HIV ASSAYS:
OPERATIONAL CHARACTERISTICS

REPORT 16
RAPID ASSAYS

World Health Organization

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WHO Library Cataloguing-in-Publication Data

HIV antigen/antibody assays : operational characteristics : report 16 rapid assays.

1.HIV antigens - analysis. 2.HIV infections – diagnosis. 3.HIV seropositivity - diagnosis. 4.AIDS serodiagnosis - methods. 5.Reagent kits, Diagnostic - standards. I.World Health Organization. II.UNAIDS.

ISBN 978 92 4 159769 2 (NLM classification: WC 503.1)

Printed in France

Contact:
Dr G. Vercauteren, Essential Health Technologies - WHO - 20, Avenue Appia - 1211 Geneva 27- Switzerland
This document is available on the internet at: www.who.int/diagnostics_laboratory/en/

HIV ASSAYS: OPERATIONAL CHARACTERISTICS
REPORT 16
RAPID ASSAYS

CONTENTS

1. Summary

Report 16 summarizes the assessment of the major operational characteristics of commercially available assays to detect antibodies to HIV-1 and HIV-2. The data that is presented was obtained in the evaluation of the following five rapid assays carried out between August 2004 and October 2005:

- HIV 1/2 Stat-Pak (Chembio Diagnostics Inc)
- HIV 1/2 Stat-Pak *Dipstick* (Chembio Diagnostics Inc)
- ADVANCED QUALITY™ HIV Rapid Test (InTec Products)
- Retrocheck HIV WB (Qualpro Diagnostics)/Core HIV 1&2 (Core Diagnostics)[1]
- DoubleCheckGold™ HIV 1&2 Whole Blood (Orgenics Ltd)

Section 2 of this report provides background information on the WHO/UNAIDS HIV Assays: Operational Characteristics series. Sections 3 and 4 provide an overview of the laboratory diagnosis of HIV and comments on assay selection. Section 5 outlines how the assessments were carried out. Details of the assay evaluations themselves are contained in the tables in section 6. Cumulative lists of the assays already assessed under the programme and the addresses of manufacturers are given in Annexes 1-3.

[1] The Retrocheck HIV WB (Qualpro Diagnostics) kit is also available under the name of Core HIV 1&2 (Core Diagnostics) under an Original Equipment Manufacturer (OEM) agreement between Core Diagnostics and Qualpro Diagnostics. The WHO laboratory evaluation was performed on both products.

2. Background information

In 1988, the World Health Organization (WHO) Global Programme on AIDS (GPA), conscious of the need to advise Member States on the laboratory diagnosis of HIV, initiated a programme to provide objective assessments of commercially available assays for detecting antibody to both types of HIV: HIV-1 and HIV-2. The laboratory aspects of this continuing programme are carried out by the WHO Collaborating Centre for HIV/AIDS Diagnostic and Laboratory Support in the Department of Microbiology, Institute of Tropical Medicine, Antwerp, Belgium and coordinated by the Department of Essential Health Technologies of WHO in conjunction with UNAIDS.

The assessments focus on the operational characteristics of these assays, such as ease of performance and their sensitivity and specificity on a panel of well-characterized sera of diverse geographical origins. The assessments also indicate their suitability for use in small laboratories such as voluntary counseling and testing centers (VCT) and blood transfusion centers in resource-limited settings. In addition, the sensitivity of the assays on eight seroconversion panels is assessed.

The assessments are published in the form of reports which are intended for use by health policy-makers, directors of blood banks, and managers of national AIDS prevention programmes. They may be used to help select HIV antibody and/or HIV antigen-antibody assays appropriate for local needs, in conjunction with other considerations, such as experience with a given assay, availability, cost, service and product support from manufacturers.

The first report was issued in March 1989, and subsequent reports have been issued on a regular basis, details of which are given in Annexes 1 and 2. Recent reports are also published on the WHO website and can be found on the Department of Essential Health Technologies site as follows: http://www.who.int/diagnostics_laboratory/en/.

Further copies of this and earlier reports are available by written request to the Department of Essential Health Technologies, World Health Organization, 1211 Geneva 27, Switzerland or by e-mail to diagnostics@who.int. Reports containing information on assays which are currently no longer available are taken out of distribution.

3. Laboratory diagnosis of HIV infection

3.1 A brief overview

The diagnosis of HIV infection is usually made on the basis of the detection of antibodies to HIV. Serological tests for detecting antibodies to HIV are generally classified as **screening assays** (sometimes referred to as **first-line** assays) or **supplemental assays** (sometimes referred to as **confirmatory** assays). First-line assays can provide the presumptive identification of antibody-positive specimens, and supplemental assays are used to confirm whether specimens found reactive with a particular screening assay contain antibodies specific to HIV and/or HIV antigen.

The most widely used screening assays are enzyme immunoassays (often referred to as **EIAs** or **ELISAs**) as they are the most appropriate for screening large numbers of specimens on a daily basis, e.g. blood donations. The earliest assays used purified HIV lysates (1st generation), and often lacked sensitivity and specificity. Improved assays based on recombinant proteins and/or synthetic peptides, which also enabled the production of combined HIV-1/HIV-2 assays, became rapidly available (2nd generation). The so-called 3rd generation or sandwich EIAs, which use labeled antigen as conjugate, are extremely sensitive and have reduced the window period considerably. Enhanced EIAs have been developed that detect both HIV antibody and antigen (4th generation assays) leading to earlier detection of HIV infection and further reducing the window period (Duong Ly et al, 2007).

A variety of simple, instrument-free assays are now available, including agglutination, immunofiltration (flow-through tests), immunochromatographic (lateral-flow tests) and dipstick tests. Specimens and reagents are often added to the test device by means of a dropper. A positive result is indicated by the appearance of a colored dot or line, or by an agglutination pattern. Most of these assays can be performed in less than 20 minutes and are therefore called **rapid assays**. Other **simple assays** are less rapid and their procedures require 30 minutes to 2 hours. The results are read visually. In general, these assays are most suitable for use in testing and counseling centers and laboratories that have limited facilities and process low numbers of specimens daily.

When a single screening assay is used for testing in a population with a very low prevalence of HIV infection, the probability that a person is infected when a positive test result is obtained (i.e., the positive predictive value) is very low, since the majority of people with positive results are not infected. This problem occurs even when an assay with high specificity is used. Accuracy can be improved if a second supplemental assay is used to retest all those specimens found reactive by the first assay. The negative predictive value will generally always approach near to 100%, irrespective of prevalence. A third assay may also be required to elucidate the correct status.

Until recently, the most commonly used confirmatory assay was the Western blot (WB). However, its use has proven to be very expensive and can, under some conditions, produce a relatively large number of indeterminate results. Similar assays, generically called line immunoassays (LIAs), based on recombinant proteins and/or synthetic peptides capable of detecting antibodies to specific HIV-1 and/or HIV-2 proteins, have been developed. Examples of this technology include the INNO-LIA™, Pepti-LAV, and RIBA™ assays. In general, these assays produce fewer indeterminate results as compared to WB, but are equally expensive. Studies have shown that combinations of EIAs and/or combinations of two or three rapid assays can provide results as reliable as the WB and LIAs at a much lower cost (Sato et al, 1994). WHO and UNAIDS therefore recommend that countries consider testing strategies which use a combination of EIAs and/or rapid tests rather than EIA/WB for HIV antibody detection (WHO, 1992).

The WHO HIV testing strategies are currently under review. Slight modifications will be made to respond to lessons learnt from country experiences and to take into consideration the characteristics of newly available assays.

In general, for the selection and use of HIV assays, the first assay should have the highest sensitivity, whereas the second and third assays should have a similar or higher specificity than the first. As assays have continued to increase in terms of quality and performance, it is now frequently the case that the assays employed have both high sensitivity and specificity values. The number of initially discordant results should not exceed 5%. If it does, quality assurance procedures should be checked and/or a new testing algorithm should be validated and adopted.

3.2 Follow up after diagnosis

A number of other assays have been introduced in recent years which assist in the establishment of the diagnosis of HIV infection and may also be used to monitor the progress of the infection and the response to therapy. These include assays that detect virus particles e.g. HIV p24 antigen EIA, or the presence of HIV viral nucleic acid (RNA or DNA) by means of nucleic acid amplification or signal amplification techniques.

Technologies based on the amplification of viral nucleic acids, such as polymerase chain reaction (PCR) and nucleic acid sequence-based amplification (NASBA) or amplification of the bound probe signal as in branched-DNA (bDNA) assays plus increased automation using real-time methods, have made it possible to detect minute amounts of viral material. In theory, as little as a single viral genome can be detected. The detection limit for most assays is around 50 copies/ml but in practice, the technique can have limited specificity. These procedures are suited to early diagnosis of mother-to-child transmission and for monitoring the viral load of individuals who are taking antiretroviral therapy. Although prices have recently decreased, the assays remain expensive, they need sophisticated equipment, rigorous laboratory conditions and highly trained staff. Many of the assays need further refinement since not all HIV-1 subtypes are equally well detected, nor is HIV-2. Therefore, it would be unwise to base a diagnosis of HIV infection on a single positive nucleic acid test result, in the absence of any other detectable marker.

3.3 Quality assurance

All laboratories and testing sites carrying out HIV testing should have a well-functioning quality management programme. It is most important that quality control and external quality assessment procedures be stringently complied with so as to maximize the accuracy of the laboratory results. Procedures for detecting both (technical) laboratory and clerical errors must be included in all standard operating protocols. For example, procedures that guarantee the correct identification of reactive units of donated blood, which must be discarded, are essential to the maintenance of a safe blood supply. It is recommended that laboratories submit to an external quality assessment scheme (also known as proficiency testing) at least once a year, but preferably more regularly. Guidelines have been developed for application of quality aspects to HIV testing with an emphasis on rapid testing in resource-limited settings. For further details see the *Joint CDC/WHO Guidelines for Assuring the Accuracy and Reliability of HIV Rapid Testing: Applying a Quality System Approach*, World Health Organization, Geneva, 2005 (ISBN 9241593563).

3.4 Safety

The testing of all clinical specimens should be performed in such a manner as to minimize occupational risk. Guidelines for good laboratory practice have been developed that, if followed, will ensure safety and keep laboratory accidents to a minimum. For further details see *Laboratory Biosafety Manual, third edition*, World Health Organization, Geneva, 2004 (ISBN 92 4 154650 6) and the Epidemic and Pandemic Alert and Response section of the WHO website: www.who.int/csr where information on laboratory biosafety and transport of infectious substances may be found.

4. Assay selection

In addition to the requirements indicated in Section 3, there are various operational factors that influence the selection of assays, including:

- desired characteristics of the assay (antigen, antibody)
- simplicity of test procedure
- equipment necessary to perform the assay
- performance time including end-point stability
- shelf-life of the reagents
- price
- storage conditions
- technical skill of laboratory staff
- laboratory infrastructure
- laboratory logistics (continuous supply of kits, stability of electrical source, maintenance of equipment, spare parts, availability of service, etc.)
- access to a referral laboratory

For use in VCT, antenatal and tuberculosis clinics, small blood-collection centers and hospitals in resource-limited settings, assays are needed that have the following specific characteristics:

- high level of sensitivity and specificity
- long shelf life at ambient temperatures
- reasonable cost
- ease of performance
- rapidity of performance

The WHO evaluations take these factors into account in assessing suitability for use in small testing facilities and/or laboratories. They show that some of the rapid assays now available, which need no or relatively simple equipment and can be read visually, are more suitable than EIAs in small centers where there are only a limited number of sera to be screened (< 40 sera per day). For testing large series of specimens, EIAs are still the most rapid and most appropriate assay type. However, they require expensive equipment which has to be well maintained.

The aim of this document is to supply managers who will decide which assays to use, and the potential users of the assays, with enough comparative data to apply their own criteria and choose the best assay for their particular circumstances. The choice of the most appropriate HIV assay also depends on the HIV variants present in a particular geographical region (e.g., HIV-1 group O). It is clear, for example, that in areas such as West Africa where HIV-2 is prevalent, an assay capable of detecting antibodies to HIV-2 as well as HIV-1 will be required. Therefore, testing algorithms should always be evaluated in the context in which they will be used before large-scale implementation.

The UN test kit bulk procurement scheme coordinated by WHO facilitates access to assays giving the most accurate results at the lowest possible cost for national HIV/AIDS control programmes. The list of HIV assays on the bulk procurement scheme is updated annually. The procurement procedure for eligible buyers is outlined in Annex 4.

5. Materials and methods of assessment

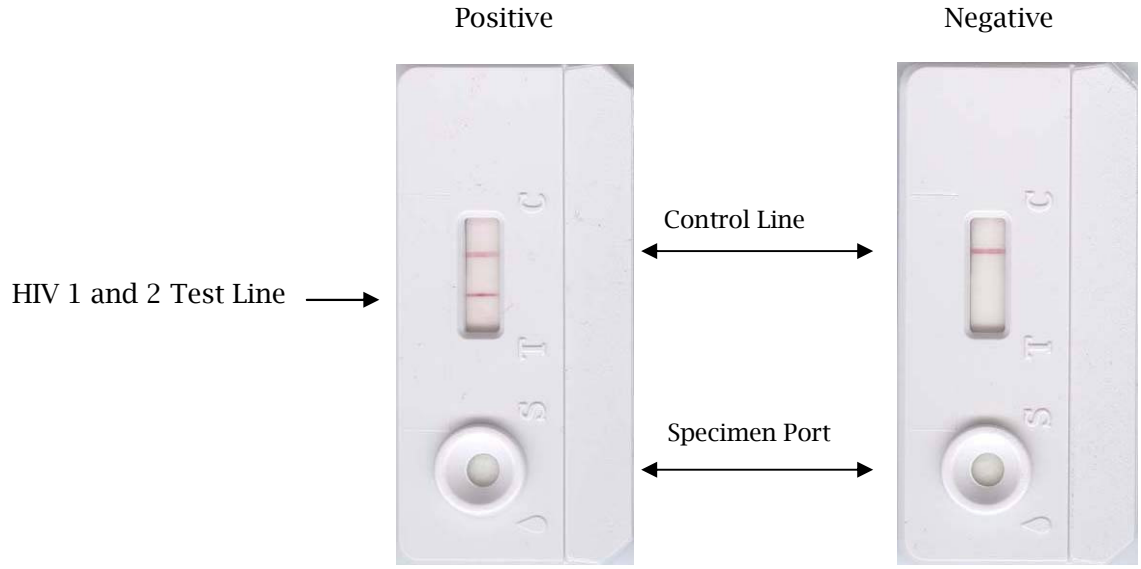
5.1 Assays

Kits for the five commercial assays listed in Section 1 were kindly provided free of charge by the manufacturers to WHO for the assessments. The manufacturers and distributors were informed that the assessments were to be carried out and that they were free to visit the assessment site and to demonstrate their assays at their own expense.

HIV 1/2 Stat-Pak® (Chembio Diagnostic Systems)

A qualitative immunochromatographic assay for the detection of antibodies to human immunodeficiency virus types 1 and 2 (HIV-1 and HIV-2) in human serum, plasma and whole blood.

