

# Laboratory testing and rapid HIV assays: applications for HIV surveillance in hard-to-reach populations

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Most HIV surveillance has been performed through serologic surveys in relatively stable, accessible populations. Similar surveillance, with or without counseling and testing, in populations that are hard-to-reach, presents logistical challenges, including the selection of laboratory testing strategy and algorithm. The advent of rapid serologic assays for HIV now allows for on-site testing, including confirmatory testing, and rapid provision of test results and counseling. The possibility of only a single contact makes repeat sampling, which current diagnostic testing recommendations include, difficult. To address the logistical complexities in surveillance in hard-to-reach populations and the increased availability of rapid tests, we propose adapting the testing strategies for HIV of the World Health Organization/the joint United Nations Programme on HIV/AIDS in order to facilitate this surveillance, including, where carried out, the provision of test results back to individuals. The choice of enzyme-linked immunosorbent assay (ELISA) versus rapid testing for these settings is discussed, as is the choice of specimen – blood, oral fluid, or urine. Three appendices summarize: (1) test algorithms for the various testing strategies; (2) advantages and disadvantages of ELISA and of rapid test formats, and (3) the characteristics and status of currently available rapid HIV tests. We also discuss the potential application of the recently developed 'detuned' methodology for estimating HIV incidence in hard-to-reach populations.

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*AIDS* 2001, 15 (suppl 3):S49–S59

**Keywords:** HIV testing strategies, HIV surveillance, HIV counseling and testing, HIV rapid test

## Introduction

Several documents outline testing algorithms and applications of HIV testing in a variety of settings [1–8]. The advent of simplified, rapid testing technology has allowed HIV testing to move on-site and away from the centralized laboratory [2,5,9]. The focus of this report is testing strategies and algorithms for surveillance where test results are not returned to individuals, as well as for surveillance with counseling and testing in hard-to-reach populations, such as migrant workers, refugees, sex workers, injecting drug users, and men who have sex with men. We present several variations, which may fit the special needs and limitations involved with surveillance in hard-to-reach populations. However, these variations may also be applicable for serologic surveillance in general.

## Strategy considerations and test applications

The types of antibody tests and, when needed, the approach to supplemental testing will depend on (a) whether or not test results are provided to individuals and (b) the HIV prevalence in the population. Under the World Health Organization/the joint United Nations Programme on HIV/AIDS (WHO/UNAIDS) testing approach, which deals with testing for both diagnostic and surveillance purposes [1,6], three strategies are proposed. Surveillance which does not involve providing test results and counseling to individuals and which is conducted in populations with an HIV prevalence over 10% would use a single test (strategy I). Similar studies in a population with prevalence less than 10% would require two different tests (strategy II) due to the higher

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relative probability for a false-positive result. For those surveillance settings where test results are provided to individuals (e.g., when counseling and testing is offered), two different tests are generally advisable, the second of these for confirmation, with a third, different, test ('tie-breaker') used in the event of discordance between the first and second (strategy III). The WHO/UNAIDS testing approach for strategy III, advised for individual diagnosis when the HIV prevalence is  $\leq 10\%$  calls for a third test even when the first and second tests are reactive [1,6].

Although not usually included in surveillance activities, patients with clinical signs or symptoms of HIV infection can be tested with strategy I in populations with  $> 30\%$  HIV prevalence, even when results are to be provided to the individuals [1,6], since a single positive reaction in a person with suggestive disease in a high prevalence population is highly predictive of an HIV infection. However, we recommend two different tests with a third test as a tie-breaker if the first two have discordant results (Strategy III), when persons are to be informed of their results.

### Surveillance test strategies

The order for running the samples with the multiple tests is outlined in the WHO/UNAIDS guidelines [1,6]. However, obtaining a second sample at a later time, as is advised in those guidelines when individuals are to be informed of a positive test result (e.g., when counseling and testing is performed in addition to surveillance), will generally not be feasible in the surveillance settings being considered for hard-to-reach populations, even when test results are being provided to individuals. However, in practice HIV positivity has typically been determined for counseling and testing by multiple tests on a single sample [7,8]. We have therefore proposed several modifications to simplify the WHO/UNAIDS testing strategies II and III (Appendix IA).

As in previous recommendations [1,6], strategy I (which assumes a prevalence of  $>10\%$  and use in a setting where survey participants will be anonymous and not advised of their test results), reactive samples are considered positive, whereas non-reactive samples are considered negative. This approach relies on selection of a screening assay (A1) with a high sensitivity ( $S > 98\%$ ) and a high negative predictive value ( $PVN > 99\%$ ).

