Comparative evaluation of 36 commercial assays for detecting antibodies to HIV*

I. Van kerckhoven,[1] G. Vercauteren,[1] P. Piot,[2] & G. van der Groen[3]

Summarized are the results of an assessment of the major operational characteristics of 36 commercially available assays for detection of antibodies to human immunodeficiency virus type 1 (HIV-1) and/or type 2 (HIV-2). For this purpose, 20 enzyme-linked immunosorbent assays (ELISAs), 11 simple immunoassays with visual reading, four supplemental assays, and one discriminatory assay were assessed using a panel of 537 sera (65% of which were of African, 26% of European, and 9% of South American origin); the prevalence of HIV-1 was 39.1% and of HIV-2, 15.7%.

The following operational parameters of the assays were investigated: ease of performance; suitability for use in small blood collection centres; sensitivity and specificity; positive predictive values at different prevalences; inter-reader variability for simple assays whose results were read visually; the proportion of indeterminate results; and, for some of the ELISA assays, δ-values, as quantitative measures of sensitivity and specificity. The results will be of use to health policy decision-makers, managers of national AIDS prevention and control programmes, directors of blood banks, and laboratory specialists in the selection of appropriate HIV antibody assays.

Introduction

The first enzyme-linked immunosorbent assays (ELISAs) for antibodies to human immunodeficiency virus (HIV) were manufactured by coating purified HIV lysates onto the surface of microtitration plates or beads (first-generation assays). More recently, ELISAs have been developed that use as antigens either HIV-recombinant polypeptides or synthetic peptides (second-generation assays). However, ELISAs require 1.5–3.5 hours to perform and need sophisticated and expensive equipment. This makes such assays technologically inappropriate for use in small laboratories in developing countries. More recently, simple agglutination and immunodot assays for HIV have been developed that do not require much equipment and that yield results after a few minutes (*1*).

HIV-2 infection, which was identified first in West Africa in 1985 (*2*), has now been found in various areas of the world (*3–15*). Incomplete cross-reactivity between HIV-1 and HIV-2 antibodies necessitates the use of combined screening assays with acceptable sensitivity and specificity for both viruses (*16*).

Even with HIV antibody screening assays that have excellent sensitivity and specificity, false-positive test results cannot be ruled out, especially when used in populations with a low prevalence of HIV antibodies (*17*). This emphasizes the need for supplemental or confirmatory testing. The most commonly used supplemental test is the Western blot, but second-generation supplemental assays have recently been developed that are based on highly purified recombinant proteins and/or synthetic peptides (*18*).

This article presents the results of an assessment of the major operational aspects of 36 commercial HIV antibody assays that were evaluated between 1988 and 1990. Among the factors considered were the ease of performance, suitability for use in small blood collection centres, sensitivity and specificity with European and African sera, inter-reader variability for simple assays whose results are read visually, and determination of δ-values, as quantitative measures of the sensitivity and specificity of the ELISAs.

Materials and methods

Sera

In the evaluation of assays for the detection of antibodies to both HIV-1 and HIV-2, a panel of 537 human sera was tested, 65% of which were of African, 26% of European, and 9% of South American origin. For assays that detected only antibodies to HIV-1 or HIV-2, sera in the panel that contained antibodies to HIV-2 or HIV-1, respectively, were omitted. The prevalence of HIV-1 was 39.1% and of HIV-2, 15.7%. All samples were stored frozen (−20 °C) in aliquots of 100 µl and thawed at least once, but four times at most.

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* From the Department of Microbiology, Institute of Tropical Medicine, Nationalestraat 155, 2000 Antwerp, Belgium.

[1] Research worker.

[2] Director.

[3] Deputy Director. Requests for reprints should be sent to Dr van der Groen.

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Types of assays

The characteristics of the 36 commercial HIV antibody assay kits, including 20 ELISAs, 11 simple assays, four supplemental assays and one discriminatory assay, as well as of the reference tests, are summarized in Table 1. Of these, 10 ELISAs, five simple assays, one supplemental assay, and one discriminatory assay were designed to detect both HIV-1 and HIV-2 antibodies (combined assays); nine ELISAs, six simple assays, and three supplemental assays were designed to detect only HIV-1 antibodies; and one ELISA was designed to detect only HIV-2 antibodies.

