

Rapid HIV Diagnostic Algorithm (rHIVda) for the Philippines

By the Health Technology Assessment Study Group – Health Policy Development and Planning Bureau

KEY MESSAGE

- The Philippines has seen an increase in new cases of human immunodeficiency virus (HIV) infection from 2008 to 2017. A faster and more accurate HIV testing method for early detection of the infection is desirable to potentially reduce further spread of the disease.
- The HIV-1 Western blot, a confirmatory test still included in the current HIV diagnostic algorithm in the Philippines, is no longer recommended by the World Health Organization (WHO) and the Center for Disease Control (CDC)/Association of Public Health Laboratories (APHL) due to evidence of false positive or indeterminate results early in the course of HIV infection.
- The WHO currently recommends the development of a nationally validated testing algorithm for HIV diagnosis.
- The rapid HIV diagnostic algorithm (rHIVda), an algorithm proposed by the Disease Prevention and Control Bureau (DPCB) of DOH, National Reference Laboratory-San Lazaro Hospital-STD/AIDS Cooperative Central Laboratory (NRL-SLH/SACCL), and the HIV National Reference Laboratory of Australia, includes rapid diagnostic tests (RDTs) that have shown comparable specificity and sensitivity and a shorter turnaround time compared with Western blot.
- The target population for rHIVda and the eligible population for the PhilHealth Outpatient HIV/AIDS Treatment (OHAT) package are different. rHIVda may be performed on both the general and key population while OHAT package is only intended for confirmed HIV/AIDS patients by SACCL or RITM.

CONTEXT

Burden of HIV

- The number of newly diagnosed cases of HIV in the Philippines was found to increase, with 1 new case per day in 2008 to 30 new cases per day in 2017¹.
- The HIV incidence rate for individuals 15 to 49 years old was 20 (95% CI 17-24) per 100,000 population in the year 2016².
- In 2016, the estimated number of people living with HIV (PLHIV) in the Philippines was 56,000 (51,00 to 62,000), but only 67% (38,000) are estimated to know their status⁽²⁾. With the reported increasing trend, there is a need for early identification of HIV cases.
- According to the World Health Organization (WHO), some reports show that HIV misdiagnosis rate is as high as 10.5%. To address this, WHO advised countries to follow their newly published guidelines on HIV Testing Services (HTS) and use nationally validated testing algorithms to improve the quality of services^{3,4}.

Policies and Service Coverage

- In response to the heavy burden of HIV/AIDS, the Department of Health (DOH) has issued a policy on the use of antiretroviral therapy (AO 2014-0031)⁵ and on the conduct of HTS in health facilities (AO 2017-0019)⁶.
- PhilHealth, on the other hand, has developed the Outpatient HIV/AIDS Treatment Package (OHAT) in 2010, which was revised last 2015^{7,8}.
- The current OHAT package, primarily for maintenance and monitoring of confirmed HIV cases by SACCL or RITM, covers drugs, laboratory examinations based on treatment guidelines, (i.e., Cluster of Differentiation 4 [CD4] level determination test, viral load, and test for monitoring of antiretroviral [ARV] drugs toxicity), and professional fees of health care providers.



Moving Forward

- WHO reports that the use of RDTs at the point of care has been an important strategy to expand access, increase the return of same-day results, and enable immediate linkage and follow-up. This is aligned with one of the overarching goals of HTS, which is to reduce HIV transmission and HIV-related morbidity and mortality³.
- This year, the National HIV/AIDS and STI Prevention and Control Program (NASPCP) of the Department of Health introduced the use of rapid HIV diagnostic algorithm (rHIVda) as the new HIV confirmatory test in the Philippines, replacing Western blot⁹.
- An administrative order that will provide implementation policies and guidelines for rHIVda is currently being proposed.

COMPARISON OF THE CURRENT HIV TESTING ALGORITHM AND THE PROPOSED rHIVda

Current National HIV Testing Diagnostic Algorithm in the Philippines

- The current HIV testing diagnostic algorithm in the Philippines (Figure 1) include screening test from referring labs⁹.
- A reactive result from the screening test will be sent to SACCL for confirmatory testing, where 2 parallel screening tests are performed.
- A reactive result on either of these tests will then require Western blot and/or nucleic acid test as supplemental confirmatory tests.