For strategy II (where prevalence is  $\leq 10\%$  or unknown and where participants will not receive test results) samples are tested as in strategy I, and reactive samples are retested with a different test. Serum- or plasma-based tests with sufficient sample volume for multiple testing, or tests based on dried blood spots, are ideal; oral fluid could also be used. Such an approach is valid only if two highly sensitive tests are used ( $S > 98\%$ ) and the negative predictive value of the algorithm is greater than 99% ( $PVN > 99\%$ ). Samples reactive in both tests are consid-

ered positive, whereas samples that are reactive with the first test but non-reactive with the second test are considered negative for surveillance purposes (although they would be considered indeterminate and retested if testing were carried out for diagnostic reasons).

For strategy III (where test results will be provided to individuals), samples are initially tested as in strategy I, and reactive samples are retested with a second test. If the second test is non-reactive, the sample is evaluated with a third test. Samples are considered positive if they are reactive on two different tests. Samples that are non-reactive with the first test are considered negative, as are those reactive on test one but non-reactive on both tests two and three.

Alternatively, for strategy III, surveillance with counseling and testing, a whole blood (from finger prick) or oral fluid-based rapid test in which the specimen is placed directly on the test apparatus may be used as a screening test, as long as the test has a sufficiently high sensitivity. However, when a rapid test is carried out directly off a blood drop or oral fluid, as opposed to using a sample collection, which would permit multiple tests, individuals would require a second sample if found reactive on the first test. In a voluntary counseling and testing setting this would complicate the flow, extending the time allocated per client. The need to immediately re-sample reactive individuals also raises concerns about confidentiality in both the surveillance and counseling settings. Therefore, a special case strategy modification is offered for on-site sampling with tests carried out directly from whole blood from finger prick or oral fluid (Appendix IB), which would be applicable for surveillance when individuals are to be informed of their test results. This incorporates the use of two rapid tests performed simultaneously at the onset. (However, dried blood spots may simultaneously be collected and stored for quality assurance and quality control or other analyses). In the event of discordance between the two tests on the first specimen, a second specimen will be needed for the tie-breaker third test but, although somewhat inconvenient, this repeat sampling should be infrequently needed and at least provides a confirmed serostatus in 45 min or less, while fulfilling the point-of-service needs of voluntary counseling and testing.

For surveillance, testing formats can be enzyme-linked immunosorbent assay (ELISA), rapid tests, or a combination of both. The preference of format will depend on the purposes of the testing (whether for surveillance data alone or whether test results will also be provided to individuals), as well as the capabilities of the setting in which testing is being carried out. ELISA is preferred where large numbers of specimens are to be run, where rapid turnaround is not necessary, and where increased sensitivity is required, such as in a population with a high frequency of recently infected individuals. Rapid tests

are preferred when small numbers of samples are being tested, limited facilities are available, and a short turn-around time to provide a result is needed. Although less demanding in terms of laboratory facilities and equipment, the rapid tests can be more labor intensive for the technician, and the rapid tests can become very laborious if large numbers of specimens are to be processed. Appendix II summarizes in more detail the advantages and disadvantages of the two test formats.

### Specimen preference

Regardless of the format, blood (serum/plasma, dried blood spots) is generally the preferred sample (on technical grounds, not necessarily from the perspective of the person tested). Blood is preferable because of the ability to do additional analyses such as viral type (HIV-1 or HIV-2) and subtype determination, molecular studies (e.g., drug resistance), RNA viral load, and incidence determinations. For surveillance purposes under difficult logistical conditions but where testing at a central laboratory is still an option, the preferred sample would be the dried blood spot rather than plasma or serum derived from a venipuncture. Once dry, such samples are stable at ambient temperatures and can be analyzed to the same extent as serum or plasma [10]. In addition, rapid testing could be run on-site using drops of whole blood, with blood spots collected for confirmatory testing and additional analyses at the main laboratory.

Non-invasive approaches – oral fluid or urine – based on ELISA methodology are commercially available. At this time, only one licensed and approved urine-based test is available (and it is not a rapid test), making strategies other than strategy I not feasible with urine testing. The current oral fluid-based ELISA testing requires an additional elution step following collection. Formats and conduct of the assays in the central laboratory would be essentially the same as for the blood-based systems. At present there are very few oral fluid-based rapid tests available (and both current tests are still under evaluation) (Appendix III), making on-site use of strategy III problematic. Although these oral fluid and urine approaches may be more appealing than blood collection to some surveillance participants (however, finger prick blood collection is not very invasive) and may present less biosafety concerns than blood collection, at present they lack many of the advantages (distinguishing HIV-1 from HIV-2, viral subtypes, antiretroviral drug resistance, ‘detuned’ methodology) offered by blood-based methods. Because of these limitations and limited commercial availability, non-blood-based testing approaches at this time would generally not be preferred. However, because of possible preference by surveillance subjects and because of lower biosafety concerns, as additional types of test kits become available the benefits as well as the limitations of non-blood-based test approaches in special settings need to be evaluated, as do their sensitivity and specificity under field conditions.