Test performance

The tests were performed according to the manufacturers instructions.

Initially reactive sera were retested once (except with the supplemental assays). Sera that yielded discrepant results were retested twice, and in this instance the outcome of the two tests that agreed determined the overall test result. Simple HIV antibody assays whose readings had to be interpreted visually were read by at least three different persons; the outcome of two tests that agreed was taken to be the final result.

Reference tests

The data obtained using the evaluated tests were compared with the results of two Western blots (HIV-1 Western blot (Du Pont de Nemours), and HIV-2 Western blot (NEW LAV Blot II, Diagnostics Pasteur). The Western blot results were interpreted according to recently revised WHO criteria (*19*), which recommend that HIV-1 or HIV-2 results are considered positive if two of three *env* bands (*env* precursor, external and transmembrane glycoproteins) with or without *gag* and/or *pol* bands are present; a Western blot result is considered negative if no HIV-specific band is present, and indeterminate when it exhibits any band pattern not considered positive.

Operational characteristics

The following performance parameters of the tests were highlighted: sensitivity and specificity of the assays with European and African sera; ease of performance; suitability for use in small blood collection centres; speed of performance; positive predictive values at different HIV antibody prevalences; inter-reader variability for simple assays with visual reading; number of indeterminate results; cost per test; and for some of the ELISA assays, δ-values for the HIV-positive and HIV-negative serum populations.

The ease of performance of a particular assay was assessed as described in the Annex. Tests were defined as very easy, easy or less easy to perform.

The suitability for use in small blood collection centres in developing countries of a particular anti-HIV kit was assessed by taking the performance parameters into consideration as described in the Annex. Tests were defined as very suitable, suitable or less suitable.

Inter-reader variability for the simple assays with visual reading was expressed as the ratio of the number of sera for which test results were differently interpreted by different readers, to the total number of sera tested.

Data analysis

Test sensitivity was expressed as the number of Western-blot-confirmed positive specimens initially detected by the HIV antibody kit under evaluation, divided by the toal number of Western-blot-confirmed positives, multiplied by 100.

Test specificity was expressed as the number of Western-blot-confirmed negative specimens detected by the HIV antibody kit under evaluation, divided by the total number of Western-blot-confirmed negatives, multiplied by 100; initially false-positive sera that yielded two negative results after repeat testing were included.

Determination of the δ-value permits comparison of the efficacy of ELISAs to separate the negative and positive HIV antibody serum populations from the cut-off value, as described by Crofts et al. (*21*) and Maskill et al. (*22*).

The δ-values for the HIV antibody-positive and antibody-negative sample populations were calculated by dividing the mean optical density (OD) ratio ($\log_{10}$) by the standard deviation for each population. OD ratios were calculated by dividing each reading by the relevant cut-off value. The sample to cut-off OD ratios of the initial test results were taken for the Western-blot-positive sera. For the Western-blot-negative sera, the OD ratios of the repeat test results were taken if the ELISA had initially given a false-positive result. The higher the positive ($\delta+$) and negative ($\delta-$) values, the greater the probability that the test will correctly identify antibody-positive and antibody-negative sera, respectively.

Results

The sensitivity and specificity together with the 95% confidence intervals (CIs) for the 36 HIV kits tested are shown in Fig. 1. A total of 15 ELISAs, two simple assays, and four supplemental assays had 100% sensitivity, whereas three ELISAs, three simple assays, and three supplemental assays had 100%

Table 1: **Characteristics of the 36 commercial HIV antibody assay kits evaluated in the study, together with those of the reference tests**

