TECHNOLOGY LANDSCAPE

HIV RAPID DIAGNOSTIC TESTS FOR SELF-TESTING

2nd Edition
1 July 2016

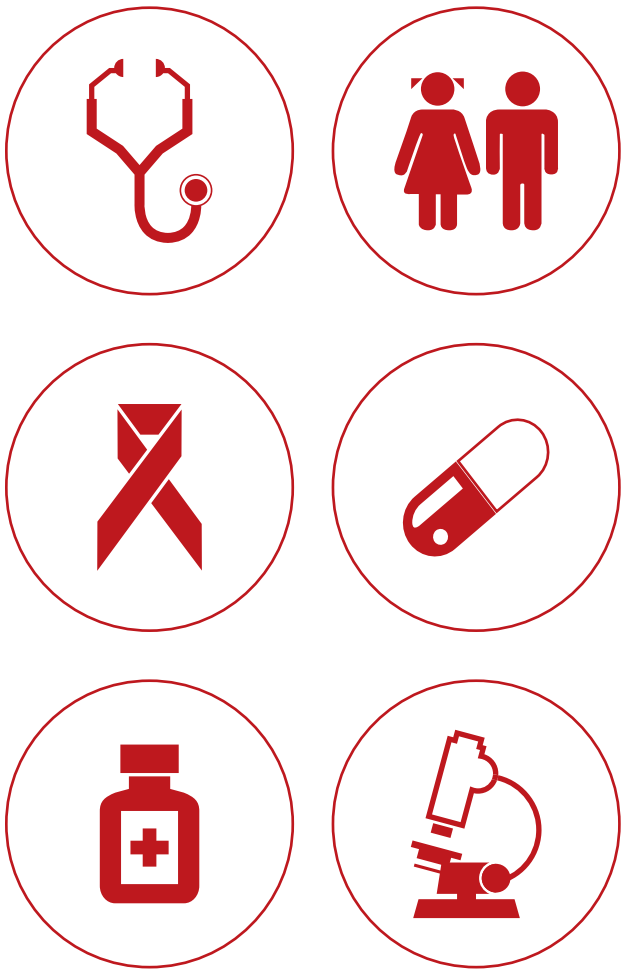

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Table of Contents

6 Acknowledgements

7 Abbreviations

9 Executive summary

12 Background

12 Public health problem

12 The potential for HIV self-testing (HIVST)

19 Technology landscape

19 Technologies available to diagnose HIV

20 Professional use of RDTs

23 HIVST target product profile

26 Current market of HIV RDTs for self-testing

32 Global HIVST demand

32 Current and estimated HIVST demand

37 Enabling environment

42 Summary and conclusions

42 Key considerations for countries, national programmes and regional bodies

43 Key considerations for donors

44 Key considerations for manufacturers

47 Annex 1. Specification sheets for HIV self-test products in the market

48 autotest VIH®

50 BioSURE HIV Self Test

51 OraQuick® In-Home HIV Test

53 INSTI HIV self-test

57 Annex 2. Specification sheets for HIV self-test products emerging in the market

58 Atomo HIV Self-Test

60 Aware™ HIV-1/2 OMT Oral HIV Self Test

61 OraQuick® HIV Self-Test

62 Exacto® HIV Screening Test

64 To be named – Chembio Diagnostic Systems Inc.

67 References

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Abbreviations

ART	antiretroviral therapy
ARV	antiretrovirals
CDC	Centers for Disease Control and Prevention
CE	European Conformity
DNA	deoxyribonucleic acid
ERPD	Expert Review Panel for Diagnostics
FDA	United States Food and Drug Administration
GHTF	Global Harmonization Task Force
Global Fund	Global Fund to Fight AIDS, Tuberculosis and Malaria
HIV	human immunodeficiency virus
HIVST	HIV self-testing
IFU	instructions for use
IPV	intimate partner violence
IVD	in vitro diagnostic
ISO	International Organization for Standardization
mL	mililitre
µL	microlitre
NA	Not available
NAT	nucleic acid testing

NGO	nongovernmental organization
PEP	post-exposure prophylaxis
PEPFAR	President's Emergency Program for AIDS Relief
PLHIV	people living with HIV
PMA	pre-market approval
PQ	prequalification
PrEP	pre-exposure prophylaxis
PSI	Population Services International
RDT	rapid diagnostic test
RNA	ribonucleic acid
STI	sexually transmitted infection
TGA	Therapeutic Goods Administration
UN	United Nations
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNICEF	United Nations Children's Fund
USA	United States of America
USAID	United States Agency for International Development
US$	United States dollar
VMMC	voluntary medical male circumcision
WHO	World Health Organization

Executive summary

This report presents HIV self-testing (HIVST) as an innovative strategy with great potential to contribute to achieving the United Nations (UN) 90–90–90 targets by 2020. It provides updates on the landscape of technologies for HIVST originally presented in the first edition of the *UNITAID/WHO Landscape on HIV self-testing (December 2015),* as well as a summary of the existing and emerging market and projections of the demand for, and supply of, HIV rapid diagnostic tests (RDTs) for self-testing. The information in this report is intended for manufacturers, donors, national programmes, researchers and other global health stakeholders who are exploring the potential role of HIVST.

HIVST is a potential approach to expand access to HIV testing services and reach those at high risk for HIV who may not otherwise test, including men, young people and key populations. The World Health Organization (WHO) defines HIVST as a specific process in which a person collects his or her specimen (oral fluid or fingerstick/blood) and then performs a test and interprets the result, often in private or with someone they trust. All individuals with a reactive self-test result must receive further testing with a complete validated testing algorithm for diagnosis from a trained provider.

The first edition of this landscape identified 52 HIV RDTs on the market, the vast majority (48) of which used fingerstick/whole blood specimens. As of June 2016, 24 HIV RDTs for professional use were identified as eligible for procurement by major donors, as they are either approved by WHO or the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund). Between 2012 and 2014, a total of 243 million HIV RDTs for professional use were reportedly procured by public agencies, averaging about 81 million HIV RDTs per year. The actual volume is likely to be much larger, as these estimates do not include HIV RDTs procured directly from manufacturers by country governments nor HIV testing services in the private and/or informal sector. Prices for HIV RDTs for professional use range from US$ 0.50 to US$ 11.00 depending on the specimen-type, procurement volume and buyer.

HIVST is a complementary approach to existing HIV testing services and the majority of HIV RDTs for self-testing are based on HIV RDTs for professional use that have been modified and repackaged. Currently, there are fewer HIV RDTs for self-testing on the market than those emerging. As of July 2016, there are only four HIV RDTs for self-testing on the market with approval by a founding

member of the Global Harmonization Task Force (GHTF) and thereby eligible for procurement with major donor funding. This includes one oral fluid and three fingerstick/whole blood products. However, prices to date are largely prohibitive for use in low- and middle-income countries (US$ 7.50–48). The pipeline of products for HIVST is much larger, with six fingerstick/whole blood-based, and three oral fluid-based RDTs for self-testing under development. All products are serology assays that use immunochromatographie (lateral flow). The majority are second generation RDTs, require between five and seven steps and include a reading time between 15 and 45 minutes.

Significant innovation would be required to meet the current HIV RDT for self-testing target product profile. Potential for innovation includes adaptation of tests with greater seroconversion sensitivity (third and fourth generation RDTs) and modifications of test kits to be more "user friendly". These modifications may include reducing the number of steps (e.g. one step), simplifying specimen collection and transfer, achieving a faster time to results, ensuring results remain stable for a longer period, improving the clarity of the space where the result appears and is read to strengthen accurate result interpretation, and optimizing packaging and instructions for use (IFU). Innovations in support tools for referral and linkage could also improve test performance as well as ensure linkage to further testing, prevention, treatment and care. Such modifications may not only benefit those who self-test, but also health workers and lay providers who often provide HIV testing services in a variety of settings where they may lack adequate training, support and supervision and who deal with challenges such as poor visibility, inadequate lighting and limited time and supplies.

Global demand for HIVST is largely uncertain. In high-income markets where HIV RDTs for self-testing are approved for use, it is estimated that 1.6 million RDTS for HIVST have been sold since 2012. Based on this information and current data about uptake and use of HIVST in low- and middle-income countries, global demand is estimated to be at least 4.8 million HIV RDTs by 2018. Work is currently under way to refine this estimate using population-level data. These estimates will focus on the African market and are planned for release in December 2016.

Despite this lack of clarity, global procurement in 2015 and the first half of 2016 significantly outpaced prior years. As of June 2016, several large buyers are signalling increased interest in HIVST; and the President's Emergency Fund for AIDS Relief (PEPFAR), the Global Fund and the Bill & Melinda Gates Foundation have all initiated procurement to support growing demand for implementation research. Furthermore, policy development at the national level gained traction in several countries since the first published landscape. Sixteen countries report the existence of a policy supportive of HIVST, while another eight are under development. WHO guidelines, a critical tool for further advancing policy development, are also expected in late 2016.

Approval pathways are also becoming more concrete. Guidelines and a sample dossier for WHO prequalification of HIV RDTs for self-testing are expected in 2016 and the Global Fund Expedited Review Panel has recently expressed interest in reviewing dossiers for HIV RDTs for self-testing for temporary approval. The establishment of these approval channels will bring more certainty to the market and further enable market entry. However, clarification of country-level policy and regulatory frameworks are urgently needed.

The growing pipeline of HIV RDTs for self-testing indicates a growing market supply, while more concrete developments in approval, policy and regulatory pathways, as well as increased procurement indicate an increasingly healthy environment in which the market demand for HIVST can flourish. However, risks that may slow market development remain, such as unanswered operational research questions, limited product innovation and unclear country-level policy and regulatory frameworks. To maximize the potential and continue to expand this market, country governments, donors and manufacturers can all take critical steps to address these risks and support further market development.

Background

Public health problem

A person's knowledge of their HIV status is essential to the success of the HIV response. HIV testing services are the gateway to treatment, prevention and care. Antiretroviral therapy (ART), voluntary medical male circumcision (VMMC), prevention of mother-to-child transmission, pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP) all contribute to reducing HIV transmission and HIV-related morbidity and mortality. ART is highly effective in reducing HIV-associated morbidity and mortality and can prevent onward transmission of HIV *(1–3)*. Thus, in October 2015, the World Health Organization (WHO) recommended ART be offered to all people living with HIV (PLHIV) immediately following diagnosis, regardless of clinical assessment *(4)*. The United Nations (UN) issued fast-track targets that could enable the end of the HIV/AIDS epidemic, by aiming to have diagnosed, by 2020, 90% of all PLHIV, for 90% of people diagnosed with HIV to receive ART, and for 90% of those on ART to have a suppressed viral load *(5)*. The first 90 – diagnosis of HIV – is both essential and a key challenge facing the HIV response today.

To date, the global scale-up of HIV testing services has been significant. From 2010 to 2014, more than 600 million people received HIV testing services in 122 low- and middle-income countries *(6)*. An estimated one half of PLHIV in Africa are now aware of their HIV status *(7)*, an increase from 2005 when only 10% of PLHIV were aware of their status *(8)*. These gains have been made possible through the expanded use of rapid diagnostic tests (RDTs), implementation of routine testing in health facilities (primarily in antenatal care and tuberculosis clinics), and expansion of community-based HIV testing and task-sharing initiatives enabling trained lay providers to perform HIV testing services. With the widespread availability of ART and the widespread use of RDTs, which in a validated testing algorithm can often provide a same-day diagnosis, HIV testing is now routinely provided with pre-test information without the requirement for pre-test counselling *(9)*.

Despite achievements in scaling up HIV testing, substantial gaps remain, as an estimated 44% of PLHIV in Africa and 43% of all PLHIV globally have yet to be diagnosed *(7)*. Depending on the local epidemiology and the approaches used to deliver HIV testing, the proportion of HIV-positive test results varies considerably. In many settings where there has been a growing number of HIV tests every year,

these tests do not necessarily reach PLHIV who are unaware of their status and others who are at high risk for HIV infection *(9)*. For instance, although 150 million HIV tests were performed in 2014 in 129 low- and middle-income countries, in this same period 81 of these countries reported that only 3% of all HIV tests performed were HIV-positive *(6)*.

Source: PATH Viet Nam, Kimberly Green

HIV testing uptake and coverage for men continues to be lower than those for women in most countries *(10)*. Nearly 70% of adult HIV tests reported in 76 low- and middle-income countries in 2014 were among women *(10)*. Global reporting suggests this is because HIV testing is integrated successfully within reproductive health services, including antenatal care, but not consistently in other relevant clinical settings, and that male partner testing is not widely implemented or taken up *(10,11)*. Thus, many men remain untested and those with HIV often continue to be diagnosed late.

