10/2/2024

NAFDAC ROADMAP FOR IMPLEMENTATION OF THE IMDRF-ToC AND TRANSITION FROM SUBMISSIONS USING SUMMARY OF TECHNICAL DOCUMENT (STED) TO SUBMISSION USING THE IMDRF-ToC FOR DOSSIER EVALUATION/REVIEW FOR MEDICAL DEVICES

-STAKEHOLDERS

VACCINES, BIOLOGICS & MEDICAL DEVICES REGISTRATION & REGULATORY AFFAIRS DIRECTORATE

NAFDAC

TABLE OF CONTENTS

Pages

1.0 INTRODUCTION:

Dear Stakeholders,

The National Agency for Food and Drug Administration and Control (NAFDAC) was formally accepted by the International Medical Device Regulators Forum (IMDRF) as an Affiliate Member on the 22nd of March 2024.

The IMDRF is a voluntary group of global medical device regulators worldwide who have come together to accelerate international medical device harmonization and convergence.

To this end, NAFDAC had to review its existing guidelines and processes to align with the IMDRF guides while also drafting new ones for relevant regulatory processes.

In view of the above, NAFDAC has reviewed its Dossier submission requirements from the Summary of Technical Documentation (STED) Template to the IMDRF ToC format. Also, NAFDAC is moving away from only using the dossier checklist process to full dossier review process, starting with IVD test kits for priority diseases (WHO PQ Classification).

Therefore, a roadmap for transitioning is hereby developed to ensure a smooth implementation of this process that allows for monitoring and evaluation.

2.0 PRESENT CONTEXT:

NAFDAC through the Vaccines, Biologics & Medical Devices Registration & Regulatory Affairs (VBM-R&R) Directorate, presently uses a checklist in reviewing dossiers submitted in the Summary of Technical Document (STED) format. The checklist is used for review of submissions for both analytical and clinical performance of submitted dossiers for completeness, and adequacy.

3.0 EXPECTED CHANGES:

The transition involves ending the acceptance of dossier submission in the Summary of Technical document (STED) format and commencing the acceptance of submissions in the IMDRF ToC format. To do this, the agency has reviewed its guidelines for both registration and renewal of registration of medical devices.
The Agency has emphasized in the reviewed documents the need to read the documents with the under-listed IMDRF documents:

- **https://www.imdrf.org/sites/default/files/docs/ghtf/archived/sg1/technical-docs/ghtf-sg1-n70-2011-label-instruction-use-medical-devices-110916.pdf**
- **GHTF SG1 Definition of the Terms 'Medical Device' and 'In Vitro Diagnostics' Medical Device's (imdrf.org)**
- **In Vitro Diagnostic Medical Device Regulatory Submission Table of Contents (IVD ToC) | International Medical Device Regulators Forum (imdrf.org)**
- **Non-In Vitro Diagnostic Device Regulatory Submission Table of Contents (nIVD ToC) | International Medical Device Regulators Forum (imdrf.org)**

Also, the Agency has developed its guidance document for compilation for submission of dossier for in vitro diagnostics using the IMDRF-ToC.

The review exercise for IVDs will commence with a review of IVDs classified as priority diseases by WHO IVD PQ. They include IVD's listed in Table 1:

Table 1

FUNCTION	TECHNOLOGY
HIV	
Diagnosis of infection	Rapid diagnostic tests Enzyme immunoassays Nucleic acid tests
Self-testing	Rapid diagnostic tests
Monitoring of infection	Flow cytometer for enumeration of lymphocyte subset including CD4+ T cells, or a technology that can be used at or