No.	Test name	Manufacturer	Test type[a]	Antigen type[b]	Coating on:[c]	Cost per test (US$)[d]
ELISAs						
A. HIV-1						
1	HIV-TEK G	Sorin Biodemica	i.e.	HL	*U̲*-plate, v8	1.0
2	Enzygnost Anti-HIV Micro	Behringwerke	c.e.	HL	*U*-plate, v16	1.8
3	Ortho HIV ELISA System	Ortho Diagnostic Systems	i.e.	HL	*U̲*-plate, h12	1.8
4	Vironostika Anti-HIV Uni-Form	Organon Teknika	c.e.	HL	*U̲*-plate, h12	2.2
5	Genetic Systems LAV EIA	Genetic Systems	i.e.	HL	*U̲*-plate, v8	1.0
6	Du Pont HIV-1 Recombinant ELISA	Du Pont de Nemours	i.e.	RP	*U̲*-plate, v8	0.9
7	Wellcozyme HIV Recombinant	Wellcome Diagnostics	c.e.	RP	*U̲*-plate, v16	1.5
8	REC VIH-KCO1	Heber Biotec	i.e.	RP	*U*-plate, complete	?
9	HIV-1 *env* Peptide EIA	Labsystems OY	i.e.	SP	*U̲*-plate, v8	3.9
B. HIV-2						
10	Genetic Systems HIV-2 EIA	Genetic Systems	i.e.	HL	*U̲*-plate, v8	1.7
C. HIV-1 + HIV-2						
11	Elavia Mixt	Diagnostics Pasteur	i.e.	HL	*U̲*-plate, v8	2.1
12	Recombinant HIV-1/HIV-2 EIA	Abbott	i.e.	RP	Beads	1.8
13	Anti-HIV-1/HIV-2 EIA ⟨Roche⟩	Hoffmann-La Roche	i.e.	RP	Beads	1.7
14	Wellcozyme HIV-1 + 2	Wellcome Diagnostics	s.e.	RP	*U̲*-plate, v8	1.5
15	Enzygnost Anti HIV-1 + 2	Behringwerke	i.e.	SP	*U*-plate, v16	2.3
16	Biochrom HIV-1/HIV-2 ELISA Modul-test	Biochrom KG	i.e.	SP	*U̲*-plate, v16	0.9
17	Detect-HIV	IAF Biochem International	i.e.	SP	*U̲*-plate, v8	2.5
18	Peptide HIV ELISA	Cal-Tech Diagnostics	i.e.	SP	*U̲*-plate, h6	0.9
19	Vironostika HIV MIXT	Organon Teknika	i.e.	HL/SP	*U̲*-plate, h12	1.8
20	Du Pont HIV-1/HIV-2 ELISA	Du Pont de Nemours	i.e.	RP/SP	*U̲*-plate, v8	1.3
Simple assays[e]						
A. HIV-1						
21	Serodia-HIV	Fujirebio	Aggl.	HL	Gelatine particles	1.1
22	Serion Immuno Tab HIV-1	Serion	Dot	HL	Nitrocellulose (comb)	2.5
23	Recombigen HIV-LA	Cambridge BioScience	Aggl.	RP	Latex particles	3.0
24	Immunocomb	PBS Orgenics	Dot	SP	Plastic card (comb)	2.5
25	Genie HIV-1	Genetic Systems	Dot	SP	Membrane	3.5
26	PATH HIV Dipstick	PATH	Dot	SP	Plastic comb	<1.5
B. HIV-1 + HIV-2						
27	Test Pack HIV-1/HIV-2 Ab	Abbott	Dot	RP	Membrane	4.8
28	Recodot	Waldheim Pharmazeutika	Dot	RP	Nitrocellulose	2.0
29	Immunocomb Bi-Spot	PBS Orgenics	Dot	SP	Plastic card (comb)	4.0
30	Genie HIV-1 and HIV-2	Genetic Systems	Dot	SP	Membrane	3.5
31	HIVCHEK 1 + 2	Du Pont de Nemours	Dot	RP/SP	Membrane	4.0
Supplemental assays						
A. HIV-1						
32	Ancoscreen	Ancos	Blot	HL	Membrane	10.8
33	HIV Western Blot Kit	Organon Teknika	Blot	HL	Nitrocellulose strip	21.0
34	RIBA HIV	Chiron	Blot	RP	Nitrocellulose strip	27.6
B. HIV-1 + HIV-2						
35	INNO-LIA HIV-1/HIV-2 Ab	Innogenetics	Lia	RP/SP	Nylon strip	18.4
Discriminatory assay						
36	PEPTI-LAV 1-2	Diagnostics Pasteur	Lia	SP	Membrane	21.5
Reference tests						
37	HIV-1 Western blot	Du Pont de Nemours	Blot	HL	Nitrocellulose strip	44.5
38	NEW LAV BLOT II	Diagnostics Pasteur	Blot	HL	Nitrocellulose strip	25.6

