PUTTING HIV TREATMENT TO THE TEST

A PRODUCT GUIDE FOR VIRAL LOAD AND POINT-OF-CARE CD4 DIAGNOSTIC TOOLS

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MEDECINS SANS FRONTIERES

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THE MSF ACCESS CAMPAIGN

In 1999, on the heels of Médecins Sans Frontières (MSF) being awarded the Nobel Peace Prize – and largely in response to the inequalities surrounding access to HIV/AIDS treatment between rich and poor countries – MSF launched the Campaign for Access to Essential Medicines. Its sole purpose has been to push for access to, and the development of, life-saving and life-prolonging medicines, diagnostics and vaccines for patients in MSF programmes and beyond.

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MSF AND HIV

MSF began providing antiretroviral therapy to a small number of people living with HIV/AIDS in 2000 in projects in Thailand, South Africa and Cameroon. At the time, treatment for one person for one year cost more than US$10,000. With increased availability of low-cost quality antiretroviral drugs (ARVs), MSF currently provides treatment to 285,000 people in 21 countries, implementing treatment strategies to reach more people, earlier in their disease progression, while increasingly encouraging patients to take on a more central role in the management of their care.

LATEST RESOURCES FROM MSF ON HIV

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Over the past 13 years, the MSF Access Campaign has been monitoring the patent barriers, prices and availability of ARVs through Untangling the Web and pushing for the uptake of policies that promote access to affordable quality medicines.

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PATENT OPPOSITION DATABASE

The Patent Opposition Database was launched by the MSF Access Campaign in October 2012 as an online space where civil society can share the resources and tools needed to oppose patents on medicines. The Database gathers contributions from around the world. It allows documents to be shared, arguments to be replicated and new alliances to be forged with the aim of successfully opposing patents and ultimately improving access to medicine in developing countries. To find out more about patents which block access to essential medicines and what you can do to challenge them, or to contribute by sharing resources, visit:

www.patentoppositions.org

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ABOUT THIS REPORT

This report is a guide for policymakers, treatment providers and advocates interested in learning more about laboratory-based and point-of-care viral load HIV diagnostic products, and point-of-care CD4 HIV diagnostic products.

The report includes:

- Information on how routine viral load (VL) monitoring improves HIV treatment outcomes
- Information on why the use of VL monitoring is particularly important for confirming treatment failure and for ensuring prevention of mother-to-child transmission of HIV (PMTCT)
- A decision guide for purchasers, and information on how to evaluate the use of point-of-care (POC) and lab-based technologies in different contexts
- Technical specifications and pricing information for 13 diagnostic tools:
  - Three POC CD4 platforms
  - Eight lab-based VL platforms
  - One POC VL platform
  - One POC VL platform for early infant diagnosis.

A second product guide, to be published in 2014, will include country-specific diagnostic prices for the same type of products, as well as an in-depth pricing analysis covering costs of platforms and general laboratory infrastructure, as well as routine costs including materials and human resources. The report will be coupled with a web-based platform that enables potential diagnostics purchasers to estimate the overall costs for these tools, based upon their programme's specific parameters.

MSF and HIV diagnostic and monitoring tools

With 285,000 people living with HIV on treatment in our programmes in 21 countries, MSF is exploring the best strategies for rolling out HIV diagnostic and monitoring tools in order to optimise treatment outcomes.

MSF is an early adopter of VL and POC CD4 testing in resource-poor settings, and is currently using, field testing or evaluating these technologies in 18 countries. With support from UNITAID, MSF is implementing a three-year project to evaluate various VL and CD4 testing technologies in eight projects across seven countries. The project will aim to establish the feasibility of routine VL testing in resource-limited settings, including assessing which existing and pipeline devices are suitable for specific resource-limited contexts, how they can have the greatest impact on treatment outcomes, and to what extent viral load testing can or should be decentralised. MSF also plans to publish its findings from on-going implementation research on the diagnostic tools selected for its programmes.

MSF believes it is medically important and operationally feasible to implement VL monitoring in developing countries, and that cost should not remain a barrier to implementation. Cost savings from optimised treatment management and adaptation of VL protocols to resource-limited settings can help mitigate higher upfront purchase costs; meanwhile, increased competition among diagnostic manufacturers is expected to reduce test prices further in the coming years.

MSF IMPLEMENTATION OF VIRAL LOAD AND POC CD4 DIAGNOSTIC TOOLS

Point-of-Care (POC) Testing:

- MSF has implemented POC CD4 diagnostics**
- MSF is in the process of implementing POC VL diagnostics

Laboratory-based Viral Load (VL) Testing:

- MSF has installed its own VL laboratory**
- MSF conducts referrals to a non-MSF VL laboratory

** Implementation in at least one MSF project in the country

- Burkina Faso
- Cambodia
- Cameroon
- Central African Republic
- Chad
- Congo
- Democratic Republic of Congo
- Ethiopia
- Guinea
- India
- Kenya
- Lesotho*
- Malawi
- Mozambique*
- Myanmar
- South Africa
- South Sudan
- Swaziland
- Uganda
- Zambia
- Zimbabwe

* MSF VL lab implementation planned

MSF currently provides HIV treatment to 285,000 people in 21 countries.

MEDECINS SANS FRONTIERES

STRONGER WHO GUIDELINES: NEW PROMISES, AND NEW CHALLENGES

More than nine million people in the developing world now receive life-saving antiretroviral treatment (ART) for HIV.[1] This represents immense progress made over the past decade – a more than 20-fold increase in the number of people on ART – but developing countries still lack access to treatment and optimised standards of care.[2] By updated World Health Organization (WHO) eligibility standards, discussed further below, as many as 25 million people in developing countries should be on ART to reduce illness and death, and to prevent new infections.[3]

In 2013, WHO is recommending a number of changes in its HIV guidelines that, when implemented, will improve treatment standards in developing countries. Two changes are particularly significant:

The first is the recommendation to start HIV treatment earlier, a protocol that is already routine in many developed countries. Treating the disease earlier in its progression not only improves health and longevity, but has also proven to drastically reduce the spread of the disease. The landmark HPTN 052 study showed that earlier HIV treatment helps to stave off opportunistic infections and reduces the risk of sexual transmission to HIV-negative partners by 96%.[4]

From now on, WHO guidelines recommend treatment initiation be triggered at CD4 counts of 500 cells/μL – typically before severe and irreversible damage has been done to the immune system – rather than at 350 cells/μL. Many more patients will thus be eligible for lifelong treatment, and for longer periods of time, intensifying the need for effective treatment monitoring and support.[5] Diagnosing people before their CD4 counts drop below 500 cells/μL, and monitoring the progression of HIV in order to determine as quickly as possible whether someone needs to be put on treatment, are critical ways to improve health outcomes in resource-poor settings.

The second, which is central to the focus of this report, is the recommendation for routine treatment monitoring with VL testing. Although WHO recognised the benefits of VL as early as 2003, the 2013 WHO guidelines strengthen recommendations and call for developing countries to roll-out routine virological monitoring, with VL tests at six and 12 months after treatment initiation, and then at least every 12 months thereafter. These important changes will allow adherence problems to be detected and corrected as they arise, and will facilitate early indication of when a switch to an alternative treatment regimen is necessary.

CD4, VIRAL LOAD, POINT-OF-CARE: THE BASICS

The goal of providing ART is to suppress HIV to undetectable levels for life. Viral suppression reduces illness, death, the development of drug resistance, and the spread of new infections. When HIV is undetectable, it means the virus isn't replicating, and people can live healthy, productive lives.

To determine when treatment should be started and whether treatment is working, the two most important diagnostic tests are CD4 count, which measures the strength of the body's immunological response, and HIV viral load, which measures the amount of viral replication in the blood. Effective HIV treatment should result in a very low (or 'undetectable') viral load and a CD4 count within the normal range.

CD4 testing, a form of immunological monitoring, measures the health of the immune system. CD4 testing is the most effective and widely used staging tool used to decide whether and when to start HIV treatment. But CD4 testing in developing countries today is mostly lab-based, which means there is a delay between when a person needs ART, and when test results that allow treatment to start are received. Point-of-care CD4 testing can accelerate treatment initiation and reduce the number of patients lost to follow-up while test results are awaited.[6]

Viral load (VL) monitoring is the optimal tool to determine if treatment is working, and has long been the standard of care for treatment monitoring in wealthy countries. HIV treatment, once started, must be taken for life, and routine treatment monitoring is necessary to ensure that a person's ART regimen continues to be effective. If treatment stops working, people become sick and the risk of drug resistance and transmission is increased. The first sign that a patient is no longer under optimal treatment is a detectable viral load – thus, the best and earliest signal that a clinical intervention is needed is the viral load measurement.

Point-of-care (POC) testing refers to medical testing at or near the point of care, conducted within 10–30 minutes of sample collection and followed by an immediate medical decision based on the results.[7] POC testing eliminates delays associated with waiting for laboratory-based test results. POC diagnostics support earlier treatment and rapid initiation. Depending on the context and the number of patients, however, POC may not be appropriate for every setting.

Together, these two changes represent important steps towards achieving HIV treatment equity in developing countries. But their implementation depends on securing adequate funding and support.

The complexity of implementing VL technology in resource-poor settings, as well as higher up-front costs compared to other diagnostic technologies, has so far hindered adoption in resource-limited, high HIV-prevalence settings, where access to optimal treatment monitoring remains dismally low. An MSF survey of 23 resource-constrained countries in 2012 found that 22 included optional (16) or mandatory (six) VL testing protocols to confirm treatment failure in their national guidelines. But only four – Botswana, Brazil, Kenya and South Africa – actually have adequate access to the technology for this purpose.[2] Thirteen countries (five mandatory, eight optional) include VL for routine monitoring in their national guidelines, but only three – Botswana, Brazil and South Africa – have VL testing available for this purpose, and therefore ten won't actually be able to implement routine monitoring unless access to VL is significantly scaled up.[2]

The inclusion of routine VL monitoring in national treatment protocols shows how some developing countries already have strong ambitions to use this technology to raise treatment standards and curb new infections. But they face immense funding and implementation hurdles that make it hard to put improved guidelines into practice.


