FEDERAL MINISTRY OF HEALTH

National HIV Testing Algorithm For Rapid Test Kits

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FOREWORD

Considerable progress has been made in Nigeria over the last five years in scaling up access to HIV testing across the country. HIV rapid diagnostic tests (RDTs) are essential tools to make the scale up of service possible, but require diagnostic algorithms. These algorithms are especially important, in that they allow decentralization of HIV testing and scale up of access. Given resource constraints, and in line with World Health Organization (WHO) guidelines, Nigeria employs a tiebreaker regimen consisting of three RDTs in series.

Multiple RDTs are marketed and available in-country. However, since the 2016 algorithms produced by the Government of Nigeria, several new tests have been evaluated but have not been integrated into the algorithm. Integrating new tests into existing algorithms is often challenging for stakeholders and requires clear guidance. This guidance therefore seeks to respond to the demand by stakeholders for harmonization of the existing algorithms and integration of newly validated test kits to increase the options.

Against this background, a standardized approach was undertaken to develop a new national algorithm, taking into consideration the performance of the tests in-country, programme needs, ease of use, among others. Building consensus was also key to developing this guidance for use at national scale.

This National HIV Algorithm Report, 2021 expands the choice of rapid test kits for use in various testing settings for diagnosis and surveillance. It also significantly expands market options, ensuring the availability of high performing test kits at various price points.

National oversight of the quality of all the tests will be monitored periodically, and the national algorithm reviewed every five years, to determine if tests are performing as expected and to accommodate new technologies and advancements in RDTs.

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Honourable Minister of Health

ACKNOWLEDGEMENT

The Federal Ministry of Health wishes to appreciate the National Quality Assurance Team and the National Laboratory Task Team on the successful completion of this new National HIV Testing Algorithm for Rapid Test Kits.

I wish to specifically extend our gratitude to all organizations and individuals who contributed to the success of the exercise including the National Agency for the Control of AIDS (NACA), National Agency for Food and Drug Administration and Control (NAFDAC), Medical Laboratory Science Council of Nigeria (MLSCN), Clinton Health Access Initiative (CHAI), United States Agency for International Development (USAID), United States Centers for Disease Control and Prevention (CDC), and our implementing partners.

We also acknowledge the very important technical contributions of the individual members of the National Laboratory Task Team.

Finally, we acknowledge the staff of NASCP for their effort in ensuring the successful completion of the process and this report.

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LIST OF ABBREVIATIONS

AHNI	Achieving Health Nigeria Initiative
AHP	African Health Project
AIDS	Acquired Immune Deficiency Syndrome
CDC	Centre for Disease Control and Prevention
CHAI	Clinton Health Access Initiative
ELISA	Enzyme Linked Immuno Sorbent Assay
FHI360	Family Health International 360
FMOH	Federal Ministry of Health
GHSC-PSM	Global Health Supply Chain - Procurement and Supply Management
GoN	Government of Nigeria
HIV	Human Immunodeficiency Virus
HMH	Honorable Minister of Health
HTS	HIV Testing Services
IHVN	Institute of Human Virology, Nigeria
IPs	Implementing Partners
LMIC	Low- and Middle-Income Countries
NACA	National Agency for the Control of HIV and AIDS
NAFDAC	National Agency for Food, Drug, Administration and Control
NASCP	National AIDS and STIs Control Programme
NHREC	National Health Research Ethics Committee
PMLL	Peak Medical Laboratories Limited
PMTCT	Prevention of Mother to Child Transmission
RTKs	Rapid Test Kits
TAT	Turn Around Time
UCH	University College Hospital, Ibadan
UNAIDS	The Joint United Nations Programme on HIV and AIDS
UNILAG	University of Lagos
WB	Western Blott
WHO	World Health Organization

DEFINITION OF TERMS

Accuracy: The ability of an assay being evaluated to correctly detect specimen containing antibody to HIV and also correctly detect specimens not containing antibody to HIV. Thus, it is the combination of sensitivity and specificity.

HIV Testing Algorithm: The sequence in which assays are performed to detect HIV antibody in a body fluid.

Sensitivity: The ability of an assay being evaluated to correctly detect specimen containing antibody to HIV.

Specificity: The ability of an assay being evaluated to correctly detect specimen that do not contain antibody to HIV.