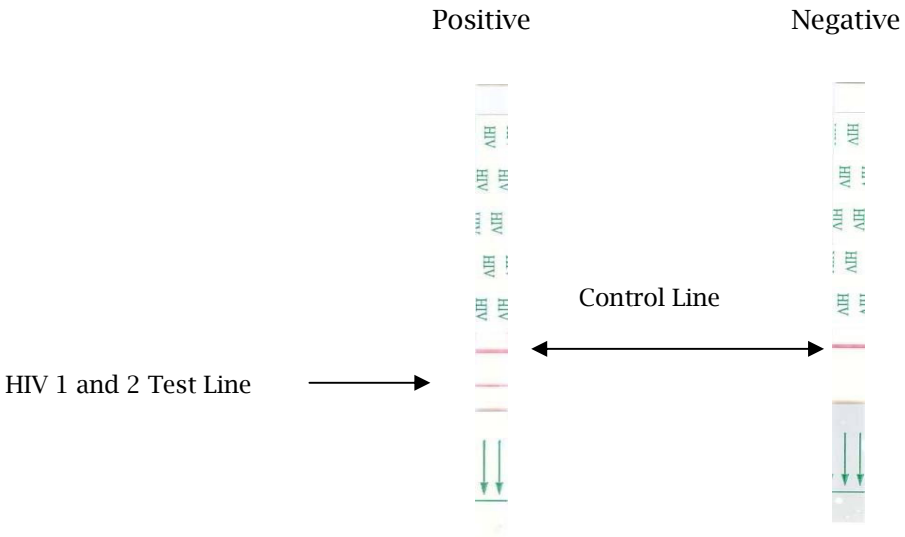
Figure 1 - Completed HIV positive and HIV negative test result with HIV 1/2 Stat-Pak®



HIV 1/2 Stat-Pak® *Dipstick* (Chembio Diagnostic Systems)

A qualitative immunochromatographic assay for the detection of antibodies to human immunodeficiency virus types 1 and 2 (HIV-1 and HIV-2) in human serum, plasma and whole blood.

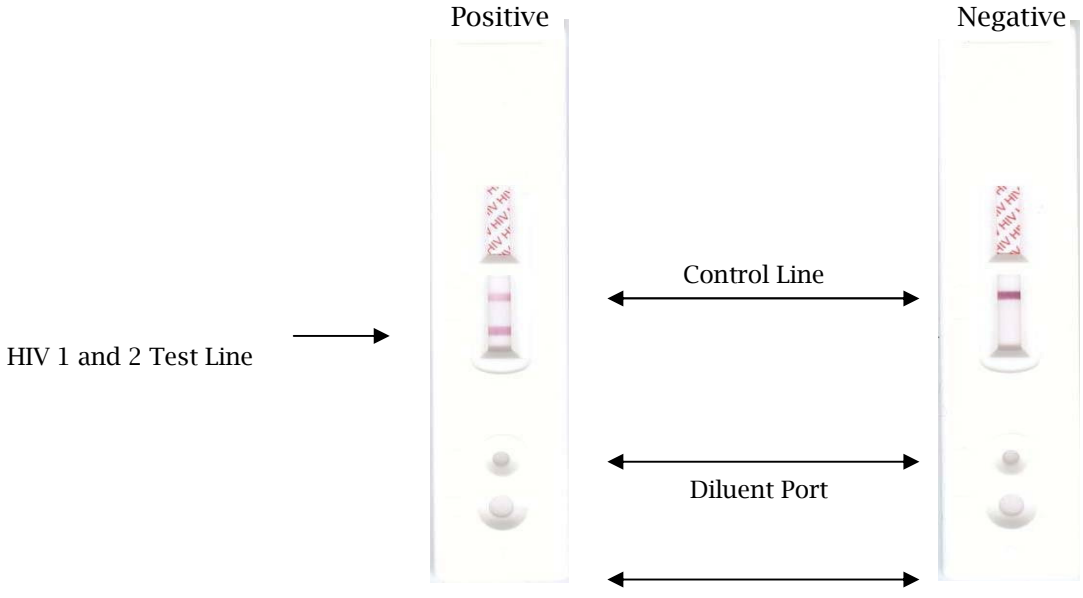
Figure 2 - Completed HIV positive and HIV negative test result with HIV 1/2 Stat-Pak® *Dipstick*



ADVANCED QUALITY™ HIV Rapid Test (InTec Products)

A colloidal gold-enhanced rapid immunochromatographic assay for the qualitative detection of antibodies to the human immunodeficiency virus types 1 and 2 (HIV-1 and HIV-2) in human whole blood, serum or plasma.

Figure 3 - Completed HIV positive and HIV negative test result with ADVANCED QUALITY™ HIV Rapid Test

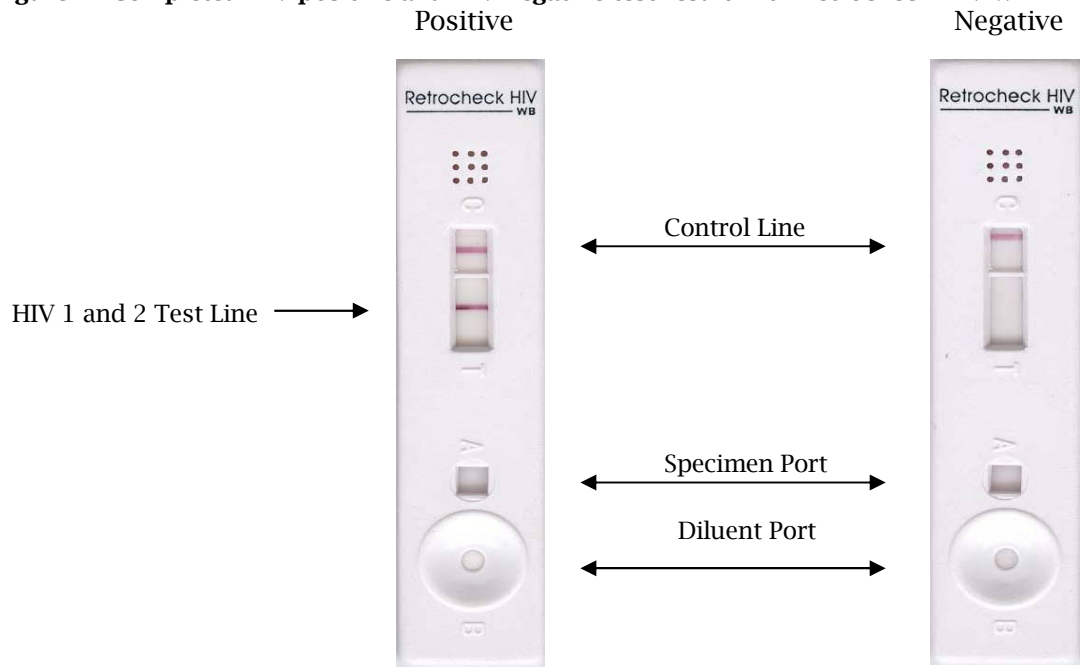


Retrocheck HIV WB (Qualpro Diagnostics)/Core HIV 1&2 (Core Diagnostics)

A rapid immunochromatographic assay for the detection of antibodies to human immunodeficiency virus types 1 and 2 (HIV-1 and HIV-2) in human serum, plasma and whole blood.

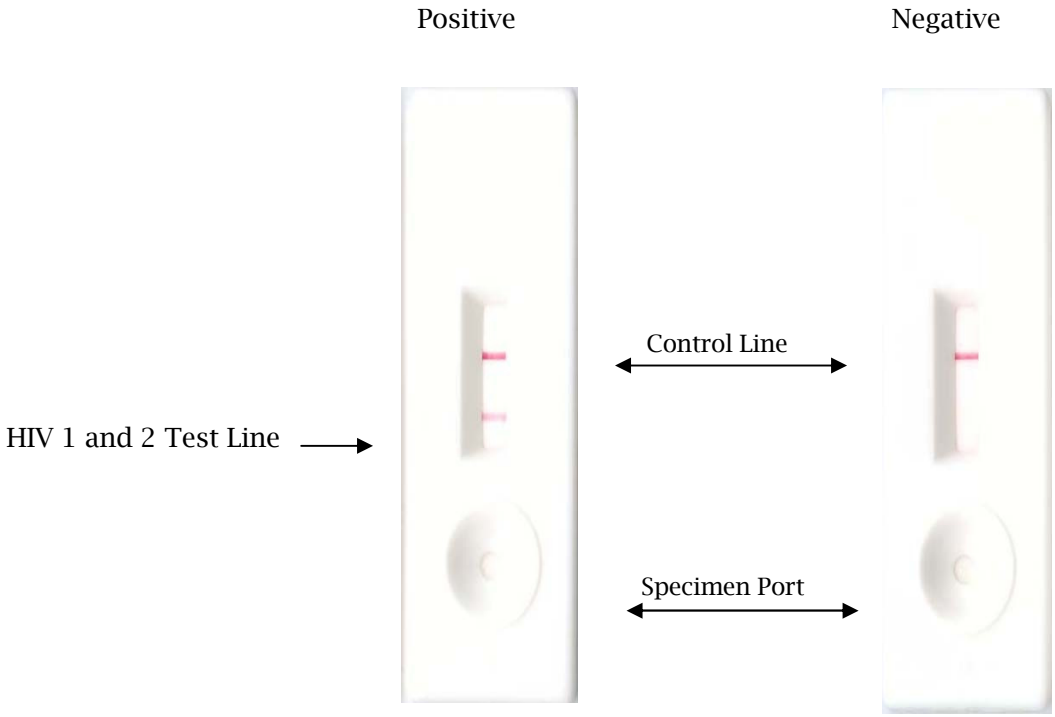
Please note that this test kit is also marketed as Core HIV 1&2 by Core Diagnostics

Figure 4 - Completed HIV positive and HIV negative test result with Retrocheck HIV WB



DoubleCheckGold™ HIV 1 & 2 Whole Blood (Orgenics)
A single reagent immunochromatographic assay for the qualitative detection of antibodies to human immunodeficiency virus types 1 and 2 (HIV-1 and HIV-2) in human serum, plasma and whole blood.

Figure 5 - Completed HIV positive and HIV negative test result with DoubleCheck Gold™ HIV 1 & 2 Whole Blood



5.2 Evaluation panels

5.2.1 WHO HIV Panel

The evaluations reported here were carried out using a panel of 769 serum/plasma (as shown in *Table A*), of which 100 were from Africa, 140 from Asia, 315 from Europe and 214 from Latin America. The panel contained 293 sera positive for HIV-1 and 21 positive for HIV-2. All samples were stored in aliquots and thawed at least once but not more than twice.

Table A - WHO HIV Specimen Reference Panel

Origin	**Positive sera**		**Negative sera**	**Total Number**
	HIV 1	HIV 2		
Africa	24	21	55	100
Asia	79	0	61	140
Europe	86	0	229	315
Latin America	104	0	110	214
Total	293	21	455	769

5.2.2 Seroconversion panels

Additionally, eight anti-HIV 1 seroconversion panels: PRB910, PRB912, PRB914, PRB917, PRB927, PRB928, PRB930 and PRB944 from Boston Biomedica (BBI) were tested. Western blot and screening EIA results provided by ITM, Belgium and HIV antigen data as provided by BBI are given in Table 6.

5.3 Test performance

The assays were performed according to the manufacturers' instructions. Usually, one person carried out all the tests. The tests on initially reactive specimenss were repeated. Specimens with discrepant results were repeated twice. Two out of three results determined the overall test outcome. Because of their extreme value, specimens belonging to the eight seroconversion panels were tested once only with each assay under evaluation.

Due to the subjective, visual nature of the reading of the rapid assays, they were read independently by three people. Two out of three reading results determined the final outcome.

5.4 Reference assays

The HIV-1 positive specimens and the HIV negative specimens included in the evaluation panel were tested by the Enzygnost Anti-HIV 1/2 Plus (Dade Behring GmbH) and Vironostika HIV Uni-Form II plus O ELISA assays (bioMérieux S.A) and the INNO-LIA HIV Confirmation assay (Innogenetics). The HIV-2 positive specimens included in the evaluation panel were tested by Western blot HIV-1 (WB HIV-1) (Genelabs Diagnostics, HIV blot (version 1.2)), NEW LAV BLOT II (WB HIV-2) (Sanofi Diagnostics Pasteur now BioRad Laboratories) and Pepti-Lav 1+2 (Sanofi Diagnostics Pasteur now BioRad Laboratories) - which is designed to differentiate between HIV-1 and/or HIV-2 infections. Following testing with the reference assays, 293 sera were considered to be HIV-1 positive, 21 specimens were HIV-2 positive and 455 were HIV negative.

A WB HIV-1 result or WB HIV-2 result was considered positive when two of three *env* bands (*env* precursor, external and transmembrane glycoproteins) with or without *gag* and/or *pol* bands were present (WHO, 1990). A WB result was considered negative when no HIV specific band was present; indeterminate when it showed any band pattern not considered positive or negative. The results of the INNO-LIA HIV Confirmation assay were interpreted according to the package insert. The evaluation panel did not include any specimens that gave an indeterminate result by WB.

The data obtained with the HIV antibody assays under evaluation were compared to the outcome of the results obtained by the above reference assays.

5.5 Analysis of the results of the assays under evaluation

5.5.1 Sensitivity, specificity and predictive values of HIV serological assays

Table B - 2 x 2 table for calculating sensitivities, specificities, predictive values, confidence intervals of assays

		True HIV status +	True HIV status –	
Results of assay under evaluation	+	**a True-positives**	b False positives	a+b
	–	c False-negatives	**d True-negatives**	c+d
		a+c	b+d	

Sensitivity = a/(a+c) Positive predictive value = a/(a+b)
Specificity = d/(b+d) Negative predictive value = d/(c+d)

Sensitivity: the ability of the assay under evaluation to detect correctly sera that contain antibody to HIV (reference assays positive). Thus sensitivity is the number of true positive sera identified by the assay under evaluation as positive (a), divided by the number of sera identified by the reference assays as positive (a+c), expressed as a percentage.

Specificity: the ability of the assay under evaluation to detect correctly sera that do not contain antibody to HIV (reference assays negative). Thus specificity is the number of true negative sera identified by the assay under evaluation as negative (d), divided by the number of sera identified by the reference assays as negative (b+d), expressed as a percentage.

NOTE: Indeterminate results, obtained with the assays under evaluation, were included in the calculation of sensitivities and specificities.

Positive Predictive Value (PPV): the probability that when the test is reactive, the specimen does contain antibody to HIV. This may be calculated in two ways:

1. using the simple formula a/(a+b) which will give an approximate value.
2. using the more precise formula which takes the prevalence of HIV in the population into account:

$$PPV = \frac{(prevalence)(sensitvity)}{(prevalence)(sensitivity)+(1-prevalence)(1-specificity)}$$

Negative Predictive Value (NPV): the probability that when the test is negative, a specimen does not have antibody to HIV. This may be calculated using:

1. the simple formula d/(c+d) which will give an approximate value.
2. the more precise formula which takes the prevalence of HIV in the population into account:

$$NPV = \frac{(1-prevalence)(specificity)}{(1-prevalence)(specificity)+(prevalence)(1-sensitivity)}$$

The probability that an assay will accurately determine the true infection status of a person being tested varies with the prevalence of HIV infection in the population from which the person comes. In general, the higher the prevalence of HIV infection in the population, the greater the probability that a person testing positive is truly infected (i.e., the greater the positive predictive value [PPV]). Thus, with increasing prevalence, the proportion of specimens

testing false-positive decreases; conversely, the likelihood that a person showing negative test results is truly uninfected (i.e., the negative predictive value [NPV]), decreases as prevalence increases. Therefore, as prevalence increases, so does the proportion of specimens testing false-negative.

Confidence intervals (CI): gives an interval estimate of likely values for the true (or population) value of sensitivity and specificity of each assay. The 95% confidence interval is a means of determining whether observed differences in sensitivity or specificity between assays are meaningful or not. Exact 95% confidence intervals for binomial proportions were calculated from the F-distribution as the proportion is nearing 1.0 (Armitage, 2002; Kirkwood, 2003).

