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Original article

# Evaluation of 9 rapid diagnostic tests for screening HIV infection, in Lomé, Togo

*Performance de 9 tests rapides de diagnostic de l'infection VIH, à Lomé, Togo*

A.Y. Dagnra *, S. Dossim , M. Salou , T. Nyasenu , K. Ali-Edje , A. Ouro-Médeli , M. Doufan , A. Ehlan , M. Prince-David

*Centre national de référence pour les tests VIH/IST-PNLS, CHU Sylvanus-Olympio, 08 BP, 8742 Lomé 08, Togo*

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**Abstract**

*Purpose.* – HIV rapid diagnostic tests (RDT) could be greatly contributive for a universal access to HIV diagnosis. However, according to the WHO, these tests need to be assessed before they can be used in routine.

*Method and results.* – We assessed 9 RDT in routine clinical use between 2009 and 2013. The sensitivity and specificity observed for 7 tests were ≥ 99% and ≥ 98%, respectively: FIRST RESPONSE HIV1-2-O PMC Medical, India, GENIE Fast HIV 1-2 and GENIE™ III HIV$^{1/2}$ Bio-Rad, France, HIV TRI-DOT + Ag; J. Mitra, INDIA; SD BIOLINE HIV$^{1/2}$ 3.0 and SD BIOLINE HIV/SYPHILIS DUO Standard Diagnostic, Korea; and VIKIA HIV$^{1/2}$; BioMérieux, France. Two tests had performances inferior to WHO recommendations: INSTI HIV1/2 Biolytical Canada; sensitivity = 97.8% and HEXAGON HIV HUMAN GmbH Germany; specificity = 94.8%.

*Conclusion.* – Seven of 9 RDT had excellent performances. Nevertheless, they can be used only after training staff, and taking into account national algorithm for their safe use.


*Keywords:* Rapid diagnostic test; HIV; Screening

**Résumé**

*Introduction.* – L'utilisation des tests de diagnostic rapide (TDR) du virus de l'immunodéficience humaine (VIH) est importante pour l'accès universel au diagnostic du VIH. Cependant, selon l'Organisation Mondiale de la santé, leur évaluation est indispensable avant la mise à disposition des prestataires.

*Méthode et résultats.* – Nous avons évalué en routine 9 TDR entre 2009–2013. La sensibilité et la spécificité observées pour 7 tests (FIRST RESPONSE HIV1-2-O PMC Medical, India, GENIE FAST HIV 1-2 et GENIE™ III HIV$^{1/2}$ Bio-Rad, France, HIV TRI-DOT + Ag ; J. Mitra, INDIA ; SD BIOLINE HIV-1/2 3.0 et SD BIOLINE HIV/SYPHILIS DUO Standard Diagnostic, Korea ; et VIKIA HIV$^{1/2}$ ; Bio Mérieux, France) étaient respectivement ≥ 99 % et ≥ 98 %. Deux tests avaient des performances en dessous de celles recommandées par l'OMS (INSTI HIV1/2 Biolytical Canada ; sensibilité = 97,8 % et HEXAGON HIV HUMAN GmbH Germany ; spécificité = 94,8 %)

*Conclusion.* – La performance observée pour 7 des 9 TDR est excellente. Cependant, leur utilisation nécessite la formation des prestataires et le respect de l'algorithme national.


*Mots clés :* HIV ; Tests de diagnostic rapide ; Dépistage

* Corresponding author.
*E-mail address:* a.dagnra@yahoo.fr (A.Y. Dagnra).