Evaluation – A process for determining whether a test system meets defined needs in the potential user's environment**.**

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EXECUTIVE SUMMARY

The Acquired Immune Deficiency Syndrome (AIDS) has presented a significant public health burden. Infection with HIV is detected by testing for antibodies to HIV, antigens of HIV and HIV RNA (nucleic acid testing). The commonest and easiest method of demonstration of HIV infection in humans is by testing for antibodies to HIV.

In Nigeria, testing for antibodies to HIV started with Enzyme Linked ImmunoSorbent Assay (ELISA) as screening test and confirmed with Western Blott (WB). This procedure requires high tech laboratories with highly proficient laboratory scientists who are skillful on ELISA and WB testing techniques. Both WB and ELISA are expensive, time consuming with resultant long turn-around time (TAT). These limitations were overcome by the use of Rapid Test Kits (RTKs). Continuous evaluation of different HIV RTKs in Nigeria led to the development of two different algorithms in 2007 and 2016**.** More RTKs have been evaluated after the 2016 algorithm. Stakeholders find it challenging integrating different available RTKs in the market due to the fact that the newly validated RTKs have not been integrated into the existing algorithms. There has been a demand by stakeholders to harmonize the existing algorithms and integrate validated RTKs into a single algorithm. Multiple RTKs options in an algorithm will increase choices for RTK use and reduce cost thereby making HIV testing services more available. This algorithm harmonized the two existing HIV testing algorithms and integrated post 2016 validated RTKs.

In the process of developing and harmonizing the existing algorithms, NASCP engaged in series stakeholders consultations which culminated into a stakeholders meeting in June 2021. The meeting reviewed the existing algorithms and made recommendations for its harmonization and integration of post 2016 validated HIV RTKs. Three Consultants were commissioned by NASCP to finalize the report of this Algorithm.

It was evident that all the protocols used for the evaluations were similar in terms of procedure, source of specimen and methodology. Quality assurance for the entire validation processes was ensured using established quality protocols. All RTKs integrated into the testing algorithm fulfilled the WHO sensitivity and specificity recommendations for HTS. In addition, they also had acceptable accuracy and composite score. RTKs with higher sensitivity, specificity and accuracy were placed for use as first line, second line and as tie breakers respectively in the testing protocol.

The recommended National Testing Algorithm for HIV following critical review and analysis of all evaluation reports and performance of all evaluated RTKs is as follows:

First Line (Screening Kit)	Second Line (Confirmatory)	Tie Breaker
Alere HIV Combo Determine	Standard Q First Response Diaquick CareStart CareUs Unigold	HIV Status Multisure Stat Pak
	Multisure	Stat Pak HIV Status
	HIV Status	Stat Pak Multisure
First Response Standard Q	Diaquick CareStart CareUs Unigold Determine	Multisure HIV Status Stat Pak
	Multisure	Stat Pak HIV Status
	HIV Status	Stat Pak Multisure
HIV Quick Check	Standard Q First Response Diaquick CareStart CareUs Unigold Determine	Multisure HIV Status Stat Pak
	Multisure	Stat Pak
Unigold	Standard Q First Response Diaquick CareStart CareUs Determine	Multisure HIV Status Stat Pak
	Multisure	Stat Pak HIV Status
	HIV Status	Stat Pak Multisure

First Line (Screening Kit)	Second Line (Confirmatory)	Tie Breaker
Wondfo Wantai	Standard Q First Response Diaquick CareStart CareUs Determine Unigold	Multisure HIV Status Stat Pak
	Multisure	Stat Pak HIV Status
	HIV Status	Multisure Stat Pak

Harmonizing the evaluation of various RTKs into one single national algorithm will help support HTS activities, achieve the goal of improving and sustaining the fight against HIV/AIDS, expand market choices for available RTKs, ensure that choice of RTKs for HIV testing services is based on scientific evidence and useful for procurement.

This national algorithm should be reviewed and updated at least every five years in order to accommodate new technologies. The performance of all RTKs in the algorithm should be monitored regularly and the algorithm should be widely disseminated across all stakeholders at all levels. This algorithm if properly adhered to by all HTS providers will tremendously improve the quality of HIV antibody testing and help HIV/AIDS intervention activities in Nigeria.

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1. Background

Acquired Immune Deficiency Syndrome (AIDS) was first reported in the early 1980s; and the first case reported in Nigerian was in 1986. The causative agent of AIDS was discovered to be Human Immunodeficiency Virus (HIV). Testing for this virus became imperative for purposes of diagnosis, surveillance and determining disease burden.

Infection with HIV is detected by testing for antibodies to HIV antigens and HIV RNA (nucleic acid testing). The commonest and easiest method of demonstration of HIV infection in humans is by testing for antibodies to HIV.