5.5.2 Inter-reader variability

The inter-reader variability is indicated in the results table when assay readings are performed without any equipment i.e. subjective assessment. Three persons independently interpret each test result. The inter-reader variability is expressed as the percentage of sera for which initial test results are differently interpreted by different readers.

5.5.3 Sensitivity in seroconversion panels

The results obtained with early seroconversion panels using the assays under evaluation were compared with those obtained using Enzygnost Anti-HIV 1/2 Plus (Dade Behring), the assay arbitrarily designated the reference for determination of relative sensitivity in these panels i.e. the benchmark assay. For each seroconversion series (panel), the first specimen in the sample sequence to become reactive with Enzygnost Anti-HIV 1/2 Plus (Dade Behring) was assigned the value "0". Results from the assays under evaluation were compared with Enzygnost Anti-HIV 1/2 Plus (Dade Behring) by determining the difference between the specimen assigned value "0"and the relative position in the sample sequence of the first specimen which showed a reactive result with each of the assays under evaluation. For example, if an assay became reactive two specimens earlier in a series than Enzygnost Anti-HIV 1/2 Plus (Dade Behring), the value assigned for that series in that assay was -2. Similarly, if an assay became reactive one specimen later than Enzygnost Anti-HIV 1/2 Plus (Dade Behring), the value assigned was +1. The assigned values over the 8 seroconversion series were averaged to determine a mean relative seroconversion sensitivity index for each assay and the 95% confidence limits were determined. These limits should be interpreted with caution as only eight panels were tested.

5.5.4 Additional analysis

The technical aspects of the assays under evaluation were assessed by the technician who performed the testing. These assessments, along with other selected assay characteristics, contributed to an overall appraisal of each assay's suitability for use in small laboratories. To enable comparison between assays, an arbitrary scoring system was used to rate specified assay characteristics.

6. Assay evaluations

Table 1 summarizes the general characteristics of each of the assays. Results of the assays evaluated as compared to the reference tests are given in Table 2. Table 3 provides further details of operational aspects. Factors taken into account in the calculation of ease of performance and suitability for use in small laboratories are listed in Table 4, and Table 5 respectively. Performance of the assays evaluated on early seroconversion panels is given in Table 6, and the relative performance of the evaluated assays as compared to the benchmark assay is given in Figure 6. Explanatory notes are provided at the end of the assay evaluation tables.

ASSAY EVALUATIONS

Table 1. General characteristics and operational aspects

NAME	HIV 1/2 Stat-Pak	HIV 1/2 Stat-Pak *Dipstick*	ADVANCED QUALITY™ HIV Rapid Test	Retrocheck HIV[2] / CORE™ HIV 1&2	DoubleCheckGold™ HIV 1&2 Whole Blood
Manufacturer	Chembio Diagnostics Inc Medford, NY USA	Chembio Diagnostics Inc Medford, NY USA	InTec Products Inc Haicang, Xiamen People's Republic of China	Qualpro Diagnostics Verna, Goa India	Orgenics Ltd Yavne Israel
Assay type	Immunochromatographic assay	Immunochromatographic assay	Immunochromatographic assay	Immunochromatographic assay	Immunochromatographic assay
Antigen type	Synthetic peptides	Synthetic peptides	Recombinant proteins	Recombinant proteins and synthetic peptides	Recombinant proteins
Individual/combined HIV 1 & HIV 2 reactivity	Combined HIV-1 & HIV-2	Combined HIV-1 & HIV-2	Combined HIV-1 & HIV-2	Combined HIV-1 & HIV-2	Combined HIV-1 & HIV-2
Solid phase	Immunochromatographic membrane	Immunochromatographic membrane	Immunochromatographic membrane	Immunochromatographic membrane	Immunochromatographic membrane
Specimen type	serum/plasma/whole blood	serum/plasma/whole blood	serum/plasma/whole blood	serum/plasma/whole blood	serum/plasma/whole blood
Number of tests per kit (product code)	20 (HIV 101) Bulk (HIV 133)	30 (HIV 301) Bulk (HIV 333)	40 (ITP02002-TC40)	10, 25, 50, 100	20 (70633020) 100 (70633100)
Batch numbers evaluated (expiry date)	HIV060404 (17/11/05) HIV062404 (08/12/05)	5504002 19/11/06) 5604003 (04/11/06) 5804004 (12/04)06)	2004121608 (06/2006) 2004121401 (06/2006) 2005012502 (07/2006) 2005012503 (07/2006)	**Retrocheck HIV** 41035 (00/10/06) 41038 (00/11/06 **CORE™ HIV 1&2** 41030 (00/07/06) 41031 (00/11/06)	0507061W (17/01/2007) 050710W (10/02/2007)
Shelf life (at °C)	18 months (8-30)	18 months (8-30)	18 months (2-30)	24 months (4-30)	18 months (2-30)
Volume of sample needed (µl) Final dilution of sample	5µl none	5µl none	5µl none	50µl none	10µl (serum/plasma) 50µl (whole blood) none
Total time to perform the assay h:min. (number of sera)	0:11 (1)	0:16 (1)	0:16 (1)	0:16 (1)	0:16 (1)
Reading	Visual	Visual	Visual	Visual	Visual
Indicative price/test US$ (as given in 2004 - 2005)	1.10 - 1.35	0.80 - 0.95	0.80 - 0.90	0.70 - 0.85	1.20 - 1.32

[2]This kit is also available under the name of Core HIV 1&2 from Core Diagnostics under an Original Equipment Manufacturer (OEM) agreement between Core Diagnostics and Qualpro Diagnostics.

Table 2. Comparison of the assays under evaluation with reference assays

NAME		HIV 1/2 Stat-Pak	HIV 1/2 Stat-Pak *Dipstick*	ADVANCED QUALITY™ HIV Rapid Test	Retrocheck HIV / CORE™ HIV 1&2	DoubleCheckGold™ HIV 1&2 Whole Blood
Final Sensitivity % (95% CI)[3] n = 314		100 (98.8 - 100)	99.4 (97.7 - 99.9)	99.7 (98.2 - 100)	100 (98.8 - 100)	100 (98.8 - 100)
Initial Specificity % (95% CI)		98.2 (96.6 - 99.2)	100 (99.2 - 100)	99.8 (98.8 - 100)	99.1 (97.8 - 99.8)	99.3 (98.1 - 99.9)
Final Specificity % (95% CI) n = 455		99.3 (98.1 - 99.9)	100 (99.2 - 100)	99.8 (98.8 - 100)	99.1(97.8 - 99.8)	99.3 (98.1 - 99.9)
Indeterminate results %		0	0	0	0.1	0
Initial inter-reader variability %		1.7	0.3	0.8	0.4	0.1
PPV	1%	60.5	100	82.1	53.5	60.5
	10%	94.4	100	98.1	92.7	94.4
NPV	1%	100	100	100	100	100
	10%	100	99.9	99.9	100	100

Note: evaluations carried out using serum/plasma specimens, see section 5.2.

[3] 95% confidence intervals

Table 3. Detailed operational aspects

NAME	HIV 1/2 Stat-Pak	HIV 1/2 Stat-Pak *Dipstick*	ADVANCED QUALITY™ HIV Rapid Test	Retrocheck HIV / CORE™ HIV 1&2	DoubleCheckGold™ HIV 1&2 Whole Blood
Dimension (cm) of kit: w-l-h	16.5 - 12.5 - 9	13.5 - 6.5 - 5	18 - 13.5 - 9	15.7 - 8.3 - 7 (10 tests) 20- 13-5 -6.7 (25 tests) 21.2 - 13.2 - 3.2 (50 tests) 26 - 13 - 19.7 (100 tests)	17.5 - 12.5 - 5.5 (20 tests) 26 - 18 - 14 (100 tests)
Storage conditions (°C)	8-30	8-30	2-30	4-30	2-30
Incubation temperature (°C)	Room temperature	Room temperature	Room temperature (18-25)	Room temperature (20-30)	Room temperature (15-30)
Reading endpoint stability (mins)	10	15-20	20	30	25
Stability after dilution/ reconstitution/ opening at (°C) - antigen (device) - controls - sample diluent - conjugate - substrate - wash buffer - running buffer	 expiry date (8-30°C) not applicable not applicable not applicable not applicable not applicable expiry date (8-30°C)	 expiry date (8-30°C) not applicable not applicable not applicable not applicable not applicable expiry date (8-30°C)	 expiry date (2-30°C) not applicable not applicable not applicable not applicable not applicable expiry date (2-30°C)	 expiry date (4-30°C) not applicable not applicable not applicable not applicable not applicable expiry date (4-30°C)	 expiry date (2-30°C) not applicable not applicable not applicable not applicable not applicable expiry date (2-30°C)
Number of sera per run minimum – maximum	1 - 10	1 - 10	1 - 10	1 - 10	1 - 10
Number of controls per test run - negative - cut-off/weak positive - positive - blank internal controls : reagent control specimen addition control	Control samples not supplied in the kit but available on order from manufacturer No Yes	Control samples not supplied in the kit but available on order from manufacturer No Yes	Control samples not supplied in the kit and are not available from the manufacturer No Yes	Control samples not supplied in the kit and are not available from the manufacturer Yes No	Control samples not supplied in the kit but available on order from manufacturer No Yes

Table 3. (continued) Detailed operational aspects

NAME	HIV 1/2 Stat-Pak	HIV 1/2 Stat-Pak *Dipstick*	ADVANCED QUALITY™ HIV Rapid Test	Retrocheck HIV / CORE™ HIV 1&2	DoubleCheckGold™ HIV 1&2 Whole Blood
Estimated time to perform one run: h. min (number of sera)	0.13 (1)	0.16 (1)	0.18 (1)	0.16 (1)	0.16 (1)
Equipment needed but not provided in the kit:[4]					
- washer	-	-	-	-	-
- incubator (water-bath)	-	-	-	-	-
- spectrophotometric reader	-	-	-	-	-
- refrigerator (storage)	±	±	±	±	±
- agitator , rocker	-	-	-	-	-
- aspiration device	-	-	-	-	-
- automatic pipette (µl)	-	-	-	-	+
- multichannel (µl)	-	-	-	-	-
- disposable tips	-	-	+	-	+
- dilution tubes/rack,	-	+	-	-	-
- microtiterplate	-	-	-	-	-
- distilled or deionised water	-	-	-	-	-
- plate covers	-	-	-	-	-
- graduated pipette; cylinder (ml) - sulfuric acid/sodium hydroxide	-	-	-	-	-
- absorbent paper	-	-	-	-	-
- disinfectant	-	-	-	-	-
- gloves	+	+	+	+	+
- reagent trough	-	-	-	-	-
- timer	+	+	+	+	+
Definition of reactive results	Appearance of pink/purple coloured lines in both the TEST and CONTROL areas	Appearance of pink/purple coloured lines in both the TEST and CONTROL areas	Both purplish red test band and control band appear on the membrane	Two coloured bands appear at the Test (T) and Control (C) regions	The Test Line and Control Line appear
Definition of grey zone or invalid result	No distinct pink/purple line in the CONTROL area	No distinct pink/purple line in the CONTROL area	If no control band is seen, test is considered invalid	Only if no control band is visible at 15 minutes	The absence of the Internal Control should be considered as an invalid result

[4] **+** : not provided in the kit but necessary to perform the test; **-** :provided in the kit or not necessary to perform the test; ± : use is optional.

Table 4a. Technician's appraisal of the test kit

NAME	Score	HIV 1/2 Stat-Pak	HIV 1/2 Stat-Pak *Dipstick*	ADVANCED QUALITY™ HIV Rapid Test	Retrocheck HIV / CORE™ HIV 1&2	DoubleCheckGold™ HIV 1&2 Whole Blood
Number of steps in the test procedure: 1-2 steps 3-5 steps >5 steps	 6 3 1	6	6	6	6	6
Clarity of kit instructions: - good - needs improvement	 2 1	2	2	2	1	2
Kit and reagent packaging and labelling: - good - needs improvement	 2 1	2	2	2	2	2
Total (out of possible 10)	10	10	10	10	9	10
Comments on the test kit		Some binding of the antigen to the solid phase impresses the membrane which may cause false positive reaction	None	Antigen-colloidal gold conjugate migrates very well - this results in a clear membrane	Traces of the coloured HIV 1/2 specific recombinant antigen-colloidal gold conjugate do not flow completely through the membrane, reading time needed extending	The reading is clear, there is no residue of the antibody HIV protein-colloidal gold complexes on the test and control area after the incubation time

Table 4b. Calculation of ease of performance

NAME	HIV 1/2 Stat-Pak	HIV 1/2 Stat-Pak *Dipstick*	ADVANCED QUALITY™ HIV Rapid Test	Retrocheck HIV / CORE™ HIV 1&2	DoubleCheckGold™ HIV 1&2 Whole Blood
Need to prepare: 1 = reagent needs no preparation 0 = reagent needs preparation					
-antigen	1	1	1	1	1
-substrate	1	1	1	1	1
-wash solution	1	1	1	1	1
-conjugate	1	1	1	1	1
-pre-dilution of serum	1	1	1	1	1
Stability after dilution/opening: 1 = expiry date 0 = less than the kit's expiry date					
-antigen	1	1	1	1	1
-controls	1	1	1	1	1
-sample diluent	1	1	1	1	1
-conjugate	1	1	1	1	1
-substrate	1	1	1	1	1
-wash buffer/running buffer	1	1	1	1	1
-sufficient reagents	1	1	1	1	1
-wash (yes=1; no =0)	1	1	1	1	1
Item needed but not provided in the kit: 1 = item provided in kit or N/A 0 = item not provided in kit					
-reagent trough	1	1	1	1	1
-automatic /multichannel pipette	1	1	1	1	0
-dilution – tubes, rack/microtiter plate	1	0	1	1	1
-distilled or deionised water	1	1	1	1	1
-plate covers	1	1	1	1	1
-graduated pipette, cylinder	1	1	1	1	1
-sulfuric acid/sodium hydroxide	1	1	1	1	1
Technician's appraisal of the test kit[1] (rating out of 10)	10	10	10	10	10
Total (out of possible 30)	30	29	30	30	29
Ease of performance: -less easy < 20 -easy $20 \leq x \leq 25$ -very easy > 25	very easy	very easy	very easy	very easy	very easy

[1] see table 4a

Table 5. Technical suitability for use in small laboratories

NAME	Score	HIV 1/2 Stat-Pak	HIV 1/2 Stat-Pak *Dipstick*	ADVANCED QUALITY™ HIV Rapid Test	Retrocheck HIV / CORE™ HIV 1&2	DoubleCheckGold™ HIV 1&2 Whole Blood
Sensitivity						
- 100%	5	5			5	5
- 98 – 100%	3		3	3		
- <98%	0					
Specificity (final)						
- >98%	5	5	5	5	5	5
- 95 – 98%	3					
- <95%	0					
Incubation temperature						
- room temp °C	3	3	3	3	3	3
- other than room temp °C	1					
Shelf-life						
- >1 year	3	3	3	3	3	3
- ≥ 6 months ≤ 1 year	2					
- < 6 months	1					
Storage at						
- room temp °C possible (opened kit)	5	5	5	5	5	5
- room temp °C possible (unopened kit)	2					
- 2-8 °C required	1					
Price per test (US$)						
- ≤ 1.0	3		3	3	3	
- >1.0 ≤ 2.0	2	2				2
- > 2.0	1					
Ease of performance						
- very easy	5	5	5	5	5	5
- easy	3					
- less easy	1					
Rapidity of performance: 1 specimen						
- < 10 min	3					
- 10 – 30 min	2	2	2	2	2	2
- > 30 min	1					
Washer/agitator						
- not needed	3	3	3	3	3	3
- needed	1					
Reading						
- visual: inter-reader variability ≤ 3%	5	5	5	5	5	5
: inter-reader variability > 3%	3					
- reading equipment	1					
Total (out of possible 40)		38	37	37	39	38
Suitability for use in small laboratories:		very suitable	very suitable	very suitable	very suitable	very suitable
- less suitable < 23						
- suitable 23 ≤ x ≤ 30						
- very suitable > 30						