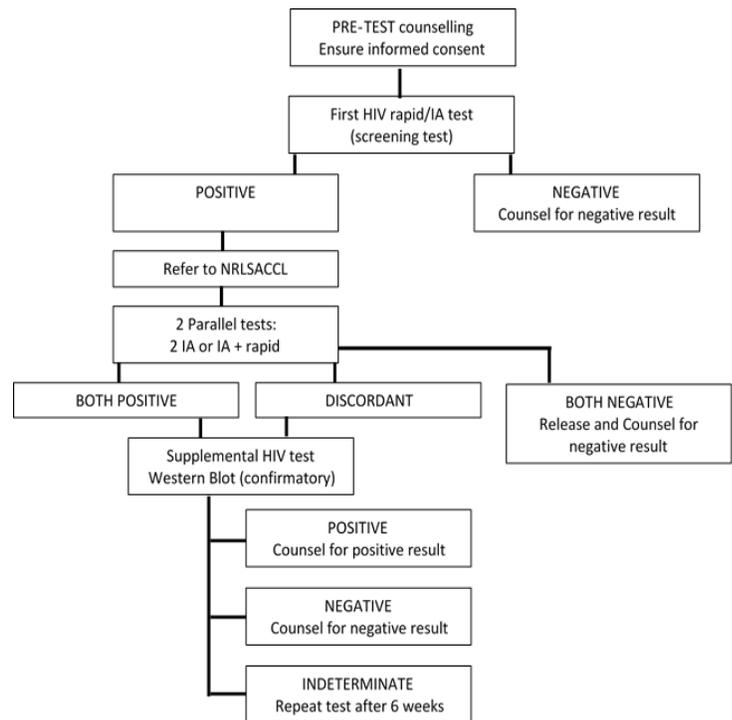


Figure 1. Current National HIV Testing Diagnostic Algorithm (Telan, 2018)

Proposed Rapid HIV Testing Diagnostic Algorithm (rHIVda) for the Philippines

- The Disease Prevention and Control Bureau (DPCB) of DOH, National Reference Laboratory-San Lazaro Hospital/STD AIDS Cooperative Central Laboratory (NRL SLH/SACCL), and the HIV National Reference Laboratory of Australia has conducted the research study to develop a rHIVda for the Philippines⁹.
- rHIVda (Figure 2), includes 2 immunoassay tests and 3 RDTs for local validation of sensitivity and specificity on general and key population in the country⁹.
 - The key population includes men who are having sex with men, people in prisons and other closed settings, people who inject drugs, sex workers, and transgender men and women⁹.
 - Selected test kits are as follows:
 - Immunoassay tests
 - Sysmex Ag-Ab (CMIA- 4th generation)
 - Vidas HIV Duo Ultra (ELFA- 4th generation)

- RDTs
 - SD Bioline HIV Ag-Ab cassette
 - Alere Determine HIV ½
 - Geenius HIV ½ Confirmatory Assay Kit
- The combination (SD Bioline + Determine + Geenius) was validated using the false positive samples referred to NRL and have resulted to 100% specificity.
- Further studies will be undertaken to validate the sensitivity and specificity of the combination of immunoassays (IAs) and RDTs on general population. Furthermore, the proposed algorithm is subject to change depending on its performance through time and the availability of new technology in the market⁹.

