingia1@gmail.com

REFERENCES:

1. Definition of the terms “medical device” and “in vitro diagnostic (IVD) medical device”. Global Harmonization Task Force; 2012 (GHTF/SG1/N071:2012;http://www.imdrf.org/docs/ghtf/ nal/sg1/technical-docs/ghtf-sg1-n071-2012-definition- of-terms-120516.pdf, accessed 20 November 2016).

2. Guidelines for submission of documentation for registration of In Vitro diagnostics, second edition 2016.

3. Principles of in vitro diagnostic (IVD) medical devices classification. Global Harmonization Task Force; 2012 (GHTF/SG1/N045:2008;http://www.imdrf.org/docs/ghtf/nal/sg1/procedural-docs/ghtf-sg1-n045-2008-principles-ivd-medical- devices-classification-080219.pdf, accessed 15 March 2016).

4. Principles of conformity assessment for medical devices. Global Harmonization Task Force; 2012 (GHTF/SG1/N78:2012;http://www.imdrf.org/docs/ghtf/nal/sg1/technical-docs/ghtf-sg1-n78-2012-conformity-assessment-medical- devices-121102.pdf, accessed 15 March 2016).

5. Clinical performance studies for in vitro diagnostic medical devices (IVDs) using specimens from human subjects – Good study practice. Geneva: International Organization for Standardization (under development, 2017).

6. Directive 98/79/EC of 27 October 1998 on in vitro diagnostic medical devices. Of cial Journal of the EuropeanCommunities;L331/1(http://eurlex.europa.eu/legalcontent/EN/TXT/PDF/?uri=CELEX:31998L0079&from= EN, accessed 20 November 2016).

7. Label and instructions for use for medical devices. Global Harmonization Task Force; 2011 (GHTF/SG1/N70:2011; http://www.imdrf.org/docs/ghtf/ nal/sg1/ technical-docs/ghtf-sg1-n70-2011-label-instruction-use-medical-devices-110916. pdf, accessed 20 November 2016).

8. Definitions of the terms manufacturer, authorized representative, distributor and importer. Global Harmonization Task Force; 2009 (GHTF/SG1/N055:2009; http://www.imdrf.org/docs/ghtf/ nal/sg1/technical-docs/ghtf-sg1-n055-definition- terms-090326.pdf, accessed 20 November 2016).

9. Registration of manufacturers and other parties and listing of medical devices. Global Harmonization Task Force; 2010 (GHTF/SG1/N065:2010; http://www. imdrf.org/docs/ghtf/ nal/sg1/technical-docs/ghtf-sg1-n065-listing-of-medical- devices-100827.pdf, accessed 20 November 2016).

10. Medical devices post-market surveillance: global guidance for adverse event reporting for medical devices. Global Harmonization Task Force; 2006 (GHTF/SG2/N54R8:2006, http://www.imdrf.org/docs/ghtf/ nal/sg2/technical-docs/ghtf- sg2-n54r8-guidance-adverse-, events-061130.pdf, accessed 20 November 2016).

11. The implementation of market surveillance in Europe. In: EC single markets and standards [website]. Brussels: European Commission (http://ec.europa.eu/growth/single-market/goods/building-blocks/market-surveillance/organisation/index_en.htm, accessed 4 April 2016).

12. Clinical investigations. Global Harmonization Task Force; 2010 (GHTF/SG5/N3:2010; http://www.imdrf.org/docs/ghtf/ nal/sg5/technical-docs/ghtf-sg5-n3- clinical-investigations-100212.pdf, accessed 20 November 2016).

13. Reportable events during pre-market clinical investigation. Global Harmonization Task Force; 2012 (GHTF/SG5/N5:2012; http://www.imdrf.org/docs/ghtf/ nal/sg5/technical-docs/ghtf-sg5-n5-2012-reportable-events-120810.pdf, accessed 20 November 2016).

14. MD SAP assessment and decision process for the recognition of an auditing organization. International Medical Device Regulators Forum; 2014 (IMDRFIMDSAP WG/N11FINAL:2014; http://www.imdrf.org/docs/imdrf/ nal/technical/imdrf-tech- 140918-assessment-decision-process-141013.pdf, accessed 20 November 2016).

15. Role of standards in the assessment of medical devices. Global Harmonization Task Force; 2008 (GHTF/SG1/N044:2008;http://www.imdrf.org/docs/ghtf/ nal/sg1/procedural-docs/ghtf-sg1-n044-2008-standards-in-assessment-of-medical-devices-080305.pdf, accessed 20 November 2016).

16. Standards applicable to the WHO prequalification of in vitro diagnostics. Geneva:

World Health Organization; 2015 (WHO technical guidance series; http://www.who.int/diagnostics_laboratory/guidance/151214_tgs1_standards_applicable.pdf?ua=1, accessed 17 March 2016).

17. ISO. Geneva: International Organization for Standardization (http://www.iso.org/iso/home.html, accessed 4 April 2016).

18. GMDN user guide – version 2010: A comprehensive guide to the global medical device nomenclature. Oxford: Global Medical Device Nomenclature; 2010 (http://www.who.int/medical_devices/innovation/GMDN_Agency_User_Guide_v120810. pdf, accessed 16 March 2016).

19. GMDN homepage. Oxford: Global Medical Device Nomenclature (https://www.gmdnagency.org/, accessed 4 April 2016).

20. Assistive products for persons with disability, Classification and terminology. Geneva: International Organization for Standardization; 2011 (ISO9999: 2016; https://www.iso.org/obp/ui/#iso:std:iso:9999:ed-5:v1:en, accessed 20 November 2016).