Table 6. Results on commercial seroconversion panels

Panel	Days since 1st bleed	HIV Ag[1]	Assays under evaluation					Enzygnost Anti-HIV1/2 Plus[2]	Vironostika HIV Uni-Form II *Plus* O[2]	INNO-LIA HIV Confirmation[2]							
			SR 1	SR 2	SR 3	SR 4	SR 5										
		S/CO						OD/CO	OD/CO	Result	Sgp120	gp41	p31	p24	p17	sgp105	gp36
PRB910-01	0	0.4	NEG	NEG	NEG	NEG	NEG	0.1	0.4	neg	-	-	-	-	-	-	-
PRB910-02	14	5.7	NEG	NEG	NEG	NEG	NEG	0.1	0.4	neg	-	-	-	-	-	-	-
PRB910-03	26	06	**POS**	**POS**	**POS**	**POS**	**POS**	**>6,7**	**8.9**	**HIV-1**	2+	3+	-	2+	2+	-	-
PRB910-04	28	0.5	POS	POS	POS	POS	POS	>6,7	8.9	HIV-1	2+	3+	-	2+	2+	-	-
PRB910-05	32	0.4	POS	POS	POS	POS	POS	>6,7	8.3	HIV-1	2+	3+	-	2+	2+	-	-
PRB910-06	35	0.4	POS	POS	POS	POS	POS	>6,7	8.4	HIV-1	2+	3+	-	2+	2+	-	-
PRB910-07	40	0.4	POS	POS	POS	POS	POS	>6,7	8.6	HIV-1	2+	3+	-	2+	2+	-	-
PRB912-01	0	10.2	NEG	NEG	NEG	**POS**	NEG	**1.8**	0.9	neg	-	-	-	-	-	-	-
PRB912-02	9	24.9	**POS**	**POS**	**POS**	POS	**POS**	>6,7	**5.4**	**HIV-1**	-	3+	-	2+	2+	-	-
PRB912-03	14	10.6	POS	POS	POS	POS	POS	>6,7	6.8	HIV-1	-	3+	-	2+	2+	-	-
PRB912-04	16	3.2	POS	POS	POS	POS	POS	>6,7	7.7	HIV-1	-	3+	-	2+	2+	-	-
PRB912-05	28	0.5	POS	POS	POS	POS	POS	>6,7	10.7	HIV-1	-	3+	-	2+	2+	-	-
PRB912-06	30	0.5	POS	POS	POS	POS	POS	>6,7	11.9	HIV-1	-	3+	-	2+	2+	-	-
PRB914-01	0	0.4	**POS**	**POS**	NEG	**POS**	**POS**	**>6,7**	**4.9**	**HIV-1**	1+	2+	-	+/-	-	-	-
PRB914-02	4	0.5	POS	POS	NEG	POS	POS	>6,7	6.5	HIV-1	1+	2+	-	1+	-	-	-
PRB914-03	7	0.5	POS	POS	NEG	POS	POS	>6,7	7.8	HIV-1	1+	2+	-	2+	1+	-	-
PRB914-04	25	0.4	POS	POS	NEG	POS	POS	>6,7	13.8	HIV-1	2+	2+	-	2+	2+	-	-
PRB914-05	31	0.4	POS	POS	NEG	POS	POS	>6,7	14.0	HIV-1	2+	2+	-	2+	2+	-	-
PRB917-01	0	0.4	NEG	NEG	NEG	NEG	NEG	0.6	0.7	neg	-	-	-	-	-	-	-
PRB917-02	53	3.9	NEG	NEG	NEG	NEG	NEG	0.1	0.3	neg	-	-	-	-	-	-	-
PRB917-03	57	21.6	NEG	NEG	NEG	NEG	NEG	0.2	0.4	neg	-	-	-	-	-	-	-
PRB917-05	65	2.4	**POS**	**POS**	NEG	**POS**	**POS**	**>6,7**	**5.7**	**HIV-1**	1+	2+	-	+/-	-	-	-
PRB917-06	67	1.6	POS	POS	**POS**	POS	POS	>6,7	6.8	HIV-1	1+	2+	-	1+	-	-	-

Notes: [1] Results obtained from Boston Biomedica Inc (now SeraCare Life Sciences).
[2] Results obtained from ITM, Antwerp.

SR1*:* HIV 1/2 Stat-Pak
SR2: HIV 1/2 Stat-Pak *Dipstick*
SR3: ADVANCED QUALITY™ HIV Rapid Test
SR4: Retrocheck HIV / CORE™ HIV 1&2
SR5: DoubleCheckGold™ HIV 1&2 Whole Blood

Table 6. (continued) Results on commercial seroconversion panels

Panel	Days since 1st bleed	HIV Ag[1] S/CO	Assays under evaluation					Enzygnost Anti-HIV1/2 Plus[2] OD/CO	Vironostika HIV Uni-Form II *Plus* O[2] OD/CO	INNO-LIA HIV Confirmation[2]							
			SR 1	SR 2	SR 3	SR 4	SR 5			Result	Sgp120	gp41	p31	p24	p17	sgp105	gp36
PRB927-01	0	0.6	NEG	NEG	NEG	NEG	NEG	0.1	0.3	neg	-	-	-	-	-	-	-
PRB927-02	28	>22.7	NEG	NEG	NEG	NEG	NEG	**2.2**	**1.8**	neg	-	-	-	-	-	-	-
PRB927-03	33	10.2	**POS**	**POS**	NEG	**POS**	**POS**	>6,7	8.3	ind	-	2+	-	-	-	-	-
PRB927-04	35	2.6	POS	POS	**POS**	POS	POS	>6,7	5.5	**HIV-1**	1+	2+	-	-	-	-	-
PRB927-05	40	1.3	POS	POS	POS	POS	POS	>6,7	6.2	HIV-1	2+	3+	-	2+	2+	-	-
PRB928-01	0	0.6	NEG	NEG	NEG	NEG	NEG	0.1	0.3	neg	-	-	-	-	-	-	-
PRB928-02	111	>22.7	**POS**	**POS**	NEG	NEG	**POS**	**4.8**	**1.5**	ind	-	1+	-	-	-	-	-
PRB928-03	120	2.2	POS	POS	**POS**	**POS**	POS	>6.7	4.0	**HIV-1**	-	3+	-	2+	-	-	-
PRB928-04	125	1.8	POS	POS	POS	POS	POS	>6.7	3.7	HIV -1	1+	2+	-	2+	1+	-	-
PRB928-05	130	1.0	POS	POS	POS	POS	POS	>6.7	5.6	HIV -1	2+	3+	-	2+	2+	-	-
PRB930-01	0	0.9	NEG	NEG	NEG	NEG	NEG	0.1	0.3	neg	-	-	-	-	-	-	-
PRB930-02	3	2.7	NEG	NEG	NEG	NEG	NEG	0.1	0.3	neg	-	-	-	-	-	-	-
PRB930-03	7	4.2	NEG	**NEG**	NEG	NEG	**POS**	**4.5**	**2.2**	ind	-	1+	-	-	-	-	-
PRB930-04	10	12.8	**POS**	POS	NEG	**POS**	POS	>6.7	8.6	**HIV -1**	-	2+	-	2+	-	-	-
PRB944-01	0	0.5	NEG	NEG	NEG	NEG	NEG	0.1	0.3	neg	-	-	-	-	-	-	-
PRB944-02	2	1.0	NEG	NEG	NEG	NEG	NEG	0.1	0.3	neg	-	-	-	-	-	-	-
PRB944-03	7	6.6	NEG	NEG	NEG	NEG	NEG	0.1	0.3	neg	-	-	-	-	-	-	-
PRB944-04	9	7.0	NEG	NEG	NEG	NEG	NEG	0.2	0.3	neg	-	-	-	-	-	-	-
PRB944-05	14	5.8	**POS**	**POS**	NEG	NEG	**POS**	**5.0**	**1.8**	**HIV -1**	-	2+	-	1+	-	-	-
PRB944-06	16	3.2	POS	POS	**POS**	**POS**	POS	>6.7	3.1	HIV -1	-	2+	-	2+	-	-	-

Notes: [1] Results obtained from Boston Biomedica Inc (now SeraCare Life Sciences).
[2] Results obtained from ITM, Antwerp.

SR1*:* HIV 1/2 Stat-Pak
SR2: HIV 1/2 Stat-Pak *Dipstick*
SR3: ADVANCED QUALITY™ HIV Rapid Test
SR4: Retrocheck HIV / CORE™ HIV 1&2
SR5: DoubleCheckGold™ HIV 1&2 Whole Blood

Table 7. Results on commercial anti-HIV 1 mixed titer performance panel

Panel ID	Expected Result	Assays under evaluation					Reference Assays									
		SR1	SR2	SR3	SR4	SR5	Coulter p24 Ag EIA[1] OD/CO	bioMérieux VIDAS HIV DUO[1] OD/CO	Abbott PRISM HIV O Plus[1] OD/CO	INNO-LIA HIV I/II Score Immunoblot[2]						Result
										sgp120	gp41	p31	p24	p17	sgp105	gp36	
PRB204-01	Inconclusive	Neg	Neg	Neg	Neg	Neg	4.0	1.0	1.2	-	1+	-	-	-	-	-	IND
PRB204-02	Positive	Pos	Pos	Pos	Pos	Pos	0.5	65.2	118.3	3+	3+	2+	3+	3+	-	-	HIV-1
PRB204-03	Negative	Neg	Neg	Neg	Neg	Neg	0.4	0.2	0.8	-	-	-	-	-	-	-	NEG
PRB204-04	Positive	Pos	Pos	Pos	Pos	Pos	0.4	65.1	80.8	3+	3+	2+	3+	3+	-	-	HIV-1
PRB204-05	Positive	Pos	Pos	Pos	Pos	Pos	3.1	66.1	128.3	2+	2+	2+	2+	2+	-	-	HIV-1
PRB204-06	Positive	Pos	Pos	Pos	Pos	Pos	0.4	67.5	107.6	3+	2+	2+	2+	3+	-	-	HIV-1
PRB204-07	Positive	Pos	Pos	Pos	Pos	Pos	0.3	66.0	135.8	3+	3+	2+	3+	3+	-	-	HIV-1
PRB204-08	Positive	Pos	Pos	Pos	Pos	Pos	0.3	64.6	133.9	3+	3+	2+	3+	2+	-	-	HIV-1
PRB204-09	Inconclusive	Neg	Neg	Pos	Pos	Pos	5.5	2.4	2.4	-	1+	-	-	-	-	-	IND
PRB204-10	Positive	Pos	Pos	Pos	Pos	Pos	0.6	65.1	21.5	1+	3+	-	3+	1+	-	-	HIV-1
PRB204-11	Positive	Pos	Pos	Pos	Pos	Pos	0.4	65.4	141.8	3+	3+	2+	3+	3+	-	2+	HIV
PRB204-12	Positive	Pos	Pos	Pos	Pos	Pos	0.4	63.8	76.1	3+	3+	2+	3+	3+	-	-	HIV-1
PRB204-13	Positive	Pos	Pos	Pos	Pos	Pos	0.3	67.0	15.2	1+	2+	-	2+	2+	-	-	HIV-1
PRB204-14	Positive	Pos	Pos	Pos	Pos	Pos	0.6	63.8	122.3	3+	3+	2+	3+	3+	-	-	HIV-1
PRB204-15	Positive	Pos	Pos	Pos	Pos	Pos	0.7	63.6	121.8	3+	2+	2+	2+	3+	-	-	HIV-1
PRB204-16	Positive	Pos	Pos	Pos	Pos	Pos	0.5	66.6	22.8	2+	3+	-	3+	2+	-	-	HIV-1
PRB204-17	Positive	Pos	Pos	Pos	Pos	Pos	2.6	68.8	28.8	2+	3+	-	3+	1+	-	-	HIV-1
PRB204-18	Positive	Pos	Pos	Pos	Pos	Pos	3.3	71.2	11.0	1+	2+	-	2+	1+	-	-	HIV-1
PRB204-19	Positive	Pos	Pos	Pos	Pos	Pos	0.6	71.5	5.1	1+	2+	-	3+	1+	-	-	HIV-1
PRB204-20	Positive	Pos	Pos	Pos	Pos	Pos	2.1	68.5	119.1	3+	3+	2+	1+	2+	-	-	HIV-1
PRB204-21	Positive	Pos	Pos	Pos	Pos	Pos	2.7	71.7	6.5	-	3+	-	3+	2+	-	-	HIV-1
PRB204-22	Positive	Pos	Pos	Pos	Pos	Pos	1.0	68.5	123.1	3+	3+	2+	2+	1+	-	-	HIV-1
PRB204-23	Negative	Neg	Neg	Neg	Neg	Neg	0.4	0.2	0.3	-	-	-	-	-	-	-	NEG
PRB204-24	Positive	Pos	Pos	Pos	Pos	Pos	2.8	2.3	4.6	1+	2+	-	1+	-	-	-	HIV-1
PRB204-25	Inconclusive	Pos	Neg	Neg	Neg	Neg	0.4	0.9	7.4	-	1+	-	-	-	-	-	IND

Notes: [1] Results obtained from Boston Biomedica Inc (now SeraCare Life Sciences).

[2] Results obtained from ITM, Antwerp.