The status and characteristics of currently available rapid test kits, both for blood and oral fluid, are summarized in Appendix III. In all cases, only tests that have been evaluated by independent, non-commercially involved organizations such as the Centers for Disease Control and Prevention (CDC) and WHO/UNAIDS [6,11] should be considered for surveillance work or for testing and counseling. The cost and labor of sampling, specimen handling, analysis, and providing test results and counseling back to individuals are sufficiently great that to depend on a test methodology that has not been fully evaluated seems unwise.

### Survey test strategies

For surveillance, several scenarios can occur, depending on the degree of interaction with the surveyed population and the logistics of the setting. On one extreme, where HIV test results are not provided to individuals and where rapid turn-around of results is not important, specimens may be brought to a regional or central reference laboratory. On the other extreme, where test results must be provided back to individuals under field conditions, on-site rapid tests must be used in order to provide test results to most hard-to-reach populations on the same day.

In the first scenario, the sample of choice would be plasma, serum or dried blood spots shipped to the regional or central laboratory for testing. The selection of either ELISA or rapid testing would be the preference of the laboratory, as either test format would be acceptable on quality grounds. The main considerations in choosing between ELISA and rapid tests at the laboratory are cost, equipment needs, and throughput. In general, the reagent cost per test for ELISA is lower than for rapid tests, but the additional costs for the necessary equipment, maintenance, cold chain, and skilled personnel often make ELISA more expensive, especially when limited numbers of specimens are to be tested, as would often be the case with hard-to-reach populations. ELISA becomes cost-effective when larger numbers of specimens are handled and when they can be batch processed. Major advantages of using a central laboratory can be realized in establishing a comprehensive quality assurance and quality control program for surveillance testing. One may also take advantage of existing specimen handling, tracking, and storage procedures.

A major disadvantage of centralized batch testing becomes evident in strategy III where test results must be returned to the hard-to-reach participant. It is not unusual for delays of 1–3 weeks to accompany the return of test results. Such delays may be complicating even in client populations that are fairly easy to reach, such as women attending antenatal clinics. Therefore, in the scenario where test results (and counseling) are to be provided to individuals and same day turn around is needed, the only viable choice is rapid tests on-site. The best option would be one in which multiple rapid tests

can be run immediately on the collected specimen, as in strategy III algorithms (the excess remaining sample may be shipped to a collaborating laboratory for additional analyses). Many whole-blood rapid tests are simple one- or two-step tests that require no additional equipment or cold storage. Their simplicity and ease of use ensure that non-laboratory personnel with limited experience can readily be trained in their use. Thus strategy III algorithms based on such tests can be quickly implemented in decentralized surveillance programs combined with voluntary counseling and testing.

A potential additional advantage of using rapid tests on-site for surveillance is that experience will be gained with field applications of this methodology. This experience will be especially helpful as more decentralized voluntary counseling and testing is performed as part of HIV prevention and for identifying infected pregnant women for interventions against mother-to-child transmission.

Quality assurance and quality control measures are important for either the central testing or the on-site testing approach. For the centralized setting, measures will be needed to ensure that specimens are suitably linked to demographic and epidemiological information, and that specimen processing, storage, and transport are adequate. Programs will also be needed that ensure rotation of test reagent stocks, maintenance of adequate supplies on-hand for bulk testing, and integration of local control sera into the testing in addition to internal test kit control standards. In decentralized settings, simple programs can be established to monitor participating facilities through distribution of blinded evaluation panels of sera and through periodic inspection. If the primary protocol involves whole blood testing from finger stick specimens, collection of additional dried blood spots on a portion (for example, 5%) of such samples for testing at a central reference laboratory can provide for quality assurance measures. All involved laboratories should participate in quarterly proficiency testing programs and in annual training reviews, including updates in technology. These programs and the training should be established and maintained by the central reference laboratory.