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## 1. Introduction

The diagnosis of human immunodeficiency virus (HIV) infection is a crucial step in the therapeutic management, blood transfusion safety, and decrease of mother to child virus transmission. Enzyme immunoassays (ELISA) and Western blotting are used for the diagnosis of HIV in Europe and in the United States. Only a few laboratories use these tests in countries with limited resources, which limit universal access to HIV testing. The introduction of rapid diagnostic tests (RDTs) in these countries over the past 15 years has significantly increased access to HIV diagnosis in many countries [1,2]. This is because RDT requires neither highly technical nor additional laboratory equipment. Thus they can be performed by personnel without any qualification in laboratory techniques. However, as with ELISA, RDTs should be regularly assessed because of genetic diversity, especially in sub-Saharan Africa, and this may have an impact on their performance; strains used to manufacture these tests are those commonly encountered in the Northern countries [3–6]. It is thus recommended to regularly assess RDTS and systematically evaluate new tests before introducing them in national algorithms. In Togo, the HIV diagnosis algorithm includes 3 tests used consecutively: a first test called screening test (ELISA or RDT), a second test called confirmation test (RDTs are always discriminating) which is used when the first test is positive, and a third test (Western or dot blot) in case of discordant results for the first 2 tests. The patient is considered as HIV-negative if the first test is negative; he is considered as HIV-positive if the first 2 tests are positive.

We report the performance of 9 RDTs for the diagnosis of HIV, in Togo.

## 2. Materials and methods

The study was conducted at the national reference center for HIV/STI testing in Lome (NRC/HIV/STI/NACP), Togo. One of the laboratory's activities, required by the Ministry of Health, is to evaluate RDTs. The samples used for test evaluation were collected in the same laboratory and stored at −20 °C. They were harvested from patients coming for voluntary testing, or patients suspected of HIV infection according to the criteria defining the WHO AIDS stage. The following tests (Table 1) were evaluated: FIRST RESPONSE HIV1-2-O test card (PMC Medical, Nani Daman, India), 1-2 GENIE Fast HIV and HIV$^{1/2}$ GENIETM III (Bio-Rad, Marnes-la-Coquette, France), HEXAGON HIV (HUMAN GmbH- 65205 Wiesbaden - Germany), HIV TRI-DOT + Ag (J. Mitra & Pvt Ltd. New Delhi-110-India Co.), INSTI HIV-1/2 (bioLytical, Canada). SD BIOLINE HIV-1/2 3.0 and SD BIOLINE HIV/SYPHILIS DUO (Standard Diagnostics, Inc., Yongin-si, Kyonggi-do, Korea) and VIKIA HIV$^{1/2}$ (BioMérieux, Marcy-Étoile, France). All the evaluated tests were third generation based on recombinant HIV antigens except for the Ag + TRI-DOT test which was a 4th generation based on recombinant antigen and monoclonal antibodies for the detection of the P24 antigen (Table 1). SD BIOLINE HIV/SYPHILIS DUO can detect HIV and syphilis, but the assessment in this study concerned only HIV testing. The tests were performed according to the manufacturer's protocol. Two reference tests were used to assess the performance of RDTs; an enzyme immunoassay, Vironostika HIV Uniform II Micro ELISA (BioMérieux, Geneva, Switzerland), and a combined test antigen/antibody systematically performed on all samples: if the test was negative, the sample was considered as negative and included as such for evaluation; a dot blot assay, INNO-LIATM HIV I/II Score (Innogenetics NV Belgium) was performed to confirm all positive ELISA results. If the test was positive, the sample was considered as positive and included for evaluation. Two groups of sample were used for the evaluation: HIV-negative samples (Vironostika negative) and positive samples (INNO-LIA Vironostika and positive). Five positive HIV-2 samples were included in the group of HIV-positive samples for the evaluation of each test. The reference tests (INNO-LIA and Vironostika) and evaluated tests were systematically retrieved in case of discordant results between reference tests and evaluated tests, to avoid the impact of sample preservation on the results. The results of each RDT were compared to the results of reference tests to determine the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The Epi-info software was used to determine the confidence interval (CI) at 95%.