SR1*:* HIV 1/2 Stat-Pak

SR2: HIV 1/2 Stat-Pak *Dipstick*

SR3: ADVANCED QUALITY™ HIV Rapid Test

SR4: Retrocheck HIV / CORE™ HIV 1&2

SR5: DoubleCheckGold™ HIV 1&2 Whole Blood

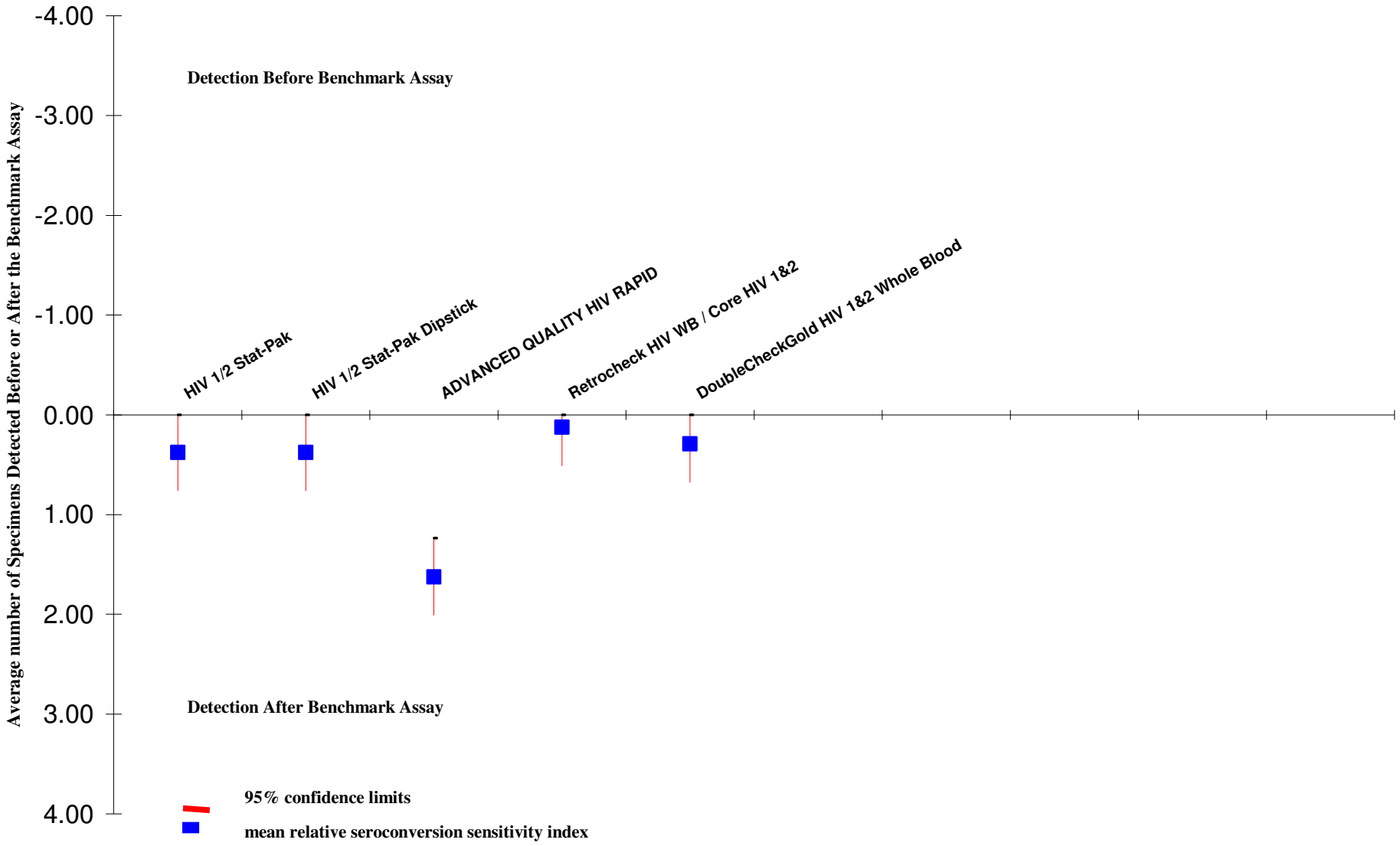


Figure 6: Relative performance on seroconversion panels as compared to the benchmark assay (Enzygnost HIV 1/2 Plus

Explanatory notes for Tables 1-6 and Figure 6

Table 1	**General characteristics and operational aspects of the assays**
Specimen type	The nature of specimen(s) that may be used in the assay
Individual/combined HIV 1 & HIV 2 reactivity	Individual: Ability to differentiate between HIV-1 and HIV-2 reactivity Combined: No ability to differentiate between HIV-1 and HIV-2 reactivity
Shelf life (at ˚C)	The maximum shelf life of the product if stored within the given temperature range
Final dilution of the serum	The dilution of the serum in the test format, e.g. 10µl serum added to 200µl diluent gives a final dilution of 1/21
Total time to perform the assay	Reflects the time needed to carry out 1 test run, i.e. the most economical use of the technique
Indicative price/test in US$	As given at the time of the evaluation by the manufacturer, or converted to USD using the currency conversion rate at the time the prices stated are meant to be catalogue prices and therefore are indicative only

Table 2	**Comparison of the results of the assays with reference assays**
Sensitivity	Calculated as described on section 5.5.1 of this document
Specificity	Calculated as described on section 5.5.1 of this document
PPV and NPV	Calculated as described on section 5.5.1 of this document
95% Confidence intervals (CI)	Calculated as described on section 5.5.1 of this document
Indeterminate results	Rapid assays - test results which could not be interpreted as clearly positive or negative were considered indeterminate
Inter-reader variability	Calculated as described on section 5.5.3 of this document

Table 3	**Detailed operational aspects of the assays**
Reading endpoint	The time period after the completion of the test procedure, including any stated incubation period, within which the result may be read. Assays which show a time period of 0.00 must be read immediately upon completion of the assay
Minimum - maximum number of sera	Minimum number = one specimen, in addition to the required controls Maximum number = the maximum number of specimens in addition to the required controls which can be simultaneously tested within the limits of the assay procedure.
Number of controls per test run	The manufacturer supplies HIV positive and negative control specimens as a separate item for 5 of the assays The manufacturer does not supply HIV positive and negative control specimens for the remaining 0 assays The number of controls shows the number of replicates of each control required for each assay run.

Explanatory notes for Tables 1-6 and Figure 6

Internal control: - specimen addition control	The following assays have a control line that shows both that the specimen has been added and the reagents functioned correctly: HIV 1/2 Stat-Pak HIV 1/2 Stat-Pak *Dipstick,* ADVANCED QUALITY™ HIV Rapid Test, DoubleCheckGold™ HIV 1&2 Whole Blood.
- reagent addition control	The following assay has a control line that which shows that the reagents have been added: Retrocheck HIV WB/Core HIV 1&2.
Definition of positive results	A specimen is interpreted as positive according to the criteria set by the manufacturer and summarized in the table
Tables 4a and 4b	**Technician's appraisal and calculation of ease of performance of the assays** The criteria for this calculation are given in the respective tables
Table 5	**Technical suitability of the assays for use in small laboratories** The criteria for this calculation are given in the respective table
Note	These criteria are primarily technical and while an assay may be regarded as "technically" suitable for use in laboratories with limited facilities or where small numbers of samples are routinely tested, the sensitivity and specificity of the assay are over-riding factors in determining the suitability of an assay for use in any laboratory
Table 6	**Performance of the assay on seroconversion panels** An assay's performance on the seroconversion panels should be viewed against both the sensitivity and specificity of the assay. Assays of relatively low specificity may appear to detect antibody to HIV earlier than other assays of higher specificity. Caution should be taken when reviewing seroconversion performance of assays tested only in 8 panels
Figure 6	**Relative performance on seroconversion panels** Eight seroconversion panels (sourced from BBI, now SeraCare Life Sciences), each containing several specimens taken at different time intervals early in the infection period (window period), were tested with rapid anti-HIV assays. The results obtained with these assays were compared to those of the combined outcome of the Enzygnost HIV 1/2 Plus benchmark assay. The mean of the difference in time period for a test to become reactive as compared to the benchmark assay was calculated and plotted. The 95% confidence intervals of the mean were also calculated

7. References

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8. Annexes

Annex 1 - Cumulative list of assays evaluated whose production has been discontinued

The names (and manufacturers) of the assays evaluated to date under the WHO programme are listed in the table below. The number of the report in which each assay is covered is given, as well as sensitivity and specificity with 95% confidence intervals, δ values for HIV antibody-positive and antibody-negative specimen populations, cost per test, ease of performance and suitability for use in small blood collection centers.

Assay (manufacturer)	Report No [a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	δ Values		Cost per test (US$) /year	nm[h]	Ease of performance	Suitability	Indeterminate results (%)
				WB pos sera	WB neg sera					
Enzyme linked immunosorbent assays										
For the detection of antibody to HIV-1										
Dupont HIV-1 Recombinant ELISA (Dupont de Nemours)	1	100.0 (98.7-100.0)	97.0 (92.7-98.8)			0.9/'88	450/410	LE	LS	NA
Enzygnost Anti-HIV Micro (Behringwerke)	1	100.0 (97.8-100.0)	100.0 (98.1-100.0)			1.8/'88	450 450/630	LE	LS	0.0
HIV-TEK G (Sorin Biomedica)	1	100.0 (96.0-100.0)	86.5 (79.5-91.8)			1.0/'88	450	LE	LS	NA
Vironostika Anti-HIV Uni-Form (Organon Teknika)	1	100.0 (97.6-100.0)	99.5 (97.3-100.0)			2.2/'88	492 492/630	LE	LS	NA
Ortho HIV ELISA System (Ortho Diagn. Systems)	1	100.0 (97.8-100.0)	98.0 (95.0-99.4)			1.8/'88	490	LE	LS	NA
HIV-1 env Peptide EIA (Labsystems)	2	96.0 (90.8-98.7)	97.0 (93.5-98.9)			3.9/'89	405 405/630	LE	LS	NA
Wellcozyme HIV Recombinant (Wellcome Diagnostics)	2	100.0 (98.2-100.0)	99.1 (96.8-99.9)			1.5/'89	450	LE	LS	NA
Genetic Systems LAV EIA (Genetic Systems)	3	100.0 (98.2-100.0)	96.3 (92.9-98.4)	9.2	-2.13	1.0/'90	450 450/615-630	LE	LS	NA

Annex 1 (continued)

Assay (manufacturer)	Report No [a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	δ Values WB pos sera	δ Values WB neg sera	Cost per test (US$) /year	nm[h]	Ease of performance	Suitability	Indeterminate results (%)
REC VIH-KCOI (Heber Biotec)	3	97.0 (93.5-98.9)	100.0 (98.3-100.0)	2.1	-4.14		492	LE	LS	NA
UBI HIV-1 EIA (United Biomedical)	6	100.0 (99.9-100.0)	88.2 (87.1-89.3)	7.5	-1.12	1.0/'92	492/620-690	LE	S	NA
Peptide HIV-1 ELISA Test System (Sero-Immuno Diagnostics)	6	82.1 (76.5-87.6)	94.1 (91.0-97.2)			0.6/'92	visual	E	VS	0.0
Peptide HIV-2 ELISA Test (Sero-Immuno Dianostics)	6	97.1 (93.0-100.0)	98.1 (96.3-99.9)			0.6/'92	visual	E	VS	NA
UBI HIV-2 EIA (United Biomedical)	7	100.0 (97.4-100.0)	96.1 (93.4-98.8)	10.5	-1.7	1.2/'93	492/620-630	LE	S	NA
Enzygnost Anti-HIV-1 (Behringwerke)	7	100.0 (98.1-100.0)	100.0 (98.8-100.0)	7.4	-3.3		450/615-690	LE	LS	0.0
Enzygnost Anti-HIV-2 (Behringwerke)	8	100.0 (96.7-100.0)	99.5 (98.5-100.0)	23.8	-3.5	6.2/'93	450/630	LE	LS	0.0
<u>For the detection of antibody to HIV-1 and HIV-2</u>										
Enzygnost Anti-HIV -1+2 (Behringwerke)	2	100.0 (98.4-100.0)	97.4 (94.0-99.2)	11.3	-2.15	2.3/'89	450 450/615-690	LE	LS	0.0
Biochrom HIV-1/HIV-2 ELISA Modul-test (Biochrom)	3	100.0 (98.6-100.0)	96.3 (92.5-98.5)	6.20	-1.69	0.9/'89	405	LE	LS	1.0
DuPont HIV-1/HIV-2 ELISA (DuPont de Nemours)	3	100.0 (98.7-100.0)	85.6 (79.8-90.2)	9.34	-0.96	1.3/'90	405 or 410 405 or 410/ 620 or 630	LE	LS	NA

Annex 1 (continued)

Assay (manufacturer)	Report No [a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	δ Values		Cost per test (US$) /year	nm[h]	Ease of performance	Suitability	Indeterminate results (%)
				WB pos sera	WB neg sera					
Vironostika HIV MIXT (Organon Teknika)	3	100.0 (98.7-100.0)	100.0 (98.1-100.0)	10.10	-2.94	1.8/'90	492	LE	LS	NA
Elavia Mixt (Diagnostics Pasteur)	4	100.0 (98.7-100.0)	95.1 (91.3-97.8)	54.33	-2.31	2.1/'90	492 492/620	LE	LS	0.0
Anti-HIV-1/HIV-2 EIA <Roche> (F. Hoffman-LaRoche)	4	100.0 (98.7-100.0)	96.9 (93.4-98.9)	11.30	-2.37	1.7/'90	492	LE	LS	NA
Clonatec HIV (1+2) Ab EIA (Clonatec)	6	99.6 (98.8-100.0)	95.9 (93.1-98.7)	7.47	-1.68	2.7'91	492	LE	S	0.0
Enzymun-Test Anti-HIV-1+2 (Boehringer Mannheim)	6	100.0 (98.7-100.0)	100.0 (98.6-100.0)	5.50	-2.48	3.0'92	405	LE	S	0.0
UBI HIV-1/2 EIA (United Biomedical)	6	100.0 (99.9-100.0)	88.7 (84.2-93.1)	7.18	-1.24	1.2/'92	492 492/620-690	LE	S	NA
Enzygnost Anti-HIV-1/HIV-2 (Behringwerke)	6	100.0 (99.9-100.0)	99.5 (98.5-100.0)	26.53	-3.50	2.6'92	450 450/615-690	LE	LS	0.0
Cobas Core Anti-HIV-1/HIV-2 EIA <Roche> (Hoffmann-La Roche)	7	100.0 (98.6-100.0)	89.2 (84.6-93.8)	10.8	-1.0	2.2'93	450	LE	LS	0.0
Biochrom HIV-1/HIV-2 ELISA Version 2 (Biochrom)	7	99.5 (99.0-100.0)	100.0 (98.6-100.0)	7.5	-7.3	1.0/'93	450	LE	LS	0.0
Wellcozyme HIV-1 + 2 (Wellcome Diagnostics)	4	100.0 (98.7-100.0)	96.9 (93.3-98.9)	38.51	-1.99	1.5/'90	492	LE	LS	NA

Annex 1 (continued)

Assay (manufacturer)	Report No [a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	δ Values [e]		Cost per test (US$) /year	nm[h]	Ease of performance	Suitability	Indeterminate results (%)
				WB pos sera	WB neg sera					
Peptide HIV ELISA (Cal-Tech Diagnostics)	5	72.6 (69.4-77.6)	95.4 (91.3-97.9)			0.9/'91	visual	E	S	0.2
Genelavia Mixt (Sanofi Diagnostics Pasteur)	5	100.0 (98.6-100.0)	98.5 (95.6-99.8)	16.77	-2.10	1.5/'91	492 492/620	LE	LS	0.0
Biotest Anti-HIV-1/-2 Recombinant (Biotest)	5	100.0 (98.6-100.0)	97.9 (94.9-99.4)	50.47	-3.08	1.2/'91	492 492/570-650	LE	LS	0.0
Innotest HIV-1/HIV-2 Ab (Innogenetics)	6	100.0 (98.8-100.0)	97.9 (95.9-99.9)	7.22	-2.30	1.9'91	450 450/620-690	LE	LS	NA
Peptide HIV-1 & HIV-2 ELISA Test (Sero-Immuno Dianostics)	6	97.6 (95.7-99.5)	98.5 (96.7-100.0)			0.6'92	visual	E	VS	NA
UBI HIV-1/2 EIA 2nd (United Biomedical)	7	99.5 (98.6 -100.0)	92.4 (88.6 - 96.2)	4.8	-1.5	1.2'93	492/620 or 630	LE	S	NA
VIDAS HIV-1+2 (Bio Merieux)	8	100.0 (98.5-100.0)	97.8 (95.6-100.0)			3.6/'93	450	VE	S	0.3
HIV 1+2 env Peptide EIA (Labsystems OY)	8	100.0 (98.6-100.0)	76.2 (70.0-82.4)			08/2.8/'93	450	LE	LS	0.0
Enzygnost Anti-HIV 1/-HIV 2 (Behringwerke)	9	100.0 (99.6-100.0)	99.5 (98.7-100.0)	24.8	-2.55	2.6'92	450 450/615-690	LE	LS	0.0
VIRONOSTIKA HIV Uni-Form II (Organon Teknika)	9	100.0 (99.6-100.0)	98.8 (97.6-100.0)	7.4	-3.0	1.7/'94	450/660 ± 40	LE	LS	NA
BIOTEST Anti-HIV-1/-2 recombinant (Biotest AG)	9	100.0 (99.6-100.0)	99.1 (98.1-100.0)	74.9	-3.3	1.2/'94	492/570-650	LE	LS	0.0
INNOTEST HIV-1/HIV-2 Ab s.p. (Innogenetics n.v.)	9	100.0 (99.6-100.0)	98.8 (97.6-100.0)	14.0	-3.8	1.5/'94	450 450/620-690	LE	LS	NA