Among **key populations**, who are disproportionately affected by HIV and comprise approximately 40% of the 2 million new HIV infections every year *(12)*, testing coverage remains low and existing reports of coverage are likely overestimates due to limited data that are not representative. Low uptake of HIV testing services among key populations is not only related to availability, but also depends on acceptability and is impacted by unfriendly services, fear of stigma, discrimination and criminalization of behaviour *(12)*.

Young people and adolescents, particularly girls and young women, are also at a significant risk of HIV infection and yet, in sub-Saharan Africa, adolescents are less likely than adults to be tested for HIV. It is estimated that fewer than one of every five girls (aged 15–19) are aware of their HIV status *(11,13)*. Uptake of HIV testing among adolescents is often low in settings with the highest HIV incidence and services for adolescents are sometimes of poor quality; uptake is further constrained due to laws and policies, for example, age of consent laws that prevent adolescents from accessing HIV testing services *(14)*.

Source:UNITAID/Eric Gauss

In addition to scaling up HIV testing services, maintaining the quality of HIV testing is critical. A systematic review identified several reports of poor quality HIV testing practices, such as poor product performance, improper storage of test kits and supplies, clerical or transcription errors, user errors in performing the test and/or interpreting the test result, lack of training, improper use of the testing strategy and/or algorithm, lack of supportive supervision and training, lack of standard operating

procedures and poor documentation and recordkeeping practices, some of which resulted in misdiagnosis of HIV status *(9)*. To address these problems, effective quality assurance systems and post-market surveillance systems must expand along with the expanded delivery of HIV testing services.

These challenges require a new focus and new approaches to reach PLHIV who remain undiagnosed early in their infection. Many countries and programmes are considering innovative approaches to delivering HIV testing services to adequately reach these people and achieve national and global testing targets.

The potential for HIV self-testing (HIVST)

HIVST has been proposed as an additional approach to help countries expand access to HIV testing services and reach those at high risk who may not otherwise test. WHO defines HIVST as a specific process in which a person collects his or her specimen (oral fluid or fingerstick/whole blood) and then performs a test and interprets the result, often in private or with someone they trust *(9)*. All individuals with a reactive self-test result must receive further testing with a complete validated testing algorithm for diagnosis from a trained provider *(9).* Self-testing is not a new concept. It is in use in the management of various health conditions, such as pregnancy, bowel cancer and diabetes. In this way, HIVST represents another step in line with task sharing initiatives and efforts to increase patient autonomy, decentralize services and create demand for existing services.

There are many models for implementing HIVST, which vary in the level of support provided and how and where HIV self-test kits are distributed. Models include support from health workers, distribution or sale in the community or a health facility, as well as sale in pharmacies, kiosks, vending machines and through the Internet. Direct or indirect assistance may also be available through a demonstration on how to self-test via an instructional video, telephone hotlines and printed instructions for use (IFU) or other package inserts *(9)*. Notably, accuracy of HIV RDTs used for self-testing can be high, particularly when using validated tests and clear and concise IFU, as well as other support tools (e.g. demonstration on how to self-test). According to a systematic review of 21 reports that assessed the performance of HIV RDTs, sensitivity ranged from 65% (95% CI 33.6–87.2%) to 98.8% (95% CI 92–99.8%) and specificity ranged from 94.7% (95% CI 84.9–98.3%) to 100%

(95% CI 99.9–100%) *(15)*. While there is a wide range in reported sensitivity, only 2/21 reports reported sensitivity less than 80% and 15/21 reported sensitivity of 90% or more *(15)*. Furthermore, there was no difference between approaches offering direct assistance compared to those that did not *(15)*.

Despite good performance, it is important to note no single HIV RDT can provide an HIV-positive diagnosis. However, a person with a nonreactive self-test result does not need to have this result confirmed *(9)*. It is recommended, as for all testing services, to provide retesting messages for people with high ongoing or recent risk exposure(s) (e.g. key populations; serodiscordant couples) *(9)*.

There are many possible advantages to HIVST. It has been shown to be a discreet and convenient approach that is also empowering and acceptable for diverse populations in various contexts who may test less frequently or not otherwise test at all *(9,16–18)*. For those with a reactive self-test result, HIVST may lead to early access to health services to establish an HIV diagnosis and link to prevention, treatment and care. For those with a nonreactive test result, HIVST may support increased uptake of prevention interventions, such as VMMC, PrEP and PEP, where the requirement for HIV testing at the time of seeking prevention services is reported as a barrier *(19–21)*. For example, in Kenya, HIVST was reported to facilitate access to PEP among health workers because accessing existing testing at their facility was a barrier *(20)* and studies in Malawi, Zambia and Zimbabwe are under way to evaluate the utility of HIVST to increase uptake of VMMC *(22)*. HIVST may also lead to increased frequency of testing, which is particularly relevant for individuals at high ongoing risk for HIV and who are advised to test every three or every six months. Several reports and models find that men who have sex with men would test more frequently if self-testing were available *(18,23)* and that increased frequency would have a public health benefit, particularly where testing coverage is low (24,25). In addition, HIVST may ease the implementation and reduce the cost of interventions, such as PrEP, where retesting is recommended every three months *(26,27)*.

HIVST may also lead to cost savings and galvanize testing scale-up in settings with low coverage and where there are health worker shortages. While the cost of an HIV RDT for self-testing is higher compared to an HIV RDT for professional use, the total cost of self-testing may be less than the total cost of standard facility-based or community-based HIV testing. The potential cost savings of self-testing has also been highlighted by a Zimbabwe-based cost-effectiveness model that states that if HIVST were delivered for US$ 3 per test over a 20-year period, Zimbabwe would save US$ 75 million and avert 7000 disability adjusted life-years *(28)*. However, since costs are highly variable across settings, further market research and cost-effectiveness analysis is needed.

HIVST has also been shown to be safe in several studies. For example, in Malawi, a two-year cluster randomized trial reported no suicides, self-harm or intimate partner violence (IPV) and while a few reports of “coercion” were documented, nearly all

Source: WITS RHI, Mohamed Majam

were among men and nearly all reported they would recommend self-testing to others *(29).* Nevertheless, it is important to note violence can occur in the context of any intervention, including existing HIV testing services, and that providing messages to mitigate risk for potential misuse and harm and implementing monitoring and reporting systems are key *(9).* To date, only one study, where 41% of participants reported IPV 12 months prior to the intervention, has identified a case of IPV following HIVST *(30).*

Using existing evidence-based strategies, such as home-based assessment or care *(31)* and couples and partner testing *(30),* has been shown to facilitate linkage to further testing and onward prevention, treatment and care. Identifying tools and strategies that support and facilitate linkage is an important area of research and several studies are under way to assess effectiveness of different tools.

Box 1 highlights tools that could potentially enhance linkage to further testing, prevention, treatment and care following HIVST.

BOX 1

Interventions and tools to support linkage to prevention, treatment and care for HIVST

Home-based treatment initiation with support and active follow-up by community-based networks has been shown to be an effective way to support linkage to care *(31).*

- **Package inserts** can be included in HIVST kits that explain the importance of further testing, and where and how to obtain prevention, treatment and care services.
- **Telephone hotlines** can be set up for people to call before or after self-testing to obtain information, including psychosocial and technical support as well as referrals and linkage to prevention, treatment and care and other non-medical services (i.e. legal support; redress for violence).
- **Mobile phone services**, which can operate like hotlines, can also provide reminders, videos and other messages and information to encourage linkage to prevention, treatment and care.
- **Internet and computer-based programmes** can support self-testers. Some approaches have included online two-way audio or video counselling services and programmes that offer step-by-step instructions on what to do following a reactive self-test result including descriptions of where and how to obtain further testing, prevention, treatment and care.
- **Vouchers, coupons, financial incentives or rebates** could assist linkage to further HIV testing, prevention, treatment and care, particularly among populations that face structural barriers to accessing services, such as long distance and costly transportation.
- **Referral or appointment cards** that provide a contact, date and/or time for an appointment for follow-up services, including HIV testing and other HIV prevention, treatment and care services could also be utilized to facilitate linkage.
- **Partner HIVST** may increase linkage to care and encourage male involvement (30). Depending on the context, offering HIVST within voluntary **partner notification services** could also promote linkage to prevention, treatment and care

Source: UNITAID/Eric Gauss

Technology landscape

Technologies available to diagnose HIV

There are two key categories of testing technologies that can be used at the point of care to diagnose HIV-1/2 infection: HIV RDTs and nucleic acid testing (NAT) technologies.

HIV RDTs are serology assays that detect HIV-1/2 antibodies and/or HIV-1 p24 antigen. HIV RDTs generally provide results between 5 and 20 minutes and are in the form of lateral flow strips or cassettes or flow through devices. When used within a national validated testing algorithm, they can accurately provide same day diagnosis. They are relatively easy to use, can be performed using capillary whole blood or oral fluid specimens, contain built-in quality controls and can be administered by trained non-laboratory personnel.

NAT is a molecular technology for detecting the presence of HIV in RNA and/or DNA in plasma, venous and capillary whole blood or dried blood spot specimens. Currently, there are few NAT technologies that can be used at the point of care in resource-limited settings. Those that are available are primarily used for early infant diagnosis.

Depending on which assays are used, HIV infection can be detected between 10 and 50 days following the initial infection (Figure 1). HIV RDTs currently in use can be classified into three groups (second, third and fourth generation) based on how quickly they can detect HIV following an exposure.

- **NAT technologies** detect HIV in RNA or DNA and have been shown to detect HIV infection in the acute infection stage. Compared to other point-of-care HIV tests, they have the shortest window period compared to other testing technologies and can detect HIV beginning 10 days after an exposure.

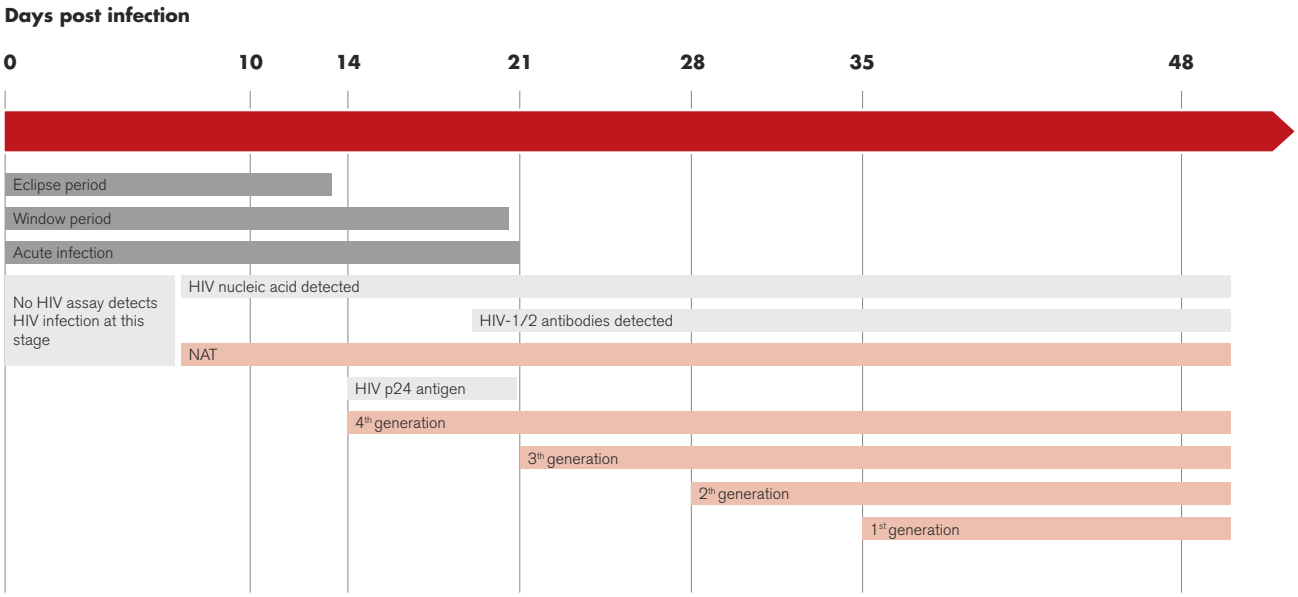
- **Fourth generation HIV RDTs** can detect both HIV-1/2 antibodies and p24 antigen. These RDTs can identify an infection beginning 14 days after an exposure. While theoretically they may be able to detect acute HIV infection using p24 antigen, field evaluations suggest that this does not occur in practice (32).

- **Third generation HIV RDTs** only detect HIV-1/2 antibodies and have been shown to have good seroconversion sensitivity. This type of test is widely used in resource-limited settings and can typically detect HIV beginning 21 days after an exposure.