## 3. Results

The evaluations were made between 2009 and 2013. Samples were collected from the population with the following characteristics: 65% of patients were < 40 years of age, 54.6% were female patients, and 20% to 23.6% depending on the year had already been tested in the previous 2 years. Between 149 and 310, samples were included in the study depending on the number of available tests (Table 2). The PPV was 100% for the following tests, INSTI HIV-1/2, GENIE IIITMHIV1/2 VIKIA HIV1/2 and SD BIOLINE HIV/SYPHILIS DUO. The NPV was 100% for HEXAGON HIV, SD BIOLINE HIV1/2 3.0, TRI-DOT Ag, GENIE Fast, SD BIOLINE HIV/Syphilis HIV DUO and VIKIA. The sensitivity of SD BIOLINE HIV1/2 3.0 was 100% for the 98 HIV-1 or HIV-2 positive samples tested (Table 2). The INNO-LIA test results for these 98 samples revealed HIV-1 ($n = 93$) and HIV-2 ($n = 5$) infection. The SD BIOLINE HIV1/2 3.0 result for 12 (12.2%) samples positive for HIV-1 and HIV-2 (double profile) which could mimic HIV-1/HIV-2 coinfection. The intensity among bands was not similar in case of dual reactivity; it was very high for the type of virus involved and very low (pale) for false positivity. This possibility was described in the package notice. The same observations were made for the HIV1-2-O FIRST RESPONSE test for 9 (8.8%) of the 102 positive samples evaluated.

Five false negative results (Table 3) were recorded for 3 tests: INSTI HIV-1/2 ($n = 2$), FIRST RESPONSE HIV1-2-O ($n = 2$), and GENIETM HIV$^{1/2}$ ($n = 1$). The INNO-LIA test allowed classifying these 5 samples as 4 samples positive for HIV-1 and 1 sample positive for HIV- 2. All the tests detected 5 samples as positive for HIV- 2 except for INSTI HIV1/2 and-O HIV1-2 FIRST RESPONSE for which one sample was falsely negative. The reactivity of the FIRST RESPONSE HIV1-2-O test for this

Table 1
Characteristics of HIV rapid diagnostic tests.
*Caractéristiques des tests évalués pour le diagnostic rapide du VIH.*

| Name | Sample | Storage (°C) | Discriminating HIV1/HIV2 | Composition | Volume (microliter)[d] | Single test cost (US $)[f] |
|---|---|---|---|---|---|---|
| HEXAGON HIV | Serum, plasma, whole blood | 2–30 | Yes | gp41, p36, p24 | 20[a]; 10[b] | 3.00 |
| FIRST RESPONSE HIV1-2-O | Serum, plasma, whole blood | 4–30 | Yes | gp41, p36, p24 | 20[a]; 10[b] | 1.41 |
| SD BIOLINE HIV-1/2 3.0 | Serum, plasma, whole blood | 2–30 | Yes | gp41, p36, p24 | 20[a]; 10[b] | 1.00 |
| HIV TRI-DOT + Ag | Plasma, serum | 2–8 | Yes | gp36, gp41, gp120, p24, anti-p24 antibody | Not specified[c] | 1.82 |
| GENIE™ III HIV1/2 | Serum, plasma, whole blood | 2–30 | Yes | Not specified | 25 | NP |
| INSTI VIH1/2 | Serum, plasma, whole blood | 2–30 | No | gp41, gp36 | 50 | NP[e] |
| GENIE FAST HIV 1-2 | Serum, plasma, whole blood | 2–30 | No | gp41, gp120, gp36 | 80 | 2.25 |
| SD BIOLINE HIV/SYPHILIS DUO | Serum, plasma, whole blood | 2–30 | No | gp36, gp41 | 20[a]; 10[b] | 1.75 |
| VIKIA HIV1/2 | Serum, plasma, whole blood | 4–30 | No | gp36, gp41 | 75 | 0.78 |

HIV: human immunodeficiency virus.
[a] Whole blood.
[b] Serum or plasma.
[c] A plastic pipette is provided with the kit; 3 drops of plasma or serum are required for the test.
[d] Required sample volume for the test.
[e] Cost not available.
[f] Single test cost in USD, 1 USD = 500 FCFA. Single test cost of national providers.

HIV-2 positive sample was extremely low and at the threshold of visibility. The INNO-LIA test electrophoretic profile of this sample was p24 and gp36positive.