Annex 1 (continued)

Assay (manufacturer)	Report No [a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	δ Values [e]		Cost per test (US$) /year	nm[h]	Ease of performance	Suitability	Indeterminate results (%)
				WB pos sera	WB neg sera					
Genelabs Diagnostics HIV-1/HIV-2 ELISA (Genelabs Diagnostics)	10	100 (99.6 -100.0)	97.3 (95.6 - 99.0)	72.2	-2.7	0.9'94	492	LE	LS	NA
HIV SCREEN (Labsystems OY)	10	100.0 (99.6 -100.0)	99.7 (99.1 -100.0)	21.51	-4.11	0.6'95	450	LE	LS	NA
HIVvisual 1 & 2 (Immuno Diagnostics Inc.)	10	90.9 (87.4 - 94.4)	94.5 (92.5 -97.3)	1.88	-1.15		450	LE	LS	NA
ETI-AB-HIV-1/2 K (Sorin Biomedica)	10	100.0 (99.6-100.0)	98.8 (97.6-100.0)	10.4	-2.5	1.5/'94	450/630	LE	LS	NA
ICE * HIV-1.O.2 (Murex Biotech Ltd.)	11	100.0 (99.6 -100.0)	99.4 (98.6 -100.0)	16.8	-4.3	0.6'95	450 450/620-690	LE	LS	NA
GENSCREEN HIV 1/2 (Sanofi Diagnostics Pasteur)	11	100.0 (99.6 -100.0)	98.5 (97.2 - 99.8)	22.8	-2.7	1.5'95	450/620	LE	LS	0.0
HIVA TEST (Lupin Laboratories Ltd)	11	100.0 (99.5 -100.0)	93.7 (91.0 - 96.4)	12.2	-1.1	0.6'98	450	LE	LS	1.5
HIV-1 and/or HIV-2 Recombigen EIA (Trinity Biotech plc)	7	100.0 (98.6-100.0)	100.0 (98.6-100.0)	10.4	-5.0	1.7/'93	490/630	LE	LS	NA

Annex 1 (continued)

Assay (manufacturer)	Report No[a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	Initial inter-reader variability (%)	Cost per test (US$) /year	Ease of performance	Suitability	Indeterminate results (%)
Simple/Rapid assays								
For the detection of antibody to HIV-1								
HIV CHEK/HIVSPOT (Genelabs Diagnostics)	1	94.5 (89.7- 97.4)	99.0 (96.4-99.9)	12.3	2.5/'88	VE	VS	
Recombigen HIV-LA (Cambridge BioScience)	1	95.2 (88.3-98.7)	96.1 (92.6-98.2)	6.0	3.0/'88	VE	S	
Immunocomb (PBS Orgenics)	1	98.8 (95.7- 99.9)	98.9 (96.0-99.9)	2.8	2.5/'89	VE	VS	
Serion Immuno Tab HIV-1 (Serion Immunodiagnostica)	2	98.9 (96.9- 99.9)	100.0 (98.3-100.0)	7.1	2.5/'90	LE	LS	1.2
Genie HIV-1 (Genetic Systems)	4	99.5 (97.4-100.0)	99.1 (96.7-99.9)	1.1	3.5/'90	VE	VS	0.2
SimpliRed HIV-1 Ab (Agen Biomedical)	5	97.5 (94.2-99.2)	91.2 (86.6-94.7)	10.5	7.8/1.5/'91	VE	S	0.7
Healthtest HIV-1 Assay (Akers Research Corp.)	6	58.7 (49.2-68.2)	89.4 (84.9-93.9)	7.0	1.4/2.3/'92	VE	S	0.2
Entebe HIV Dipstick (Hepatika Laboratories)	6	97.0 (94.4-99.6)	99.1 (97.8-100.0)			E	VS	
Abbott Retrocell HIV 1 (Abbott GmbH)	9	100.0 (99.6 -100.0)	100.0 (99.7-100.0)	2.2	1.45/'94	VE	S	0.6
PATH HIV Dipstick (PATH)	4	99.5 (97.3-100.0)	98.2 (97.1.99.1)	1.3	<1.5'91	E	VS	0.0
SUDS Murex HIV-1 Ab test (Murex Corporation)	5	100.0 (98.5-100.0)	75.1 (69.3-80.9)	22.9	4.5/'91	VE	S	11.7

Annex 1 (continued)

Assay (manufacturer)	Report No[a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	Initial inter-reader variability (%)	Cost per test (US$) /year	Ease of performance	Suitability	Indeterminate results (%)
<u>For the detection of antibody to HIV-1 and HIV-2</u>								
Test Pack HIV-1/HIV-2 Ab (Abbott)	2	100.0 (98.5-100.0)	95.9 (92.0-98.2)	1.4	4.8/'89	VE	VS	0.0
Immunocomb Bi-Spot (PBS Orgenics)	3	98.5 (96.3-99.6)	100.0 (98.1-100.0)	7.6	4.0/'90	VE	VS	0.9
HIV CHEK 1+2/HIVSPOT 1+2 (DuPont de Nemours)/(Genelabs Diagnostics)	3	99.3 (97.4-99.9)	100.0 (98.1-100.0)	7.2	4.0/'90	E	VS	1.0
Recodot (Waldheim Pharmazeutika)	4	98.9 (97.0-99.8)	88.6 (82.2-93.3)	31.7	2.0/'90	LE	LS	12.3
Genie HIV-1 and HIV-2 (Genetic Systems)	4	99.3 (97.5-99.9)	99.5 (97.2-100.0)	11.8	3.5/'90	VE	VS	0.0
Clonatec rapid HIV 1-HIV 2 Ab (Clonatec)	5	98.9 (96.8-99.8)	99.5 (97.2-99.8)	15.9	4.3/'91	E	VS	0.4
Recobead LA Assay (Waldheim Pharmazeutika)	6	59.8 (53.9 -65.7)	94.8 (91.7 - 97.9)	22.3	1.7/2.2/'91	VE	S	0.4
Recombigen HIV-1/HIV-2 Rapid Test Device (Trinity Biotech plc)	7	100.0 (98.7-100.0)	94.5 (91.2-97.8)	11.4	4.0/'93	E	VS	2.8
MicroRed HIV-1/HIV-2 Ab Test (Agen Biomedical)	9	98.5 (97.0-100.0)	95.5 (93.2-97.7)	1.5	1.5/1.0/'94	VE	S	0.5
SimpliRed HIV-1 /HIV-2Ab Test (Agen Biomedical)	9	99.2 (98.2 -100.0)	87.3 (83.7 -90.9)	9.5	4.0/3.0/'94	VE	S	0.3
HIV (Sav) 1&2 Rapid Sero Test (Diatech (Savyon) Diagnostica Ltd.)	10	97.7 (95.9 -99.5)	96.7 (94.8 -98.6)	5.1	1.9'94	VE	S	0.2
ENTEBE HIV Dipstick (Hepatika Laboratories)	10	100.0 (99.6 -100.0)	96.4 (94.4 -98.4)	5.0	0.8'94	VE	VS	1.3

Annex 1 (continued)

Assay (manufacturer)	Report No[a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	Initial inter-reader variability (%)	Cost per test (US$) /year	Ease of performance	Suitability	Indeterminate results (%)
Dipstick-HIV 1 + 2 (Pacific Biotech Co., Ltd.)	10	100.0 (99.6- 100.0)	98.2 (96.8 -99.6)	1.0	0.5'94	E	VS	0.3
DIA (Dot Immuno Assay) HIV 1 + 2 (Weiner Lab.)	10	99.6 (98.8-100.0)	99.4 (98.6-100.0)	0.8	<1.0'94	VE	VS	0.2
SERO•STRIP HIV-1/2 (Saliva Diagnostic Systems)	11	98.9 (97.6 -100.0)	100.0 (99.7 -100.0)	1.5	1.5'95	VE	VS	0.0
RED-DOT HIV 1&2 (Cal-Test Diagnostics Inc.)	11	100.0 (99.6 -100.0)	94.9 (92.5 - 97.3)	9.5	2.9'94	VE	S	1.9
HIVCHEK System 3 Test Kit (Ortho Diagnostic Systems)	11	99.6 (98.9 -100.0)	99.7 (99.1 -100.0)	1.0	4.35'95	E	VS	0.2
AccuSpot HIV-1 and 2 (Specialty BioSystems Inc.)	11	100.0 (99.6 -100.0)	86.3 (82.5 - 90.1)	10.8	2.5'95	VE	S	5.0
SEROCARD HIV (Trinity Biotech plc)	11	100.0 (99.6 -100.0)	97.9 (96.4 - 99.1)	1.5	4.0/'94	VE	VS	0.2
EasiDot HIV/EasiSpot HIV (Nubenco Diagnostics)	11	95.3 (92.7 - 97.9)	71.3 (66.4 - 76.2)	23.7		VE	S	12.5
For the detection of antibody to HIV-1 and HIV-2 and HIV-1 p24 antigen								
Genscreen® Plus HIV Ag/Ab (Bio-Rad Laboratories)	15	100 (97.7-100)	98.3 (96.1-99.4)	NA	0.62-0.68/'04	LE	LS	0.0
Supplemental assays								
For the detection of antibody to HIV-1 or HIV-2								
RIBA HIV-1 (Chiron)	1	99.4 (96.6-100.0)	100.0 (97.9-100.0)	NA	27.6/'88	E	S	
HIV Western Blot Kit (Organon Teknika)	3	100.0 (98.2-100.0)	100.0 (98.0-100.0	NA	21.0/'90	LE	S	10.5
Wespage HIV-1 Western blot Kit (Bio Genex)	6	100.0 (99.9-100.0)	100.0 (99.9-100.0)	NA	21.6/'92	LE	VS	12.8
Wespage HIV-1 Western blot Kit II (Bio Genex)	7	100.0 (98.5 -100.0)	100.0 (98.7 -100.0)	NA	17.7/'93	LE	S	12.4
CBC HIV-2 Western blot kit (Cambridge Biotech)	7	100.0 (97.0-100.0)	100.0 (98.5-100.0)	NA	16/'93	LE	S	13.9

Annex 2 - Cumulative list of assays evaluated; currently commercially available

The names (and manufacturers) of the assays evaluated to date under the WHO programme are listed in the table below. The number of the report in which each assay is covered is given, as well as sensitivity and specificity with 95% confidence intervals, δ values for HIV antibody-positive and antibody-negative specimen populations, cost per test, ease of performance and suitability for use in small blood collection centers.

Assay (manufacturer)	Report No [a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	δ Values [e]		Cost per test (US$) /year	nm[h]	Ease of performance	Suitability	Indeterminate results (%)
				WB pos sera	WB neg sera					
Enzyme-linked immunosorbent assays - Evaluations on serum/plasma										
<u>For the detection of antibody to HIV-1 and HIV-2</u>										
Detect-HIV™ (Biochem Immunosystemes now Adaltis)	3	100.0 (98.6-100.0)	97.4 (94.0-99.2)	12.65	-2.21	2.5/'90	450 450/600-650	LE	LS	NA
Abbott Recombinant HIV-1/HIV-2 3rd Generation (Abbott)	7	100.0 (98.5-100.0)	100.0 (98.5-100.0)	11.5	-4.3	1.7/1.8'93	492	LE	LS	NA
UBI HIV 1/2 EIA (United Biomedical Inc.)	9	100.0 (99.6-100.0)	100.0 (99.7-100.0)	10.8	-3.2	1.0/'94	492 492/620-690	LE	LS	NA
HIV EIA (Labsystems OY now Anilabsystems)	10	100 (99.6 -100.0)	99.4 (98.6 -100.0)	14.20	-3.85	0.6'95	450	LE	LS	NA
IMx HIV-1/HIV-2 3rd generation Plus (Abbott GmbH Diagnostika)	11	99.6 (98.9 -100.0)	97.9 (96.4- 99.4)	9.1	-2.1	3-4'95	Imx system	VE	S	0.3
Enzygnost Anti-HIV 1/2 Plus (Behringwerke AG now Dade Behring)	11	100.0 (99.6 -100.0)	99.7 (99.1 -100.0)	19.1	-6.6	1.0'95	450 450/615-690	LE	LS	0.0
Vironostika Uni-Form II *plus* O (Organon Teknika nv (now bioMérieux)	11	100.0 (99.6 -100.0)	100.0 (99.7 -100.0)	17.2	-4.1	1.5'97	450 450/620-700	LE	LS	NA

Annex 2 (continued)

Assay (manufacturer)	Report No[a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	Initial inter-reader variability (%)	Cost per test (US$) /year[g]	Ease of performance	Suitability	Indeterminate results (%)
Rapid tests - Evaluations on serum/plasma								
For the detection of antibody to HIV-1								
Serodia-HIV (Fujirebio)	1	100.0 (97.6-100.0)	96.9 (93.4-99.0)	0.8	1.1/'88	E	S	0.0
For the detection of antibody to HIV-1 and HIV-2								
Serodia-HIV-1/2 (Fujirebio)	8	100 (98.5-100.0)	100 (98.5-100.0)	6.3	2.8/'93	LE	S	0.0
SPAN COMBAIDS VISUAL (Span Diagnostics.)	8	96.5 (93.5-99.5)	100.0 (98.3-100.0)	0.8	0.4/'93	E	VS	0.0
CAPILLUS HIV-1/HIV-2 (Trinity Biotech plc)	9	100.0 (99.6-100.0)	98.8 (97.6-100.0)	0.0	2.2/'94	VE	VS	0.0
Immunocomb II BiSpot HIV 1&2 (PBS Orgenics)	9	100.0 (99.6-100.0)	99.7 (99.1-100.0))	4.5	1.7/'94	VE	VS	0.2
SPAN COMBAIDS VISUAL (Span Diagnostics Ltd.)	10	100.0 (99.6-100.0)	88.0 (84.5-91.5)	6.3	0.5'94	E	S	3.2
HIV TRI-DOT (J. Mitra & Co. Ltd.)	11	99.6 (98.9 -100.0)	99.7 (99.1 -100.0)	3.2	2.0'96	VE	VS	0.2
BIONOR HIV-1&2 (Bionor A/S)	11	100.0 (99.6 -100.0)	98.8 (97.6 -100.0)	1.0	2.5/'95	VE	S	0.2
HIV 1 & 2 DoubleCheck (Orgenics)	11	100 (99.6 -100.0)	99.4 (98.6 -100.0)	0.8	2.0/'96	VE	VS	0.2
*Instant*CHEK™-HIV 1+2 (EY Laboratories Inc)	14	99.4 (96.5 - 110.0)	97.6 (95.2 - 99.0)	4.6	1.0'03	E	S	0.0
GENIE II HIV-1/HIV-2 (Bio-Rad)	14	100 (97.7 - 100)	99.7 (98.1 - 100)	0.7	2.55/'03	E	VS	0.2

Annex 2 (continued)