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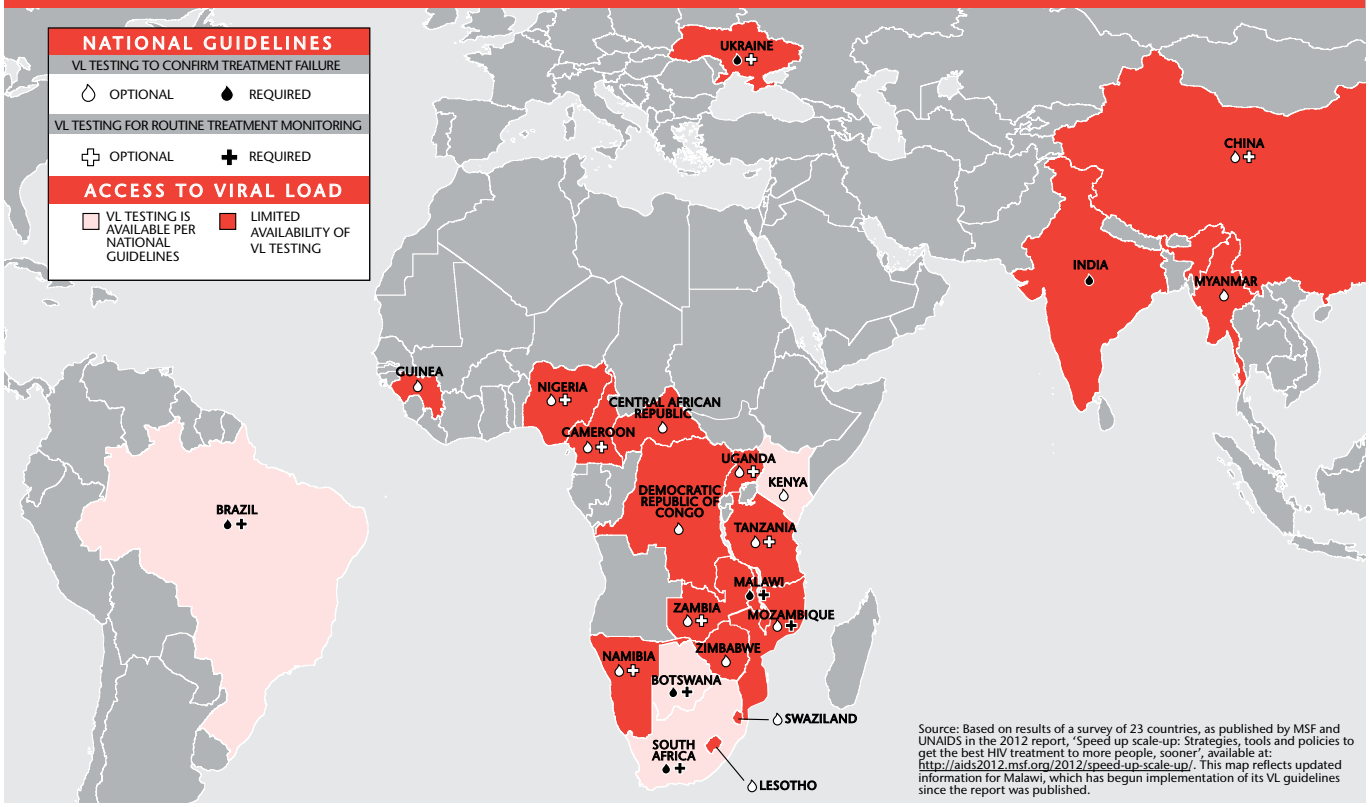
VL TESTING HELD BACK BY LIMITED ACCESS



Source: Based on results of a survey of 23 countries, as published by MSF and UNAIDS in the 2012 report, 'Speed up scale-up: Strategies, tools and policies to get the best HIV treatment to more people, sooner', available at: http://aids2012.msf.org/2012/speed-up-scale-up/. This map reflects updated information for Malawi, which has begun implementation of its VL guidelines since the report was published.

GETTING TO UNDETECTABLE: HOW CD4 AND VIRAL LOAD WORK TOGETHER FOR OPTIMAL HIV TREATMENT

CD4 testing is routinely and effectively used for treatment initiation…

…but is not so effective for optimised treatment monitoring.

CD4 testing determines whether and when an HIV-positive person should initiate treatment, based on CD4 cell count thresholds in national guidelines. CD4 testing is also recommended to measure immune function after ART is initiated, to confirm that the CD4 cells have reconstituted and remain in an acceptable range (preferably above 500 cells/μL, but definitely above 200 cells/μL).

However, once CD4 cells have rebounded, CD4 testing is not particularly effective for long-term treatment monitoring. CD4 can't detect early signs of adherence problems or treatment failure, because CD4 counts naturally fluctuate a great deal and measuring CD4 count can't detect the source of the problem – increasing viral load. Effective treatment should result in an undetectable viral load within six to 12 months after treatment initiation; a detectable viral load after this period is a sign that the treatment is not effective and could be failing.[8] CD4 testing can detect the effects of increasing viral load on the immune system, but does not offer timely enough information to initiate an optimised treatment response.[9]

In fact, the 11-country MONET trial on treatment simplification reported that if treatment was working and viral load was suppressed, CD4 monitoring offered no added value.[10] This was confirmed by a recent study showing that patients with CD4 counts ≥300 cells/μL had a 97.1% probability of retaining durable CD4 counts ≥200 cells/μL for four years, if their viral load stayed below 200 copies/mL, and this was increased to 99.2% if non-HIV causes of a CD4 cell drop were excluded.[11]

VIRAL LOAD monitoring ensures effective treatment and prevention…

…but is only sparsely available in developing countries.

VL testing determines the level of HIV in the blood, and indicates whether antiretroviral treatment is working. VL monitoring coupled with enhanced adherence support, helps deliver improved health outcomes both for individuals, by reducing morbidity and mortality, and for communities, by reducing transmission of the virus.

Viral load can also be used to initiate treatment, and has been proposed as a criteria for ART initiation, with patients initiated at high viral loads (>100,000 copies/mL), even when they have high CD4 counts.[51] This is because ongoing HIV replication is harmful.[52]

The benefits of VL monitoring for people and programmes in resource-poor settings are well established.[14, 15, 16, 17] But while viral load testing is the standard of care for patients in wealthy countries, routine virological monitoring is sparsely available in resource-limited settings, owing to cost and complexity.

VL is the gold standard for treatment monitoring because it:

Ensures treatment efficacy

- Detects adherence problems early, often before drug resistance develops
- Prolongs the use of more affordable, well-tolerated, one-pill-a-day first-line drugs

Supports treatment adherence

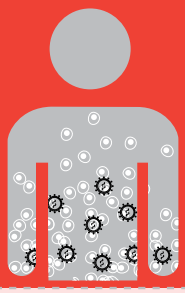
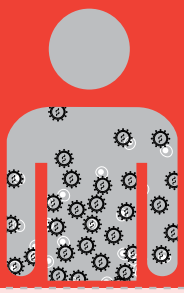
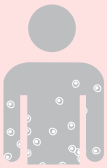
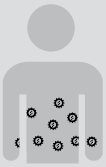
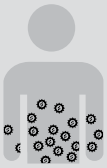
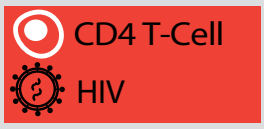
- Triggers need for intensive adherence counselling that can result in viral re-suppression
- Contributes to treatment literacy and motivation to reach and maintain an 'undetectable' viral load

Identifies risk of treatment failure early

- Prevents unnecessary switches, based on non-specific immunological monitoring, to more expensive second-line drugs
- Once non-adherence has been addressed, enables early and specific confirmation of treatment failure due to drug resistance mutations
- Enables timely switching to a more effective drug regimen, before drug resistance mutations accumulate and reduce the efficacy of second- and third-line regimens

Identifies risks for transmission, for example from mother to child (in utero, at birth, and during breast-feeding) and between sexual partners.[12, 13]

VIROLOGICAL MONITORING DETECTS TREATMENT PROBLEMS EARLIER THAN IMMUNOLOGICAL MONITORING

TREATMENT IS WORKING	EARLY DETECTION OF TREATMENT PROBLEMS	LATE DETECTION OF TREATMENT PROBLEMS	VERY LATE DETECTION OF TREATMENT PROBLEMS
			
WHAT CD4 TESTING REVEALS:			
 CD4 T-cells within acceptable range	 CD4 T-cells within acceptable range	 CD4 T-cell count is dropping	 CD4 T-cell count has plummeted
CD4 TESTING MISSES EARLY WARNING SIGNS THAT TREATMENT ISN'T WORKING. IN THE MEANTIME, THE DISEASE CONTINUES TO PROGRESS AND THE PATIENT CAN FALL SERIOUSLY ILL.			
WHAT VL TESTING REVEALS:			
 Virus level is undetectable	 Virus is replicating	 Virus level is high due to high viral replication	 Virus level is sky high due to unrestrained viral replication
PROGNOSIS MADE POSSIBLE WITH VL TESTING:			
• Virological suppression	• Viraemia (virus is detectable) • Possible virological failure • Drug resistance may not yet have developed	• Immunological failure • Viological failure • Drug resistance may have developed	• Clinical failure: severe immunosuppression opportunistic infections • Immunological failure • Virological failure: unless caused by non-adherence, new drugs required • Drug resistance has likely developed
INTERVENTION TRIGGERED BY VL TESTING:			
• Routine bi-annual or annual VL testing, according to national guidelines	• If viraemia is due to non-adherence, viral re-suppression is still possible with improved adherence • Targeted adherence counselling – retest in 3–6 months	• If no drug resistance, viral re-suppression is still possible with improved adherence • Targeted adherence counselling – retest in 3–6 months • If multiple consecutive high VL results, after ruling out non-adherence, evaluate for new regimen	• If multiple consecutive high VL results, after ruling out non-adherence, evaluate for new regimen 
VL TESTING DETECTS TREATMENT PROBLEMS EARLY. EARLY INTERVENTION CAN ENABLE RE-SUPPRESSION BEFORE DRUG RESISTANCE DEVELOPS, AND BEFORE THE PATIENT FALLS SERIOUSLY ILL.			