## 4. Discussion

This was the second assessment of its kind in Togo. The first was performed in 2002 on 3 RDT and 5 ELISA [7]. This study was made only on RDT. Using RDTs can increase the number of patients tested and allow access to testing in areas without any laboratory [8]. The diagnosis of HIV infection is based on a strategy using a combination of at least 2 RDTs in most resource-limited countries. In Togo, HIV diagnosis for the prevention of mother to child transmission (PMTCT) has relied on RDT since 2010, performed by midwives, birth attendants, and health centers midwives. This allows the country to have over 500 PMTCT centers; the availability of a laboratory is no longer a limiting factor for the creation of PMTCT centers. This also allowed shortening the delay before results, in turn improving the rate of result withdrawal for screened patients.

We observed that 7 of the 9 RDT used were efficient compared to the results of benchmark tests. The INSTI test had a sensitivity of 97.8%, below the sensitivity recommended by the WHO. But this test was reported to have a sensitivity of 99% [9] for the diagnosis of HIV-1, in patients predominantly infected with subtype B treated by antiretroviral therapy. Some Canadian data also suggest that it is more effective at detecting patients in seroconversion than other tests commonly used in laboratories [10–12]. These inconsistent results justify a preliminary evaluation of all diagnostic tests prior to use in a given region, because of the genetic diversity of HIV. However, other factors may be the cause of these conflicting results: errors in batch manufacture, transport and storage conditions, and particularly for reagents exposed to high temperatures for too long, even for tests that can be stored at room temperature.

We observed that SD BIOLINE HIV1/2 3.0 and FIRST RESPONSE HIV1-2-O could give a dual HIV-1/VHI-2 positive profile for samples positive for 1 type of virus. These possibilities are mentioned in the test indications, but routine reading can be a real problem in case of true coinfection, as observed in West Africa.

The routine use of the 7 effective RDTs assessed in this study for the national algorithm of Togo will depend on several factors: type of sample (whole blood or serum/plasma), completion time, time before results, discriminating effectiveness, and storage temperature. Whole blood should be used for early screening strategy in PMTCT and peripheral centers. Whole blood can be used with all tests except for the TRI-DOT + Ag. All the tests can be stored at room temperature except for the TRI-DOT + Ag. Nevertheless, in the West African region including Togo, room temperature can exceed 40 °C during the dry season. The effectiveness of these tests may decrease in these conditions.

Three of the 7 RDTs could not discriminate between HIV-1 and HIV-2 (Table 1). Both types of virus co-circulate in West Africa and identifying the type are required for the selection of antiretroviral drugs. Therefore, the non-discriminating tests should be used with a discriminating test in this region, either as first-line or as a confirmation test.

It should be noted that our national algorithm recommends using at least 2 tests to confirm HIV infection. In any case, training users in strict accordance with the algorithm defined by the national program for the prevention of HIV/AIDS, and regularly organizing an external quality assessment are essential for the quality of results.

All the evaluated tests come in single kits. This presentation is better than the one of DETERMINED (Alere, Israel),

Table 2
Performance of HIV rapid diagnostic tests.
*Performance des tests évalués pour le diagnostic rapide du VIH.*