Assay (manufacturer)	Report No [a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	Initial inter-reader variability (%)	Cost per test (US$) /year	Ease of performance	Suitability	Indeterminate results (%)
Efoora HIV Rapid (Efoora Inc)	14	96.2 (91.9 - 98.6)	98.9 (95.6 - 99.3)	3.8	0.75-2.60/'03	VE	S	0.4
OraQuick HIV-1/2 Rapid HIV-1/2 (OraSure Technologies Inc)	14	98.1 (94.5 - 99.6)	100.0 (98.8 - 100)	2.4	NA	VE	VS	0.4
SD Bioline HIV 1/2 3.0 (Standard Diagnostics)	14	100.0 (97.7 - 100.0)	99.3 (97.6 - 99.9)	3.5	1.10/'03	VE	VS	0.0
Hema • Strip(R) HIV 1/2 (Chembio Diagnostics Inc)	14	98.1 (94.5 - 99.6)	100.0 (98.8 - 100.0)	3.3	1.85-2.5/'03	VE	VS	0.0
HIV 1/2 STAT-PAK (Chembio Diagnostics Inc)	14	97.6 (93.6 - 99.3)	100.0 (98.8 - 100.0)	0.7	0.75-1.25/'03	VE	VS	0.0
HIV (1+2) Antibody (Colloidal Gold) (KHB Shanghai Kehua Bioengineering Co. Ltd)	14	100 (97.7 - 100.0	100.0 (98.8 - 100.0)	0.2	1.50/'03	VE	VS	0.0
GENEDIA(R) HIV 1/2 Rapid 3.0 (Green Cross Life Science Corp)	14	100 (97.7 - 100.0)	99.7 (98.1 - 100.0)	1.8	0.93-1.15/'03	VE	VS	0.0
DoubleCheckGold™ HIV 1&2 (Orgenics Ltd)	14	Lot A 99.4 (96.5 - 100.0) Lot B 100.0 (97.7 - 100.0)	Lot A 95.6 (92.6 - 97.6) Lot B 94.6 (91.4 - 96.9)	2.4	0.65-0.70/'03	VE	VS	Lot A 0.9 Lot B 2.0
HIV 1/2 Stat-Pak (Chembio Diagnostics Systems)	16	100 (98.8 - 100)	99.3 (98.1 - 99.9)	1.68	1.10-1.35/'05	VE	VS	0.0
HIV 1/2 Stat-Pak *Dipstick* (Chembio Diagnostic Systems)	16	99.4 (97.7 - 99.9)	100 (99.2 - 100)	0.26	0.80-0.95/'05	VE	VS	0.0
ADVANCED QUALITY™ HIV Rapid Test (InTec Products)	16	99.7 (98.2 - 99.8)	99.8 (98.8 - 100)	0.78	0.80-0.90/'05	VE	VS	0.0
Retrocheck HIV WB / Core HIV 1&2 (Qualpro Diagnostics / Core Diagnostics)	16	100 (98.8 - 100)	99.1 (97.8 - 99.8)	0.40	0.70-0.85/"05	VE	VS	0.13

Annex 2 (continued)

Assay (manufacturer)	Report No [a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	Initial inter-reader variability (%)	Cost per test (US$) /year	Ease of performance	Suitability	Indeterminate results (%)
DoubleCheckGold™ HIV 1&2 Whole Blood (Orgenics Ltd)	16	100 (98.8 - 100)	99.3 (98.1 - 99.9)	0.13	1.20-1.32/"05	VE	VS	0.0
For the detection of antibody to HIV-1 and HIV-2 and HIV-1 p24 antigen								
Enzygnost HIV Integral II (Dade Behring)	15	100 (97.7-100)	100 (98.7-100)	NA	NA/'04	LE	LS	0.0
Genedia® HIV AG-Ab ELISA (Green Cross)	15	100 (97.7-100)	99.7 (98.1-100)	NA	0.40-0.45/'04	LE	LS	0.0
Murex HIV Ag/Ab Combination (Abbott Diagnostics)	15	100 (97.7-100)	99.3 (97.6-99.9)	NA	0.80-1.20/'04	LE	LS	0.0
Vironostika® HIV UniForm II Ag/Ab	15	100 (97.7-100)	99.0 (97.1-99.8)	NA	1.48-1.95/'04	LE	LS	0.0
Supplemental assays- Evaluations on serum/plasma								
For the detection of antibody to HIV-1								
Ancoscreen (Ancos)	2	100.0 (97.8-100.0)	90.4 (82.6-95.5)	NA	10.8/21.5/'89	LE	LS	31.4
IFA anti-HIV-1 (Waldheim Pharmazeutika)	5	98.9 (96.9-99.8)	100.0 (98.3-100.0)	13.8	5.6/'91	LE	LS	0.7
New Lav-Blot-I (Sanofi Diagnostics Pasteur)	5	100.0 (98,.1-100.0)	100.0 (96.8-100.0)	NA	11.6/'91	E	S	30.6
HIV-1 Western Blot Kit (Open Tray Procedure) (Bio Genex)	7	100.0 (98.5-100.0)	100.0 98.7-100.0)	NA	17.7/'93	LE	S	6.7

Annex 2 (continued)

Assay (manufacturer)	Report No [a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	Initial inter-reader[f] variability (%)	Cost per test (US$) /year[g]	Ease of performance[i]	Suitability[j]	Indeterminate results[k] (%)
<u>For the detection of antibody to HIV-2</u>								
IFA anti-HIV-2 (Waldheim Pharmazeutika)	5	98.7 (93.1-99.7)	100.0 (98.2-100.0)	11.0	6.0/'91	LE	LS	1.8
<u>For the detection of antibody to HIV-1 and HIV-2</u>								
INNO-LIA HIV-1/HIV-2 Ab (Innogenetics)	2	100.0 (98.6-100.0)	100.0 (98.0-100.0)	NA	18.4/'89	LE	S	4.3
Speedscreen HIV (British Bio-Technology)	4	100.0 (99.4-100.0)	66.4 (57.9-74.1)	NA	17.0/'90	LE	S	16.9
Pepti-Lav 1-2 (Sanofi Diagnostics Pasteur)	4	99.3 (96.4-99.9)	100.0 (98.1/100.0)	NA	21.5/'90	LE	S	0.7

Annex 2 (continued)

Assay (manufacturer)	Report No [a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	Initial inter-reader[f] variability (%)	Cost per test (US$) /year[g]	Ease of performance[i]	Suitability[j]	Indeterminate results[k] (%)
Rapid assays - Evaluations on whole blood specimens								
For the detection of antibody to HIV-1 and HIV-2								
Determine™ HIV-1/2 (Abbott Laboratories Dainabot Co. Ltd)	12	100.0 (95.5-100.0)	99.4 (96.7-100.0)	1.6	1.20/'01	VE	VS	0.0
InstantScreen™ HIV-1/2 (Gen 2) (Gaifar GmbH)	12	100.0 (90.0-100.0)	100.0 (97.0-100.0)	0.7	8.00-12.00/'01	VE	VS	0.0
ADVANCED QUALITY™ Rapid HIV Test (InTec Products Inc.)	12	98.8 (93.2-100.0)	100.0 (97.9-100.0)	2.0	0.80-1.20/'01	VE	VS	0.8
MedMira Rapid HIV Test (MedMira Laboratories Inc.)	12	100.0 (95.5-100.0)	97.6 (94.1-99.6)	14.4	3.00/'00	E	VS	0.8
First Response™ HIV-1/HIV-2 WB (PMC Medical Pty.)	12	100.0 (95.5-100)	98.8 (95.8-99.9)	0.4	1.15/'01	VE	VS	0.0
CAPILLUS™ HIV-1/HIV-2 (Trinity Biotech PLC)	12	100.0 (95.5-100.0)	100.0 (97.9-100.0)	0.0	2.20/'01	VE	VS	0.0
Uni-GoldTMHIV (Trinity Biotech PLC)	12	100.0 (95.5-100.0)	100.0 (97.9-100.0)	0.4	2.34/'01	VE	VS	0.0
Rapid and ELISA assays - Evaluations on oral fluid specimens								
For the detection of antibody to HIV-1 and HIV-2								
SMLX Technologies Diagnostic test (SMLX Technologies)	13	62.7 (51.0-74.0)	74.8 (67.0-82.0)	22.5	NA	E	S	7.7
OraScreen HIV Rapid Test (Beacon Diagnostics Inc)	13	56.0 (44.0-68.0)	98.6 (95.0-100.0)	11.3	NA	E	S	4.1
Salivax™-HIV (ImmunoScience Inc)	13	79.4 (67.0-89.0)	96.0 (91.0-99.)	8.5	NA	E	S	2.7
Wellcozyme HIV 1+2 GACELISA (Murex Biotech Ltd)	13	100 (95.2-100.0)	99.0 (95.0-100.0)	NA	NA	LE	LS	0.0

Annex 2 (continued)

Assay (manufacturer)	Report No [a]	Sensitivity (%)[b,c]	Specificity (%)[c,d]	δ Values [e] WB pos sera	WB neg sera	Cost per test (US$) /year[g]	nm[h]	Ease of performance[i]	Suitability[j]
Elisa and Western blot - Evaluations on urine specimens									
For the detection of HIV-1									
Calypte™HIV-1 Urine EIA, Fc (Calypte™ Biomedical Corporation)	13	97.8 (92.4-99.7)	100.0 (98.2-100)	2.4	-4.4	3.00-4.25/'02	405 405/630	E	LS
Calypte™ HIV-1 Urine EIA (Recombinant) (Calypte™ Biomedical Corporation)	13	98.9 (94.2-100)	98.6 (95.8-99.7)	2.28	-2.42	3.00-4.25/'02	405 405/630	E	LS
Cambridge Biotech HIV-1 Urine Western Blot Kit (Calypte™ Biomedical Corporation)	13	98.9 (94.2-100)	NA	NA	NA	26.00/'02	Visual	E	LS/S

Legend for Annexes 1 and 2

a: Operational characteristics of commercially available assays to detect antibodies to HIV-1 and/or HIV-2 in human sera:

Report 1 - unpublished document GPA/RES/BMR/89.4
Report 2 - unpublished document GPA/RES/BMR/90.1
Report 3 - unpublished document GPA/RES/BMR/91.1
Report 4 - unpublished document GPA/RES/DIA/91.6
Report 5 - unpublished document GPA/RES/DIA/92.8
Report 6 - unpublished document GPA/RES/DIA/93.4
Report 7 - unpublished document GPA/RES/DIA/93.6
Report 8 - unpublished document GPA/RES/DIA/94.4
Report 9,10 - unpublished document WHO/BLS/98.1
Report 11 - unpublished document WHO/BTS/99.1
Report 14 - ISBN 92 4 159216 8
Report 15 - ISBN 92 4 159237 0

b,c,d: Sensitivity, specificity and 95% confidence intervals were calculated as described section 5.5.1 of this document.

e: δ-values were calculated as described in previous documents , see above.

f: Inter-reader variability was calculated as described section 5.5.3 of this document.

g: Prices quoted are those in effect at the time of the evaluation.

h: The wavelength(s) of the spectrophotometer (single and/or double) is specified by the manufacturer.

i: Ease of performance is defined on table 4b.

j: Suitability for use in small laboratories is defined on table 5.

k: Indeterminate results were calculated as described in the explanatory notes on page 30.

Annex 3 - Cumulative list of assay manufacturers' addresses

Abbott GmbH, Diagnostika, Max-Planck-Ring 2, 65205 Wiesbaden, Germany.
Tel: +49 6122 58 16 23; Telex: 4182555; Fax: +49 6122 58 16 12

Adaltis, 10900 rue Hamon, Montréal (Québec), Canada H3M 3A2.
Tel: +1 514 335 9922; Telex: 058-27642 IAF BCM MTL; Fax: +1 514 335 9919

Agen Biomedical Ltd, 11 Durbell Street, P.O. Box 391, Acacia Ridge, Queensland 4110, Australia.
Tel: +61 7 173 6266; Fax: +61 7 273 6224

Akers Laboratories Inc., 201 Grove Road, Thorofare, New Jersey 08086, USA.
Tel: +1 609 848 8698; Fax: +1 609 848 0269

Ancos Denmark ApS., Tengslemarkvej 4, 4573, H□jby, Denmark.
Tel: +45 59 30 65 55; Telex: 42580 ancos dk; Fax: +45 59 30 60 45

Anilabsystems, Pulttitie 8, P. O. Box 8, 00881 Helsinki, Finland.
Tel: +358 0 75821; Telex: 123569 Labsy sf; Fax: +358 0 7557610

Biochem Immunosystèmes, See Adaltis

Biochrom KG, Leonorenstrasse 2-6, 12247 Berlin, Germany.
Tel: +49 30 77 99 06 00; Telex: 185 821 bio d; Fax: +49 30 771 0012

Bio Genex, 4600 Norris Canyon Road, San Ramon, CA 94583, USA.
Tel: +1 510 275 0550, Fax: +1 510 276 0580

bioMérieux S.A., 69280 Marcy-l'Etoile, France.
Tel: +33 78 87 20 00; Fax: +33 78 87 20 90

BIONOR A/S, P.O. Box 1868, N-3705 Skien, Norway
Tel: +47 35 53 84 88; Fax: +47 35 53 71 30

Bio-Rad Laboratories, 3, boulevard Raymond Poincaré, 92430 Marnes-la-Coquette, France
Tel: +33 1 47 95 60 00; Fax: +33 1 47 41 91 33

Biotest AG, Landsteiner Str. 5, 63303 Dreieich, Germany.
Tel: +49 6103 80 10; Telex: 4185429; Fax: +49 6103 80 11 30

Boehringer Mannheim GmbH, Sandhofer Strasse 116, 68298 Mannheim, Germany.
Tel: +49 621 759 8838; Telex: 463193 bmd/462420 bmd; Fax: +49 621 759 8842

British Bio-Technology Ltd, Watlington Road, Cowley, Oxford OX4 5LY, England.
Tel: +44 865 748747; Telex: 838083 BIOTEC G; Fax: +44 865 717598

Cal-Tech Diagnostics, 1580 A. West San Bernardino Road, Covina, CA 91722, USA.
Tel: +1 818 331 9763, (1 818) 571 6826, (1 818) 369 3755; Fax: +1 818 331 1882, (1 818) 280 4846; Telex: 9102409630 Cal-Tech UQ.