	near the patient Nucleic acid tests for measuring viral load
Hepatitis C virus	
Diagnosis of infection	Rapid diagnostic tests Enzyme immunoassays
Aid to diagnosis of infection and monitoring of anti-viral therapy	Nucleic acid tests
Hepatitis B virus	
Diagnosis and monitoring of infection	Rapid diagnostic tests Enzyme immunoassays
Monitoring of infection and anti-viral therapy	Quantitative nucleic acid tests
Malaria parasites	
Diagnosis of infection	Rapid diagnostic tests
Human papilloma virus	
Diagnosis of infection (for cervical cancer prevention)	Nucleic acid tests
Glucose-6-phosphate dehydrogenase (G6PD) enzyme	
Enzyme deficiency detection	Technologies/formats to be used at or near the patient
Toxigenic Vibrio cholerae	
Detection of outbreaks or surveillance for the disease	Rapid diagnostic tests
Rapid diagnostic tests Treponema pallidum (Syphilis)	
Screening and aid to diagnosis of infection	Rapid diagnostic tests
Mycobacterium tuberculosis complex and resistance to first and/or second-line anti-tuberculosis drugs	
Diagnosis of infection	Qualitative nucleic acid tests
SARS-CoV-2	
Diagnosis of infection	Rapid diagnostic tests Qualitative nucleic acid tests
Blood glucose	
Monitoring of diabetes	Handheld systems
HbA1c	
Monitoring response to therapy in people with diabetes or as an aid to diagnosis of type 2 diabetes	Point-of-care analyzers

The Directorate is still working on the IMDRF-ToC for non-IVDs. While this activity is ongoing, the Agency will accept submissions using the STED for non-IVD medical devices. The Agency anticipates full transition to IMDRF ToC submission for both IVD and Non-IVD medical devices by the end of 1st quarter of 2025.

4.0 ENQUIRIES:

Enquiries regarding the transition should be forwarded to the Biologics, Vaccines, and Medical Devices Registration and Regulatory Affairs Directorate (VBM-R&R) via email: bvmregistration@nafdac.gov.ng.

5.0 TECHNICAL DOCUMENTS

The under-listed documents may be consulted in the compilation of submitted IVD dossiers:

- **NAFDAC guidance document for compilation of product dossier for registration of in vitro Diagnostics ToC**

- **WHO Technical Guidance Series:**

TGS 1 Standards applicable to the WHO Prequalification of in vitro diagnostic medical devices: identifies standards and guidance relating to a range of issues that are encountered in the manufacture, verification, and validation of IVDs.

https://extranet.who.int/prequal/sites/default/files/document_files/WHO_PQT_TGS-1_2.0.pdf

TGS 2 Establishing stability of in vitro diagnostic medical devices: provides IVD manufacturers with guidance on possible approaches to determining stability and describes WHO prequalification requirements for stability testing.

https://extranet.who.int/prequal/sites/default/files/document_files/WHO-BS-TGS-2_20172304.pdf

Annex to TGS 2 Establishing component stability for in vitro diagnostic medical devices: provides recommendations for establishing the stability of components for IVDs, with examples of the change from establishing stability for multi-use dropper bottles to establishing stability for single-use vials.

https://apps.who.int/iris/bitstream/handle/10665/311345/WHO-MVP-EMP-RHT-PQT-2019.03-eng.pdf?ua=1

TGS 3 Principles of performance studies: identifies the key principles that apply when conducting and reporting the study design, results, and conclusion of analytical and clinical performance studies that support performance claims for IVDs undergoing assessment for WHO prequalification.

https://apps.who.int/iris/bitstream/handle/10665/258985/WHO-EMP-RHT-PQT-TGS3-2017.03-eng.pdf?sequence=1

TGS 4 Test method validation for in vitro diagnostic medical devices: guides manufacturers on the validation of the test methods used in establishing the design, development, and manufacture of an IVD.

http://apps.who.int/iris/bitstream/10665/258971/1/WHO-EMP-RHT-PQT-TGS4-2017.04-eng.pdf?ua=1

TGS 5 Designing instructions for use for in vitro diagnostic medical devices: guides manufacturers on best practices when designing the instructions for use (IFU), which are an opportunity for the manufacturer to interact directly with end users and inform them about their product.

https://extranet.who.int/prequal/sites/default/files/document_files/WHO_PQT-TGS5-201705.pdf

TGS 6 Panels for quality assurance and quality control of in vitro diagnostic medical devices: provides IVD manufacturers with guidance on possible approaches to the preparation of validation panels for quality assurance (QA) and quality control (QC) and describes WHO prequalification requirements for the QA and QC information that must be submitted for prequalification assessment.