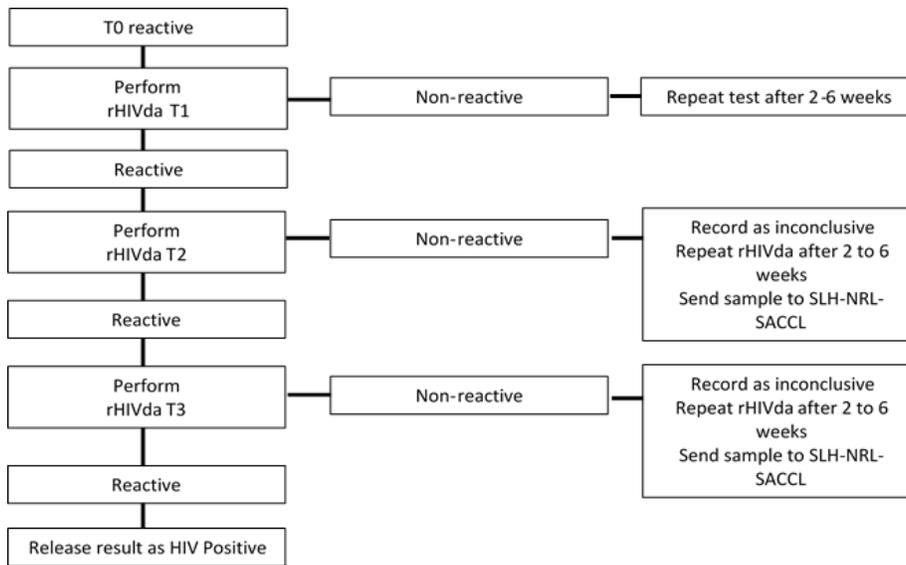


Figure 2. Proposed algorithm of rHIVda Confirmatory Testing (Telan, 2018)

The following tests are used in rHIVda Confirmatory Testing for NRL-SLH/SACCL:

- T1- Sysmex HISCL HIV Ag+Ab Assay Kit
- T2- Vidas HIV Duo Ultra or SD HIV-½ 3.0 or Alere Determine HIV ½
- T3- Geenius HIV ½ Confirmatory Assay Kit

Alignment of the Current and Proposed Algorithm to WHO recommendations

- WHO recommends the following in developing an algorithm³:
 - Recommendation 1: HIV testing services may use combinations of RDTs or combinations of RDTs/enzyme immunoassays (EIAs)/supplemental assays rather than EIA/Western blot combinations.
 - Recommendation 2: Three different serological assays that do not share the same false reactivity must be included in the algorithm.
 - Recommendation 3: Among the serological assays, first test must be the most sensitive of the three. Succeeding tests, on the other hand, must have superior diagnostic specificity.
- Table 1 summarizes the description of the current and proposed algorithm against WHO recommendations. It illustrates the greater adherence of the proposed algorithm than the current algorithm.

Table 1. Comparison of the Current and Proposed Algorithm against the WHO Recommendations

WHO recommendations	Current algorithm		Proposed algorithm	
Recommendation 1: Combination of RDTs or RDTs/EIAs	Western blot as supplemental confirmatory test	✓	A combination of RDTs and EIAs	✓
Recommendation 2: Three different serological assays	Use of 2 IAs or a combination of an IA and an RDT, followed by Western blot	✓	Use of an IA, followed by another IA or an RDT, then confirmed by an immunochromatographic test	✓
Recommendation 3: First test must be the most sensitive and superior specificity of succeeding tests	Unknown	-	First test showed the lowest number of false positives based on the validation study. Third test showed the highest specificity	✓

EIA=enzyme immunoassay; IA=immunoassay; RDT=rapid diagnostic tests.

Source: WHO, 2015; WHO, 2016; Telan, 2018

RAPID DIAGNOSTIC TESTS VERSUS WESTERN BLOT

- Table 2 illustrates the comparison between RDTs and the Western blot based on various parameters sourced from the product information. There is comparable sensitivity and specificity between RDTs and Western blot and a greater reduction in turnaround time using RDTs¹⁰⁻¹⁶.