| Name | Year of evaluation | Number of samples | True positive | False positive | False negative | True negative | Sensibility % (CI) | Specificity % (CI) | PPV % (ICCI | VPN % (IC) |
|---|---|---|---|---|---|---|---|---|---|---|
| HEXAGON HIV | 2009 | 149 | 52 | 5 | 0 | 92 | 100 (91.4–100) | 94.8 (87.8–98.1) | 91.2 (80.0–96.7) | 100 (95–100) |
| FIRST RESPONSE HIV1-2-O | 2010 | 206 | 102 | 1 | 2 | 101 | 99 (93.9–99.9) | 98.1 (92.5–99.7) | 98.1 (92.5–99.7) | 99 (93.9–99.9) |
| SD BIOLINE HIV-1/2 3.0 | 2011 | 200 | 98 | 2 | 0 | 100 | 100 (95.3–100) | 98 (92.4–99.7) | 98 (92.3–99.7) | 100 (95.4–100) |
| HIV TRI-DOT + AG | 2012 | 198 | 93 | 2 | 0 | 103 | 100 (95.1–100) | 98 (90.8–99.2) | 96.9 (90.5–99.2) | 100 (95.4–100) |
| GENIE$^{TM}$ III HIV$^{1/2}$ | 2012 | 200 | 99 | 0 | 1 | 100 | 99 (93.8–99.9) | 100 (95.4–100) | 100 (95.3–100) | 99 (93.8–99.9) |
| INSTI VIH1/2 | 2009 | 192 | 90 | 0 | 2 | 100 | 97.8 (91.6–99.6) | 100 (95.4–100) | 100 (94.9–100) | 98 (92.4–99.7) |
| GENIE FAST$^{TM}$ HIV 1-2 | 2012 | 200 | 100 | 2 | 0 | 100 | 100 (95.4–100) | 98 (92.3–99.7) | 98 (92.4–99.7) | 100 (95.3–100) |
| SD BIOLINE HIV/SYPHILIS DUO | 2013 | 310 | 107 | 0 | 0 | 203 | 100 (95.7–100) | 100 (97.7–100) | 100 (95.7–100) | 100 (97.7–100) |
| VIKIA HIV$^{1/2}$ | 2013 | 200 | 100 | 0 | 0 | 100 | 100 (95.4–100) | 100 (95.4–100) | 100 (95.4–100) | 100 (95.4–100) |

Table 3
Profile of samples with discordant results with reference tests.
*Profil des échantillons ayant des résultats discordants avec les tests de référence.*

| Samples | Reference tests | Tests evaluated | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | HEXAGON HIV | INSTI VIH1/2 | FIRST RESPONSE HIV1-2-O | SD BIOLINE HIV-1/2 3.0 | HIV TRI-DOT + AG | GENIE FAST$^{TM}$ HIV 1-2 | GENIE$^{TM}$ III HIV$^{1/2}$ | SD BIOLINE HIV/ SYPHILIS DUO | VIKIA HIV$^{1/2}$ |
| HT09-89 | N | P | N | N | N | N | N | N | – | – |
| HT09-102 | N | P | N | P | N | N | N | N | – | – |
| HT09-831 | N | P | N | N | N | N | N | N | – | – |
| HT09-1507 | N | P | N | N | N | N | N | N | – | – |
| HT09-2320 | N | P | N | N | N | N | N | N | – | – |
| HT11-102 | N | –* | – | – | P | – | – | – | – | – |
| HT11-766 | N | – | – | – | P | N | N | N | – | – |
| HT12-010 | N | – | – | – | – | P | N | N | N | N |
| HT12-154 | N | – | – | – | – | P | N | N | N | N |
| HT12-346 | N | – | – | – | – | N | P | N | N | N |
| HT12-900 | N | – | – | – | – | N | P | N | N | N |
| HT09-521 | P | P | N | P | – | – | – | – | – | – |
| HT09-826 | P | P | N | P | – | – | – | – | – | – |
| HT10-1025 | P | – | – | N | P | – | – | – | – | – |
| HT10-1056 | P | – | – | N | P | – | – | – | – | – |
| HT12-015 | P | – | – | – | – | P | P | N | P | P |

N: negative result; P: positive result; –*: sample not tested.

which comes as a strip, because it reduces the risk of contamination during handling, especially by staff without any training in laboratory techniques; it also offers more safety for sample identification.

The results obtained in this study for SD BIOLINE SYPHILIS HIV/concerned only HIV testing. The test allows testing for HIV and syphilis, but our results cannot be extended to the test effectiveness for the screening of syphilis.

## 5. Conclusion

The results of our evaluation show that 7 RDT can be used in the Togo national algorithm. We suggest that these 7 tests be used as follows:

- test 1 (test): SD BIOLINE HIV/SYPHILIS DUO VIKIA HIV or HIV GENIE FASTTM 1-2;
- test 2 (confirmation test): $^{1/2}$ GENIETM III HIV, HIV TRIDOT + AG, SD BIOLINE HIV1/2 3.0 or FIRST RESPONSE HIV1-2-O.

## Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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