A GUIDE TO TERMINOLOGY AND THRESHOLDS

CD4 measurements:	CD4 count is the main eligibility criteria for ART initiation today. CD4 count measures the number of CD4 cells (T lymphocytes or T-cells) in the blood, the most important cells in the body's immune system and the primary targets of HIV. CD4 percentage measures the percentage of all lymphocytes that are CD4 cells. This percentage is more stable than the absolute number of CD4 cells, and is often used in paediatric staging and monitoring. CD4 count is measured in cells per microliter (cells/μL) of blood; equivalent to cells per cubic millimetre (cells/mm^3). A normal CD4 count falls between about 500 and 1,500 cells/μL. For CD4%, the normal range is between 20% and 40%. A CD4 percentage below 14% indicates serious immune damage.
Treatment initiation:	In 2013, WHO recommendations for ART initiation will change to include patients with CD4 counts of ≤500 cells/μL, up from ≤350 cells/μL in the current guidelines. Patients without access to CD4 testing can also be initiated on treatment based on WHO clinical staging guidelines. Different WHO guidelines exist for special populations, e.g. pregnant mothers and children, people co-infected with TB and sero-discordant couples. As most people who start ART are subsequently treated for life, treatment monitoring and adherence to treatment is critical to preventing resistance from developing.
Viraemia and viral load testing:	Viraemia refers to the presence of HIV in the blood, as measured by viral load. Viral load testing measures the number of 'copies' of HIV genetic material, ribonucleic acid (RNA), per millilitre of blood (copies/mL or c/mL or c/mL HIV RNA). When virus is detected in the blood (viraemia) at sufficient levels, this is considered virological failure. When treatment is working, viraemia remains at a low level, for example between <20 copies/mL to <1,000 copies/mL. High level viraemia can exceed 100,000 copies/mL.
Treatment adherence:	Good adherence means following the treatment regimen closely every day – taking the correct dose of each HIV medication at the correct time and exactly as prescribed. Adherence is very important to effectively suppress viral replication and to prevent drug resistance from developing.
Undetectable:	When treatment is working, HIV is suppressed to a very low level, and viral load is said to be 'undetectable.' Health is restored and the risk of transmission is low.
Treatment failure:	Failure can be defined by virologic, immunologic or clinical measures. In HIV disease progression, virological failure occurs first, often before drug resistance develops, followed by immunological failure, then clinical failure.[18] Definitions for virological and immunological failure vary widely between contexts and continue to evolve as the science changes.
Virological failure:	Treatment is failing to suppress the virus, and viral load is high, either due to adherence problems, drug resistance or other problems, including drug interactions or poor absorption of drugs. Specific thresholds to define virological failure vary widely by context, and it is sometimes defined as two consecutive measurements at ≥1,000 copies/mL. Values of >5,000 copies/mL are associated with clinical progression and a decline in the CD4 cell count. Transient increases in viral load ('blips'), which are common in successfully treated patients, can cause false alarms. A measurement of >1,000 copies/mL is a reasonable trigger for intensive targeted adherence counselling, as it would not register 'blips' as false alarms, but would still identify problems before drug resistance develops.
Immunological failure:	CD4 cell counts are low, and the immune system is not rebounding in response to the current treatment regimen. Thresholds for immunological failure vary by context, but are usually defined by a steep drop in CD4 count, or the failure to increase CD4 count above a specific threshold over a specific period of time.
Clinical failure (clinical progression):	Clinical failure occurs as a result of virological and immunological failure. Clinical progression means that a significant, potentially dangerous, clinical event has already occurred and many signs of clinical progression (e.g. opportunistic infections) can put the patient at significantly increased risk of death.

THE BENEFITS OF ROUTINE VIRAL LOAD

The long-term benefits of viral load monitoring, both in terms of treatment affordability and health outcomes, more than warrants investment in viral load testing today. This section provides an overview of the benefits of introducing the tool in resource-limited settings.

VL SUPPORTS TREATMENT ADHERENCE

Routine viral load monitoring allows early detection of viraemia, triggering targeted adherence interventions before treatment failure due to drug resistance occurs.[19, 20] Targeted adherence interventions can successfully resolve viraemia in the majority of patients: a study comparing programmes in three countries found significantly lower attrition and fewer deaths in programmes with viral load monitoring.[16] A global systematic review and meta-analysis of adherence to ART among pregnant women, including during the post-partum period, revealed that only 73.5% of women achieved optimal adherence, with ante-partum adherence higher than post-partum.[21] Critically, optimal adherence was defined differently across studies (ranging from 80–100%), although at least 95% adherence is required to prevent development of resistance.[22]

A number of studies have investigated whether viral load can be used effectively to reinforce adherence. After a range of different types of adherence interventions, a recent systematic review and meta-analysis[23] of eight studies across eight different countries found that viral re-suppression was achieved in 70.5% of cases overall across five studies that reported viraemic re-suppression (ranging from 56.6% to 84.4%). In the other three studies, mean viral load levels declined. Importantly, delayed onset of routine viral load monitoring was associated with the emergence of drug resistance. For example, the study in Khayelitsha, South Africa, where patients attending the MSF-supported clinic are enrolled for targeted adherence counselling as soon as their viral load becomes detectable, found that 71% of patients who met criteria for virologic failure were able to achieve viral suppression to undetectable levels within four months after a viral load-triggered adherence intervention.[24] Early adherence, and adherence support, is key to achieving long-term viral suppression and treatment success.[25] Using viral load testing to trigger targeted interventions allows counsellors to focus their time on the patients who need it most, and increase the chances of re-suppression of the virus. For example, although rates of second-line failure are high in low-resource settings, the limited number of studies that have assessed whether or not this failure is due to drug resistance or poor adherence seem to point to poor adherence as the main cause.[26] This is an especially important distinction where further treatment options are limited.

Viral load monitoring also improves treatment adherence by acting as a motivational benchmarking tool to track and resolve adherence problems. MSF and other treatment providers are finding that viral load monitoring can act as a powerful motivator for people to adhere to their treatment (see box).

Importantly, in order for VL to be effective as an adherence-boosting tool, adequate adherence support measures must be in place. This can include nurses and clinicians that engage their patients in troubleshooting adherence problems, facility-based adherence counsellors, community health workers providing home-based follow up care, and access-friendly treatment strategies that makes treatment convenient and close to where people live.

VL CONFIRMS TREATMENT FAILURE EARLY, BEFORE CD4 DECLINE

Viral load treatment monitoring may simplify the monitoring of treatment failure. Detection of treatment failure using standard immunological definitions (i.e. with CD4) is poorly implemented in resource-limited settings. Only 1.6% of people receiving treatment from MSF-supported HIV programmes in 19 countries have been switched to second-line therapy, suggesting very poor levels of detection.[28] Monitoring CD4 changes over time is challenging for clinicians, especially in overburdened clinics. In contrast, routine virological monitoring provides a clearer measurement of treatment efficacy using a single time point.

Viral load monitoring helps to avoid unnecessary switches to more expensive and difficult drug regimens, potentially conserving first-line therapy, which is typically simpler and cheaper than second-line therapy.[14, 29] This also allows for greater treatment options in the future.

For people experiencing treatment failure due to drug resistance to first-line drugs, clear and early confirmation using VL allows timely switching to effective therapy before their immune system is further damaged, and avoids the development of cross-resistance to other drugs.[5, 30] The cost of WHO-recommended second-line treatment has fallen, thanks to generic competition, by a substantial 75% since 2006, from US$1,200 to $300 ppy for today's most affordable second-line combination.[31]

When to switch therapy is a particularly critical decision in resource-poor settings; if first-line ART is switched prematurely, months or years of potential effectiveness in terms of survival benefit might be lost.[18]

While it is preferable to perform virological testing routinely during the time that countries are scaling up testing, it can also be useful in more limited instances, to confirm treatment failure in patients failing clinically or immunologically, thereby preventing unnecessary switches to second-line ART.[32] Resource-limited countries, such as India, Malawi and Ukraine, have updated their guidelines to require targeted viral load testing for this purpose.[2]

FROM THE FIELD... SOUTH AFRICAN PERSPECTIVES

VL REVEALS PREVIOUSLY-HIDDEN HIGH VIRAL LOADS, THEN HELPS REDUCE THEM

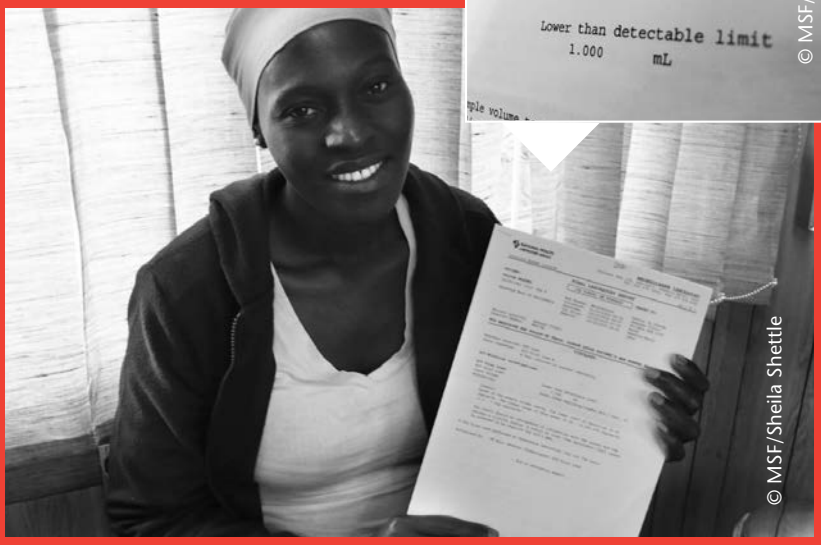
Viral load testing is a key enabling technology at the heart of new community models of care that are patient-centred and patient-empowering. Viral load monitoring allows people to measure and track viral suppression, providing patients and clinicians with critical data to measure treatment efficacy and craft appropriate adherence support programmes; and acting as a powerful motivational tool that contributes to long-term retention in care and treatment adherence.