[a] c.e. = competitive ELISA; i.e. = indirect ELISA; s.e. = sandwich ELISA; Aggl. = agglutination assay; Dot = immunodot assay; Blot = immunoblot assay; Lia = line immunoassay. [b] HL = HIV lysate; RP = recombinant protein; SP = synthetic peptide. [c] *U̲*-plate = microplate with U-bottomed wells; *U*-plate = microplate with flat-bottomed wells; h12, h6 = horizontal strips composed of 12 wells and 6 wells, respectively; v8, v16 = vertical strips composed of 8 wells and 16 wells, respectively. [d] Costs were provided by the distributor of the test in Belgium during the period of the evaluation. The costs may have changed, since the first kits (No. 1, 2, 3, 4, 6, 21, 23, 24 and 34) were evaluated in 1988; kits No. 7, 9, 12, 15, 16, 22, 27, 32 and 35, in 1989; and the remaining kits, in 1990. Costs vary also with the number of tests ordered, and for different countries. [e] Simple assays: non-ELISA HIV-antibody immunoassays with visual reading.

Fig. 1. **Sensitivity and specificity with 95% confidence intervals (see footnotes *a*, *b*, and *c*, Table 2) of the 36 commercial HIV assays, tested on sera of African or European origin. Test No. 1–20: ELISA; No. 21–31: simple HIV immunoassay with visual reading; No. 32–35: supplemental assays; No. 36: discriminatory assay.**

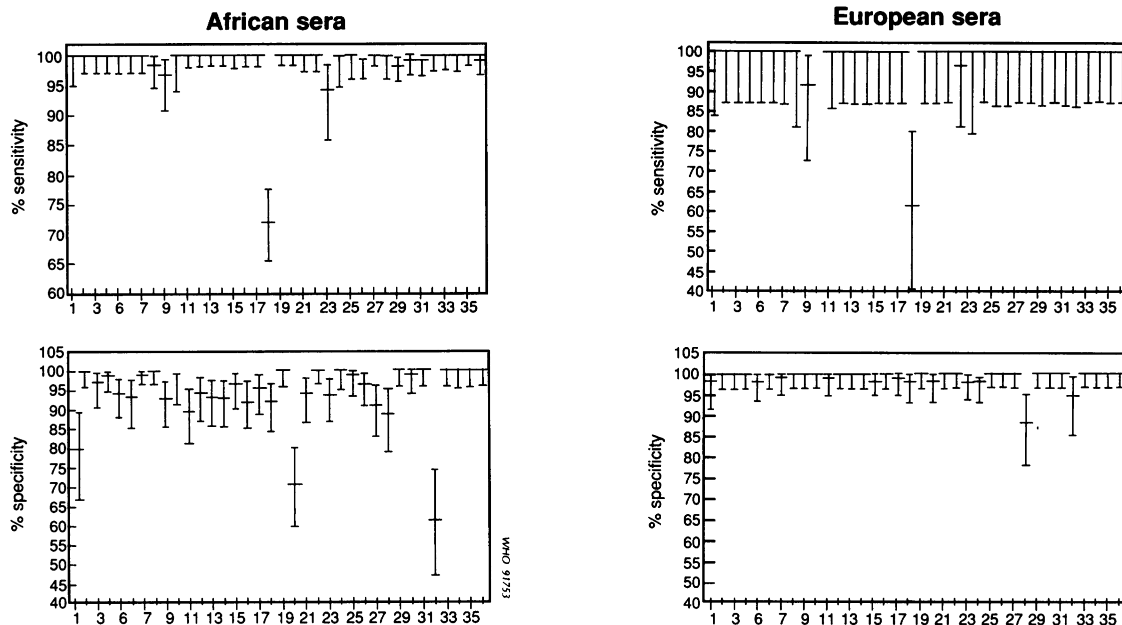

Table 2: **δ-Values for HIV antibody-positive and antibody-negative serum populations and sensitivity and specificity for 12 of the ELISAs tested**