https://apps.who.int/iris/bitstream/handle/10665/259408/WHO-EMP-RHT-PQT-2017.10-eng.pdf?sequence=1

TGS 7 Risk management for manufacturers of in vitro diagnostic medical devices: developed to help manufacturers of IVDs adopt the appropriate risk management approach within their quality management system before compiling a product dossier for submission to WHO and in preparation for site inspection as part of WHO prequalification assessment.

https://apps.who.int/iris/bitstream/handle/10665/274300/WHO-EMP-RHT-PQT-2018.02-eng.pdf?ua=1

TGS 8 Quality control for in vitro diagnostic medical devices for WHO prequalification: developed to guide IVD manufacturers to develop QC criteria, focusing on determining whether quality requirements for the product are being met, and specifically to identify any defects in the products produced.

https://apps.who.int/iris/bitstream/handle/10665/311795/WHO-EMP-RHT-PQT-2019.05-eng.pdf?ua=1

❖ **WHO Technical Specification Series**

- **TSS 1 - Human immunodeficiency virus (HIV) rapid diagnostic tests for professional and/or self-testing** https://apps.who.int/iris/bitstream/handle/10665/251857/9789241511742-eng.pdf?sequence=1

- **TSS 2 - In vitro diagnostic medical devices to identify glucose-6-phosphate dehydrogenase (G6PD) activity**
https://apps.who.int/iris/bitstream/handle/10665/252628/9789241511865-eng.pdf?sequence=1

- **TSS 3 - Malaria rapid diagnostic test**
https://iris.who.int/bitstream/handle/10665/255038/9789241512275-eng.pdf?sequence=1

- **TSS 4 - In vitro diagnostic medical devices used for the detection of high-risk human papillomavirus (HPV) types in cervical cancer screening**
https://apps.who.int/iris/bitstream/handle/10665/272282/9789241513814-eng.pdf?ua=1

- **TSS 5 - Rapid diagnostic tests used for surveillance and detection of an outbreak of cholera**
https://apps.who.int/iris/bitstream/handle/10665/260469/9789241513715-eng.pdf?sequence=1

- **TSS 6 - Syphilis rapid diagnostic tests**
https://apps.who.int/iris/bitstream/handle/10665/277285/9789241515160-eng.pdf?ua=1

- **TSS 7 - see 2021 version update TSS 16 below**

- **TSS 8 - Immunoassays to detect hepatitis C antibody and/or antigen**
https://apps.who.int/iris/bitstream/handle/10665/327936/9789241516518-eng.pdf?ua=1

- **DRAFT TSS 9 - Immunoassays to detect HIV antibody and/or antigen**
https://extranet.who.int/prequal/sites/default/files/document_files/TSS_9_Immunoassays_Draft.pdf

- **TSS 10 - In vitro diagnostic medical devices used for the qualitative and quantitative detection of hepatitis C RNA**
https://apps.who.int/iris/bitstream/handle/10665/366372/9789240057487-eng.pdf

- **TSS 11 - In vitro diagnostic medical devices used for the quantitative detection of HIV-1 nucleic acid**
  https://apps.who.int/iris/bitstream/handle/10665/366373/9789240057500-eng.pdf

- **TSS 12 - In vitro diagnostic medical devices used for the qualitative detection of HIV-1 and HIV-2 nucleic acid**
  https://apps.who.int/iris/bitstream/handle/10665/366070/9789240039346-eng.pdf

- **TSS 13 - Rapid diagnostic tests to detect hepatitis B surface antigen**
  https://apps.who.int/iris/bitstream/handle/10665/366331/9789240063068-eng.pdf

- **TSS 14 - Immunoassays to detect hepatitis B virus surface antigen**
  https://apps.who.int/iris/bitstream/handle/10665/366463/9789240063082-eng.pdf

- **TSS 15 - In vitro diagnostic medical devices used for the quantitative detection of hepatitis B DNA**
  https://apps.who.int/iris/bitstream/handle/10665/366330/9789240064393-eng.pdf