In Nigeria, testing for antibodies to HIV started with Enzyme Linked ImmunoSorbent Assay (ELISA) as screening test and confirmed with Western Blott (WB). This procedure requires high technology laboratories with highly proficient Medical Laboratory Scientists who are skillful in ELISA and WB testing techniques [1]. Western Blott together with ELISA are considered to be highly expensive, time consuming with long turn-around time (TAT). These limitations were initially overcome by the use of Rapid Test Kits (RTKs) notably using Capillus, as screening test and Genie II as confirmatory test [1]. These two Kits also suffered limitation of use because they are cold chain dependent and therefore cannot be deployed where there is either no electricity supply or electricity supply is not reliable[2].

The advent of non-cold chain dependent RTKs revolutionized HIV testing in Nigeria. They have the advantage of short TAT (less than or equal to 30 minutes) and can be used where there is no electricity thus, they make HIV antibody testing results easily available for decision making. These test kits are used in combinations to maximize the benefits of the properties of each Kit and accurately predict the presence of HIV antibodies. The combinations of two or more RTKs in testing a single specimen is called testing algorithm. The RTKs are therefore evaluated and put in combinations to design HIV testing algorithm in Nigeria.

In 2003, a national algorithm was adopted following the HIV sentinel survey[1]. Furthermore, in August 2005, with the support of the US Centers for Disease Control and Prevention (CDC), the Government of Nigeria (GoN) constituted a working group to evaluate HIV RTKs. The first national HIV testing algorithm was developed in 2007. However, subsequent efforts have been made to develop new algorithm using data generated from evaluation of RTKs.

At the onset, Nigeria adopted parallel testing algorithm where two Kits were used to test specimen concurrently and a tie breaker was used to resolve discordance from the parallel testing. Subsequently, with decreasing prevalence and resultant low positivity in antibody testing, the country opted for serial testing algorithm where screening test result of negative is issued as test result and the positive screening is confirmed by a second kit. Discordance between the screening test and the second kit is resolved with a tie breaker otherwise the result is issued as positive in the absence of discordance [1, 2]

2. Statement of Problem

Continuous evaluation of different HIV RTKs in Nigeria led to development of two different algorithms in 2007 and 2016**.** More Kits have been evaluated after the 2016 algorithm. Stakeholders find it challenging to integrate different available RTKs in the market without the necessary guidance. New RTKs evaluated since 2016 have not been integrated into the algorithms.

3. Justification

There has been a demand by stakeholders to harmonize the existing algorithms and integrate validated RTKs into a single algorithm. Multiple RTKs options in an algorithm will increase choices for RTKs and help reduce cost thereby making HIV testing services more available.

4. Goal

The goal is to produce a single HIV testing algorithm for Nigeria**.**

4.1 Objectives

- To harmonize the two existing HIV testing algorithms.
- To integrate post 2016 validated RTKs into the harmonized algorithm.

5. Methodology

NASCP convocated all stakeholders meeting. Stakeholders reviewed the existing algorithms and how they were arrived at and made recommendation for harmonization and the integration of validated HIV testing RTKs. The recommendations were presented to the National HIV Laboratory Task Team (NHLTT). They reviewed and adopted the recommendation of the

stakeholders meeting. NASCP commissioned a team of three Consultants to produce the final report.

6. Findings

The stakeholders in their review of the processes leading to the review of existing algorithm found that:

- HIV test kits evaluation preceded the development of each of the two algorithms;
- All evaluation protocols received ethical approval from the National Health Research Ethics Committee (NHREC);
- All the protocols for evaluation were similar in terms of procedure, source of specimen and methodology;
- Quality assurance for the entire validation processes was ensured using established quality assurance measures;
- The characteristics used to evaluate and determine performance levels were the same;
- All RTKs evaluated met World Health Organization (WHO) sensitivity and specificity recommendations for HTS;
- All Kits had composite score of 95%;
- RTKs with higher sensitivity are placed for use on first line;
- RTKs with higher specificity are placed for use on second line;
- RTKs with higher accuracy are placed for use as tie breakers;
- The final algorithm was produced using 14 different RTKs.

The summary of the evaluation of all RTKs from 2016-2021 showing their different levels of sensitivity specificity, accuracy and composite score are presented in the figures below.