Test No.[a]	Sensitivity (%)[b]	Specificity (%)[c]	δ-Values[d] WB-positive sera	δ-Values[d] WB-negative sera
HIV-1 + HIV-2				
11	100.0 (98.7–100.0)	95.3 (91.3–97.8)	54.33	−2.31
12	100.0 (98.5–100.0)	97.4 (94.1–99.2)	3.78	−1.50
13	100.0 (98.7–100.0)	96.9 (93.4–98.9)	11.30	−2.37
14	100.0 (98.7–100.0)	96.9 (99.3–98.9)	38.51	−1.99
15	100.0 (98.4–100.0)	97.4 (94.0–99.2)	11.28	−2.15
16	100.0 (98.6–100.0)	96.3 (92.5–98.5)	6.20	−1.69
17	100.0 (98.6–100.0)[e]	97.4 (94.0–99.2)	12.65	−2.21
19	100.0 (98.7–100.0)	100.0 (98.1–100.0)	10.10	−2.94
20	100.0 (98.7–100.0)	85.6 (79.8–90.2)	9.34	−0.96
HIV-1				
5	100.0 (98.2–100.0)	96.3 (92.9–98.4)	9.20	−2.13
8	96.6 (93.0–98.6)	100.0 (98.3–100.0)	2.10	−4.14
HIV-2				
10	100.0 (94.0–100.0)	98.6 (95.9–99.7)	17.39	−3.06

[a] See Table 1.
[b] The % sensitivity was calculated by dividing the number of Western-blot-confirmed positive specimens detected initially by the HIV kit under evaluation, by the total number of Western-blot-confirmed positives, and multiplying this by 100.
[c] The % specificity was calculated by dividing the number of Western-blot-confirmed negative specimens detected by the HIV kit under evaluation, by the total number of Western-blot-confirmed negatives, and multiplying this by 100; initially false-positive sera that twice gave a negative result after repeat testing were included in the calculation.
[d] δ-Values for the HIV antibody-positive and antibody-negative samples were calculated by dividing the mean of the $\log_{10}$ sample to cut-off optical density ratios by the standard deviation of each population. WB = Western blot.
[e] Figures in parentheses are the 95% confidence intervals, calculated using data in ref. *20*.

specificity, with both European and African sera.

The δ-values for 12 HIV ELISA kits, as well as their sensitivities and specificities, with 95% CIs, are shown in Table 2.

The major operational characteristics of the 36 assays evaluated are summarized in Table 3.

Discussion

Specificity and sensitivity

Most assays evaluated in the study had excellent sensitivity (Fig. 1). There were essentially no differences between the sensitivities, except for the Peptide HIV ELISA assay (No. 18), whose sensitivity was significantly lower. The specificities were generally somewhat lower than the sensitivities, but only the HIV-TEK G (No. 1), Du Pont HIV-1/HIV-2 ELISA (No. 20), Recodot (No. 28), and Ancoscreen (No. 32) assays had a significantly lower specificity. This arose because of the high number of false-positive results obtained with African sera, which indicates the importance of including such sera in evaluations of HIV antibody kits (*23*).

Recent evaluation of an improved version of the Ancoscreen assay indicates that its specificity is 100%, with 10.8% of results being indeterminate; this modification has improved its ease of performance and suitability for field use.

First- and second-generation assays performed comparably in terms of sensitivity and specificity (Fig. 1 and Table 1).

The sensitivity and specificity of the assays to detect simultaneously antibodies to HIV-1 and HIV-2 were as high as those of the separate assays for HIV-1 or HIV-2.

Delta values (δ-values)

The δ-value provides a statistical estimate of the test sensitivity and specificity and permits differentiation between ELISAs of similar sensitivity and specificity.

In Table 2 positive δ-values reflect the ability of an ELISA to consistently produce high sample/cut-off OD ratios for HIV antibody-positive sera; negative δ-values reflect the ability of the assays to consistently produce sample OD ratios that lie far below the cut-off OD for HIV antibody-negative sera.

Although the sensitivity and specificity of most of the combined ELISAs were not significantly different, there were differences in the δ-values (Table 2). The highest positive δ-values were obtained from the Elavia Mixt (No. 11), and the Wellcozyme HIV-1 + 2 (No. 14). These assays therefore have a larger margin for variation with HIV antibody-positive sera, without producing false negatives, compared with the other assays in Table 2. The Recombinant HIV-1/HIV-2 EIA (Abbott, No. 12) had the lowest positive δ-value, i.e., a less clear separation of the positive sera from the cut-off.