Additional flexibility in surveillance design and test strategy will emerge as new tests become available. HIV test methodology is evolving quickly, and it is important to stay abreast of new developments, particularly in terms of rapid test technology (Appendix III). This is the impetus behind the active support of WHO/UNAIDS and CDC for continuous evaluation and monitoring of HIV diagnostic reagents. Similarly, national or multi-country regional programs should be established and maintained to monitor product quality and reliability. Expanded communications and data sharing with others evaluating available technologies will also be necessary to establish regional standards for surveillance.

### Incidence evaluation

Estimates of the rate of recent new infections – incidence – can be extremely valuable for evaluating the current risk of HIV infection. Differentiating individuals with recent HIV infection from those infected for longer periods of time has previously been difficult and costly, requiring repeated testing of the same individuals. Incidence estimates from cohorts are biased due to the exclusion from observation of the persons at highest risk (who are likely to be infected already) and self-selection and continued cohort participation of persons who are more likely to reduce their risk. The recent modification of a commercially available serologic assay termed 'detuned' or 'standardized testing algorithm for recent HIV seroconverters' (STARHS), now makes it possible to determine whether an HIV-infected person has seroconverted within an average of about 130 days prior to collecting the sample [12]. This ability to distinguish recent from older infections permits estimation of recent HIV incidence based on a single cross-sectional survey. However, this methodology has been fully evaluated only for HIV-1 subtype B. Current evaluation of the assay in non-B subtypes suggest that the test will require modification of the window period or cut-off value, or possibly even the test format, to obtain reliable incidence estimates. Due to this uncertainty, incidence estimates cannot yet be made using the assay in areas with non-B subtypes, and any such estimates should be interpreted with caution. The possible use of dried blood spots in the assay for subtype B is currently being investigated. However, there is now some uncertainty about the future availability of the test kit which served as the basis for the original 'detuned' assay format; consequently, there is a growing need to develop and evaluate comparable testing protocols.

In addition to the laboratory issues, there will still be a need to determine epidemiologically the most effective applications of incidence estimation methodology for surveillance purposes. Relatively large numbers of 'detuned' seropositive results (i.e., recently infected persons) will be needed (the 'numerator' in calculations of incidence) in a given study population to be able to make meaningful incidence estimates. However, in hard-to-reach populations, the number of people tested, and therefore the number of recently infected persons, may be limited. Thus, in addition to standardizing the laboratory methodology, further work will be needed to assess the utility of applying the 'detuned' methodology to estimate HIV incidence in such populations.

### Conclusion

HIV serologic surveillance in hard-to-reach populations presents several challenges that will influence the selection of testing algorithms and strategies. Typically only one contact with hard-to-reach individuals included in the surveys will be possible, which limits the algorithms

to those which can be performed from a single specimen collection. A key determinant in selecting the testing algorithms and strategies will be whether test results will be provided back to individuals, in which case rapid tests carried out at the site of sampling will generally be required. The other key determinant in selecting the testing strategy will be the expected HIV prevalence in the population study. The logistical conditions, including availability of refrigeration, specimen preparation and handling capacity, and the availability and extent of training of laboratory personnel will also influence the selection of tests. Oral fluid and urine collection may be more appealing to some test subjects, but blood-based testing still offers many advantages at this time, and finger-stick specimens both fresh and dried on filter paper are relatively simple to collect.

Incidence estimation through the 'detuned' test performed on cross-sectional survey specimens would be very valuable. Test evaluation is continuing at present, and the test has not yet been standardized for HIV subtypes other than B. The applicability of the 'detuned' approach needs to be evaluated epidemiologically in hard-to-reach populations in the field, especially when the numbers of persons available to be tested are limited.

### Acknowledgements

The authors wish to acknowledge the Robert Koch Institute for hosting the Workshop on HIV Surveillance in Hard-to-Reach Populations, at which this review was initially presented. They also acknowledge Carl Campbell and Bernard Branson of CDC for helpful discussions of rapid test applications in counseling and testing settings, and Christopher Murrill of CDC and Peter Ghys of UNAIDS for helpful comments on the manuscript.