- **Second generation HIV RDTs** only detect HIV-1/2 antibodies and have the longest window period compared to other generations as they can typically detect HIV beginning 28 days after an exposure.

FIGURE 1

Detecting HIV-infection with various formats and generations of IVDs over the natural history of infection



Sources: WHO 2015 (9); Rosenberg 2015 (33).

Professional use of RDTs

The market of professional use RDTs for HIV is large. A review performed for the first edition of this report in December 2015[a] identified 52 HIV RDTs available for professional use, the majority of which (48) use fingerstick/whole blood specimens and only four that use oral fluid specimens. As of June 2016, 24 HIV RDTs for professional use are eligible for procurement by main donors,

as per WHO[b] or the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund)[c] listing. Of those listed, 13 fingerstick/whole blood-based RDTs and two oral fluid-based RDTs are WHO prequalified; and 9 other fingerstick/whole blood products are undergoing the WHO prequalification process.[d]

Between 2012 and 2014, a total of 243 million HIV RDTs for professional use were reportedly procured by the Global Fund, the Partnership for Supply Chain Management Systems (SCMS), the United Nations Children's Fund (UNICEF) and WHO, averaging about 81 million HIV RDTs per year. In total, more than 242.2 million HIV RDTs using fingerstick/whole blood were procured, averaging about 80.7 million annually. During the same period, nearly 750 000 HIV RDTs using oral fluid were procured, averaging about 250 000 annually.

The volume is likely to be much larger, as these estimates reflect what is reported by donor agencies and do not include HIV RDTs procured directly from manufacturers by countries and HIV testing services that take place in the private and/or informal sector.

In 2014, the cost of HIV RDTs for professional use ranged from US$ 0.95 to US$ 1.08 per test, using volume weighted average prices per smallest unit per year across the Global Fund, SCMS, UNICEF and WHO (excluding any distributor markups and assuming ex-works). However, ranges were wide: the cost per HIV RDT for professional use procured by the Global Fund ranged from about US$ 0.50 per test to about US$ 3.30 per fingerstick/whole blood test, whereas the cost of HIV RDTs using oral fluid ranged from US$ 4.00 to US$ 11.00. See Table 1 and Table 2 for summary of products listed by WHO or the Global Fund.

TABLE 1

Summary table of WHO prequalified HIV RDTs for professional use (oral fluid)

Assay name (manufacturer)	Sensitivity*	Specificity*	Approval status
DPP® HIV 1/2 Assay (Chembio Diagnostic Systems Inc., USA)	100%	99.9%	**WHO PQ**
OraQuick® HIV 1/2 Rapid Antibody Test (OraSure Technologies Inc., USA)	99.1%	99.8%	**WHO PQ**

* sensitivity and specificity estimates for oral fluid as a specimen type

[a] UNITAID/WHO Landscape on HIV RDTs for self-testing. First edition, November 2015: http://unitaid.org/images/marketdynamics/publications/HIV_ST_Landscape_Nov_2015-_UNITAID_WHO.pdf

[b] WHO Prequalification of IVDs Programme list of prequalified products 16 June 2016: http://www.who.int/diagnostics_laboratory/evaluations/160615_prequalified_product_list.pdf?ua=1

[c] Global Fund: http://www.theglobalfund.org/documents/psm/PSM_ProductsHIV-WHO_List_en/

[d] WHO Prequalification of IVDs Programme list of active applications products 16 June 2016: http://www.who.int/diagnostics_laboratory/160608_rapid_test_v1.pdf?ua=1

TABLE 2

Summary table of WHO prequalified or Global Fund approved HIV RDTs for professional use (fingerstick/whole blood)

Assay name (manufacturer)	Sensitivity*	Specificity*	Approval status
ABON™ HIV 1/2/O Tri-Line Human Immunodeficiency Virus Rapid Test Device (ABON Biopharm (Hangzhou) Co. Ltd, China)	100%	99.7%	**WHO PQ**
Alere Determine HIV-1/2 (Alere Medical Co. Ltd, Japan)	100%	99.4%	**WHO PQ**
Alere HIV Combo (Alere Medical Co. Ltd, Japan)	100%	99.72%	**CE marked**
Anti-HIV 1/2 (Turk Lab, Turkey)	100%	10%	**CE marked**
DIAQUICK HIV 1&2 Ab Cassette (DIALAB GmbH, Austria)	100%	100%	**CE marked**
First Response™ HIV 1-2-0 Card Test (Premier Medical Corporation, Nani Daman, India)	100%	98.8%	**CE marked**
Genie Fast HIV 1/2 (Bio-Rad Laboratories, Marnes La Coquette, France and Steenvoorde, France)	100%	99.9%	**CE marked**
Hexagon HIV (Human Gesellschaft für Biochemica und Diagnostica mbHGermany)	100%	99.9%	**CE marked**
HIV 1/2 STAT-PAK® Dipstick (Chembio Diagnostic Systems Inc., USA)	100%	99.7%	**WHO PQ**
HIV 1/2 STAT-PAK™ (Chembio Diagnostic Systems Inc., USA)	99.3%	100%	**WHO PQ**
ImmunoComb® II HIV 1&2 BiSpot (Orgenics Ltd, Israel)	100%	99.4%	**WHO PQ**
INSTI HIV-1/HIV-2 Antibody Test (BioLytical Laboratories Inc., Canada)	100%	99.7%	**WHO PQ**
Multispot HIV-1/HIV-2 Rapid Test (Bio-Rad Laboratories, Marnes La Coquette, France and Steenvoorde, France)	100%	99.3%	**FDA/ PMA**
Multisure HIV Rapid Test (MP Biomedicals Asia Pacific, Singapore)	100%	99.12%	**CE marked**
ONE STEP Anti-HIV(1&2) Test (InTec PRODUCTS INC., Haicang, Xiamen, China)	99.8%	99.23%	**CE marked**
Rapid Test for Antibody to Human Immunodeficiency Virus (HIV) (Colloidal Gold Device) Beijing Wantai Biological Pharmacy Enterprise Co. Ltd, China)	100%	98.48%	**WHO PQ**
SD Bioline HIV Ag/Ab Combo (Standard Diagnostics Inc., Republic of Korea)	100%	99.1%	**WHO PQ**
SD BIOLINE HIV/Syphilis Duo (Standard Diagnostics Inc., Republic of Korea)	100%	99.5%	**WHO PQ**
SD BIOLINE HIV-1/2 3.0 (Standard Diagnostics Inc., Republic of Korea)	99.8%	99.9%	**WHO PQ**

Assay name (manufacturer)	Sensitivity*	Specificity*	Approval status
SURE CHECK® HIV 1/2 Assay (Chembio Diagnostic Systems Inc., USA)	99.8%	99.9%	**WHO PQ**
Uni-Gold™ HIV (Trinity Biotech Manufacturing Ltd, Ireland)	99.8%	99.9%	**WHO PQ**
VIKIA HIV 1/2 (bioMérieux SA, France)	99.4%	99.9%	**WHO PQ**

PMA: Pre-market approval

HIVST target product profile

The current technology utilized for HIVST is primarily adapted and repackaged versions of HIV RDTs for professional use. There are many inherent characteristics of an HIV RDT that may need adaptation to make it more suited for HIVST, but there are also modifications to the packaging and IFU that further optimize a product for HIVST.

In 2014, PATH developed a target product profile for HIVST *(34)*. The summary below provides an overview of that profile, as well as some additional considerations for the ideal HIV RDT for self-testing.

Test generation. At the moment, the self-testing products on, and emerging in, the market are primarily second generation HIV RDTs. The use of second generation HIV RDTs for self-testing has raised some concerns, as they reportedly have poorer seroconversion sensitivity compared to third and fourth generation HIV RDTs. There is one third generation HIV RDT for self-testing on the market currently, and another that is emerging in the market.

Adapting tests that are highly sensitive, have high seroconversion sensitivity and a shorter window period, including third and fourth generation RDTs and NAT technologies that can be used at the point of care for self-testing, may be particularly advantageous for populations that require frequent retesting and are at high risk for HIV (e.g. high incidence). The development of third and fourth generation HIV RDTs for self-testing is advancing, however, the development of self-operated NAT technologies are not being developed at this stage.

In addition, possible concern about the use of second generation HIV RDTs for self-testing should be weighed against several factors. First, NAT technologies and fourth generation tests currently have limited availability in low- and middle-income technologies. Where used, third and fourth generation tests may require volumes of fingerstick/whole blood specimen, which is difficult for self-testers to collect, and fourth generation tests may increase the risk of false-reactive results. Current NAT

Source: Atomo Diagnostics, Anna Wang

technologies are optimized for specificity, not sensitivity, which may also make them less appropriate for a "test for triage" approach with self-testing.

Multiplex technology. There is also the potential for self-testing to improve diagnosis for other sexually transmitted infections (STIs) through multiplex testing. Combinations could include HIV, syphilis, hepatitis B and hepatitis C, among others. Introducing multiplex self-testing for HIV and other STIs reduces the chance of missed opportunities for STI screening outside facility-based settings. This could be particularly beneficial for high-risk groups who are hard to reach, as described above. At this time, the potential for multiplex self-testing has not been fully explored and there are few multiplex RDTs for professional use. Only one HIV and syphilis RDT is WHO prequalified. There are multiplex RDTs for HIV and hepatitis B and C, but none is currently undergoing WHO prequalification. Despite the limited number of multiplex RDTs that could be adapted for self-testing, if successful, they may be a way to reach people at high risk and increase the public health impact of self-testing.

Reduced steps. Each step for HIV testing, from the specimen collection to interpreting the final result, is critical for a correct result. The more steps, the greater the risk is for user error that may then result in a greater risk of an incorrect test result. Collecting and transferring specimen (either fingerstick/whole blood or oral fluid) has been shown to be particularly prone to error for self-testers, resulting in test system failures, invalid results and suboptimal performance *(15)*. Thus, an HIV RDT for self-testing with few steps, or ideally one single step, could substantially reduce the risk of a number of user errors. Opportunities to develop integrated components, such as specimen collection and transfer devices as well as integrated buffer systems may be useful, including less painful lancets and other components that are automated to regulate the volume of specimen collected and how the specimen is transferred.

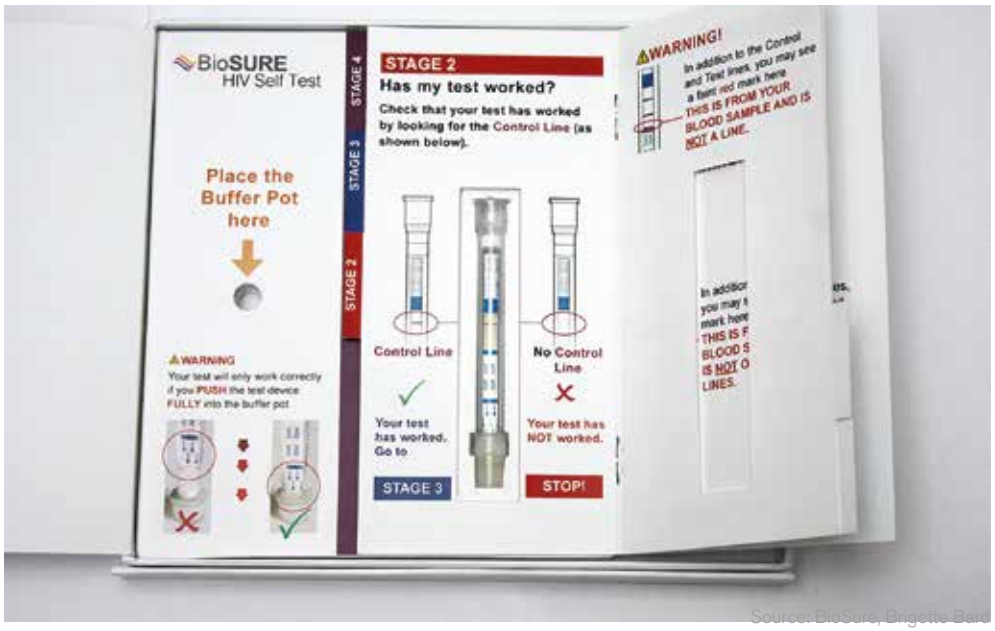
Easy interpretation. Interpretation of test results can be challenging, particularly if lines are faint or blurred, if the size of the read window is small, if the incubation time is narrow and if the read time is lengthy. It is well documented that errors interpreting

RDT results occur among trained users, for example, incorrect interpretation of "faint lines" and failure to read results within the stipulated time *(15).* It is likely that using existing RDTs for self-testing will have similar challenges.