The estimated specificities for nine combined HIV-1 + HIV-2 ELISAs were not significantly different, with the exception of Du Pont HIV-1/HIV-2 (No. 20), which had a significantly lower specificity and the lowest negative δ-value (Table 2). The Vironostika HIV Mixt (No. 19) had the highest negative δ-value. As a result, this assay has a greater margin for variation in test results, without the occurrence of false positives, and this increases confidence in the specificity estimates (Table 2).

Genetic Systems HIV-2 EIA assay (No. 10) had high positive and negative δ-values, indicating a clear separation of positive and negative specimens from the cut-off (Table 2). The newly developed anti-HIV-1/HIV-2 combined ELISAs have δ-values that are comparable with those of the specific HIV-1 ELISAs evaluated (Table 2).

Operational characteristics

There was no significant difference in the sensitivity and specificity of the simple assays, whose results were read visually, and the ELISAs, irrespective of the type of antigens used (Fig. 1). The simple tests were easier to perform and more suitable for use in small blood collection centres, where only a few sera have to be screened (Table 3). For testing large series of sera, i.e., hundreds per day, ELISAs are the most rapid and appropriate method; on the other hand, they require rather expensive equipment which has to be well maintained. The accuracy of the visual reading of simple tests is reflected in the inter-reader variability (Table 3), which ranged from 0.8% to 31.7% for the different assays. The Serodia-HIV (No. 21), Genie HIV-1 (No. 25), PATH HIV Dipstick (No. 26), and Test Pack HIV-1/HIV-2 Ab (No. 27) had the lowest inter-reader variability, while the Recodot and Genie HIV-1 and HIV-2 had the highest.

Supplemental assays

Although the specificity of most of the HIV antibody kits was high, their positive predictive values, especially for populations with a low prevalence of antibodies (0.01%) were low (Table 3), indicating the need for further confirmation of positive screening results. The supplemental assays evaluated in the study exhibited high sensitivities and specificities, except for the Ancoscreen (No. 32), which performed poorly with the African sera. The INNO-LIA HIV-1/HIV-2 Ab test (No. 35) permits simultaneous detection of antibodies to HIV-1 and HIV-2 and scored a lower number of indeterminate results than the classical Western blot assays for HIV-1 or HIV-2.

Table 3: **Comparative evaluation of various operational characteristics of the 36 commercially available assays to determine antibodies to HIV-1 and/or HIV-2, and of the reference test used**

No.[a]	Ease of performance[b]	Time (h. min) for:		Suitability[c]	PPV:[d]		Inter-reader variability (%)[e]	Indeterminate results (%)[f]
		90 sera	1 serum		0.01%	6%		
ELISAs								
A. HIV-1								
1	LE	3.35	3.00	LS	0.1	32.1	NA[g]	NA
2	LE	2.10	1.45	LS	100.0	100.0	NA	NA
3	LE	3.15	2.50	LS	0.5	76.1	NA	NA
4	LE	2.35	2.15	LS	2.0	92.7	NA	NA
5	LE	3.30	2.40	LS	0.3	63.5	NA	NA
6	LE	2.25	2.05	LS	0.3	68.0	NA	NA
7	LE	1.55	1.30	LS	1.1	87.6	NA	NA
8	LE	1.35	1.00	LS	100.0	100.0	NA	NA
9	LE	2.45	2.20	LS	0.3	61.1	NA	NA
B. HIV-2								
10	LE	3.35	2.40	LS	0.7	81.7	NA	NA
C. HIV-1 + HIV-2								
11	LE	4.30	3.05	LS	0.2	57.6	NA	NA
12	LE	2.35	2.20	LS	0.4	71.4	NA	NA
13	LE	2.15	1.40	LS	0.3	67.4	NA	NA
14	LE	2.15	1.45	LS	0.3	67.3	NA	NA
15	LE	2.10	1.40	LS	0.4	71.1	NA	NA
16	LE	2.30	1.45	LS	0.3	63.4	NA	1.0[h]
17	LE	2.30	1.45	LS	0.4	71.2	NA	NA
18	E	2.15	1.10	S	0.2	50.0	18.5	0.2
19	LE	2.05	1.40	LS	100.0	100.0	NA	NA
20	LE	2.25	2.00	LS	0.1	30.7	NA	NA
Simple assays								
A. HIV-1								
21	E	3.00	2.05	S	0.3	67.3	0.8	NA
22	LE	5.10	4.00	LS	100.0	100.0	7.1	1.2
23	VE	1.36	0.06	S	0.2	60.9	6.0	NA
24	VE	2.30	0.35	VS	1.0	86.3	2.8	NA
25	VE	2.35	0.12	VS	1.1	87.5	1.1	0.2
26	E	2.05	0.27	VS	0.6	77.9	1.3	0.0
B. HIV-1 + HIV-2								
27	VE	1.35	0.05	VS	0.2	61.2	1.4	0.0
28	LE	2.25	1.25	LS	0.1	35.6	31.7	12.3
29	VE	1.25	0.40	VS	100.0	100.0	7.6	0.9
30	VE	2.35	0.12	VS	1.9	92.4	11.8	0.0
31	E	1.0	0.05	VS	100.0	100.0	7.2	1.0
Supplemental assays								
A. HIV-1								
32	LE	3.45	2.00	LS	0.1	40.0	NA	31.4
33	LE	5.10	2.25	S	100.0	100.0	NA	10.5
34	E	5.0	3.15	S	100.0	100.0	NA	NA
B. HIV-1 + HIV-2								
35	LE	4.05	2.05	S	100.0	100.0	NA	4.3
Discriminatory test								
36	LE	3.25	1.45	S	100.0	100.0	NA	0.7
Reference tests								
37	LE	20.40	18.40	LS	100.0	100.0	NA	6.7
38	LE	4.55	3.45	LS	100.0	100.0	NA	12.3