CAL-TEST DIAGNOSTICS, 13760 Mountain Avenue, Chino, CA 91710, USA.
Tel: +1 909 902 0550, Fax: +1 909 902 0044

Cambridge Diagnostics Ireland Ltd., See Trinity Biotech plc

Catalina Bio-Diagnostic Consulting, Inc. 5595 E. 7th Street, Long Beach, CA 90804, USA.
Tel: +1 310 983 8111; Fax: +1 310 987 0670

Chembio Diagnostic Systems Inc., 3661 Horseblock Road, Medford, BY 11763, USA
Tel: +1 631 924 1135; Fax: +1 631 924 6033

Chiron Corporation, 4560 Horton Street, Emeryville, CA 94608-2916, USA.
Tel: +1 510 655 8730; Fax +1 510 655 9910

Clonatec Diagnostics S.A., 60 rue de Wattignies, 75580 Paris Cedex 12, France.
Tel: +33 1 43 42 43 88; Telex: 214044F; Fax: +33 1 43 40 48 86

Core Diagnostics, Aspect Court, 4 Temple Row, Birmingham B2 5HG, United Kingdom.
Tel: + 44 121 609 4720; Fax: + 44 121 609 4721

Dade Behring Marburg GmbH, Postfach 1149, 35001 Marburg, Germany.
Tel: +49 6421 39 4478; Fax: +49 6421 66064

Efoora Inc., 900 Asbury Drive, Buffalo Grove, Illinois, USA 60089
Tel: +1 847 634 6400; Fax: +1 847 634 0476

EY Laboratories, Inc., P.O. Box 1787, 107 N. Amphlett Blvd., San Mateo, CA 94401, USA
Tel: +1 650 342 3296; Fax: +1 650 342 2648

Fujirebio Inc., 19th floor, Shinjuku Daiichi Seimei Building, 7-1 Nishi-Shinjuku 2-Chome, Shinjuku-Ku, Tokyo 163-07, Japan.
Tel: +81 3 3348 0947; Telex: J 28612; Fax: +81 3 3342 6220
Fujirebio Europe BV, Takkebijsters 69c, 4817 BL Breda, The Netherlands
Tel: +31 76 571 0440; Fax: +31 76 587 2181

Genelabs Diagnostics, See MP Biomedicals

Genetic Systems Corporation, 3005 First Avenue, Seattle, WA 98121, USA.
Tel: +1 206 728 4900; Telex: 532050 Genetic Systems; Fax: +1 206 728 4950

Green Cross Life Science Corporation, 227-3, Gugal-li, Giheung-eup, Yongin-shi, Kyonggi-do, Korea
Tel: +82 31 260 9300; Fax: +82 31 260 9491

Heber Biotec S.A., Calle 8, No. 306, Miramar, Havana, Cuba.
Tel: +537 291187; Telex: 511269 cimex cu; Fax: +537 222261

Hepatika Laboratories, Yayasan Hati Sehat, Jalan Bung Hatta 3A, Mataram, Lombok, Indonesia, under license from the Concept Foundation Program for Appropriate Technology in Health (PATH), Seattle, WA, USA.
Tel: +62 3 64 31 662; Fax: +62 3 64 35642

Hoffmann-La Roche F. AG, Grenzacherstr 124, 4058 Basel, Switzerland.
Tel: +41 61 688 55 55; Fax: +41 61 681 98 67

Human GmbH, Max-Planck-Ring 21, D 65205, Wiesbaden, Germany.
Tel: +49 6122 99880; Fax: +49 6122 9988 100/99

Immuno-Chemical Laboratories., See Pacific Biotech Co.Ltd.

Immuno Diagnostics, Inc., 85 Great Arrow Avenue., Buffalo, New York 14216, USA.
Tel: +1 716 873 9400; Fax: +1 716 876 7919

InTec Products Inc., 332 Xinguang Road, Xinyang Industry Area, Haicang, Xiamen, 361022 P R China.
Tel: +86 5926 807 188; Fax: +86 592 651 9161

Innogenetics S.A., Technologiepark 6, 9052 Ghent, Belgium
Tel: +32 9 329 1329; Fax: +32 9 329 1911

J. Mitra & Co. Ltd, A-180, Okhla Industrial Area, Phase-1, New Delhi-110 020, India
Tel: +91 11 681 8971, +91 11 681 8973, +91 11 681 3995, +91 11 681 3989; Fax: +91 11 681 0945, +91 11 681 8970

Johnson & Johnson International, Roissy Pole B.P. 10784, 1, Place de Londres, F-95727 Roissy CDG Cedex, France.
Tel: +33 1 48 62 08 75; Fax: +33 1 48 62 00 54

KHB Shanghai Kehua Bio-engineering Co. Ltd., 1189 N Qinzhou Road, Shanghai, 200233, People's Republic of China
Tel: +86 21 64851188 +86 21 64853370 +86 21 8203370; Fax: +86 21 64854051

Labsystems OY, See Anilabsystems

Lupin Laboratories Ltd., 159, CST Road, Kalina, Santacruz (E), Mumbai 400098, India.
Tel: +91 22 611 3391; Fax: +91 22 611 4008
Annex 3, continued

Murex Biotech Limited, Central Road, Temple Hill, Dartford, Kent DA1 5LR, England.
Tel: +44 1322 27 77 11; Telex MUREX G 896113; Fax: +44 1322 27 32 88

MP Biomedicals, Halle de Frêt, P. O. Box 1015, 1215 Geneva 15 Airport, Switzerland.
Tel: +41 22 788 1908; Fax +41 22 788 1986

Nubenco Enterprises, Inc. One Kalisa Way, Suite 207 Paramus, New Jersey 07652-3508, USA. Tel: +1 201 967 9000; Fax +1 201 967 9444

OraSure Technologies, Inc., 150 Webster Street, Bethlehem, PA 18015, USA
Tel: +1 610 882 1820

Organon Teknika N.V., See bioMérieux

Orgenics Ltd., P.O. Box 360, Yavne 70650, Israel
Tel: +972 8 9429212; Fax: +972 8 9438758

Ortho Diagnostic Systems Inc., US Route 202, Raritan, N.J. 08869, USA.
Tel: +1 201 218 1300; Telex: 833 425; Fax: +1 201 218 8582

Pacific Biotech Co., Ltd. 6 Ladprao 110 (Sonthiwattana 3), Ladprao Road, Bangkapi, Bangkok 10310, Thailand.
Tel: +66 2 530 4608 or 530 2754; Fax: +66 2 530 4619

PBS Orgenics, Parc de l'Innovation, B.P. 209, 67405 Illkvich Cedex, Strasbourg, France.
Tel: +33 88 67 08 30; Telex: 890665; Fax: +33 88 67 38 61
North Industrial Zone, P. O. Box 360, Yavne, 70650 Israel.
Tel: +972 8 43 87 52-2; Fax: +972 8 43 87 58

Program for Appropriate Technology in Health (PATH), 4 Nickerson Street, Seattle, WA 98109, USA.
Tel: +1 206 285 3500; Telex: 47 100 49 PATH UI; Fax: +1 206 285 6619

Qualpro Diagnostics, Plot Nos. 88/89, Phase II C, Verna Industrial Estate, Verna, Goa, 403 722, India.
Tel: + 91 832 2783140; Fax: + 91 832 2783139

Saliva Diagnostic Systems (SDS), SDS International Ltd., 11 Sovreign Close, Sovereign Court, London E1)HW, UK
Tel: +44 171 415 0550; (Fax: +44 171 415 0553
Saliva Diagnostic Systems, (SDS), 11719 NE 95th Street, Vancouver, WA 98682, USA
Tel: +1 360 696 4800; Fax: +1 360 254 7942

Sanofi Diagnostics Pasteur, See Bio-Rad Laboratories

Savyon Diagnostics, LTD, Kiryat Minrav, 3 Habosem, Ashdod 77101, Israel.
Tel: +972 8 562920; Fax +972 8 563258

Serion Immunodiagnostica, Bronnbachergasse 18a, 8700 Würzburg, Germany. Tel: +49 931 14079; Telex: 68480 virion d; Fax: +49 931 52650

Sero-Immuno Diagnostics, P.O. Box 616, 2177-J Flintstone Drive, Tucker, GA 30084, USA.
Tel: +1 404 496 1370; Telex: 750747 SERO UD; Fax: +1 404 938 7189

Sorin Biomedica SpA, Divisione Diagnostici, 13040 Saluggia (Vercelli), Italy.
Tel: +39 161 487243; Telex: 200064 I SORIN; Fax +39 161 487672

Span Diagnostics PVT-Ltd, 173-B New Industrial Estate UDHNA-394210 (SURAT), India. Tel: +91 261 67 71 43; Telex: 0188284 span in; Fax: +91 261 66 57 57

Specialty BioSystems, Inc. 5870 Pacific Center Boulevard, Suite A, San Diego, California 92121 USA.
Tel: +1 619 457 9927; Fax: +1 619 457 2425

Standard Diagnostics, Inc., 575-34 Pajang-dong, Jangan-ku, Suwon-si, Kyonggi-do, Korea 440-290
Tel: +82 31 258 2994; Fax: +82 31 258 2995

Trinity Biotech plc, IDA Business Park, Bray, Co. Wicklow, Ireland.
Tel: +353 1276 9800; Fax: +353 1276 9888

United Biomedical Inc., 25, Davids Drive, Hauppauge, NY 11788, USA.
Tel: +1 516 273 2828; Fax: +1 516 273 1717

Waldheim Pharmazeutika GmbH, Boltzmanngasse 11, 1091 Vienna, Austria.
Tel: +43 1 319 1456; Telex: 116487 wamed a; Fax: +43 1 319 1456-44;

Wiener Laboratories, Riobama 2944, 2000 Rosario, Argentina.
Tel: +54 41 39 01 73/8; Fax: +54 41 37 13 77

Wellcome Diagnostics, See Abbott GmbH Diagnostika

Annex 4 - WHO HIV Test Kit Bulk Procurement Scheme

World Health Organization, Geneva

WHO HIV Test Kit — Bulk Procurement Scheme

"ensuring access to high quality, low cost HIV test kits"

The Issue

HIV test kits are essential for:

- ✓ Diagnosis of HIV infection
- ✓ Screening of donated blood
- ✓ Surveillance
- ✓ Voluntary counselling and testing
- ✓ Prevention of mother-to-child transmission

However…

- HIV test kits account for a substantial proportion of the budgets of most National AIDS Control Programmes.
- National and local blood transfusion services in many countries do not have the financial resources to purchase the required number of test kits.
- Many countries have interrupted supplies of test kits.
- Many countries require additional information to ensure that the kits they do purchase are of high quality and are suitable for their particular situation.

The Response

WHO established the HIV Test Kit Bulk Procurement Scheme in 1989. The goals of the scheme are to:

- Facilitate access to:
  - ✓ *high quality* test kits
  - ✓ at a *low cost*
  - ✓ through an *easy purchase procedure*
- Provide additional information and assistance to those selecting/purchasing test kits to ensure that the chosen kits will be appropriate for the conditions in which they will be used and will meet the overall testing objectives.

The Bulk Procurement Scheme is directed towards and assists:

- National AIDS Control Programmes
- Blood transfusion services
- UN agencies
- Nongovernmental organizations
- Donor supported HIV/AIDS projects
- Other recognized groups

High Quality

All HIV test kits available through the Bulk Procurement Scheme have been evaluated by WHO. These evaluations assess the operational characteristics of the tests i.e. sensitivity, specificity, ease of performance and storage conditions. To be eligible for inclusion in the Bulk Procurement Scheme, the evaluated test kits must meet current standards. All test kits included in the Bulk Procurement Scheme are reviewed annually.

The Bulk Procurement Scheme encompasses the main types of tests used to detect HIV antibodies today – Enzyme Linked ImmunoSorbent Assays (ELISAs), Simple/Rapid assays and Confirmatory assays. There are 22 tests on the current Bulk Procurement Scheme List of Available Assays, including a greater number of Simple/Rapid Assays than ever before.

When selecting a test kit, the following issues should be considered:

- The number of samples to be tested
- The laboratory facilities available
- The level of laboratory staff training
- The objective of the testing
- The testing strategy being followed

No single test is suitable for all testing objectives in all settings. It is important to choose the test kit which will produce the best working performance in actual, routine use.

In addition to the Bulk Procurement Scheme, recommendations and guidelines have been developed by WHO to assist with the selection of appropriate kits.

Annex 4, continued

Low Cost

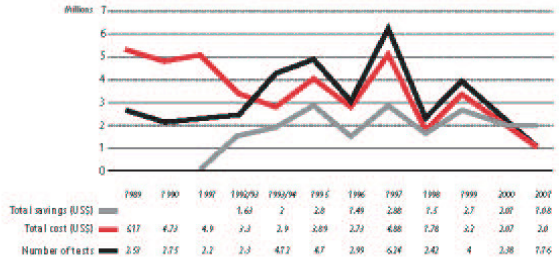
WHO negotiates prices for all assays in the Bulk Procurement Scheme directly with the manufacturers. This process enables WHO to offer a per test cost approximately half that of the open market price.

Main types of tests	Range – Open Market Price (US$)*	Average – Bulk Procurement Price (US$)*
ELISA	1.00 to 2.00	0.50
Simple/Rapid	2.00 to 8.00	1.00
Confirmatory	20.00 to 30.00	11.00

*Prices as of 2000

The resulting savings are substantial, enabling countries with limited resources to buy more HIV test kits with their funds, or to channel more resources into other areas of need, such as HIV care. The savings for 1999-2000 amounted to US$ 5 million.

HIV Bulk Purchase 1989–2001



Easy Purchase Procedure

The HIV Test Kit Bulk Procurement Scheme accepts purchase requests from programmes/institutions/organizations in 3 categories:

- Category A – WHO programmes & UN agencies
- Category B – WHO Member States & NGOs in official relations with WHO
- Category C – Other clients ie. Donor supported AIDS projects, regulatory bodies

The HIV Test Kit Bulk Procurement Scheme provides an easy-to-follow purchase procedure. Simply complete the steps indicated by this symbol ⓘ and let WHO do the rest!

ⓘ Step 1: Prepare a request which includes the following information:
- Name of requesting programme
- Contact person (ie. name, telephone)
- Test kit name & manufacturer*
- Order code*
- Number of test kits required (indicate number of tests per kit where necessary)

*as on the Bulk Procurement List

ⓘ Step 2: Submit this request to one of the appropriate offices for your category:
- WHO Headquarters, Geneva (Category A)
- WHO Regional Office (Category A, B)
- WHO Country Representative (Category B)
- UNAIDS Representative (Category B, C)
- Ministry of Health (Category C)

Step 3: Payment will be debited from your account (Category A) or a proforma invoice will be issued to you (Category B and C). Goods must be paid for in full before purchase is initiated.

Step 4: Procurement Services purchases the requested kits.

Step 5: WHO ships the goods to the airport of destination.

Step 6: The consignee is responsible for customs clearance and delivery of the goods.

Further Information

Further information on the WHO HIV Test Kit Bulk Procurement Scheme is available from the following sources:

WHO Headquarters —

for procurement assistance:
Procurement Services
Tel: +41 22 791 2801 Fax: +41 22 791 4196
Email: procurement@who.int

for technical assistance:
Blood Safety and Clinical Technology
World Health Organization
Avenue Appia 20, 1211 Geneva 27
Switzerland

Internet —
Visit the BCT section of the WHO website at www.who.int/bct and follow the links to Key Initiatives, HIV Diagnostics, HIV Test Kit Bulk Procurement Scheme. In addition to general information, PDF versions of the WHO HIV Test Kit Bulk Procurement Scheme Information Booklet, several fact sheets, and this brochure are (or will soon be) available for downloading. In addition, information on Test Kit Evaluation is available on this website.

Regional Offices/Country Representatives —
Contact your WHO Regional Office, WHO Country Representative, or nearest UNAIDS representative.

If you are a manufacturer and wish to submit your kit for evaluation by WHO to become eligible for inclusion in the Bulk Procurement Scheme, please visit our website or contact Blood Safety and Clinical Technology:
Fax: +41 22 791 4836
Email: bloodsafety@who.int

August 2002

9. Acknowledgements

We would like to thank the following for supplying sera to the WHO specimen panel:

Dr P. Ghys, Projet Retro-ci, Abidjan, Côte Ivoire; Dr E Vinelli, Programa Nacional de Sangre, Comayaguela, Honduras; Dr O'Charoen, National Blood Transfusion Service, Bangkok, Thailand; Dr E Sabino, Fundación Pró-sangue, Sao Paulo, Brazil; AIDS Reference Centre, Institute of Tropical Medicine, Antwerp, Belgium; National Blood Transfusion Center, Phnom Penh, Cambodia.

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ISBN 978 92 4 159769 2