Current RDTs that are being used for self-testing should not be read for at least 15 minutes after the sample is applied and should not be read more than 60 minutes afterward. This requirement may be challenging for individuals who do not have timers readily available and result in misinterpretation of results by users reading too early or too late *(15)*. Settings where mobile phones or other timers and clocks are available may minimize this problem.

To address these challenges, the ideal RDT for self-testing should provide a result in one to five minutes and have stable incubation times where results are stable. Result windows should be clear and easy to read, particularly to prevent faint lines that can be especially challenging to interpret. Current HIV RDTs being used for self-testing, however, do not have these characteristics and would need to be developed.

Robustness and durability. The product design for HIV RDTs for self-testing should consider transport, use and storage in uncontrolled settings that require a degree of robustness and durability. Products that can withstand high temperatures, user errors and other conditions that promote product instability may be an advantage for self-testers and those that distribute the test kits, particularly in resource-limited settings. Lastly, while robustness and durability are critical, packaging is also a key consideration to maximize product acceptability. Potential users may find bulky or heavy packaging unattractive, particularly those seeking privacy and discretion. The inclusion of multiple tests in a single pack may be desired in order to facilitate repeat testing or partner testing.



Source: BioSure, Brigette Bard

IFU and support tools. Several studies have indicated that HIV RDTs for self-testing perform best when IFU have been developed and validated among intended user populations. Pictorial IFU are most ideal as literacy levels vary highly across intended user populations and settings. Because of cultural and language differences, special attention to detail will be needed as instructions will have to be translated and validated before implementation. Other support tools such as videos, telephone hotlines and demonstrations on how to self-test and interpret the result can also improve performance. These tools can also be utilized to facilitate linkage to prevention, treatment and care.

Disposal and waste management. In general, RDTs for self-testing should be designed to be disposable as they will be designed for single use. Although RDTs that use oral fluid specimens pose minimal biohazardous risk, concerns have been raised about such risks with fingerstick/whole blood-based RDTs. However, no data yet conclusively support this concern. Across all products for HIVST, lessons learnt from blood glucose monitoring and other self-tests or self-monitoring devices should be considered in order to minimize risk of exposure to biohazardous material.

Cost. HIV RDTs for self-testing are intended for a single use where all components are individually packaged. Therefore, costs are typically higher than professional use HIV RDTs that can be sold in bulk. While the test kit costs may be higher in some cases, for comparison purposes the cost of the testing event should be considered, for example, health worker time, facility costs and community outreach costs.

Second generation HIV RDTs for self-testing may be slightly lower cost than third and fourth generation RDTs, and all RDT costs will be much lower than NAT technologies at the point of care (estimated to be as much as US$ 20 per test for professional use). Although NAT could be potentially more accurate and able to diagnose HIV in the acute stage, a high cost for a self-use tool can lead to low uptake of, and access to, HIVST.

Current market of HIV RDTs for self-testing

Available and pipeline products. Currently, there is one oral fluid and three whole blood-based RDTs for self-testing eligible for procurement with major donor funds, including from the Global Fund and UNITAID. These products are registered and approved for use by a founding member of the Global Harmonization Task Force (GHTF). However, the pipeline is much larger, with six fingerstick/whole blood-based

and three oral fluid-based RDTs for self-testing under development. All products use immunochromatographie (lateral flow) and serology. The majority are second generation RDTs, with one third generation RDT on the market and one under development.

Current and emerging products require between five and seven steps and include a reading time between 5 and 45 minutes. Significant product innovation would be required to meet the target product profile description outlined above.

Tables 3A, 3B, 4A and 4B summarize the current pipeline. Detailed product specifications can be found in Annex 1 and Annex 2.

TABLE 3A

Fingerstick/whole blood-based HIV RDTs for self-testing on the market

Assay name (manufacturer)	Generation	Sensitivity	Specificity	Approval status	Approximate price per test (US$)
autotest VIH® (AAZ Labs, France)	2nd generation	100%	99.8%	CE marked; submitted WHO PQ	25–28 (to consumer)
Private sector version BioSURE HIV Self Test (BioSURE, United Kingdom)	2nd generation	99.7%	99.9%	CE marked	42–48 (to consumer)
Public sector version BioSURE HIV Self Test (BioSURE, United Kingdom)	2nd generation	99.7%	99.9%	CE marked	7.50–15 (to public sector)
INSTI HIV Self Test (bioLytical Laboratories, Canada)	3rd Generation	100%	99.8%	CE marked	36 (to consumer)

TABLE 3B

Oral fluid-based HIV RDTs for self-testing on the market

Assay name (manufacturer)	Generation	Sensitivity	Specificity	Approval status	Approximate price per test (US$)
OraQuick® In-Home HIV Test (OraSure Technologies Inc., USA)	2nd generation	91.7%	98.7%	FDA	40 (to consumer)
OraQuick® In-Home HIV Test (OraSure Technologies Inc., USA)	2nd generation	100%	99.8%	Completed CE procedure, pending CE certificate	NA

TABLE 4A

Pipeline of fingerstick/whole blood-based HIV RDTs for self-testing emerging in the market

Assay name (manufacturer)	Generation	Sensitivity	Specificity	Approval status	Approximate price per test (US$)
Atomo HIV Self-Test (AtomoDiagnostics, Australia)	3rd generation	NA	NA	No info	NA
Exacto® HIV Screening Test (Biosynex Medtech, France)	3rd generation	NA	NA	Submitting dossier for CE mark	NA
HemaDiagnostics Self-Test (Hema Diagnostics Systems LLC, USA)	NA	NA	NA	No info	NA
To be named (Chembio Diagnostics Systems Inc., USA)	2nd generation	NA	NA	No info	NA
To be named (Alere, USA)	NA	NA	NA	No info	NA
To be named (Trinity Biotech Manufacturing Ltd, Ireland)	NA	NA	NA	No info	NA

TABLE 4B

Pipeline oral fluid-based HIV RDTs for self-testing emerging in the market

Assay name (manufacturer)	Generation	Sensitivity	Specificity	Approval status	Approximate price per test (US$)
To be named (Sedia Biosciences, USA)	NA	NA	NA	No info	NA
Aware™ HIV-1/2 OMT Oral HIV Self Test (Calypte Biomedical Corporation, USA)	2nd generation	NA	NA	No info	NA
HIV Self-Test (OraSure Technologies, Bangkok, Thailand)	2nd generation	NA	NA	No info	Price available upon request

Market entry. HIV self-test products have launched in only a few countries. This includes the United States Food and Drug Administration (FDA)-approved OraQuick® In-Home HIV Test (OraSure Technologies, Bethlehem, PA, United States), an oral fluid-based RDT, available in the United States, as well as two CE marked fingerstick/whole blood RDTs available in France (autotest VIH®, AAZ Labs, Rungis Cedex, France) and the United Kingdom (BioSURE HIV Self-Test, BioSURE Ltd, London, United Kingdom). Although the OraQuick® In-Home HIV Test has completed CE mark procedures, it is not yet marketed in Europe. In July 2016, the INSTI HIV Self-Test (bioLytical Laboratories, British Columbia, Canada) was CE marked and will be launched in European markets in late 2016 .

Plans for future market introduction of RDTs for HIVST vary widely. The majority of products, both oral fluid and whole blood, are intended for deployment in low- and middle-income markets.

Currently, target markets in Africa routinely cited for both fingerstick/whole blood and oral fluid-based HIVST include Kenya and South Africa. Interest in other African markets is limited and inconsistent across manufacturers. Most manufacturers expect demand in these African markets will come from the public sector (e.g. governments and international donors) and that the private sector will comprise small volumes. Manufacturers' interest outside of Africa is primarily in markets with concentrated epidemics and large populations. Eastern Europe is of interest to manufacturers of both fingerstick/whole blood and oral fluid products, particularly those already present in other European countries or those pursuing CE-marking. The interest in this market may be particularly important given evidence of increasing HIV incidence in Eastern Europe and the potential for developed markets to drive innovation for low-income markets (35).

Source: AAZ Labs, Laure Poignant

While these targets markets suggest where interest in the market currently sits, targets markets are in flux and are likely highly sensitive to any shift in demand. At the moment, there is a high degree of uncertainty about the potential scope of the target market and what the incentives for entering the HIVST market might be (e.g. potential market size; profitability; demand). While there are many drivers for this, one particularly cited by manufacturers is the uncertainty of and not yet defined country-level regulatory and registration processes. Additionally, there are also questions and concerns about the significant financial and human resource investments needed to pursue registration for each country. For many manufacturers, decisions about entering a specific market are being driven by identification of markets with the most clear and conducive policy and regulatory environments. Because there are few countries with clear policies and regulatory standards, particularly in resource-limited settings where the need for HIV testing is highest, the development of WHO guidelines and criteria for WHO prequalification are viewed as a priority by manufacturers.

Pricing. HIV RDTs for self-testing that are currently available have a recommended consumer price of between US$ 25 and US$ 48 in markets in the United States and the European Union: (i) OraQuick® In-Home HIV Test (OraSure Technologies, Bethlehem, PA, USA): US$ 40/test in the United States; (ii) BioSURE HIV Self-Test (BioSURE Ltd, London, United Kingdom): US$ 42–48/test in the United Kingdom; (iii) autotest VIH® (AAZ Labs, Rungis Cedex, France): US$ 25–28/test in France; and INSTI HIV Self-Test® (bioLytical Laboratories, British Columbia, Canada): US$36/test in European markets. In the United Kingdom, BioSURE has also made a public sector version of its product, with a different version of packaging, available at US$ 7.50–15 to the National Health Service and nongovernmental organizations (NGOs). Price information for HIV RDTs for self-testing outside these markets is limited and largely unreported. This is because HIVST has not been widely implemented and is occurring informally or in the context of research. HIV RDTs for self-testing used within the context of research in low- and middle-income settings are priced at between US$ 3.15 and US$ 16 per test. Pricing varies based on packaging requested, volumes procured, country policies and regulation, importation taxes and fees, among other factors.

The cost of HIV RDTs for self-testing in informal markets also varies, particularly through sale in private pharmacies and the Internet. Anecdotal reports from Kenya suggest pricing as low as US$ 1 per test *(36)*, while self-tests reportedly available in South Africa, through pharmacies or online, retail for as much as US$ 10 *(37).* In Namibia, HIV self-tests currently retail direct to consumers for US$ 4–12 *(38).* At the high end of this price range, in both Namibia and South Africa, some products include multiple tests.

Manufacturers sense significant price pressure in the market – in both the public and private sectors. In the public sector, manufacturers recognize growing demands from donors and country governments to develop a lower-cost product and there is consistent agreement that volumes may help reduce price.

However, costs associated with the development and the production of a single-use product continues to limit manufacturer ability to reduce prices to levels cited as targets by donors and country governments. Furthermore, the lack of clear demand signals in low- and middle-income countries makes it difficult to forecast demand that may indicate the volumes necessary to achieve further cost savings and reduce price.

Manufacturing capacity. Manufacturing capacity is not a barrier for meeting current demand for HIV RDTs for self-testing where they are available on the market. However, it is important to note that there is only one oral fluid-based RDT manufacturer and two fingerstick/whole blood-based RDT suppliers and they share the same source manufacturer. This suggests some risk to the sustainable supply of product, if current demand was to increase exponentially or either manufacturing site was to experience operational challenges.

Based on current reported manufacturing capacity and demand estimates, future demand for HIV RDTs for self-testing can most likely be met. Analysis of available data indicates manufacturing capacity is an unlikely barrier to the development of the HIVST market in the short term, particularly because most HIVST products on the market or in development are based upon an existing professional-use RDTs. Thus, production lines for most professional-use RDTs have spare capacity that can be easily used to meet HIVST demand. Only minor modifications to manufacturing lines would be required for inclusion of tailored IFU and packaging. Furthermore, the automation of existing lines may further expand capacity with minimal investment. However, if demand increases considerably and at a quicker rate than regulatory approvals of new products, this may become a challenge, particularly as user preferences become more polarized (e.g. oral versus blood). Furthermore, the lead time associated with current manufacturing lines has not been evaluated and will need additional consideration as demand forecasts are clarified.

Critically, this analysis of manufacturing capacity assumes the use of re-purposed HIV RDTs. If significant product innovation were to take place, bringing products in-line with the target product profile, investments in manufacturing may be required.

Global HIVST demand

Current demand for HIVST products remains low, as compared to its estimated potential. It is estimated that since 2012, approximately 1.6 million RDTs for HIVST have been sold. Procurement in 2015 and the first half of 2016 significantly outpaced prior years and several large buyers are signalling increased interest in HIVST. Policy development efforts gained traction in several countries since the first published landscape, and key steps have been taken to formalize additional approval pathways. Combined, these factors suggest the growth of a much healthier environment in which the market demand for HIVST can flourish.