### References

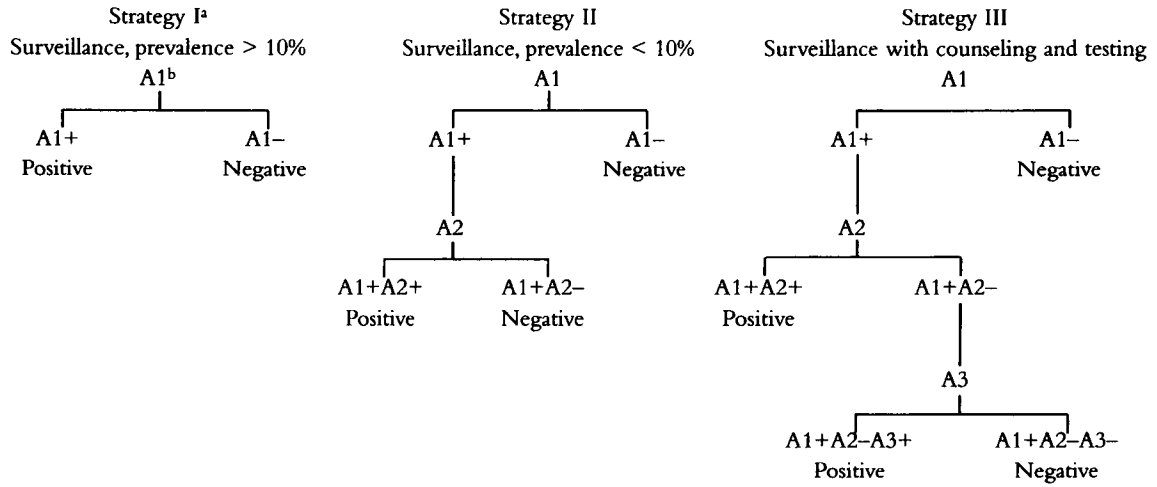
1. World Health Organization. **Revised recommendations for the selection and use of HIV antibody tests.** *Wkly Epidemiol Rec* 1997, 72:81–87.
2. World Health Organization. **The importance of simple/rapid assays in HIV testing.** *Wkly Epidemiol Rec* 1998, 73:321–326.
3. Centers for Disease Control. **HIV counseling and testing using rapid tests – United States, 1995.** *MMWR* 1998, 47:211–215.
4. George JR, Schochetman G, (eds). *Detection of HIV Infection Using Serologic Techniques in AIDS Testing: a Comprehensive Guide to Technical, Medical, Social, Legal, and Management Issues*, 2nd edn. New York: Springer-Verlag, 1994.
5. Stetler HC, Granade TC, Nuñez CA, *et al.* **Field evaluation of rapid HIV serologic tests for screening and confirming HIV-1 infection in Honduras.** *AIDS* 1997, 11:369–375.
6. *Operational Characteristics of Commercially Available Assays to Determine Antibodies to HIV-1 and/or HIV-2 in Human Sera.* World Health Organization/the joint United Nations Programme on HIV/AIDS, Geneva, Switzerland. Report 11. WHO/BTS/99.1; UNAIDS/99.5.
7. The Voluntary HIV-1 Counseling and Testing Efficacy Study Group. **Efficacy of voluntary HIV-1 counselling and testing in individuals and couples in Kenya, Tanzania, and Trinidad: a randomized trial.** *Lancet* 2000, 356:103–112.
8. Fylkesnes K, Haworth A, Rosensvärd C, *et al.* **HIV counselling and testing: overemphasizing high acceptance rates a threat to confidentiality and the right not to know.** *AIDS* 1999, 13: 2469–2474.
9. Branson BM. **Rapid tests for HIV antibody.** *AIDS Reviews* 2000, 2:76–83.
10. Lew J, Reichelderfer P, Fowler M, *et al.* **Determinations of levels of human immunodeficiency virus type 1 RNA in plasma: reassessment of parameters affecting assay outcome.** *J Clin Microbiol* 1998, 36:1471–1479.
11. World Health Organization. **HIV test kit: main report.** [http://www.who.int/pht/blood\\_safety/](http://www.who.int/pht/blood_safety/) 3 Mar 2000
12. Janssen RS, Satten GA, Stramer SL, *et al.* **New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes.** *JAMA* 1998, 280:42–48.

Please note: Appendices are shown on the following pages.