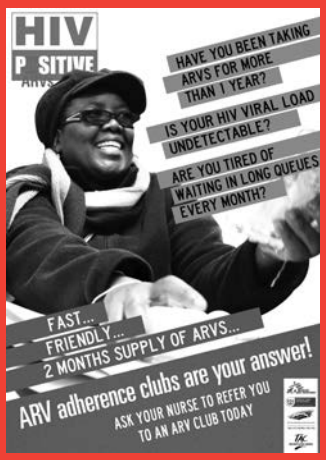
South Africa has the fourth highest adult HIV prevalence in the world (17.3%), with 5.6 million people estimated to be HIV-positive.[27] HIV treatment programmes have been progressively scaled up over the past decade, and the country's National Strategic Plan 2012-2016 aims to ensure that 80% of the estimated 3 million people who need treatment are receiving it by 2016. By early 2013, South Africa had initiated 1.9 million people on ART, but studies estimate retention rates are lower than 70% after three years on ART. As pressure on the health system increases, with many more people being initiated on ART, retention in care and adherence of patients on ART decreases.

In KwaZulu-Natal (KZN), where MSF supports the KZN Department of Health to manage 8,100 HIV patients across eight clinics, implementation of consistent viral load testing and data analysis revealed that average annual viral detectability was 35.3% in 2011, much higher than in previous years when VL testing was still being ramped up. In 2012, however, after MSF teams trained and mentored facility-level health staff on enhanced adherence counselling protocols and VL monitoring, average annual viral detectability decreased to 21.7%. This drop occurred despite an almost threefold increase in the number of people started on ART each month.

"In our enhanced adherence counselling programmes, we conduct a lot of patient education on viral load, and it is amazing to see them discussing their results and competing on who has the best value!"

– **Dr. Ruggero Giuliani**, Deputy Field Coordinator, MSF KwaZulu-Natal, South Africa





In 2007, as a way to decongest health centres, MSF began piloting adherence clubs with support from the Western Cape Department of Health and the Treatment Action Campaign (TAC) in a large community health centre ART site in Khayelitsha, Cape Town. Adherence clubs shift the majority of consultations and ART distributions for stable patients to 'clubs' organised by lay counsellors or peer educators. The pilot demonstrated that club participation was associated with sustained virological suppression and immunologic recovery. Over 40 months, 97% of club patients remained in care, compared to 85% of those who qualified for clubs but remained in mainstream care. Club participants were also 67% less likely to experience virological rebound, indicating better adherence in clubs compared to mainstream care. From January 2011 to December 2012, after adoption for phased roll out by Western Cape Government Health, more than 600 ART clubs have been set up in Cape Town, providing ART care to over 16,000 patients.

"Routine viral load monitoring is a lynchpin of the adherence club model. Club patients are only seen by their clinician once a year, and their viral load result ensures identification of a patient who is no longer stable and needs to be removed from the club to return to mainstream clinical care for regular clinical follow up and enhanced adherence support. Viral load is also a critical benchmarking tool that helps motivate and empower people to maintain good adherence to treatment."

– **Lynne Wilkinson**, Project Coordinator, MSF Khayelitsha, South Africa

VL ENABLES PROGRAMME DECENTRALISATION AND TASK-SHIFTING

As both an early indicator of treatment failure and a tool to improve treatment adherence, viral load monitoring supports decentralisation and peer- or self-managed therapy. This involves strategies such as peer antiretroviral therapy groups, which can boost adherence and relieve the burden on individuals and on health systems.

VL also allows for less frequent clinical follow-up and for further task shifting. Simplification of treatment monitoring for stable patients on therapy for more than a year, using an annual clinical visit with review of the viral load, could significantly reduce the number of clinical contacts required, having both a cost-saving effect and reducing the burden on patients and healthcare workers alike.[33]

VL IMPROVES TREATMENT EFFICACY

Observational studies have shown VL treatment monitoring to be the superior treatment monitoring tool, leading to better treatment outcomes,[16] more timely and appropriate switching to second-line ART,[14, 32, 34, 35] and a reduced development of drug resistance.[14, 36]

For example, a recent study at an MSF-supported HIV programme in Kenya showed that when clinico-immunological criteria were used to predict virological failure (above 5,000 copies/mL), the sensitivity, specificity, and positive and negative predictive values were 36.4%, 83.5%, 12.3% and 95.4%, respectively.[37] This means that although clinico-immunological monitoring might be able to rule in treatment failure, it definitely cannot rule out treatment failure. And the results are dismally inaccurate for paediatric diagnosis: a paediatric study in South Africa found that immunological monitoring had a sensitivity of just 5%, and a positive predictive value of 42%, compared to the gold standard, virological treatment monitoring.[38]

These studies add to growing evidence that clinical or immunological monitoring does not correlate closely enough with virological measures, and thus is not sufficient to provide patients with optimal monitoring.

Randomised clinical trials have not directly proven that laboratory monitoring leads to better patient outcomes as measured by mortality or significant morbidity compared to clinical monitoring.[39, 40, 41, 42] However, these trials are typically of short duration (three to five years) and thus may not follow patients for sufficient time to demonstrate differences in clinical outcomes, and, furthermore, patient outcomes in carefully-managed trials may be far better than those in real-world health settings. It is therefore questionable whether the results can be generalised. In addition, trials usually focus on long-term outcomes, such as mortality, while beneficial outcomes such as viral suppression, limited development of drug resistance, adherence, development of certain co-morbidities, and prevention of transmission may be much more relevant in the short term.

VL HELPS TO MEET PROGRAMME-WIDE GOALS

Beyond the benefits of viral load monitoring of individual patients,[12] recent modelling shows that ART programmes with routine viral load testing, as opposed to ART programmes with immunological monitoring alone, can lead to a 31% greater reduction in community viral transmission, and a subsequent reduction in HIV incidence.[17] Furthermore, using viral load testing to identify mothers on suboptimal ART is important to prevent mother-to-child transmission of HIV (PMTCT) in utero, at birth and during breastfeeding. As more and more countries and national reproductive health programmes move towards the implementation of PMTCT 'option B+' (whereby pregnant and breast-feeding women are started on triple ART irrespective of CD4 count), viral monitoring will be an important tool for tracking treatment efficacy.

In addition to helping programmes meet targets, programme managers and policy makers can use viral load monitoring among patient cohorts, as well as community-wide viral load measurements, to monitor progress against targets and identify areas needing more attention. One systematic review involving almost 10,000 people on ART showed 76% with virological suppression at one year on ART, short of the 95% target to maximise population-level results.[53]

VIRAL LOAD MONITORING IMPROVES EARLY INFANT DIAGNOSIS

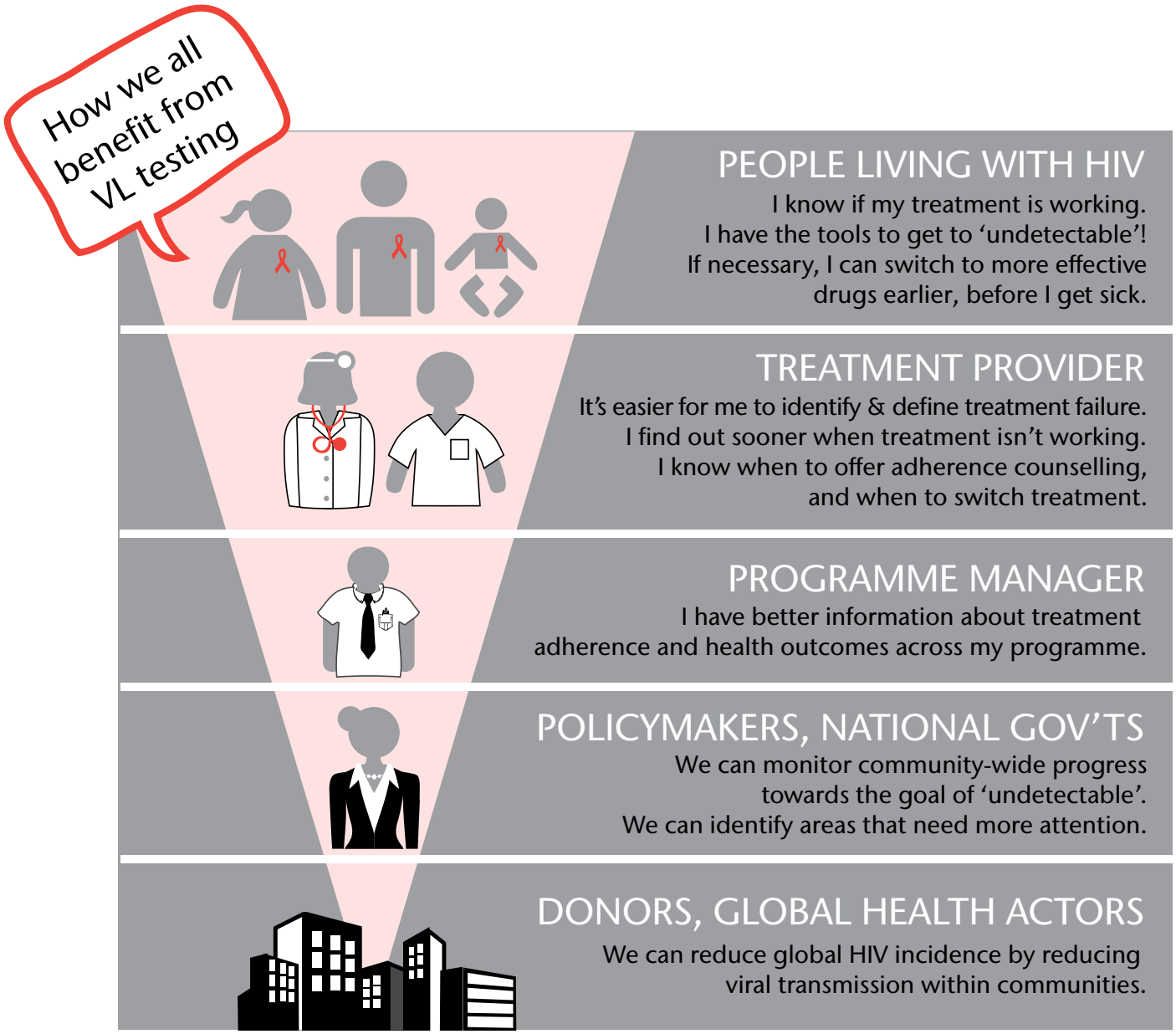
Early infant diagnosis (EID) – currently recommended by WHO to be performed at six weeks post-birth – is critically important because of the high risk of mortality associated with HIV infection in infants. Mortality peaks at 2–3 months of age, and those infected in utero or intra-partum are at a higher risk than those infected post-partum (e.g. during breast-feeding).[43, 44] POC testing could play a useful and important role in being able to diagnose and initiate infants on the same day and before they are lost to follow-up.[45]