Current and estimated HIVST demand

Demand estimates. The December 2015 *WHO/UNITAID Landscape on HIV self-testing* estimated that the potential demand for HIVST could be at least 4.8 million by 2018 depending on the number of new users reached, the impact of HIVST on testing frequency and the level of substitution in which users replace standard HIV testing services with self-testing. The details of this analysis can be found at the following link: http://unitaid.org/en/statements/1500-unitaid-and-who-review-emerging-landscape-for-hiv-self-testing

Efforts are currently under way to refine this estimate, particularly in sub-Saharan Africa where the need and demand for HIVST is likely to be highest. A more refined model is under development and will estimate the HIVST market size in nine African countries – Kenya, Malawi, Mozambique, Nigeria, South Africa, Uganda, United Republic of Tanzania, Zambia and Zimbabwe. The model will begin by examining the potential market for all HIV testing, disaggregated by age, sex and key population group. Using data on existing HIV testing and emerging research on HIVST uptake across various distribution models and populations, the model will estimate the adoption of HIVST among both new and existing users across both existing (community and facility) and new (pharmacy) channels. Estimates will be further refined to take into account estimated testing

Source: UNITAID/Eric Gauss

frequency, price and the presence of a range of factors in the enabling environment. Estimates will be generated through 2020, and will be framed in the context of existing HIV RDT procurement. These estimates will be formally released in 2016 and further refinement of model assumptions will be undertaken when WHO normative guidance is released.

Consumer demand. Efforts to estimate the size of the market for HIV RDTs for self-testing draw heavily on the increasing body of evidence that suggests that consumer demand for HIV self-test products can be high across a diversity of channels.

In high-income settings (France, United Kingdom, United States), where HIVST products are registered and available, the majority of distribution occurs through the private sector. Between July 2012 (when the OraQuick® In-Home HIV Test was FDA-approved) and June 2016, nearly 1.6 million HIV RDTs for self-testing products have been sold in the private and public sectors of these markets.

- Nearly 1 million OraQuick® In-Home HIV Tests[e] were sold in the United States, primarily through over-the-counter pharmacy sales.

- Approximately 50 000 BioSURE HIV Self-Test kits were sold in the product's first year on the United Kingdom market between April 2015 and February 2016.[f] Most sales were through online retail outlets; no over-the-counter product was available in the United Kingdom pharmacies and there was limited distribution in the public sector. According to reports, as of February 2016,

Source: UNITAID/Eric Gauss

among self-tests sold in the country, 75% were sold to men and 75% were sold outside metropolitan areas. About 50% of users were first-time testers and 10% ordered a test more than once *(39)*.

- In France, AAZ Labs estimated that between 35 200 and 92 800 autotest VIH® kits were sold between September 2015 and February 2016.[g] Sales of the autotest VIH® are restricted to online retailers and pharmacies, supported by government-led campaigns to promote HIV testing. One study of pharmacies reporting sales of 900 kits found that 66% of purchasers were male and 42% were first-time testers; 54% of users reported that they would not have tested if a self-test was unavailable *(40)*.

In developing markets where tests are not yet formally available, growing research indicates high levels of consumer demand can be achieved through a variety of channels. In Malawi, a study of community-based distribution of HIV self-test products in Blantyre found a population-level uptake of 76.5% over a two-year period *(29)*. Uptake was highest among younger age groups, and 44% of participants were first-time testers *(29)*. Additionally, uptake among men was 68%, which is substantially

[e] This is estimate is based on OraSure's public reports from 2012 to present, divided by the estimated cost to distributers (US$ 28). It also factors in publicly available procurement reports, as well as reports from contacts with past and ongoing implementation projects.

[f] Brigette Bard, BioSURE, personal communication, 29 June 2016.

[g] Laure Poignant, AAZ Labs, personal communication, 27 June 2016.

higher than national estimates of testing coverage among men *(29)*. In Zimbabwe, a pilot of community-based distribution in one rural district found similarly high levels of uptake, including high uptake among men. Importantly, distribution reached a high proportion of PLHIV who were previously undiagnosed *(41)*. Evaluations of secondary test distribution, in which an individual is provided multiple self-test products for distribution to their sexual partners, also suggest strong demand. In Kenya, women attending antenatal and postpartum care, as well as female sex workers, were offered a self-test kit for themselves and for their sexual partners. Between 75% and 91% of participants reported secondary distribution of the test *(30)*.

Additional studies are under way to generate further evidence of consumer uptake of HIVST, including linkage to further testing, and prevention, treatment and care following HIVST. This includes the UNITAID/ Population Services International (PSI) HIV Self-Testing AfRica (STAR) Project, which is evaluating several HIVST distribution models in Malawi, Zambia and Zimbabwe, including community-based models, facility-based distribution in public and private clinics, and distribution through peer educators to reach key population groups *(22)*. Studies in Australia *(43),* Brazil *(44),* China *(45),* Netherlands *(46),* Thailand *(47),* the United Kingdom *(39,49),* the United States *(48)* and Viet Nam *(50)* are examining HIVST distribution among key populations, while several studies in Kenya, South Africa, Uganda and Zambia are evaluating other community- and facility-based distribution models to reach the general population, as well as young people and key populations *(51)*. Several planned and forthcoming studies are also examining how uptake of HIVST may vary for blood-based tests versus those with oral fluid. These data will be critical to the formulation of supportive policies and implementation guidance for HIVST.

The potential for consumer demand through the private sector in developing countries, particularly sub-Saharan Africa is unknown although several manufacturers are interested in entering this market. Assessments and anecdotal reports of the informal sale of HIV RDTs in the private sector indicate that HIV RDTs for self-testing have been available informally for more than a decade in sub-Saharan Africa. In Namibia and South Africa, it was reported that HIV RDTs for self-testing have been available for sale in private pharmacies as of 2001 and 2002, respectively *(52)*. Likewise, in Kenya and other sub-Saharan African countries, a high proportion of health workers are already self-testing for HIV*(53,54)*. Outside of Africa, HIV RDTs for self-testing are also reportedly available informally in private pharmacies and through the Internet, including in China *(55),* Malaysia *(58),* Peru *(57),* the Philippines *(59)* and the Russian Federation *(56)*. None of these products are known to be quality assured and sell at a range of prices, as outlined earlier in this report.

Although most private sector markets are informal and unregulated in resource-limited settings, they indicate the potential to capture significant latent demand for self-testing. However, formal work to evaluate potential demand in this sector remains limited, particularly in sub-Saharan Africa *(55)*. A small study of pharmacy distribution of HIVST in Kenya is under way, but further work is needed to understand private sector demand and inform the development of market entry strategies *(36)*.

Source: UNITAID/Eric Gauss

Government and donor-based procurement. In the last year, public procurement of HIV self-test kits grew exponentially with support from several major HIV funding agencies.

- **UNITAID** is supporting the largest HIVST implementation study in Malawi, Zambia and Zimbabwe. The focus of this study, as described above, is to identify the most acceptable, ethical and effective approaches for delivering HIVST and reaching populations at high risk who may not otherwise test, such as young people, men, and female sex workers. Under this project, PSI and UNITAID procured 382 000 RDTs for HIVST in sub-Saharan Africa, as of June 2016. An additional 2.4 million tests will be procured over the course of the project.

- **President's Emergency Fund for AIDS Relief (PEPFAR)** is also supporting ongoing and planned pilot programmes and operational research studies in Brazil, Haiti, Lesotho, Mozambique, Namibia, Nigeria, Senegal, South Africa, Thailand, the United Republic of Tanzania, Viet Nam, Zambia and Zimbabwe. Currently, PEPFAR has been focusing HIVST implementation research in "DREAMS districts" to reach adolescent girls and young women, as well as their male partners, key populations and other vulnerable populations. Procurement of RDTs for self-testing is planned to support these implementation studies. Further expansion of procurement through PEPFAR is expected in the coming years.

- **Bill & Melinda Gates Foundation** is supporting several HIVST implementation studies through the International Initiative for Impact Evaluation and WITS

Reproductive Health and HIV Institute, including pilot studies in Kenya, South Africa, Uganda and Zambia. Other investments include work to understand the HIVST market, including emerging supply and the potential market size for HIV RDTs for self-testing. The Bill & Melinda Gates-funded work has resulted in the procurement of more than 12 000 RDTs for HIVST.

- **Global Fund** currently supports one "assisted" HIVST project in Ukraine because trained lay provider and community-based HIV testing is illegal. Since 2015, over 200 000 test kits have been procured for this project. Global Fund support for self-testing is expected to increase after the March 2016 release of the Briefing note: Operational research to improve implementation and uptake of HIV self-testing. The note outlines key implementation considerations regarding HIVST to inform the inclusion of HIVST pilot programmes in reprogramming or new applications.

This movement in the public sector market is critical to building a stable HIVST product supply as discussions with manufacturers indicate that nearly all expect that bulk procurement through the public sector will drive their revenue models.

Enabling environment

Approval pathways and eligibility for procurement. For many countries, particularly low- and middle- income countries, evaluations and approvals by WHO, the United States Agency for International Development (USAID), the United States Centers for Disease Control and Prevention (CDC), the Global Fund and stringent regulatory authorities[h] are utilized to guide local decisions in the absence of a national mechanism or national regulation of in vitro diagnostics (IVDs). The procurement policies of main international funders for HIV programmes (Global Fund, PEPFAR, UNITAID) require IVDs to be manufactured according to the applicable International Organization for Standardization (ISO) or equivalent standards and for the IVD to be reviewed and approved or recommended by founding members of the GHTF and/or agencies listed above. In addition, the Expert Review Panel for Diagnostics (ERPD), supported by UNITAID and the Global Fund and hosted by WHO, provides expert recommendations on the use of needed IVDs that have not yet obtained stringent approval or WHO prequalification, leading to temporary eligibility for procurement by main donor institutions.

Similar to approvals from stringent regulatory authorities, WHO prequalification of an HIV RDT for professional use involves an assessment of a product dossier that contains comprehensive information provided by the manufacturer, supporting safety and

[h] Stringent regulatory authority refers to founding members of the GHTF, including the regulatory authorities from Australia, Canada, the EU, Japan and the United States.

performance, and undertakes an onsite inspection, evaluating manufacturing quality and risk management. The prequalification assessment relies on best international practices and is based on globally accepted standards and guidance documents. In addition, the WHO prequalification assessment includes a performance evaluation of sensitivity and specificity, an assessment of invalid rates and inter-reader variability and an assessment of operational aspects. In general, the other approval mechanisms of non-regulatory authorities are usually comprised of an assessment of performance through a laboratory evaluation in the hands of trained users in a controlled setting.

In addition to recognizing the assessment work of international bodies, such as those noted above, some countries also have national-level product evaluation and approval requirements. Evaluation requirements may call for an HIV RDT to be assessed in the country setting or as part of a national algorithm before the IVD can be officially approved for use. Ad hoc in-country evaluations are also often used, instead of pre-market regulatory reviews, to inform product selection at the country level. Once approved for use in a country, an IVD could be procured and dispensed through the public or private sector. Lastly, within a national HIV testing policy there may also be generic regulations on how and where HIV RDTs can be used and distributed as well as who can collect specimens, perform the test, interpret the results and issue a diagnostic report.

Given the potential for the emergence of diverse and complex regulatory requirements across markets, efforts to harmonize diagnostic regulation within specific regions may be needed. Entities such as the Pan African Harmonisation Working Party and Asian Harmonization Working Party could play an important role in standardizing approaches across countries in order to streamline country registration processes and decrease market entry barriers for manufacturers.

Approval for HIV RDTs for self-testing. At the time of this publication, no HIV RDTs for self-testing have been approved for procurement by WHO, USAID or the CDC or recommended for temporary procurement by ERPD. WHO is currently developing the criteria and approval pathway for HIVST. While the products in Tables 3A and 3B are available and can be procured, current pricing is prohibitive to the public sector and other low- and middle-income buyers. The establishment of these approval channels is intended to bring more certainty to the market and drive greater demand and market entry – enabling costs and prices to decrease.

The WHO Prequalification of IVDs Programme undertakes a comprehensive assessment of individual IVDs through a standardized procedure aimed at determining if the product meets WHO prequalification requirements on quality, safety and performance. The prequalification assessment process includes three components:

- review of a product dossier;
- performance evaluation, including operational characteristics;
- manufacturing site(s) inspection.