21. Guidance for regulatory authority assessors on the method of assessment for MD SAP auditing organizations. International Medical Device Regulators Forum; 2015 (IMDRF/MDSAP WG/NSFINAL:2015; http://www.imdrf.org/docs/imdrf/nal/technical/imdrf-tech-151002-mdsap-auditing-organizations.pdf, accessed 20 November 2016).

22. Medical device regulatory audit reports. International Medical Device Regulators Forum; 2015 (IMDRF/MDSAP WG/N24 FINAL; 2015 http://www.imdrf.org/docs/ imdrf/nal/technical/imdrf-tech-151002-mdra-audit-report.pdf, accessed 20 November 2016).

23. Summary technical documentation (STED) for demonstrating conformity to the essential principles of safety and performance of in vitro diagnostic medical devices. Global Harmonization Task Force; 2011 (GHTF/SG1/N063:2011; http://www.imdrf.org/docs/ghtf/ nal/sg1/technical-docs/ghtf-sg1-n063-2011- summary-technical--documentation-ivd-safety-conformity-110317.pdf, accessed 20 November 2016).

24. Assembly and technical guide for IMDRF table of contents (ToC) submissions (ToC-based submissions). International Medical Device Regulators Forum; 2015 (IMDRF/RPS WG (PD1)/N27R1; http://www.imdrf.org/docs/imdrf/ nal/consultations/imdrf-cons-rps-atg-imdrf-toc-150409.pdf, accessed 20 November 2016).

25. In vitro diagnostic medical device market authorization table of contents (IVD MA ToC). International Medical Device Regulators Forum; 2015 (IMDRF/RPS WG/N13FINAL:2014; http://www.imdrf.org/docs/imdrf/ nal/technical/imdrf-tech- 140630-rps-ivd-toc.pdf, accessed 20 November 2016).

26. Manual on borderline and classi cation in the community regulatory framework for medical devices. Brussels: European Commission; 2010 (http://ec.europa.eu/consumers/sectors/medical-devices/ les/wg_minutes_member_lists/version1_7_borderline_manual_en.pdf, accessed 16 March 2016).

27. Guidance on legislation, borderlines between medical devices and medicinal products. In: Gov.uk/guidance [website]. Medicines and Healthcare products Regulatory Agency; 2013 (https://www.gov.uk/guidance/decide-if-your-product- is-a-medicine-or-a-medical-device, accessed 16 March 2016).

28. Medical device donations: considerations for solicitation and provision. Geneva: World Health Organization; 2011 (WHO Medical Device Technical Series; http:// apps.who.int/iris/bitstream/10665/44568/1/9789241501408_eng.pdf, accessed 20 November 2016).

29. Harper SR. Global import regulations for pre-owned (used and refurbished) medical devices. Washington (DC): Of ce of Microelectronics, Medical Equipment and Instrumentation International Trade Administration/Trade Development, US Department of Commerce (http://www.trade.gov/td/health/usedequipment.pdf, accessed 18 March 2016).

30. Placing on the market of fully refurbished medical devices. Brussels: European Co-ordination of Noti ed Bodies MedicalDevices; 2000 (NB-MED/2.1/Rec5; https://www.mdc-ce.de/ leadmin/user_upload/Downloads/Leitlinien/NB-Med/Recommendation-NB-MED-2_1-5_rev5_Placing_on_the_market_of_fully_ refurbished_medical_devices.pdf, accessed 21 March 2016).

31. In vitro diagnostics and laboratory technology, Prequalification of in vitro diagnostics. WHO/Programmes [website].Geneva:WorldHealth Organization; 2016 (http://who.int/diagnostics_laboratory/evaluations/en/, accessed 4 April 2016).

32. Instructions for compilation of a product dossier. Geneva: World Health Organization (http://www.who.int/diagnostics_laboratory/evaluations/140828_pqdx_018_dossier_instructions_v3.pdf?ua=1&ua=1, accessed 5 December 2016).

33. WHO list of prequalified in vitro diagnostic products. WHO/In vitro diagnostics and laboratory technology [website].Geneva:WorldHealthOrganization(http://www.who.int/diagnostics_laboratory/evaluations/PQ_list/en/, accessed 16 March 2016).

34. The GHTF Regulatory Model. Global Harmonization Task Force; 2011 (GHTF/ AHWG-GRM/N1R13: 2011; http://www.imdrf.org/docs/ghtf/ nal/steering-committee/ technical-docs/ghtf-sc-n1r13-2011-ad-hoc-regulatory-model-110413.pdf).

35. International Medical Device Regulators Forum (IMDRF) [website] (http://www.imdrf. org/, accessed 20 November 2016).

36. Medical devices regulations. WHO/medical devices [website]. Geneva: World Health Organization (http://www.who.int/medical_devices/safety/en/, accessed 20 November 2016).

37. Medical devices regulations; global overview and guiding principles. Geneva: World Health Organization; 2003 (http://apps.who.int/iris/ bitstream/10665/42744/1/9241546182.pdf).

38. Medical devices, managing the mismatch. Geneva: World Health Organization; 2010 (http://apps.who.int/iris/bitstream/10665/44407/1/9789241564045_eng.pdf, accessed 20 November 2016).

39. Wong J, Tong RKY, editors. Handbook of medical devices regulatory affairs in Asia. Singapore: Pan Stanford; 2013.