Traditionally, EID has been performed using a qualitative virological test for HIV DNA, however, the new molecular platforms are dual purpose for both HIV DNA and HIV RNA (viral load) testing. Furthermore, infants may also be diagnosed with a viral load test, as the purpose is to measure whether the virus is present or not – and both an HIV DNA and an HIV RNA test suit this purpose just as well. Viral load testing performed on whole blood using reverse transcriptase PCR will amplify both the DNA and RNA (total nucleic acid) and thus maximises sensitivity by capturing all possible HIV nucleic acid.

There are two emerging and important considerations in the context of EID:

- It is critically important that infants receive a confirmed virological diagnosis prior to treatment initiation for two reasons: (1) Serological tests, such as rapid diagnostic tests (RDTs) commonly used to diagnose HIV in adults, may not be used in infants aged <18 months because of the presence of maternal antibodies. As such, where no access to EID is available, infants suspected of being HIV-infected are often started on treatment empirically, after which they still require a confirmed diagnosis; and (2) If an infant has been treated empirically, then performing a serological diagnosis post-18 months of age may be false negative because infants, if placed on treatment quite soon after infection, can serorevert. If an infant is incorrectly taken off treatment this will have significant impact on morbidity and mortality. Furthermore, depending on how long the infant has received empirical treatment, even the HIV DNA test result, usually performed on a very small sample of blood from a heel stick, may be false negative.[46, 47]
- With the roll-out of PMTCT services, treatment exposure can make virological tests less sensitive because treatment inhibits viral replication.[48, 49] Performing infant diagnosis at birth (if the mother gives birth at a facility) or within one week of birth (for example, when the infant is brought in for their BCG vaccination), makes sense for two reasons: (1) Early infections are diagnosed as soon as possible and infants who are already infected can start on combination therapy, rather than receiving monotherapy prophylaxis; and (2) Risk of mortality is diminished by earlier treatment. However, should the infant test negative, additional testing post-prophylaxis will be required to detect post-partum infections. Assuming prophylaxis is taken until six weeks of age, a test at 10–12 weeks should allow sufficient time for viral replication to again maximise diagnostic sensitivity. In addition, virological confirmatory testing may be required after breast-feeding to confirm infection status as some evidence points to the fact that, depending on the drug, ART exposure through breast-milk may also limit viral replication in the infant.[50]

VL DELIVERS SYSTEMIC BENEFITS, FROM THE INDIVIDUAL TO THE INSTITUTION



"We were able to use some very simple techniques to overcome staffing, cost, and logistical constraints to get people in very remote communities the gold standard for monitoring HIV therapy. We have to keep trying these field-adapted solutions to ensure that the benefits of viral load monitoring reach as many patients as possible."

– **Dr. Laura Triviño Duran,** Medical Coordinator, MSF Thyolo, Malawi

GOING ROUTINE: FEASIBILITY AND COSTS OF ROLLING OUT VIRAL LOAD MONITORING

The limited uptake of viral load in developing countries is largely attributable to barriers related to the cost and the complexity of the technology.[15] Nevertheless, evidence is mounting that some of the cost and implementation barriers holding back VL implementation in resource-poor settings are being overcome.[54] Other factors relate to operational or technical innovation, or to the fact that new products and manufacturers are driving down the cost and complexity of VL implementation. MSF and other treatment providers are simplifying protocols and adapting implementation plans to resource-poor contexts, while stronger WHO guidelines may catalyse funders and countries to prioritise scaling up access.

COST: VL HAS COST BENEFITS FOR PROGRAMMES

Results from observational studies and field implementations are helping to build models to reflect on some of the early cost benefits of VL monitoring in developing countries. It is clear that the contribution from preventing the development of drug resistance through targeted adherence counselling and limiting transmission will play a major role in cost-effectiveness.[55, 56] In two recent modelling studies, one found that routine virological monitoring could reduce transmitted drug resistance by as much as 80% [20] while the other found that, if the baseline transmitted drug resistance was <10% or between 10-20%, which reflects current rates,[57, 58] then it could be as high as 17% and 34% in 45 years' time, respectively.[13] Depending on what drug classes predominate going forward, primary resistance to existing regimens may be either more or less of a problem.

Viral load monitoring can yield cost savings in a number of areas, including:

Reducing the cost of drugs, by preserving first-line therapy: Prices for first-line treatment continue to fall, and patient-friendly and robust one-pill-a-day regimens are now available for less than $140 per person per year. Despite substantial price drops since 2006, second-line treatment remains more than twice the cost of first-line treatment, at approximately $300 ppy, while the most affordable third-line regimen costs almost 15 times more, at $2,000 ppy.[31]

Maintaining people on effective first-line treatment for longer therefore yields costs savings. A modelling study comparing CD4 to viral load treatment monitoring head-to-head showed that any additional diagnostic costs are balanced by cost savings from avoiding unnecessary switches to new drug regimens, due to the more frequent misdiagnosis of ART failure when using CD4.[55] In one observational study of HIV-positive adults and children, 25% of patients in one cohort would have been incorrectly switched to more expensive second-line treatment if not for viral load monitoring.[32] High adherence to treatment reduces healthcare costs, particularly hospitalisations.[59]

With prohibitively high prices for third-line drugs keeping them out of reach of most patients in developing countries, the preservation of first- and second-line treatment is even more critically important.

Reduced costs associated with redundant testing: VL monitoring could completely replace CD4-based immunological monitoring for people who are stable on treatment.[11] Viral load is recognised as the more effective technology for treatment monitoring, while CD4 testing for stable patients fails to even influence their care, since patients with high CD4 cell counts so rarely dip below clinically-meaningful thresholds.[9] The elimination of CD4 tests in virologically stable patients with a CD4 count above at least 200 cells/μL will positively impact overall programme costs.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Reduced costs for VL equipment and operation: The price of viral load testing is expected to fall with the entry of new products and manufacturers into the market, as competition drives prices down. In addition, the introduction of newer, innovative technologies that are cheaper to produce and that require no- or low-maintenance will also reduce costs. For example, automated, high throughput testing will allow for efficiency and volume-based discounts.

Today viral load tests cost, on average, two to four times more than CD4 tests.[55, 60] However, cost of the test itself does not always reflect the full cost of the intervention, nor does it account for cost-savings from other interventions due to the integration of viral load monitoring into treatment programmes.

Reduced cost of testing through use of pooled samples: In an attempt to assess how to overcome cost barriers to routine viral load monitoring, MSF evaluated the accuracy of, and cost-savings from, pooling samples for the monitoring of patients on ART in Thyolo, Malawi. MSF showed that by using mini-pools of five dried blood spot (DBS) samples, pooled sample VL testing is feasible, accurate, efficient and cost-saving.[61]

All patients in the Thyolo district were monitored routinely – a population of 620,000 with an HIV prevalence of 14.5%, requiring 23,000 viral load tests per year for those on treatment. When there was detectable virus in the pooled sample, individual viral load testing for each of the patients in the pool was done. At a viral load test price of $24, the total cost of testing would have totalled $552,000 per year. Using a threshold of 1,000 copies/mL to diagnose virological failure, pooling would have saved $157,800 per year (28.6% efficient), whereas using a threshold of 5,000 copies/mL would have saved $283,700 per year (51.4% efficient). Promising evidence exists to support these models, but more data is needed.[62]

FEASIBILITY: STRIKING THE RIGHT BALANCE BETWEEN POC CONVENIENCE AND LAB-BASED EFFICIENCIES

The second obstacle preventing wider uptake of VL tools relates to complexity. Here too, change is afoot, or strategies can be adopted to mitigate this barrier.

Looking to the pipeline: Several simple and point-of-care tests are expected to become available soon, which will greatly increase the feasibility of monitoring viral load in decentralised, resource-limited settings.[63] In addition, laboratory-based tests are becoming increasingly automated, with the large, centrally based platforms almost entirely automated, reducing the level of laboratory infrastructure, skill and hands-on time required.