BOX 1
Examples of approval pathways for HIV RDTs for self-testing

In high-income settings, there are examples of how HIV RDTs for self-testing were evaluated and then licensed and registered for use. In the United States, the FDA pre-market approval of an HIV RDT for self-testing required a three-phase clinical trial:

1. evaluation of the RDT in the hands of trained users in a controlled setting;

2a. observed evaluation of untrained users interpreting a panel of contrived test results in a controlled setting;

2b. observed evaluation of untrained users, with high, unknown and low risk of HIV, performing the RDT and interpreting the test results in a controlled setting;

3. established performance of the test system as a whole in the hands of untrained intended and expected users in the actual intended use (in-home) setting as a measure of clinical utility (61).

In addition, a performance standard was established and a risk–benefit assessment was conducted to determine the public health benefit (61).

In France and the United Kingdom, the conformity assessment conducted for the CE marking process required the completion of both phase 2a and 2b studies in each country. For instance, the Medicines and Healthcare Products Regulatory Agency (MHRA) guidance states no threshold for performance and outlines that IVDs for self-testing will be evaluated in terms of usability and suitability for self-testing population (e.g. validated IFU; labelling and packaging studies) (62).

In Australia, the Therapeutic Goods Administration (TGA) outlines guidance similar to that in France and the United Kingdom, but specifies thresholds for sensitivity and specificity for professional use, and states products for self-testing with a "user" sensitivity less than 90% would not be acceptable, whereas user specificity between 90% and 95% "could be considered acceptable where evidence of significant public health benefits can be demonstrated and where thorough risk mitigation strategies have been put in place to minimise the risk of false negative and false positive results" (63).

All HIV RDTs with self-testing as the intended use submitted for WHO prequalification will undergo a prequalification assessment, as per the process described above. However, any WHO assessment that has already been undertaken for HIV RDTs intended for professional use will be leveraged according to a risk-based approach. The information required to support any

claim made by the manufacturer needs to be directly linked to the intended use of the assay. In this instance, self-testing. Verification and validation data are, therefore, required in the hands of both professional users and self-testers.

The WHO Prequalification of IVDs Programme released a sample dossier for an IVD intended for HIVST in December 2015 and is currently drafting a Technical Specifications Series for prequalification of HIV RDTs including both professional and self-testing intended uses. The dossier and the Technical Specifications Series guide outline the requirements and procedures for a dossier submission. Formal release is expected in mid- to late-2016 *(60)*.

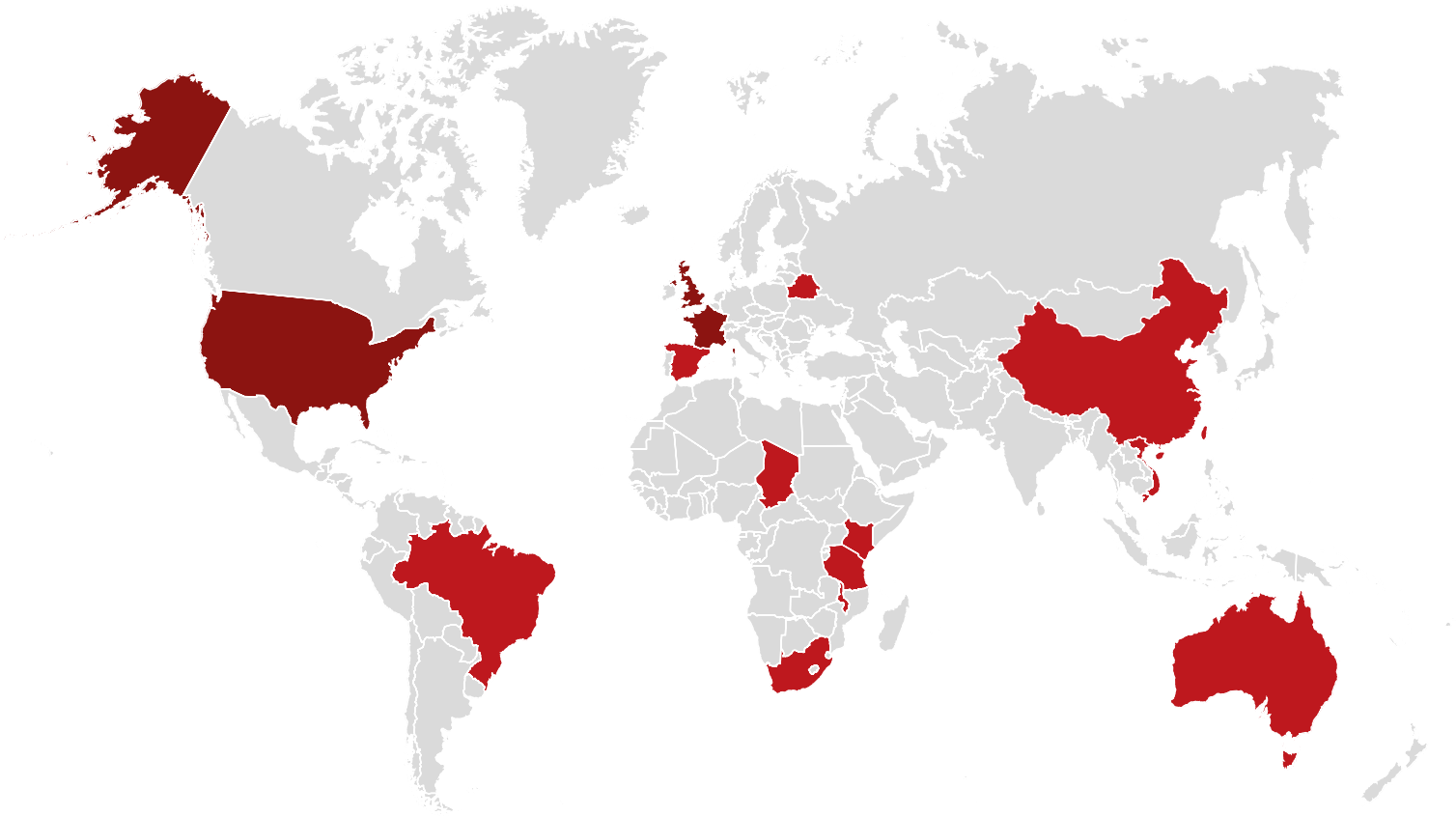
To facilitate the procurement of quality tests while no product has yet been found to meet WHO prequalification requirements, the Global Fund and UNITAID launched an ERPD for HIV RDTs for self-testing. ERPD for HIV RDTs for self-testing will not replace WHO prequalification, but instead act as an interim solution, while a stringent review is under way. An invitation to manufacturers to submit an expression of interest for consideration by ERPD was issued in February 2016 and closed in April 2016. The results of this process are expected in July 2016. It is likely that there will be additional ERPD's which include HIV RDTs for self-testing in 2016/2017. Under this ERPD review, HIV RDTs for self-testing may be procured with the Global Fund and UNITAID's funds for a 12-month period. Box 2 summarizes examples of regulatory approval pathways for HIVST.

National policy. Within national HIV testing policies, several countries permit HIVST and outline standards for approval of RDTs, how they fit within the national HIV strategy, how RDTs for self-testing should be distributed and who can distribute or sell them. Only three countries (France, United Kingdom and the United States) have a policy allowing self-testing and at least one product approved for use. Some countries have a policy allowing HIVST, but do not yet have a product with regulatory approval for use. Additionally, several other countries report having a policy in development and/or informal sale and use of RDTs for self-testing (Figure 2).

Key changes since the first landscape include data reported in the Global AIDS Response Programme Reporting (WHO, UNAIDS, UNICEF) as of 23 June 2016 and the WHO review of more than 100 national policies and regulatory frameworks *(64)*. In particular, the pharmaceutical council in South Africa lifted the ban on the sale of HIV self-test kits in private sector pharmacies; however, the Department of Health is working to develop an official policy and the standards and criteria for HIVST. In Brazil, an HIVST national policy was released in December 2015 and it is planned for HIV self-test kits to be in private pharmacies by the end of 2016. To continually track the evolving policy environment for HIVST, please reference HIVST.org for the most up-to-date information.

FIGURE 2

Map of countries with policies supporting HIVST (n=16)



- **Countries with Policy Supporting HIVST**
  Australia, Belarus, Chad, China, Kenya, Lesotho, Malawi, Rwanda, South Africa, Spain, United Republic of Tanzania
- **Countries with Policy Supporting HIVST & Products Approved For HIVST**
  France, United Kingdom, United States Of America

[1]Australia, Malawi, Rwanda, Spain and the United Republic of Tanzania report that while there is a policy in place, implementation has not yet begun.

[2] Brazil plans to introduce a product for HIVST in pharmacies in late 2016.

[3] While the South African Pharmaceutical Council lifted the ban on the sale of HIVST in May 2015, the Ministry of Health has not provided official policy, criteria or standards.

Sources: Global AIDS Response Programme Reporting (WHO, UNAIDS, UNICEF) 23 June 2016; WHO, 2016 (64).

Summary and conclusions

The demand for HIV testing to achieve the first 90 goal – diagnosis of 90% of all PLHIV by 2020 – is of paramount importance to achieving global targets and stemming the tide of the HIV epidemic. The additional approach of self-testing may have an important impact on demand for HIV RDTs, particularly if uptake is high among new users not previously reached and the frequency of testing increases among new and existing users. Existing estimates of demand, however, remain limited and forthcoming size estimates will be critical to understanding the potential for HIVST to shape or impact the HIV RDT market and further maximize the public health impact of this approach.

Although more evidence is needed to fully understand the potential public health and market impact of HIVST, this landscape provides a review of the existing and forthcoming technologies, as well as a strategic summary of the supply and demand for HIVST. The available data may inform strategic planning among diverse global health stakeholders exploring the potential role of HIVST.

Key considerations for countries, national programmes and regional bodies

- To facilitate the market for low-cost and quality-assured products for HIVST, it is important for international and national policy to be implemented. Creation of these policies and guides, which outline necessary approval channels, processes and location of HIVST within the national algorithm and testing strategy, will build confidence in demand estimates, providing greater certainty to manufacturers and catalysing market entry in settings where barriers are few and market incentives are many. There are several country examples of existing policies and regulations, however, WHO guidance is essential, particularly for many low- and middle-income countries.

- Countries and programmes should consider how HIVST can contribute to achieving national testing targets, particularly in specific populations with low testing uptake, high incidence and prevalence and high risk of infection. These decisions should be reflected in national strategies to further inform demand forecasts and advance implementation planning. This should include plans for establishment of strategies that further optimize linkage, as already recommended by WHO for existing testing services.

- While adapting existing professional use HIV RDTs for self-testing has many benefits, it is important that countries, programmes and regional bodies work to adapt and validate IFU, translations and other support materials to ensure they are appropriate for their setting and context. Country governments should engage with manufacturers to streamline processes for adaptation of IFU.

- Complex regulatory environments at the country level may pose a significant constraint to market development. Country governments should move quickly to outline clear and streamlined registration processes. These processes should ensure entry of quality of products without imposing unnecessary requirements.

Key considerations for donors

- WHO guidelines are forthcoming in late 2016, however, key operational research questions to guide implementation scale-up remain. This includes questions around linkage to prevention, treatment and care and effective means for targeting HIVST to reach those at highest risk. Operational research to answer these questions should be supported in parallel with rapid adoption of WHO guidelines, development of donor policies and scale-up of evidence-based approaches.

- To achieve scale-up in low- and middle-income markets, manufacturers must obtain necessary approvals (USAID, Global Fund and WHO) for donor procurement. Ensuring clear guidance and rapid review of applications will be crucial to ensure rapid evolution of the HIVST market.

- HIV RDTs for self-testing may have a higher unit cost compared to HIV RDTs for professional use. However, donors should consider the full cost of a testing event and the potential cost savings and increased cost-effectiveness of self-testing. Nevertheless given increased testing need and reduced donor budgets, it will be critical to coordinate across donor agencies and take on collaborative efforts to ensure the affordability of HIV RDTs for self-testing as the market evolves.

Key considerations for manufacturers

- Existing technologies for HIVST still rely heavily upon adaptation of existing technologies for professional use, notably second generation RDTs. In the short term, this has some advantages, particularly to hasten market entry while national and international policies and regulatory processes are still evolving. Existing mechanisms, such as ERP-D and WHO prequalification should be pursued as quickly as possible, particularly after WHO finalizes standards and procedures, to speed entry in the public sector market. Engagement with country governments regarding registration should also begin. However, in the medium and long term, there is significant need to further optimize existing HIV RDTs for self-testing, in line with the target product profile. These modifications may translate into higher performing tests, greater uptake and frequency of testing among users and thus a greater market size.