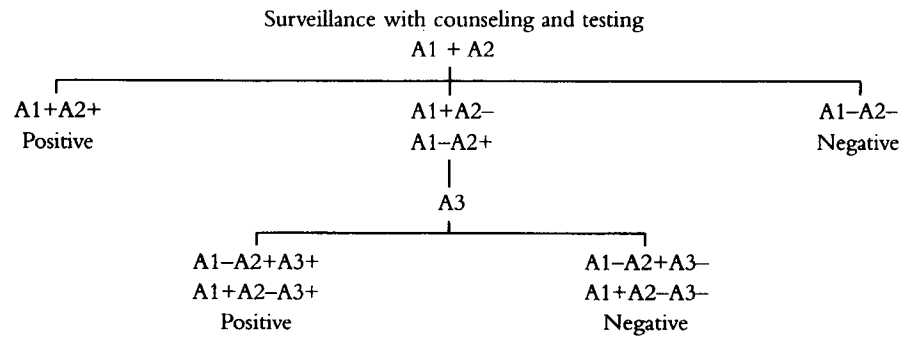
## Appendix I

### Proposed modifications of WHO/UNAIDS HIV testing strategies [1,6] for surveillance in hard-to-reach populations

#### A. Testing of collected, processed specimens



#### B. Rapid testing on unprocessed specimens directly from the subject



<sup>a</sup>Unchanged from WHO/UNAIDS strategy I [1,6]. <sup>b</sup>A1, A2, and A3 represent three different assays.

## Appendix II

### ELISA and rapid tests: advantages and disadvantages

Technology	Advantages	Disadvantages
ELISA <sup>a</sup>	<ul style="list-style-type: none"> <li>Batch capability</li> <li>Can be automated</li> <li>Centralized (QA/QC)</li> <li>May be highly sensitive (for seroconverters)</li> </ul>	<ul style="list-style-type: none"> <li>Less flexible (minimum numbers needed for maximum efficiency)</li> <li>Time to result (&gt; 1.5 h)</li> <li>Skilled technician required</li> <li>High maintenance equipment</li> <li>Refrigerated reagents</li> </ul>
Rapid test <sup>b</sup>	<ul style="list-style-type: none"> <li>Flexible (1 to multiple tests at a time)</li> <li>Minimal equipment/reagents required</li> <li>On site testing</li> <li>Skilled staff not required</li> <li>Interpretation straight forward</li> <li>Time to result (&lt;30 min)</li> <li>Ambient temperature stability with newer tests</li> <li>Non-invasive (oral fluid)</li> <li>No sharps (oral fluid)</li> </ul>	<ul style="list-style-type: none"> <li>Small numbers for each test run</li> <li>QA/QC at multiple sites</li> <li>Some products less sensitive (for seroconverters)</li> <li>Choice of testing algorithm may require multiple samples</li> <li>Limited comparative products (oral fluid)</li> <li>Less sensitive (oral fluid)</li> <li>Testing strategy may require two types of specimen (i.e. oral fluid and blood)</li> </ul>

ELISA, enzyme-linked immunosorbent assay; QA/QC, quality assurance/quality control. <sup>a</sup>Applies to plasma, serum, oral fluid, and urine.

<sup>b</sup>Applies to whole blood, plasma, serum, oral fluid, but not urine.

## Appendix III

### Rapid testing: methodology and degree of implementation

#### Methodology and degree of implementation

##### Agglutination

Capillus HIV-1/HIV-2                      Implemented for voluntary counseling and testing (VCT)

##### ImmunoDot

SeroCard HIV                                  Evaluated, Implemented for VCT  
 HIVSav 1&2                                  Evaluated, Implemented for VCT  
 MultiSpot HIV-1/HIV-2                      Implemented for emergency blood screening  
 HIVCHEK System 3                          Implemented for emergency blood screening  
 HIV Spot                                      Implemented for emergency blood screening and VCT  
 Genie II HIV-1/HIV-2                      Evaluated, successfully field-tested  
 SalivaCard                                  Currently under evaluation

##### Immunochromatography

Sero-Strip HIV-1/2                          Evaluated, successfully field-tested  
 Determine HIV-1/2                          Evaluated, Implemented for VCT  
 Hema-Strip HIV-1/2                          Evaluated, Implemented for VCT  
 DoubleCheck HIV 1&2                      Evaluated, Implemented for VCT  
 Uni-Gold HIV Recombinant                  Currently under evaluation  
 OraQuick HIV 1&2                          Currently under evaluation

##### Magnetic Bead

Bionor HIV-1&2                              Evaluated, successfully field-tested, implemented

#### Complexity (All cited tests are designed to be simple and rapid, but protocols vary)

##### Level 1 – No additional equipment and little or no laboratory experience needed

Determine HIV-1/2                          Uni-Gold HIV Recombinant  
 HemaStrip HIV-1/2  
 OraQuick HIV 1&2

##### Level 2 – Requires multiple reagents or pipetting; centrifugation or optional equipment beneficial

Capillus HIV-1/HIV-2                      SalivaCard HIV  
 DoubleCheck HIV 1&2                      SeroCard HIV  
 Genie II HIV1/HIV2                      Sero-Strip HIV-1/2  
 HIVSav 1&2  
 HIVSpot

##### Level 3 – Requires multi-step assay with reagent and sample preparation or additional equipment

Bionor HIV-1&2  
 HIVCHEK System 3  
 HIV Spot  
 MultiSpot HIV-1/HIV-2

Appendix III continues overleaf.