- **TSS 16 - Hepatitis C rapid diagnostic tests for professional use and/or self-testing, 2021 update**
  https://apps.who.int/iris/bitstream/handle/10665/366073/9789240033757-eng.pdf

- **TSS 17 - In vitro diagnostic medical devices used for the qualitative detection of Mycobacterium tuberculosis complex DNA and mutations associated with drug-resistant tuberculosis**
  https://apps.who.int/iris/bitstream/handle/10665/366068/9789240055865-eng.pdf

- **TSS 18 - Haemoglobin A1c point-of-care analysers for professional use**
  https://extranet.who.int/prequal/node/29977

- **TSS 19 - In-vitro diagnostic medical devices for monitoring of blood glucose in capillary blood**
  https://iris.who.int/bitstream/handle/10665/374321/9789240082939-eng.pdf

- **TSS 20 - In vitro diagnostic medical devices used for the qualitative detection of SARS-CoV-2 nucleic acid**
  https://iris.who.int/bitstream/handle/10665/373081/9789240077751-eng.pdf

- **TSS 21 - SARS-CoV-2 antigen rapid diagnostic tests for professional use and self-testing**
  https://iris.who.int/bitstream/handle/10665/373082/9789240077775-eng.pdf

❖ WHO SAMPLE PRODUCT DOSSIER

- **Sample product dossier for a qualitative nucleic acid-based testing technology for HIV-1 and HIV-2**
  https://apps.who.int/iris/bitstream/handle/10665/255402/9789241512336-eng.pdf?sequence=1

- **Sample product dossier for a quantitative nucleic acid-based testing technology to measure HIV-1 RNA**
  https://apps.who.int/iris/bitstream/handle/10665/255403/9789241512251-eng.pdf?sequence=1

- **Sample product dossier for WHO prequalification: Simu POC CD4 System: THE Manufacturing Company®**
  https://apps.who.int/iris/bitstream/handle/10665/330061/WHO-MVP-EMP-RHT-PQT-2014.03-eng.pdf?ua=1

❖ **OTHER STANDARDS**

- **International Organization for Standardization standards**
  https://www.iso.org/standards-catalogue/browse-by-ics.html

- **Clinical Laboratory and Standards Institute standards**
  https://clsi.org/standards/

6.0 TRANSITION PROCESS:

Phase 1: Notice to all applicants applying for registration of IVDs to submit dossiers using the **NAFDAC instruction for compilation of dossiers for IVD medical devices** (IMDRF-ToC) format from December 2024 – **Notice to be published on 1st week of October 2024**

Phase 2: Commencement of pilot review of Dossiers for IVDs on table 1 (Two IVDs for malaria testing and two IVDs for HIV testing from applications on the NAPAMs e-portal) – **2nd week of December 2024**

Phase 3: All applicants applying for registration of Non-IVD medical device would submit dossiers for review using the developed NAFDAC compilation of dossiers for non-IVD medical devices IMDRF-ToC format. – **January 2025**

Phase 4: Establishment of Dossier review for both IVDs and Non-IVDs application **– 31st July 2025**

7.0 TRANSITION PERIOD

The transition period will begin from 1st week of October 2024 to 31st July 2025.

8.0 CONCLUSION:

NAFDAC is well-positioned to develop this transition plan that includes both high-level strategies as well as considerations for transitioning from using the STED checklist to ensure completeness, adequacy, and conformity to the Essential Principles of Safety and Performance of Submissions.

This transition plan would draw on the individual and collective experiences and successes of other IMDRF members, which would generate stakeholder confidence in the resulting output of the process. The transition plan includes content related to WHO Prequalification of IVD medical devices and allows for a structured approach to operationalization while maintaining sufficient flexibility to account for country-specific needs and variations.

The Agency believes that with the full transition and implementation of the dossier review process for both IVD and non-IVD medical devices, NAFDAC will be complying with relevant globally harmonized standards and processes as a global player in the medical devices space.

Thank you.

Prof. Mojisola Christianah Adeyeye ***PhD, FAS***
Director-General