- There is significant potential for cross-over between markets for RDTs for professional use and RDTs for self-test use. Investments in RDTs for self-testing may catalyse optimization of existing, and development of new, HIV tests for use by professionals, addressing the challenges facing professionals who work in settings where conditions are poor, training and supervision are infrequent, and resources and health worker time are limited. There may be greater market incentives for manufacturers who can develop products that can unify the market for decentralized HIV testing services, for example, in community-based settings and low-level facilities and clinic settings, with the market for HIVST.

- IFU are likely to require significant adaptation across markets. Manufacturers should work to develop pictorial instructions that minimize written text and that may be easily tailored to various cultural context (e.g. replacement of photos with individuals who reflect the intended user demographic or use of symbols in line with the target market culture). Manufacturers should engage with governments in target markets to establish streamlined process for adaptation.

- Many procurement decisions by countries and donors are driven by price, particularly in low- and middle-income markets. Manufacturers who are able to reduce price and shrink the gap between HIV RDTs for self-testing and HIV RDTs for professional use may have a significant amount to gain. It may be possible to achieve this by identifying innovation in product design, manufacturing, packaging or shipment that could reduce product price.

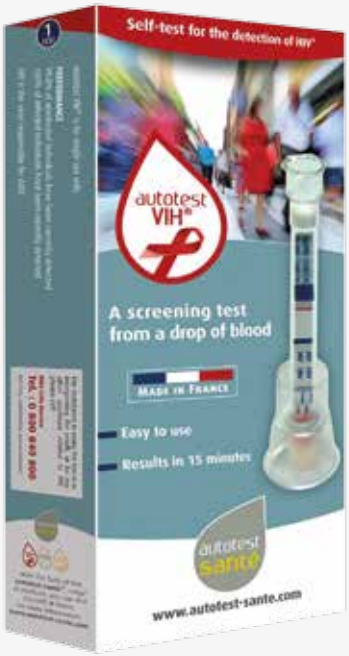
ANNEX 1

SPECIFICATION SHEETS FOR HIV SELF-TEST PRODUCTS IN THE MARKET

The following specification sheets provide information shared by manufacturers and through public evaluations of HIV RDTs by a founding member of the GHTF.

Please note that sensitivity and specificity denotes the performance in the hands of self-testers, and not the performance in the hands of professional users. The information was provided by manufacturers and reflects what is stated in manufacturer IFU and what is reported by recognized regulatory authorities (e.g. FDA; CE; TGA) or other international approval systems (e.g. WHO prequalification; Global Fund; USAID). Sensitivity and specificity reported in the literature, but not recognized by a regulatory authority, is not reflected.

AUTOTEST VIH®

Product specification	
Commercial name (trademark)	autotest VIH®
Professional test basis (commercial professional use name-trademark)	SURE CHECK® HIV-1/2
HIVST product photo	
Approval status for professional use product	CE, FDA, WHO prequalification
Company	AAZ-LMB
Manufacturing site	Rungis Cedex, France
Type of technology	Immunochromatographie (lateral flow)
Generation (2nd, 3rd or 4th)	2nd

Product specification	
Antigen type	Synthetic: gp36,gp41,gp120 Control line: Protein A
Output	Qualitative immunoassay, HIV-1/2 antibody detection
HIVST sensitivity	100%
HIVST specificity	99.8%
HIVST invalid rate	0.8%
Sample type	Capillary whole blood
Volume of sample required	2.5 µL (integrated blood sampling system)
Capacity	Single specimen – one-time use
Volume of buffer required	150–200 µL (350 µL pre-measured enclosed in sealed buffer pot included)
Time to result	15 minutes
Read window	Do not read after 60 minutes
Protocol complexity – steps required[i]	1. Set up the stand and buffer 2. Remove lid from safety lancet and apply to finger 3. Sample collection (use end of barrel to collect sample) 4. Push on test device through top of buffer to activate migration 5. Interpretation of test result
Shelf life of test kit	24 months
Storage requirements	8–30 °C – do not store in direct sunlight or open foil packet until ready to use the test
Test kit components	1 foil pouch containing test cassette, buffer cap, desiccant packet, bandage, safety lancet, test stand, disinfectant wipe, sterile pad and IFU
Not included in test kit	Timer
Restrictions for use	Wash hands and ensure they are clean and dry before testing Do not open pouch until ready to perform test Not intended for individuals with HIV-1 or HIV-2 who are on ART
Controls	Test has an internal control (in the control line) to indicate that human specimen has been added and that it has well migrated Control specimens (e.g. test kit controls) are available but sold separately
Approvals for HIVST product	CE marked WHO prequalification dossier submitted in 2016
HIVST pricing (US$/per test)	US$ 25–28 is the recommended consumer price in Europe; US$ 8–15 for distributors and NGOs depending on format (e.g. bulk; individual box), volume and conditions of payment.
Additional details	Test kit has been evaluated formally among people using ARV drugs for treatment and for prevention (e.g. PrEP or PEP) although the current product does not make an intended use claim for people on PrEP or PEP

[i] Steps are defined here as those beginning with the setup of the test kit and steps focused on specimen collection, specimen transfer, addition of buffer and ending with interpretation of result.

BIOSURE HIV SELF TEST

Product specification	
Commercial name (trademark)	BioSURE HIV Self Test
Professional test basis (commercial professional use name-trademark)	SURE CHECK® HIV-1/2/Stat-View HIV-1/2
HIVST product photo	
Approval status for professional use product	CE
Company	BioSURE United Kingdom Ltd
Manufacturing site	United Kingdom
Type of technology	Immunochromatographie (lateral flow)
Generation (2nd, 3rd or 4th)	2nd
Antigen type	Synthetic : gp36,gp41,gp120 Control line: Protein A
Output	Qualitative immunoassay, HIV-1/2 antibody detection
HIVST sensitivity	99.7%
HIVST specificity	99.9%
HIVST invalid rate	0.16%
Sample type	Capillary whole blood
Capacity	Single specimen – one-time use
Volume of sample required	2.5 µL (integrated blood sampling system)
Volume of buffer required	150–200 µL (350 µL pre-measured enclosed in sealed buffer pot included)
Time to result	Do not read before 15 minutes
Read window	Do not read after 60 minutes
Protocol complexity – steps required	1. Place pre-measured buffer pot into stand in box 2. Remove lid from safety lancet and apply to finger 3. Sample collection (place end of barrel onto drop of blood to naturally collect sample) 4. Place test device into the buffer pot by pushing device tip down firmly through foil lid to the bottom of the pot 5. Wait 15 minutes 6. Interpretation of test result through integrated section of HIVST packaging
Shelf life of test kit	24 months after manufacture

Product specification	
Storage requirements	8–30 °C – do not store in direct sunlight or open foil packet until ready to use test
Test kit components	A carton or paper-based box including 1 foil pouch (containing test device, safety lancet, bandage), IFU booklet, integrated results reading booklet, disposal bag, product insert
Not included in test kit	Timer
Restrictions for use	Wash hands and ensure they are clean and dry before testing Do not open pouch until ready to perform test Not intended for individuals with HIV-1 or HIV-2 who are on ART
Controls	Test has a control to indicate that human specimen has been added Control specimens (e.g. test kit controls) are available but sold separately
Approval status for HIVST product	CE
Pricing (US$/per test)	US$ 42–48 United Kingdom recommended retail price (including tax) for direct to consumer sales via e-commerce and United Kingdom private sector pharmacies US$ 7.50–15 for sale to the public sector, including the United Kingdom NGOs and the National Health Service (NHS)
Additional details	Test kit has not been evaluated formally among people using ARV drugs for prevention (e.g. PrEP or PEP)

ORAQUICK IN-HOME HIV TEST

Product specification	
Commercial name (trademark)	OraQuick® In-Home HIV Test
Professional test basis (commercial professional use name-trademark)	OraQuick® *ADVANCE*® Rapid HIV-1/2
HIVST product photo	
Approval status for professional use product	FDA/CE

Product specification	
Company	OraSure Technologies LLC
Manufacturing site	Bethlehem, PA, USA
Type of technology	Immunochromatographie (lateral flow)
Generation (2nd, 3rd or 4th)	2nd
Antigen type	Synthetic peptides representing the HIV envelope region and a goat anti-human IgG procedural control immobilized onto a nitrocellulose membrane in the Test (T) zone and the Control (C) zone
Output	Qualitative immunoassay, HIV-1/2 antibody detection
HIVST sensitivity	FDA: 91.7% CE: 100%[j]
HIVST specificity	FDA: 99.98% CE: 99.8%[k]
HIVST invalid rate	FDA: 1.1% CE: 1.8%
Sample type	Oral fluid
Capacity	Single specimen – one-time use
Volume of sample required	NA
Volume of buffer required	1 mL
Time to result	Do not read before 20 minutes
Read window	Do not read after 40 minutes
Protocol complexity – steps required	1. Remove cap of developer solution 2. Set buffer vial in stand 3. Collect sample (oral swab) 4. Insert sample in buffer 5. Interpret Result
Shelf life of test kit	30 months
Storage requirements	Store at 2–27 °C – do not open foil packet until ready to use test
Test kit components	Plastic package encasing a divided pouch (containing test device, desiccant, developer solution vial), test/buffer stand, pencil, disposal bag, IFU and informational booklets about HIV
Not included in test kit	Timer
Restrictions for use	Do not eat, drink or chew gum for at least 15 minutes before testing or use mouth cleaning products 30 minutes before taking the test Do not open pouch until ready to perform test Not intended for individuals with HIV-1 or HIV-2 who are on ART Operate at 15–37 °C
Controls	Addition of procedural quality control (band appears when human specimen is added and sample has flown up the device)
Approval status for in-home HIV test product	FDA Formal CE mark pending as product has not yet been launched in the EU

Product specification	
Pricing (US$/per test)	Distributor price not available US$ 40 is recommended consumer price in the USA; recommended prices outside the USA not yet available
Additional details	Detects HIV-1 seroconversion 2.5 days (95% CI: 1.2–3.8) later than CE marked enzyme immunoassay (EIA) Test kit has not been evaluated formally among people using ARV drugs for prevention (e.g. PrEP or PEP)

INSTI HIV SELF TEST

Product specification	
Commercial name (trademark)	INSTI HIV Self Test
Professional test basis (commercial professional use name-trademark)	INSTI® HIV-1/HIV-2 Antibody Test
HIVST product photo	
Approval status for professional use product	CE/FDA/HealthCanada/WHO prequalification CLIA Complexity: waived for fingerstick whole blood and moderate for venous whole blood and plasma
Company	bioLytical Laboratories
Manufacturing site	Richmond, British Columbia, Canada
Type of technology	Immunofiltration
Generation (2nd, 3rd or 4th)	3rd generation
Antigen type	gp41 and gp36 antigen Control: Protein A
Output	Qualitative immunoassay, HIV-1/2 antibody detection
HIVST sensitivity	100%
HIVST specificity	99.8%
HIVST invalid rate	0%

[j] Note this is preliminary information, as the product has not yet been officially launched in Europe.

[k] Note this is preliminary information, as the product has not yet been officially launched in Europe.

Product specification	
Sample type	Fingerstick whole blood
Volume of sample required	50µL
Capacity	Single specimen – one-time use
Volume of Buffer required	1.5mL sample diluent, 1.5 mL colour developer, and 1.5 mL of clarifying solution
Time to result	Instant results after completion of procedure
Read window	Do not read after 5 minutes
Protocol complexity – steps required	1. Remove cap of sample diluent 2.Collect sample (fingerprick) 3.Insert sample into sample diluent 4. Sequentially invert and pour sample diluent, colour developer and clarifying solution on to test device 5. Interpret Results
Shelf life of test kit	15 months
Storage requirements	Store at 15 – 30°C. The kit can be refrigerated (2-8oC) if required.
Test kit components	1 cardboard box containing test device, sample diluent, colour developer, clarifying solution, IFU, HIVST Booklet, 2 sterile single-use lancets, 2 pipettes, an adhesive bandage, and disposal bag
Not included in test kit	Not required
Restrictions for use	Not suitable for users who have a bleeding disorder Not suitable for users below the age of 18 Not suitable for users who are taking ARV drugs for treatment or prevention (i.e. ART, PrEP or PEP) Not suitable for users who have participated in a HIV vaccine study.
Controls	Built in procedural control of protein A which detects the human IGg antibodies. Test kit quality controls available upon request.
Approval status for in-home HIV test product	CE Marked
Pricing (US$/per test)	$36 is recommended consumer price in Europe Pricing information for distributors and NGOs available upon request.
Additional details	Test kit has not been evaluated formally among people using ARV drugs for prevention (e.g. PrEP or PEP). Extra pipette and lancet provided in the kit, but not required for use.