Using novel sample transportation strategies: The use of dried blood spots (DBS) has greatly simplified the transportation of patient samples to the laboratory.[64] MSF has successfully implemented and validated the use of fingerprick-based DBS in Thyolo district, Malawi, using the bioMérieux platform: compared to viral load in plasma and similar to viral load in venous (full blood) DBS specimens, viral load in fingerprick (capillary blood) DBS samples had a sensitivity of 90.8% and a specificity of 96.7% at a 1,000 copies/mL cut-point; and a sensitivity of 88.8% and specificity of 100% at a 5,000 copies/mL cut-point.[65] These results show how DBS using fingerprick capillary blood is an accurate method that can enable the decentralisation of routine viral load monitoring.

Priorities for VL roll-out: Where it is not feasible to fully introduce and integrate VL testing into all aspects of a programme, a phased implementation approach can enable logistical and technical laboratory capacity to be firmly established before scaling up to routine virological monitoring for everyone. Some possible approaches include:

- Use VL to confirm treatment failure before switching to second-line ART and implement a triggered VL testing approach, using a clear algorithm to identify patients with CD4 reductions of 30% or more, with specific clinical signs and/or with poor adherence
- Select specific populations for VL testing that are identified as being at higher risk of failure, e.g. children and adolescents, and prioritise EID
- Monitor ARV-treated pregnant women before birth and during breast-feeding to confirm viral suppression and prevent mother-to-child transmission

Although these approaches represent suboptimal use of viral load testing, they represent some initial implementation priorities for consideration.

Striking the right balance between the convenience of point-of-care tests, and lab-based efficiencies: Diagnostic testing has traditionally been confined to laboratories and performed by technicians. But decentralisation – getting care out of hospitals and laboratories and into community clinics and local health posts – has been the cornerstone of expanding access to ART. Shifting healthcare tasks to the community level eases the strain on the central health system and supports faster treatment scale up. Policies to enable task-shifting include allowing non-physicians, including nurses, to initiate ART, and allowing lay workers to dispense antiretrovirals.

Decisions on where to place testing must take many factors into account, including: patient volume and characteristics, for example to what degree transient, remote or stigmatised populations are linked to the health care system; cost per test and anticipated levels of instrument usage, which can yield different cost efficiencies; human resource skill level and task-shifting policies and consequences; and the time to a result-based intervention.[66–69]

CD4 testing in developing countries is today mostly lab-based, which means there is a delay between when a person needs ART, and when the diagnostic results can confirm eligibility and a

medical decision can be made. POC tests, on the other hand, ideally require minimal training, use few resources (such as electricity), are easy to transport and quick to set up at primary health centres, health posts and mobile clinics.

The evidence suggests that POC CD4 testing can reduce the number of patients lost to follow-up between the time that someone is diagnosed as HIV-positive and the time they are deemed eligible to start treatment, and thus can ensure that more people can access effective therapy.[6, 70] If serological and CD4 testing can be performed in succession, and eligibility is determined, ART initiation can possibly happen on the same day as diagnosis. This not only gets people on treatment as soon as possible, but also prevents the loss of patients who would otherwise not have returned to the clinic for their laboratory-based CD4 test result; in other words, it helps retain patients in the HIV care continuum. In addition, if mobile HIV counselling and testing is offered, people who receive an immediate CD4 test result, as opposed to waiting for a follow-up clinic visit, are more likely to visit a referral clinic afterwards. Thus, empowering people with immediate knowledge about their eligibility for treatment seems to improve linkage to care, even where treatment is not immediately available at the testing site.[71] These are important points considering that, in sub-Saharan Africa, 59% of patients are lost to follow-up between the time they receive serological HIV testing and the time they receive their CD4 result (or clinical staging).[72]

On the flip side, moving diagnostic testing to the point of care has important human resource consequences: unless a technician is placed on site to perform the testing, nurses will be tasked with administering these new tests, and must undergo on-going training, and perform quality-assurance testing and reporting. POC testing can strain overburdened clinicians at the community level. In addition, throughput of test processing will be low since only one sample can be processed at a time, which may be burdensome time-wise.

If task-shifting is allowed, trained lay-workers may be trained to perform simpler sample preparation and testing procedures, thus allowing for POC services without placing an extra burden on clinicians. In any case, sufficient human resource and quality requirements will become a critical factor in the feasibility of POC testing.

For viral load testing, in some contexts, such as high-prevalence settings with existing sample transport systems, laboratory-based VL testing makes more sense, particularly when test results do not necessarily require an immediate clinical intervention – for example, when people are already enrolled in care and the aim of the viral load test is to confirm that treatment is working effectively.

In other contexts, the forthcoming POCs will be an important catalyst in promoting adoption of VL, and in ensuring better patient outcomes: POC viral load may have particular benefits in hard to reach areas or specific 'vulnerable' patient groups (pregnant women, adolescents and young adults etc.), for reaching patients in remote or rural areas, and for the simplification of patient management and cross-checking their adherence.

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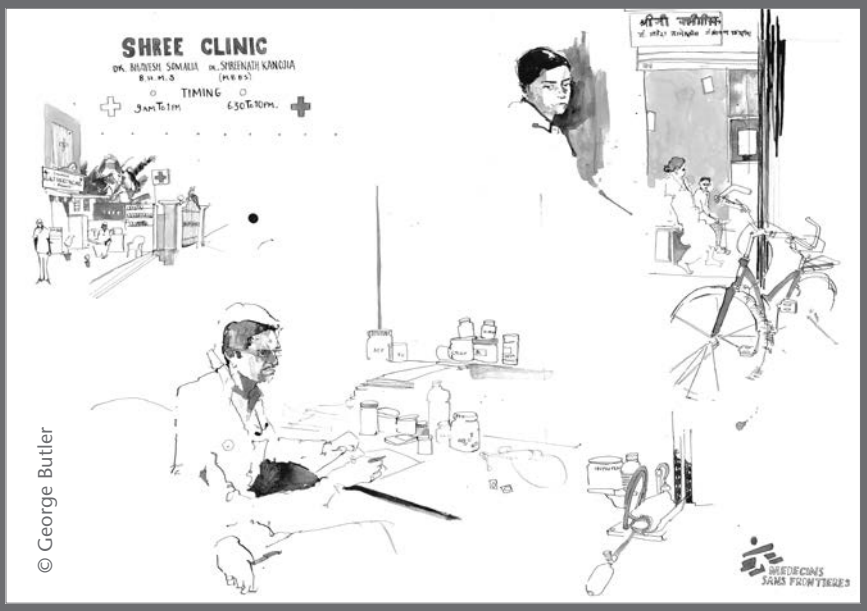
RUNNING OUT OF TREATMENT OPTIONS

In many developing countries, access to third-line treatment regimens is severely limited, primarily due to prohibitively high costs and few treatment options. Yet a limited but growing number of patients in resource-poor settings require third-line, or salvage, ART. The acute fear of running out of treatment options means that first- and second-line treatment must be carefully managed and preserved, where medically appropriate. This is best done with the aid of viral load monitoring and strong clinician adherence support.



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Managing second-line failure in Mumbai, India

MSF's Mumbai HIV/MDR-TB project started in 2006, at first caring for 'excluded' HIV-infected populations, including migrants, and gradually expanding to focus on 'medical' exclusions such as HIV-2 infection, second- and third-line ART, and co-infections, especially HBV, HCV, HPV and TB/MDR-TB. In 2012, MSF conducted a retrospective, observational cohort study of 40 patients with suspected failure of second-line ART; patients were referred to MSF and followed for at least 12 months. Targeted interventions included structured patient-centred adherence counselling and health education for patients and their families.

With intensive psychosocial and medical interventions, 78% of those failing second-line ART were able to re-suppress within six months. Of those that were switched to third-line, 78% were able to achieve viral suppression, while two patients failed third-line treatment due to extensive antiretroviral drug resistance.

"With viral load monitoring and intensive adherence support, we were able to prevent 31 out of 40 patients from unnecessary switches to expensive and sparsely available third-line regimens. However, there is an increasing need for access to medications that can be used in third-line antiretroviral regimens. The cost of such medications and inadequate access to HIV viral load monitoring and drug-resistance testing are major barriers to the management of patients failing second-line ART."

– **Petros Isaakidis**, Medical Epidemiologist and Senior Operational Research Fellow, MSF India

The 'Risk of Treatment Failure' Clinic in South Africa

In 2011, about 482 (7%) of the 6,000-patient cohort at the Ubuntu clinic in Khayelitsha, Cape Town, were on second-line treatment. MSF launched a targeted adherence and support programme for patients who were failing second-line ART, in an effort to increase durability of the second-line regimen and decrease the need for costly third-line regimens. All patients were offered a comprehensive package of integrated clinical and adherence support, which included regular consultations with experienced staff. More than two-thirds of the patients failing second-line ART achieved re-suppression, without changing their regimen, following an enhanced patient support intervention, and the majority re-suppressed within three months of enrolment in the programme.[76] MSF is now piloting a programme, based on viral load monitoring and structured adherence support, to address patients failing first-line ART.

"The findings are promising as they demonstrate that patients failing second-line treatment can become adherent following targeted, enhanced adherence support. By increasing the time on second-line ART and decreasing the need for genotypes and costly third-line ART, this intervention may reduce programmatic costs."

– **Dr. Karien Conradie**, Risk of Treatment Failure Programme Manager, MSF Khayelitsha, South Africa

THE PRODUCT GUIDE FINDINGS – IN BRIEF

PRODUCT SUMMARY

This report compiles information that manufacturers were willing to share on commercially available products, except for POC VL diagnostic platforms, which are still pipeline products, and which were included only if pricing information was made available.