Table 2. Comparative evaluation of RDTs and Western Blot

Parameter	Rapid Diagnostic Tests			Western Blot
	SD Bioline HIV Ag-Ab cassette	Alere Determine HIV ½	Geenius HIV ½ Confirmatory Assay Kit	
Description	Immunochromatographic assay	Qualitative immunoassay	Immunochromatographic assay	Qualitative immunoassay
Markers that can be detected	Antibodies to all isotypes (IgG, IgM, IgA) specific to HIV Type 1 including subtype-O and HIV Type 2	HIV Type 1 p24 Ag and Ab to HIV Types 1 and 2	Antibodies to HIV Types 1 and 2	Antibodies to HIV 1 and 2
Specimen	Whole blood, plasma/serum	Serum, plasma, capillary (fingerstick) whole blood or venipuncture (venous) whole blood	Fingerstick whole blood, venous whole blood, serum or plasma samples	Serum/Plasma
Sensitivity	100%	99.9%	100%	100%
Specificity	99.87%	99.6%	100%	100%
Turnaround Time	10-20 mins	20-30 mins	20-30 mins	7-21 days



Cost**	PHP 50	PHP 150	PHP 1,500	PHP 3,500
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Note: costs for each test was obtained from the minutes of the meeting on presentation of final draft AO on rapid HIV diagnosis last June 20, 2018
 Ab=antibody; Ag=antigen; HIV=human immunodeficiency virus; Ig=immunoglobulin; RDT=rapid diagnostic test.
 Source: Alere, 2013; Bernard et al., 2014; Bio-rad, 2013; CDC, 2018; J. Mitra and Co., 2015; Standard Diagnostics Inc., 2018; CDC, 2017

Additional International Experience

- The Centers for Disease Control and Prevention (CDC) and Association of Public Health Laboratories (APHL) in the United States recommend that laboratories use 4th generation HIV screening immunoassay as initial test¹⁷.
 - A reactive result shall be followed by an HIV-1/HIV-2 antibody differentiation immunoassay.
 - When the differentiation assay interpretation is negative or indeterminate for HIV-1, an HIV-1 nucleic acid test is recommended.
- The update from CDC’s previous guideline (i.e., guideline which recommended the use of the HIV-1 Western blot and HIV-1 indirect immunofluorescence assay) are due to advances in technology with FDA approving HIV assays that allow detection of HIV sooner after infection than previous immunoassays.

SAFEGUARDS AGAINST ABUSE OF HIV TESTING SERVICES

Population and Frequency of HTS

The current policy on HIV testing services⁶ specify subsets of the population that should undergo routine HIV testing, including a recommendation on the frequency of testing⁶⁻⁸.

Table 3. Comparison of Population Based on Existing and Proposed Policies

Current PhilHealth OHAT Package	DOH-Philippines (AO 2017-0019)
<p>Only confirmed HIV/AIDS cases by SACCL or RITM</p> <p>The package does not state coverage on the costs for screening and/or diagnosis of HIV.</p>	<p>HIV testing should be routinely offered, prioritized for, and promoted to the following:</p> <ul style="list-style-type: none"> • Key populations including adolescents • High risk individuals who have not been tested recently • Partners, infants, and children of PLHIV • Patients showing signs and symptoms consistent with AIDS defining illness • Patients with Sexually Transmitted Infections • Patients with Hepatitis B and C • Patients with undernutrition and not responsive to interventions • All confirmed tuberculosis patients • All pregnant women regardless of risk <p>Frequency of Testing</p> <ul style="list-style-type: none"> • Every 3 months for key populations • Every trimester and at least once while breastfeeding for pregnant women who belong to the key population or a partner of a PLHIV

AIDS=acquired immune deficiency syndrome; AO=Administrative Order; DOH=Department of Health; HIV=human immunodeficiency virus; PLHIV=person living with HIV; STD=sexually transmitted disease.
 Source: PhilHealth, 2015; PhilHealth, 2018; DOH, 2017.

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Information briefs are based on a limited literature search and are not systematic reviews. The intent is to provide a list of sources of the best evidence on the topic that the Health Technology Assessment (HTA) Study Group could identify using all reasonable efforts within the time allowed.

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Research Center for Health System Development (RCHSD)

rlc.rchsd.doh@gmail.com

651-7800 loc 1326

Research Division - Health Policy Development and Planning Bureau
Department of Health

Building 3 2/F San Lazaro Compound, Rizal Avenue, Sta. Cruz, Manila

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