Manufacturer/Distributor	Product Description	Sensitivity	Specificity	Field use	Comments <sup>a</sup>	Status	Cost/Test <sup>f</sup>
Abbott Laboratories Abbott Park, Illinois, USA www.abbott/diagnostics.com Manufacturer: Dainabot Co., Ltd. Tokyo, Japan	Determine HIV-1/2 Immunochromatographic Recombinant antigens and synthetic peptides for HIV-1/2 Single reagent Uses whole blood, plasma, or serum	97.9–100% <sup>a</sup>	100% <sup>a</sup>	Limited	Complexity: 1 Store at 2–30°C	For sale	US\$ 3.80 Negotiable
BIONOR A/S Skien, Norway www.bionor.no	Bionor HIV-1&2 Magnetic particle-bound EIA Synthetic peptides for HIV-1/2 Multiple reagents Uses whole blood, plasma, or serum	99.8–100% <sup>a,b</sup>	95.6–100% <sup>a,b</sup>	Moderate	Complexity: 3 Store at 2–8°C Requires Bionor equipment	For sale WHO- evaluated	Negotiable
Sayvon Diagnostics Ltd. Ashdod, Israel www.hctech.com/sayvon	HIVSav 1&2 Microfiltration-bound EIA Recombinant antigens and synthetic peptides for HIV-1/2 Multiple reagents Uses plasma or serum	95–99% <sup>a,c</sup>	96–99.9% <sup>a,c</sup>	Extensive	Complexity: 2 Store at 2–25°C <sup>d</sup> Optional: centrifuge	For sale WHO- evaluated	Negotiable
Orasure Technologies, Inc. Bethlehem, Pennsylvania, USA www.orasure.com	OraQuick HIV-1/2 Immunochromatographic Synthetic peptides for HIV-1/2 Single reagent Uses oral fluid, whole blood, plasma, or serum	100% <sup>a,c</sup>	100% <sup>a,c</sup>	Limited	Complexity: 1 Store at 18–30°C	Evaluations ongoing	Negotiable
Genelabs Diagnostics, Pte, Ltd. Singapore Parent Company: Genelabs Technologies, Inc. Redwood City, California, USA www.genelabs.com.sg	HIV SPOT Microfiltration-bound EIA Recombinant antigens and synthetic peptides for HIV-1/2 Multiple reagents Uses plasma or serum	97–99% <sup>a,c</sup>	96–99% <sup>a,c</sup>	Extensive	Complexity: 2 Store at 2–25°C <sup>d</sup> Optional: centrifuge	For sale WHO- evaluated	US\$ 1.20–1.80
Orgenics, Ltd. Yavne, Israel www.orgenics.com	DoubleCheck HIV 1&2 Immunochromatographic Recombinant antigens for HIV-1/2 Single reagent Use with plasma, or serum	100% <sup>a,c</sup>	99.5–100% <sup>a,c</sup>	Moderate	Complexity: 2 Store at 2–30°C <sup>d</sup> Optional: centrifuge	For sale WHO- evaluated	Negotiable