POINT-OF-CARE CD4	COST PER TEST RESULT, IN US$[1]
Alere Pima Analyzer *Well-established and fairly widely implemented in resource-poor settings*	**$6–$12[2]**
Burnet Institute/Omega Diagnostics Semi-quantitative CD4 Test/Visitect CD4 *Disposable, instrument-free test (reader is optional)*	**$5[3]**
Partec CyFlow miniPOC *One of only two POC tests that measures CD4% for paediatric staging and monitoring; can also measure total lymphocyte count*	**$4[4]**
LABORATORY-BASED VIRAL LOAD	
Abbott RealTime HIV-1 assay *Different throughput options (m24sp and m2000sp); HIV RNA extraction from whole blood is about 90% RNA-specific (extraction conditions "prefer" RNA to DNA); R&D to improve RNA-specificity is on-going*	**$15–70[5]**
Biocentric Generic HIV viral load assay *Multi-manufacturer approach has a small footprint and allows for low instrument and test prices without the need for high volumes to bring costs down*	**$13 (manual)[6]** **$16 (automatic)[6]**
bioMérieux NucliSENS EasyQ HIV-1 v2.0 *The only RNA specific amplification platform and the only platform having received regulatory approval to use DBS as a sample type*	**$25[7]**
Cavidi ExaVir Load *A non-molecular platform and therefore not affected by amplicon contamination; not as dependent on precision pipetting; not automated and very hands-on; only medium throughput; can only be used with plasma*	**$12–25[8]**
Qiagen artus HI Virus RG/QS-RGQ RT-PCR *Not widely used in low-resource settings*	**$16–35[9]**
Roche COBAS Ampliprep/COBAS TaqMan HIV-1 monitor version 2.0 *Different throughput options (Taqman 48 and Taqman 96); current extraction method extracts DNA and RNA so not suitable to measure viral load from whole blood below 3,000 copies/mL; R&D to improve RNA-specificity is on-going (e.g. using DNase)*	**$11–25[10]**
Siemens VERSANT HIV-1 RNA 3.0 Assay (bDNA) *Not widely used in low-resource settings; might be discontinued*	**$36–72[11]**
Siemens VERSANT HIV-1 RNA 1.0 Assay (kPCR) *Not widely used in low-resource settings; expensive*	**$54–72[11]**
POINT-OF-CARE VIRAL LOAD	
Northwestern Global Health Foundation LYNX HIV p24 Antigen Test *Non-molecular test; only suitable for early infant diagnosis, not for treatment monitoring; commercially available in late 2013*	**$6–15[12]**
Northwestern Global Health Foundation LYNX HIV Viral Load Test Kit and sample processor *Expected to be commercially available in late 2014 or early 2015*	**<$10[12]**

(1) Incoterms for prices are FCA, unless otherwise noted

(2) These prices are for illustration value only and need to be negotiated in the different regions in the world with the local business unit; Alere have a programme with special pricing for low-income countries in response to the HIV epidemic – please enquire with the local business unit

(3) FCA Glasgow, at cost, no markup

(4) EXW; includes consumables

(5) EXW; inclusive of all items to run assay: amplification, extraction, controls, calibrators, but does not include consumables

(6) EXW; includes consumables

(7) EXW; includes reagent kit and disposables (extraction, amplification, detection)

(8) Includes consumables and reagents

(9) EXW; includes extraction, controls, reagents and consumables

(10) CPT; Prices provided include consumables and are all CPT unless insurance is required, then it's CIF

(11) Includes all items to run assay: amplification, extraction, controls, calibrators; price estimate from UNITAID HIV/AIDS Diagnostics Technology Landscape – 2nd Edition (June 2012)[73]

(12) EXW

CD4 POINT-OF-CARE TESTS

The currently available POC CD4 tests surveyed are priced quite competitively, within the $4–6 range per test. The fully commercialised Pima Analyzer (Alere), which is well-established and fairly widely implemented, currently costs around $6 per test. The CyFlow CD4 miniPOC (Partec) costs $4 per test, and is available at tiered prices based on country income. The Visitect CD4 test (Burnet Institute/Omega Diagnostics), one example of the newer disposable, instrument-free tests coming on to the market, will cost around $5 a test.

Of the current and pipeline tests, the CyFlow CD4 miniPOC is the only point-of-care test able to measure CD4 percentage (for the treatment eligibility testing and monitoring of children under five years of age). However, as the new 2013 WHO guidelines will recommend ART initiation regardless of CD4 and CD4% for all HIV-positive children under five years of age, and as viral load testing becomes increasingly available, the need for CD4 percentage to monitor treatment efficacy following immune reconstitution will decline.

The CyFlow CD4 miniPOC, being a mini flow cytometer, is not as amenable to decentralisation as the Pima Analyzer, because the equipment is not as easily transportable and it relies on a venous blood draw (cannot accept fingerprick/capillary blood samples). However it offers a much higher throughput, and therefore may be better placed at district level.

Market availability of a number of additional POC tests for CD4, as described in the HIV/AIDS Diagnostic Technology Landscape published by UNITAID,[63, 73] some without power requirements, will increase competition and is expected to drive prices down, and allow for further decentralisation.

VIRAL LOAD TESTS

Only commercially available laboratory-based products were included. Although many in-house assays have been developed, and are often cheaper and better regionally optimised for locally circulating strains, they are not covered in this report.

We included pricing information on the laboratory-based Generic HIV viral load assay (Biocentric), NucliSENS EasyQ HIV-1 V2.0 (bioMérieux), ExaVir Load Version 3 (Cavidi), artus HI Virus-1 RG/QS-RGQ RT-PCR (Qiagen), and COBAS AmpliPrep/COBAS TaqMan HIV-1 Test v2.0 (Roche).

Abbott and Siemens were not willing to provide specific pricing at this time, as they only provide country-specific pricing, but technical details for their tests are included, along with estimated prices from Abbott directly and Siemens pricing from the HIV/AIDS Diagnostic Technology Landscape published by UNITAID.[73]

Prices ranged upwards of $13 per test. Roche provides preferential pricing for least-developed countries ($11–25 versus $35–90). The Generic HIV Viral Load assay is the cheapest option at $13–16 per test, followed by the ExaVir Load at $12–25 per test.

A cost modelling study has revealed that both the test price and the cost of second-line ART are important determinants of cost-effectiveness of new POC VL technologies, as is the threshold used to define virological failure. Critically better evidence on the effect of adherence support to prevent treatment failure and transmission is needed to improve modelling outcome estimates for these important factors.[56]

Most POC VL tests are still pipeline products, and have therefore not yet been priced. The exceptions are the Northwestern Global Health Foundation's p24 infant diagnostic and RNA viral load tests, which are $6.50–15 and about $10 per test, respectively, with tiered pricing anticipated based on volume. Similarly to CD4, the imminent availability of these products will ensure further competition, and therefore price decreases, as well as facilitating decentralised testing. Further technical information on these tests may be found in the HIV/AIDS Diagnostic Technology Landscape published by UNITAID.[63, 73]

WHAT THIS MEANS FOR PROGRAMMES: A DECISION GUIDE FOR PURCHASERS

When deciding which diagnostic tool is the best fit for a programme, considering the following information, along with context-specific information, will assist in choosing the right tool.

1. Don't rely on a single manufacturer

Using at least two products for the same purpose will give more price negotiating power between suppliers, increase competition (which brings about further price decreases), and ensures that, if there are any supply problems with one product, there is at least one other supplier to depend on. Although the distribution, transport, training, maintenance and quality requirements will increase with multiple tests from different manufacturers, a compromise may be reached between the capacity to introduce multiple products versus the resources required to ensure quality of testing.

2. Check whether a local service provider is available to facilitate training and support

Local representatives of the company, or a third party designated by the manufacturer, are important for procurement, training and maintenance, and local service should ideally be available. It is good to investigate whether a local or regional office is available for the product of interest.

3. When deciding between using a centralised laboratory-based approach and a decentralised point-of-care based approach, consider throughput per site

Price per test is maximally reduced when instruments are used efficiently. For example, if a POC test can perform eight tests per day, but it would only be used an average of once or twice per day at clinic level, then it may be better to install a POC test platform at district level for low throughput needs. Similarly, in high-prevalence settings, where a single POC test at clinic or district level is unlikely to meet throughput needs, and many instruments would place an undue burden on staff, it might make more sense to install an automated, high-throughput laboratory-based instrument at provincial level. Throughput needs should also take into account likely scale-up over the next few years.

4. Make sure staff are well trained in the performance of the test

Even the simple performance of diagnostic tasks, including sample acquisition (for example, from a lancet-derived fingerprick of blood) requires adequate training and quality surveillance. For example, if a capillary sample is taken too superficially, the blood sample will be diluted by the interstitial fluid, with an erroneous reading as a result. Manufacturers should provide a thorough training, and refresher training, for all end-users.

5. Enrol in an external quality-assurance programme

Post-training, the most effective way to monitor the ongoing proficiency of testing is to enrol in an external quality-assurance programme. The test should also have in-built internal controls, which, upon analysis, will flag an error so that the result may be rendered invalid. Instruments with connectivity options will allow for information to be sent to a server from all testing sites so that monitoring can be done in real time. A list of external quality-assessment resources is available on the CDC website[74] and some of these, such as the CDC's proficiency testing programme, are currently available free of charge. In addition, regional training centres, such as the African Centre for Integrated Laboratory Training (NICD, Johannesburg, South Africa), provide training courses for laboratory staff and present courses for managers and policy makers.

6. Consider purchasing polyvalent platforms

Healthcare systems, especially those at public health clinic level, are often integrated in terms of diagnostic requirements. For example, a tuberculosis clinic may want to test people for HIV, and vice versa; HIV clinics may want to be able to perform viral load testing for HIV as well as hepatitis B and C, and high-risk HPV screening for women as part of cervical cancer screening. For this reason, when faced with choosing between similar platforms, it may be prudent to choose one that offers multiple disease-specific testing requirements. This will obviate the need to purchase new instrumentation for different disease requirements. It will still be important, however, not to rely on a single supplier – both from a cost and a reliability point of view.