[a] See Table 1. [b] VE = very easy; E = easy; LE = less easy. See Annex. [c] Suitability for use in small blood collection centres. VS = very suitable; S = suitable; LS = less suitable. See Annex. [d] Positive predictive value in populations where the prevalence of HIV is 0.01% or 6%. [e] The percentage of sera whose test results were interpreted differently by different readers, relative to the total number of sera tested. [f] The percentage of sera that yielded an indeterminate result, relative to the total number of sera tested. [g] NA = not applicable. [h] The results were considered indeterminate for sera that twice yielded an optical density that lay in the "grey area" defined by the manufacturer.

Conclusions

No single test or sequence of tests was appropriate for all situations; the particular test to be used depends on many parameters, some of which have been highlighted in the study. We chose arbitrarily the criteria for ease of performance and suitability for field use and these may not necessarily correspond to those selected by other investigators. Our objective was to provide potential users of the tests with comparative data to enable them to arrive at a decision of their own, depending on their needs and circumstances. More detailed information on these assays is available upon request from the WHO Global Programme on AIDS.[a–d]

Acknowledgements

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Résumé

Evaluation comparative de 36 tests du commerce pour le dépistage des anticorps anti-VIH

Les caractéristiques de fonctionnement de 20 titrages immuno-enzymatiques (ELISA), 11 tests simples à lecture visuelle, 4 tests supplémentaires et 1 test de discrimination pour le dépistage des anticorps dirigés contre le virus de l'immunodéficience humaine type 1 (VIH-1) et/ou type 2 (VIH-2) ont été étudiées. A cette fin, une série de 537 sérums a été utilisée, dont 65% étaient d'origine africaine, 26% d'origine européenne et 9% d'origine sud-américaine. La prévalence du VIH-1 était de 39,1% et celle du VIH-2 de 15,7%.

Les tests HIV-1 Western blot (Du Pont) et HIV-2 Western blot (Pasteur) ont été utilisés comme tests de référence. A l'exception des tests ci-après, la sensibilité et la spécificité de tous les tests essayés étaient excellentes: un test ELISA avait une sensibilité sensiblement plus faible, et deux tests ELISA, un test simple et un test supplémentaire présentaient une spécificité sensiblement plus faible, en particulier pour les sérums africains. La sensibilité et la spécificité des tests simples à lecture visuelle étaient aussi bonnes que celles des ELISA, quel que soit le type d'antigène utilisé. D'autre part, les tests simples étaient plus faciles à exécuter et plus adaptés à l'emploi dans de petits centres de transfusion sanguine, qui n'analyseront que peu de prélèvements (<90). La variabilité inter-lecteurs pour les divers tests simples allait de 0,8% à 31,7%. Les résultats des tests de première et de deuxième génération (ELISA et non ELISA) étaient comparables. Les tests pour la détection simultanée des anticorps dirigés contre le VIH-1 et le VIH-2 avaient une sensibilité et une spécificité comparables à celles des tests recherchant séparément le VIH-1 et le VIH-2. La détermination des valeurs δ offrait une mesure quantitative de la sensibilité et de la spécificité des tests et facilitait la différenciation entre les ELISA de sensibilité et de spécificité similaires.