Manufacturer/Distributor	Product Description	Sensitivity	Specificity	Field use	Comments	Status	Cost/Test*
Ortho-Clinical Diagnostic Systems Parent Company: Johnson & Johnson New Brunswick, NJ, USA www.orthoclinical.com	HIVCHEK System 3 Microfiltration-bound EIA Recombinant antigens and synthetic peptides for HIV-1/2 Multiple reagents Uses plasma or serum	98.2-100% <sup>a,b</sup>	98.8-100% <sup>a,b</sup>	Extensive	Complexity: 3 Store at 2-25°C <sup>d</sup> Optional: centrifuge	For sale WHO- evaluated	Negotiable
Saliva Diagnostic Systems, Ltd Medford, New York, USA www.salv.com	Sero-Strip HIV-1/2 Immunochromatographic Synthetic peptides for HIV-1/2 Single reagent and buffer Uses plasma or serum Hema-Strip HIV-1/2 Immunochromatographic Synthetic peptides for HIV-1/2 Single reagent Uses whole blood, plasma, or serum	98.4-99.9% <sup>a,b,c</sup>	99.6-100% <sup>a,b,c</sup>	Moderate	Complexity: 2 Store at 2-25°C <sup>d</sup> Optional: centrifuge	For sale WHO- evaluated	US\$ 1.50
Saliva Diagnostic Systems, Ltd Medford, New York, USA www.salv.com	Saliva-Strip HIV-1/2 Immunochromatographic Synthetic peptides for HIV-1/2 Single reagent and buffer Uses oral fluid	99.6% <sup>a</sup>	99.9% <sup>a</sup>	Limited	Complexity: 1 Store at 20-33°C	For sale	US\$ 3.00 Negotiable
Sanofi Diagnostics Pasteur, S.A. 92430 Marne La Coquette, France Parent Company: BioRad Hercules, California, USA www.bio-rad.com	MultiSpot HIV-1/HIV-2 Microfiltration-bound EIA Recombinant antigens and synthetic peptides for HIV-1/2 Multiple reagents Uses plasma or serum Genie II HIV1/HIV2 Microfiltration-bound EIA Recombinant antigens and synthetic peptides for HIV-1/2 Multiple reagents Uses plasma or serum	99.3-100% <sup>a,c</sup>	98.5-100% <sup>a,c</sup>	Extensive	Complexity: 2 Store at 2-25°C <sup>d</sup> Requires vortex	For sale WHO- evaluated	US\$ 4.00 -5.00
Sanofi Diagnostics Pasteur, S.A. 92430 Marne La Coquette, France Parent Company: BioRad Hercules, California, USA www.bio-rad.com	MultiSpot HIV-1/HIV-2 Microfiltration-bound EIA Recombinant antigens and synthetic peptides for HIV-1/2 Multiple reagents Uses plasma or serum Genie II HIV1/HIV2 Microfiltration-bound EIA Recombinant antigens and synthetic peptides for HIV-1/2 Multiple reagents Uses plasma or serum	97.8-100% <sup>a,b</sup>	99.7-100% <sup>a,b</sup>	Limited	Complexity: 2 Optional: centrifuge	For sale	Negotiable

Manufacturer/Distributor	Product Description	Sensitivity	Specificity	Field use	Comments <sup>f</sup>	Status	Cost/Test <sup>f</sup>
Trinity Biotech, Plc Dublin, Ireland www.trinitybiotech.com	Capillus HIV-1/HIV-2 Latex bead agglutination Recombinant antigens and synthetic peptides for HIV-1/2 Multiple reagents Uses plasma or serum SalivaCard HIV Microfiltration-bound EIA Synthetic peptides for HIV-1/2 Multiple reagents Uses oral fluid SeroCard HIV Microfiltration-bound EIA Synthetic peptides for HIV-1/2 Multiple reagents Uses whole blood, plasma, or serum UniGold HIV Recombinant Immunochromatographic Recombinant antigens for HIV-1/2 Single reagent Uses whole blood, plasma, or serum	98.6–99.9% <sup>a,b</sup>	98.2–99.6% <sup>a,b</sup>	Extensive	Complexity: 2 Store at 2–8°C Optional: reader & centrifuge	For sale WHO- evaluated	US\$ 1.50
		98.9% <sup>a</sup>	98.8% <sup>a</sup>	Limited	Complexity: 2 Store at 2–8°C Requires: Orapette device	For sale	Negotiable
		99.8–100% <sup>a,b</sup>	99.5% <sup>a,b</sup>	Extensive	Complexity: 2 Store at 2–8°C	For sale	US\$ 1.80
		99.8% <sup>a</sup>	100% <sup>a</sup>	Limited	Complexity: 1 Store at 2–27°C	For sale	US\$ 2.25 Negotiable

<sup>a</sup> Sensitivity and specificity data supplied by manufacturer as determined for blood/serum/plasma against multiple HIV-1/2 subtypes. <sup>b</sup> Published sensitivity and specificity data against multiple HIV-1/2 subtypes (see [5,6,9]). <sup>c</sup> Sensitivity and specificity data from Centers for Disease Control evaluation against multiple HIV-1/2 subtypes. <sup>d</sup> Stable at room temperature (20–33°C), but shelf life improved with refrigeration. <sup>e</sup> Although all tests are designed to be simple, some require multiple steps, including pipetting, and performance may improve with centrifugation. In these instances limited training and laboratory experience are useful. Complexity rating: (1) specimen may be whole blood, venipuncture not required, sample manipulation limited to application followed by addition of buffer reagent or wash, easily read; (2) specimen limited to plasma or serum, centrifugation or optional equipment beneficial; (3) reagent or sample preparation may be required, multi-step assay. <sup>f</sup> Prices vary dependent on market and availability; they are provided solely as a point of reference. EIA, enzyme immunoassay.