ANNEX 2

SPECIFICATION SHEETS FOR HIV SELF-TEST PRODUCTS EMERGING IN THE MARKET

The following specification sheets provide information shared by manufacturers regarding products that are under development or are in the process of seeking and receiving approvals by a founding member of the GHTF[1] or through other international approval systems (e.g. WHO prequalification; Global Fund; USAID). Furthermore, these specification sheets are not comprehensive, as there are other products under development for which available information was either inadequate or confidential.

Please note all information and product characteristics described are subject to change.

Please note that sensitivity and specificity is the performance in the hands of self-testers, and not the performance in the hands of professional users. The information was provided by manufacturers and reflects what is stated in manufacturer IFU and what is reported by recognized regulatory authorities (e.g. FDA; CE; TGA) or other international approval systems (e.g. WHO prequalification; Global Fund; USAID). Sensitivity and specificity reported in the literature, but not recognized by a regulatory authority, is not reflected.

ATOMO HIV SELF-TEST

Product specification	
Commercial name (trademark)	Atomo HIV Self-Test
Professional test basis (commercial professional use name-trademark)	AtomoRapid™ HIV (1&2)
HIVST product photo	
Approval status for professional use product	CE; submitted dossier for WHO prequalification
Company	Atomo Diagnostics
Manufacturing site	Australia
Type of technology	Immunochromatographie (lateral flow)
Generation (2nd, 3rd or 4th)	3rd

[1] Founding members of the GHTF include Australia, Canada, the European Union, Japan and the United States. Approval by these bodies is considered stringent regulatory approval.

Product specification	
Antigen type	Recombinant and synthetic peptides for HIV-1 and HIV-2
Output	Qualitative immunoassay, HIV-1/2 antibody detection, including subtype O
HIVST sensitivity	NA
HIVST specificity	NA
HIVST invalid rate	NA
Sample type	Capillary whole blood
Capacity	Single specimen – one-time use
Volume of sample required	10 uL
Volume of buffer required	2–4 drops (sufficient mL to initiate fluid flow on the test strip)
Time to result	Do not read before 15 minutes
Read window	Do not read after 20 minutes
Protocol complexity – steps required[m]	1. Pull green tab to remove lancet cap 2. Push grey button firmly to prick finger 3. Squeeze finger firmly to extract blood and touch blood to tip of blood tube and fill tube 4. Flip blood tube over to the well 5. Add 2-4 drops of buffer solution 6. Interpret test results
Shelf life of test kit	24 months
Storage requirements	2–30 °C; do not store in direct sunlight or open foil packet until ready to use test
Test kit components	IFUs, foil packet containing test cassette and desiccant, buffer solution, disposable bag, care card
Not included in test kit	Timer, bandage, sterile swab or tissue
Controls	The device has a self-contained internal control: if the purple colour band (control line) is not visible within the result window after performing the test, the result is considered invalid. However the test does not include a control for human specimen. Control specimens (e.g. test kit controls) are available but sold separately
Restrictions of use	Wash your hands and ensure they are clean and dry before starting the test Not suitable for blood donors or people with blood clotting or bleeding disorders (e.g. haemophilia) Not intended for people with HIV-1/2 using ART
Approval status for HIVST product	None
Pricing (US$/per test)	Current or recommended price is not yet available for distributors or for sale direct to consumers
Additional details	Used or unused test should be placed in disposal bag, sealed and disposed in general waste system Test kit has not been evaluated formally among people using ARV drugs for prevention (e.g. PrEP or PEP)

[m] Steps are defined here as those beginning with the setup of the test kit and steps focused on specimen collection, specimen transfer, addition of buffer and ending with interpretation of result.

AWARE™ HIV-1/2 OMT ORAL HIV SELF TEST

Product specification	
Commercial name (trademark)	Aware™ HIV-1/2 OMT Oral HIV Self Test
Commercial professional use name (trademark)	Aware™ HIV-1/2 OMT, Oral HIV Rapid Test
HIVST product photo	 
Approval status for professional use product	USAID waiver list; WHO prequalification application under review
Company	Calypte Biomedical Corporation
Manufacturing site	Thailand
Type of technology	Immunochromatographie (lateral flow)
Generation (2nd, 3rd or 4th)	2nd
Antigen type	gp36,gp41
Output	Qualitative immunoassay, HIV-1/2 antibody detection
HIVST Sensitivity	NA
HIVST Specificity	NA
HIVST Invalid rate	NA
Sample type	Oral fluid (oral mucosal transudate)
Volume of sample required	NA
Volume of buffer required	1 mL
Sample storage	2–30 °C
Time to result	Do not read before 20 minutes
Read window	Do not read after 45 minutes
Protocol complexity – steps required	1. Insert test tube into stand 2. Remove test tube cap 3. Collect specimen by swabbing gum line 4. Transfer specimen to test tube containing buffer 5. Insert test strip into test tube 6. Remove test strip 7. Interpret test result
Shelf life of test kit	18 months (unopened); 7 days (opened)
Storage requirements	2–30 °C – do not store in direct sunlight or open foil packet until ready to use test
Test kit components	IFU, frequently asked questions, 1 foil pouch (containing 1 test strip, 1 desiccant, 1 capped test tube containing 1 mL of buffer, 1 collection swab and 1 test kit box (box also used as a stand)

Product specification	
Not included in test kit	Timer
Restrictions for use	Do not eat, drink or chew anything 10 minutes before testing Do not open pouch until ready to perform test Not intended for people with HIV-1/2 using ART
Controls	Control specimens (e.g. test kit controls) are available but sold separately All control specimens are derived from inactivated human plasma. None of the controls were designed to produce an invalid test result.
Approval status for HIVST product	None
Professional use pricing (US$/per test)	Current or recommended price is not yet available for distributors or for sale direct to consumers
Additional details	Test kit has not been evaluated formally among people using ARV drugs for prevention (e.g. PrEP or PEP)

ORAQUICK® HIV SELF-TEST

Product specification	
Commercial name (trademark)	OraQuick® HIV Self-Test
Professional test basis (commercial professional use name-trademark)	OraQuick® Rapid HIV-1/2 Antibody Test
HIVST product photo	
Approval status for professional use product	WHO prequalification
Company	OraSure Technologies LLC
Manufacturing site	Thailand
Type of technology	Immunochromatographie (lateral flow)
Generation (2nd, 3rd or 4th)	2nd
Antigen type	Synthetic peptides representing the HIV envelope region and a goat anti-human IgG procedural control immobilized onto a nitrocellulose membrane in the Test (T) zone and the Control (C) zone
Output	Qualitative immunoassay, HIV-1/2 antibody detection
HIVST sensitivity	NA

Product specification	
HIVST specificity	NA
HIVST invalid rate	NA
Sample type	Oral fluid
Capacity	Single specimen – one-time use
Volume of sample required	NA
Volume of buffer required	1 mL
Time to result	Do not read before 20 minutes
Read window	Do not read after 40 minutes
Protocol complexity – steps required	1. Remove cap of developer solution 2. Set buffer vial in stand 3. Collect sample (oral swab) 4. Insert sample in buffer vial 5. Interpret Result
Shelf life of test kit	30 months
Storage requirements	Store at 2–27 °C– do not open foil packet until ready to use test
Test kit components	A divided pouch (containing test cassette, desiccant, vial of buffer), test/buffer stand and IFU
Not included in test kit	Timer
Restrictions for use	Do not eat, drink or chew gum for at least 15 minutes before testing or use mouth cleaning products 30 minutes before taking the test Do not open pouch until ready to perform test Not intended for individuals with HIV-1 or HIV-2 who are on ART Operate at 15–37 °C
Controls	Test has a control to indicate that human specimen has been added (i.e. band appears when human specimen is added) Control specimens (e.g. test kit controls) are available but sold separately
Approval status for HIVST product	None
Pricing (US$/per test)	Pricing available from OraSure Technologies upon request
Additional details	Test kit has not been evaluated formally among people using ARV drugs for prevention (e.g. PrEP or PEP)

EXACTO® HIV SCREENING TEST

Product specification	
Commercial name (trademark)	Exacto® HIV Screening Test
Professional test basis (commercial professional use name-trademark)	EXACTO® Test HIV

Product specification	
HIVST product photo	
Approvals for professional use product	CE
Company	Biosynex Group
Manufacturing site	France
Type of technology	Immunochromatographie (lateral flow)
Generation (2nd, 3rd or 4th)	2nd
Antigen type	Synthetic: gp41,gp36
Output	Qualitative immunoassay, HIV-1/2 antibody detection
HIVST Sensitivity	Not specified
HIVST Specificity	Not specified
HIVST Invalid rate	Not specified
Sample type	Capillary whole blood
Volume of sample required	Not specified
Capacity	Single specimen – one-time use
Volume of buffer required	2 drops[n]
Time to result	Do not read before 10 minutes
Read window	Do not read after 20 minutes
Protocol complexity – steps required	1. Remove lid from safety lancet and apply to finger 2. Squeeze finger and use inverted cup/capillary tube to collect sample 3. Add drop of blood to the test cassette where marked “Blood” 4. Add buffer to the test cassette where marked “diluent” 5. Interpret result
Shelf life of test kit	Not specified
Storage requirements	2–30 °C – do not store in direct sunlight or open foil packet until ready to use test
Test kit components	1 foil pouch with test cassette and desiccant, 1 buffer solution, 1 bandage, 1 alcohol-wipe, 1 sterile pad, 1 lancet and 1 inverted cup/capillary tube, IFU, disposal bag
Not included in test kit	Timer

[n] Amount in mL not specified.

Product specification	
Restrictions for use	Wash hands and ensure they are clean and dry before testing Test must be run immediately after the capillary blood has been collected Not intended for individuals with HIV-1 or HIV-2 who are on ART Test should be run in setting with 15–30 °C
Controls	Test has a control to indicate that human specimen has been added Control specimens (e.g. test kit controls) are available but sold separately
Approvals for HIVST product	CE mark pending
HIVST pricing (US$/per test)	Price to distributors and consumers not yet available
Additional details	Validation study from CE mark; study did not provide sensitivity and specificity but stated that 99.5% of participants obtained interpretable result and 98% of the results were interpreted correctly Test kit has not been evaluated formally among people using ARV drugs for prevention (e.g. PrEP or PEP)

TO BE NAMED – CHEMBIO DIAGNOSTIC SYSTEMS INC.

Product specification	
Commercial name (trademark)	To be named
Professional test basis (commercial professional use name-trademark)	SURE CHECK® HIV-1/2/Stat-View® HIV-1/2 assay
HIVST product photo	NA
Approvals for professional use product	CE/FDA/WHO prequalification CLIA Complexity: waived for fingerstick and venous whole blood/moderate for serum and plasma
Company	Chembio Diagnostic Systems Inc.
Manufacturing site	Medford, NY, USA
Type of technology	Immunochromatographie (lateral flow)
Generation (2nd, 3rd or 4th)	2nd
Antigen type	Synthetic: gp36,gp41,gp120 Control line: Protein A
Output	Qualitative immunoassay, HIV-1/2 antibody detection
HIVST Sensitivity	NA
HIVST Specificity	NA
HIVST Invalid rate	NA

Product specification	
Sample type	Capillary whole blood
Volume of sample required	2.5 µL (integrated blood sampling system)
Capacity	Single specimen – one-time use
Volume of buffer required	150–200 µL (350 µL pre-measured enclosed in sealed buffer pot included)
Time to result	Do not read until 15 minutes
Read window	Do not read after 20 minutes
Protocol complexity – steps required	1. Set up the stand and buffer 2. Remove lid from safety lancet and apply to finger 3. Sample collection (use end of barrel to collect sample) 4. Place test device on top of buffer 5. Push on test device through to activate buffer solution 6. Interpretation of test result
Shelf life of test kit	24 months from date of manufacture
Storage requirements	8–30 °C – do not store in direct sunlight or open foil packet until ready to use test
Test kit components	1 foil pouch containing test cassette, buffer cap, desiccant packet, bandage, safety lancet, test stand
Not included in test kit	Timer
Restrictions for use	Wash hands and ensure they are clean and dry before testing Do not open pouch until ready to perform test Not intended for individuals with HIV-1 or HIV-2 who are on ART
Controls	Test has a control to indicate that human specimen has been added Control specimens (e.g. test kit controls) are available but sold separately
Approvals for HIVST product	None Two private label version of the product are CE marked for self-testing in the European Union (BioSURE HIV Self-Test and autotest VIH®)
HIVST pricing (US$/per test)	Current or recommended price is not yet available for distributors or for sale direct to consumers
Additional details	Test kit has not been evaluated formally among people using ARV drugs for prevention (e.g. PrEP or PEP)

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