[a] *Operational characteristics of commercially available assays to determine antibodies to HIV-1; report 1.* WHO unpublished document GPA/BMR/89.4.

[b] *Operational characteristics of commercially available assays to determine antibodies to HIV-1 and/or HIV-2 in human sera; report 2.* WHO unpublished document GPA/BMR/90.1.

[c] *Operational characteristics of commercially available assays to determine antibodies to HIV-1 and/or HIV-2 in human sera; report 3.* WHO unpublished document GPA/RES/DIA/90.

[d] *Operational characteristics of commercially available assays to determine antibodies to HIV-1 and/or HIV-2 in human sera; report 4.* WHO unpublished document GPA/RES/DIA/91.6.

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Annex

Ease of performance

For a particular HIV antibody assay, ease of performance was assessed by giving a score of +1 to each of the performance parameters outlined below.

• If there is no need to prepare: 1) antigen, 2) substrate, 3) wash, 4) conjugate; if there is no need to 5) predilute serum (in dilution tubes or plates that differ from the "test-plate" or "test-tubes"; 6) dilute serum (immediately into the test plate or test tubes); 7) if the volume of serum needed to perform the test is less than 25 µl; 8) if the test can be performed at ambient temperature without need of an incubator; if the following reagents after opening, reconstitution, or dilution remain stable until their expiry date: 9) antigen, 10) controls, 11) sample diluent, 12) conjugate, 13) substrate, and 14) wash buffer; 15) if sufficient reagents are available in the kit for all tests, performing the smallest number of sera possible per run (e.g., one strip for an ELISA); 16) if washing procedures are not necessary; if the following equipment is not needed to perform the assay: 17) wash device, 18) incubator/water-bath, 19) spectrophotometric reader, 20) refrigerator (storage), 21) agitator, 22) aspiration device, 23) automatic pipette, 24) multichannel pipette, 25) dilution tubes, rack, 26) distilled water, 27) microtitration plate, 28) plate covers, 29) graduated pipettes, 30) sulfuric acid/sodium hydroxide (to stop the enzymatic reaction of the conjugated enzyme with the substrate).

We defined a test as very easy (VE), easy (E), or less easy (LE) to perform if scores of ⩾25, ⩾20, or <20 were obtained, respectively.

Suitability for use in small blood collection centres

This was assessed by taking the performance parameters outlined below into consideration (a score of 1–3 (shown in parentheses) was given).

• If the positive predictive value (PPV) of a positive test result in a population with a 6% prevalence of HIV antibody lay in the range 90–100% (3), 80–90% (2), <80% (1); if the negative predictive value (NPV) of a negative test result in a population with a 6% prevalence of HIV antibody was 100% (3), 99.9% (2), ⩽99.8% (1); if the test can be performed at ambient temperature (3) or must be performed at a well-controlled incubation temperature (1); if the test has a long shelf-life (⩾6 months at ambient temperature or ⩾1 year at 2–8 °C) (2), or a short shelf-life (<6 months at ambient temperature or <1 year at 2–8 °C) (1); if storage of the kit at ambient temperature is possible (2) or a refrigerator (2–8 °C) is required (1); if the price per test is <US$ 1.5 (2), or ⩾US$ 1.5 (1); if the ease of performance is very easy (3), easy (2), or less easy (1); if the time necessary to test a single serum is <30 minutes (3), 30–60 minutes (2), or >60 minutes (1); if the time necessary to test 90 sera at a time is <120 minutes (3), 120–180 minutes (2), or >180 minutes (1); if visual reading of the test result is possible (3) or a spectrophotometer is required (1).

A maximum score of 27 could be obtained; we defined a test as very suitable (VS) if it had a total score of ⩾21, suitable (S) if its score was ⩾17, or less suitable (LS) if its score was ⩽16.