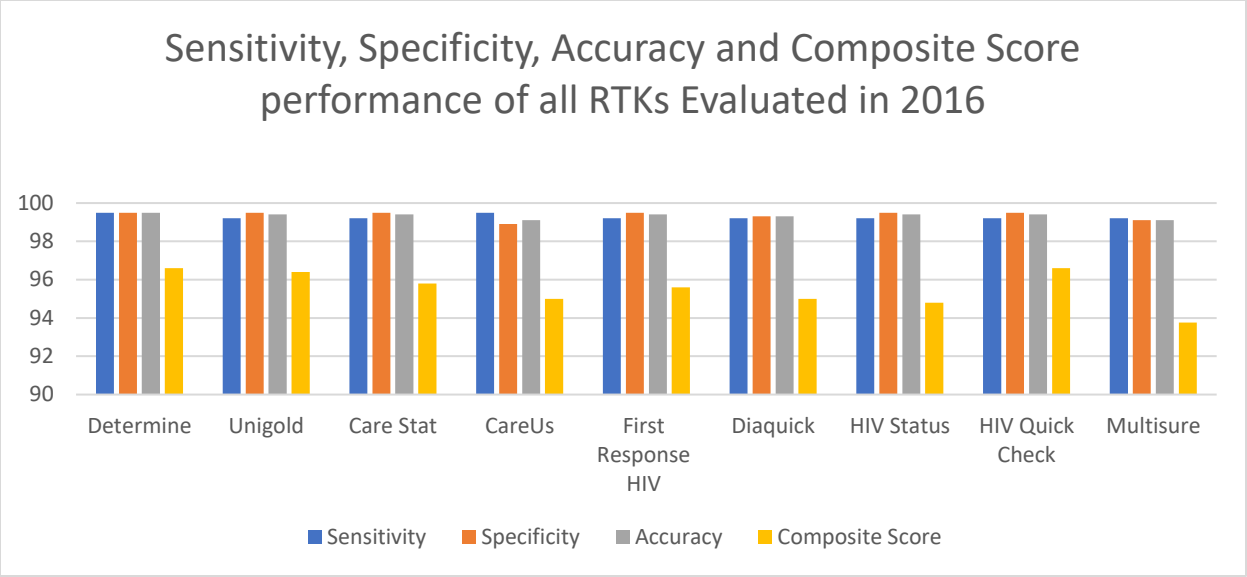

Figure 1

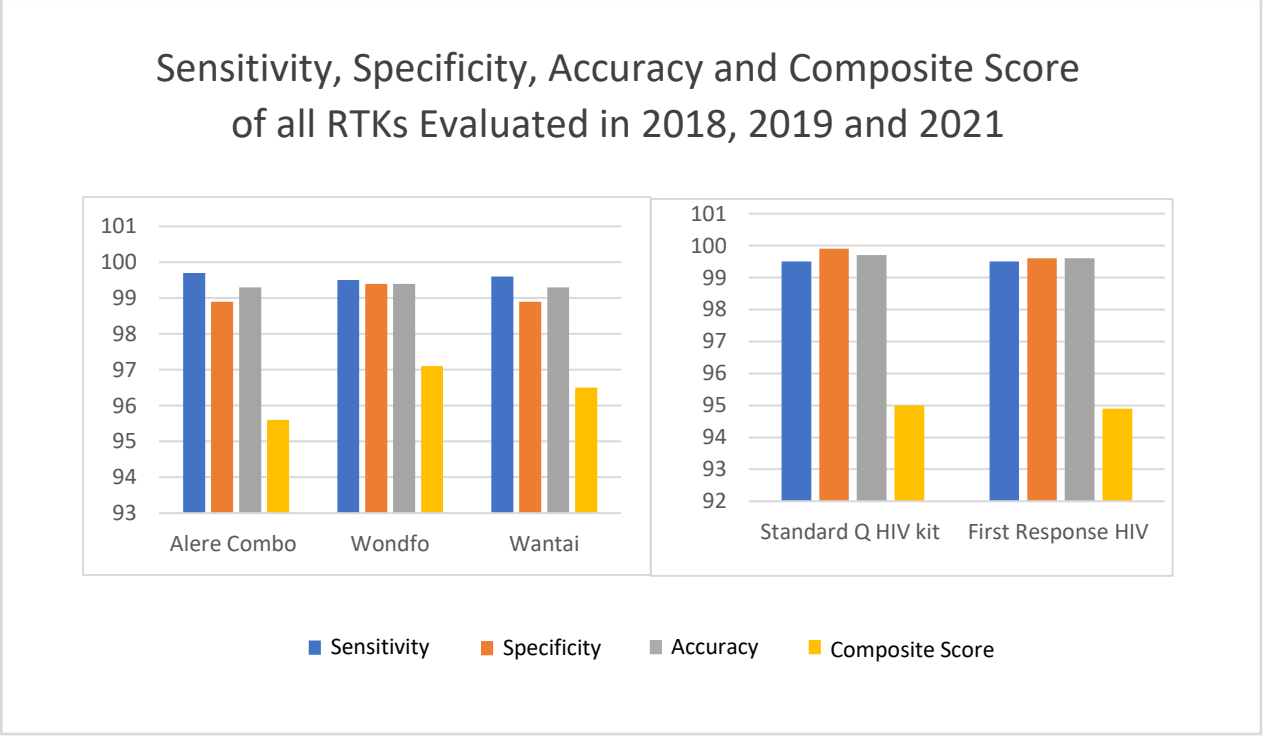

Figure 2

7. Discussion

For several years, different efforts have been made to evaluate more HIV Rapid Test Kits (RTKs) with a view to integrating them into existing national algorithm. However, since 2016, there has been no process to update the algorithm; and this has limited the use of validated RTKs available within the country.

Harmonizing the evaluation of various RTKs into one single national algorithm will help support HTS activities, achieve the goal of taking forward the fight against HIV/AIDS, expand market choices for available RTKs, ensure that choice of RTKs for HIV testing services is based on scientific evidence and useful for procurement. Availability of national algorithm also streamline and standardize the utilization of RTKs for HTS.

One good observation from previously validated RTKs which are used to update the available national algorithm is that all the RTKs exhibited similar laboratory performance characteristics. From the performance characteristics, it was observed that some RTKs could comfortably be deployed for both screening (first line) and confirmation (second line) test kits.

8. Recommendations

8.1 Algorithm.

The recommended National Testing Algorithm for HIV following critical review and analysis of all evaluation reports and performance of all evaluated RTKs are as follows:

Table 1: Algorithm Table

First Line (Screening Kit)	Second Line (Confirmatory)	Tie Breaker
Alere HIV Combo Determine	Standard Q First Response Diaquick CareStart CareUs Unigold	 HIV Status Multisure Stat Pak
	Multisure	Stat Pak HIV Status
	HIV Status	Stat Pak Multisure
Unigold	Standard Q First Response Diaquick CareStart CareUs Determine	Multisure HIV Status Stat Pak
	Multisure	Stat Pak HIV Status
	HIV Status	Stat Pak Multisure

First Line (Screening Kit)	Second Line (Confirmatory)	Tie Breaker
HIV Quick Check	Standard Q First Response Diaquick CareStart CareUs Unigold Determine	Multisure HIV Status Stat Pak
	Multisure	Stat Pak
Wondfo Wantai	Standard Q First Response Diaquick CareStart CareUs Determine Unigold	Multisure HIV Status Stat Pak
	Multisure	Stat Pak HIV Status
	HIV Status	Multisure Stat Pak
First Response Standard Q	Diaquick CareStart CareUs Unigold Determine	Multisure HIV Status Stat Pak
	Multisure	Stat Pak HIV Status
	HIV Status	Stat Pak Multisure

8.2 ***Notes on Algorithm:***

- *RTKs used as first line test **MUST** not be repeated for confirmation test (second line) for the same specimen.*
- *RTKs used for confirmation **MUST** not be repeated as tie breaker for the same specimen.*

8.3 The available national algorithm **SHOULD** be reviewed and updated at least every Five years in order to accommodate new technologies.

8.4 The performance of all RTKs in the algorithm **SHOULD** be monitored regularly and remedial action(s) taken if required.

8.5 This algorithm **SHOULD** be widely disseminated across all stakeholders at all levels.

9. Conclusion

This algorithm for all practical purposes and integration of the two earlier algorithms with the addition of subsequently validated RTKs showed comparable characteristics. The algorithm if properly adhered to by all HTS will tremendously help in intervention activities for HIV/AIDS in Nigeria.

REFERENCES

1. Federal Ministry of Health Report on Laboratory Evaluation of Amethyst HIV 1 & 2 Test Kit (saliva cassette). 2016; pp 12
2. Federal Ministry of Health Report on Laboratory Evaluation of Alere HIV Combo (AHC) Rapid Test Kit. 2018; pp3.

ANNEXURE

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List of Stakeholders Present at HIV RTKs Harmonization Meeting June 8-9, 2021.

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