7. Consider "open" or multi-manufacturer platforms to bring costs down

With the introduction of generic drug options, prices for antiretroviral therapy have plummeted over the years – proving that competition is the best strategy for lowering prices. Although there is no precise analogy for diagnostic tests, the closest example of this would be the use of open, multi-manufacturer platforms. This means that, rather than ordering everything from a single manufacturer, as is usually the case, the instrumentation and reagents can be sourced from

Continued overleaf ···

What this means for programmes continued

multiple manufacturers. This has the advantage of sourcing the best-priced item, but also optimising the test for best performance in the particular population of interest on which it will be used. For example, for viral load testing, subtype and circulating recombinant forms inclusion is a critical component of test selection. A caveat of this approach is that, once optimised, the test must be standardised for routine use and for submission to a strict regulatory authority. But this is possible. One example, included in the report, is the Generic HIV viral load assay, developed by the Agence nationale de Recherche sur le Sida (ANRS) and made available as an all-in-one platform by Biocentric (France). Biocentric then offer the entire package of different products, plus the test kit, to end-users, perform the platform installation and training of technicians, and are available for post-market trouble-shooting. The test has also been submitted for CE marking and WHO prequalification. The Qiagen artus HI Virus-1 RG/QS-RGQ RT-PCR also meets this criteria, although to a lesser extent, as the test has been validated for use with other non-Qiagen amplification instrumentation.

8. Consider a leasing or reagent rental option

If national and/or donor regulation permits, an instrument leasing option or reagent rental option may be preferable compared to purchasing expensive instrumentation outright. This option will allow for end-user flexibility to adopt newer and more efficient technologies as they emerge in the market.

9. When using a threshold for virological failure below 3,000 copies/mL and a whole blood sample, choose an RNA-specific technology for performing viral load testing

If viral load testing is being performed for the purposes of treatment monitoring, an RNA-specific technology is currently the preferred method. HIV virus is present in the body in both a DNA and an RNA form. The DNA form incorporates into the human genomic DNA so that the RNA form may be produced from this template. Amplification technologies that use reverse transcriptase PCR can amplify both DNA and RNA (as RNA is reverse transcribed into DNA), whereas RNA-specific techniques, such as nucleic acid sequence based amplification (NASBA), can only amplify RNA (as the temperature does not get hot enough to cleave the double-stranded DNA in order to allow for amplification). Because DNA is only present in the cellular part of the blood, this differentiation is only important when using whole blood (instead of plasma or serum, the non-cellular part of the blood) as a sample type. Venous whole blood may be used to prepare dried blood spots or directly as a fresh fingerprick or heel-stick blood for use with point-of-care assays. This differentiation is also only important at low viral loads – below 3,000 to 5,000 copies/mL. This is because, above that threshold, there is so much RNA virus in the plasma that the "contamination" from cellular nucleic acid is negligible. However, for programmes that wish to use a threshold of 1,000 copies/mL to define virological failure, this will be an important consideration when using whole blood.[75] Alternatively an RNA-specific extraction method can be used. Roche and Abbott are both conducting research and development in this regard to try to make their tests more RNA-specific.

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QUALITY ASSURANCE

This report is a pricing guide and, apart from indicating whether the product has received regulatory approval, does not include detailed information about the quality of the products listed. However, quality is an important factor in procurement decisions. This section provides a brief overview of the key entities that provide quality assessments of diagnostic tools.

1. WHO PREQUALIFICATION

More commonly known as WHO Prequalification, the WHO List of Prequalified Diagnostic Products was initiated by WHO and developed in collaboration with other United Nations organisations, principally for procurement by UN agencies. The project evaluates diagnostic and monitoring test manufacturers according to WHO-recommended standards of quality and compliance with Good Manufacturing Practices.[77]

The WHO Prequalification Programme is a benchmark for the identification of quality diagnostics for HIV/AIDS, malaria and hepatitis B and C and includes both a laboratory evaluation (to assess the operational and performance characteristics) and site inspection (to assess manufacturing quality). However, the programme is still is its infancy relative to medicines prequalification and, as such, many products have yet to be prequalified.

A key factor of success has been that financial support to national programmes has been dependent on purchasing medicines and diagnostics respecting clear quality assurance criteria. In this the WHO Prequalification Programme has played an important role, providing guidance to purchasers on the quality of diagnostics and thereby creating a positive market dynamic where manufacturers strive to reach WHO standards in order to comply with procurement policies.

WHO recognises the evaluation of products by regulatory authorities that apply stringent standards for quality similar to those recommended by WHO, such as the US Food and Drug Administration (US FDA), and the European Economic Area conformity mark (CE mark). However, in order to comply with the standards set by WHO, which may be more suited to resource-limited areas, further information may be required from manufacturers.

It is important that manufacturers approach WHO for guidance before submitting a dossier.

2. US FOOD AND DRUG ADMINISTRATION

The US FDA is a public organisation offering strict regulatory approval for medical devices, including in vitro diagnostics.[78] Approval based on a pre-market notification (510K) may be issued to products only needing to demonstrate substantial equivalence to an already-approved product, whereas, for Class III (the highest-risk category) medical devices, a more stringent pre-market approval is required.

3. EUROPEAN CONFORMITY

European standards for medical devices are based on the European Council Directive 93/42/EEC for CE marking.[79] Under this directive, private notified bodies in each country are responsible for the CE marking of medical devices, with stringency based on a Class system – Class A (the highest-risk category) requiring the most stringency. Products submitted under low-risk categories (such as diagnostic tests for tropical diseases) only require a self-declaration for certification, and are therefore not well scrutinised. This is due to the fact that disease-risk classifications may not always coincide between Europe and low-resource settings, and illustrates the point that low- and middle-income countries require their own strict regulatory authorities to mitigate the problems of relying on regulation of products by richer countries.

4. INTERNATIONAL MEDICAL DEVICE REGULATORS FORUM

The International Medical Device Regulators Forum (IMDRF) was founded in February 2011, replacing the Global Harmonisation Task Force. It is composed of a voluntary group of medical device regulators from countries around the world with the aim of accelerating harmonisation and convergence.[80]

5. ISO CERTIFICATION

ISO International Standards are a benchmark for safety, reliability and quality. The ISO13485:2003 standard, used to assess the manufacturing quality of medical devices, may be used to assess the quality of the management system for production.[81] It is one of the requirements to gain approval from a strict regulatory authority.

6. DONOR PROCUREMENT POLICIES

The Global Fund to fight AIDS, Tuberculosis and Malaria has a quality assurance policy for the procurement of diagnostic products that is effective from March 2011.[82] It refers to the WHO "List of HIV diagnostics eligible for procurement by WHO in 2012". As this list is currently limited to serological and antigen-based tests, countries may procure other products as long as a regulatory authority member belonging to the IMDRF authorises them for use.

7. POST-MARKET SURVEILLANCE

It is important to note that authorisation by a strict regulatory body is only a starting point. It is critical that continuous post-market surveillance on the performance and quality of the product, as used on the population of interest, be captured so that any problems may be addressed.

METHODOLOGY

This report includes technical and price information for all known commercially available HIV viral load tests and point-of-care CD4 diagnostic devices, including some pipeline products.

Commercially available viral load tests were featured with company-provided data, as well as publically available information; Siemens pricing information was sourced from UNITAID.[73] Pipeline viral load test companies that provided pricing information were included. Additionally, CD4 point-of-care companies were included in the pricing report when pricing information was provided.

A list of additional companies developing or producing these products, but not providing pricing information, is available in the 2012 MSF report *"Undetectable: How Viral Load Monitoring Can Improve HIV Treatment in Developing Countries."*[12]

Questionnaires were sent to companies producing or developing viral load diagnostics as well as companies producing and developing POC CD4 technologies. The companies were requested to provide technical and pricing information.

The data was collected between January and April 2013. All companies known to be developing and producing viral load diagnostics or CD4 point-of-care tests were included in the survey.

Some important preliminary remarks on the data presented in this report:

- The information in this report provides information on the costs of products. It does not include costs linked to equipment shipping, standing laboratory, staff, sample transport, external quality control, maintenance and other overheads.
- The manufacturers provided the prices listed in this publication (except for Siemens product prices, which were sourced from UNITAID.[73]) These are indicative prices, not price lists. Therefore the actual costs paid on these items may be higher or lower, depending on specific contexts.
- Companies use different trade terms (known as incoterms).* These trade terms outline the responsibilities of the manufacturer and purchasers with regards to transport, international freight and insurance costs. In order to provide comparable pricing, companies were requested to provide pricing information using FCA.
- The price per test calculation consists of the total price of reagents, buffers, and controls needed per test result. It does not factor in the price of instrumentation, consumables required but not supplied by the manufacturer, infrastructure, or labour.

***For more information on Incoterms, please refer to the Glossary.**

HOW TO READ THE PRODUCT TABLES

1. GENERAL INFORMATION

HIV diagnostic companies were requested to provide information on their products' technical specifications; pricing information; volume-based and tiered pricing; maintenance, training and warranty information; and contact information; all information that was received is included here. Both company-provided and publically available information were included. The narrative provides additional information on the products.

All prices are quoted in United States Dollars (US$). When currency was converted from Euro (€) to (US$) a currency exchange rate of €1 to $1.3 was used, as requested by companies.

2. TECHNICAL SPECIFICATIONS

Technological set-up refers to the type of assay (either laboratory or point-of-care), instrument compatibility with other brands, and the extent to which processes are automated or manual.

The mean time between failures refers to the elapsed time between inherent failures of a system during operations.

Polyvalency refers to the platform's capability to be used for multiple disease assays.

3. PRICING INFORMATION

When applicable, pricing for diagnostics assays were divided into categories: whether consumables, instruments, or required materials are or are not provided by the company. When applicable, sample extraction and preparation items were separated from items required for amplification and detection. If manual or automated options are available, both were included.

The sample throughput capacity, and therefore the number or size of the instruments required, will vary depending on the laboratory and context. Therefore, the number of samples per run and run times for instruments are provided, when available. Prices are displayed according to the incoterm provided by the company.

The price per test is the sum cost of reagents and controls per test result. When manual or automated options exist, these costs per tests are differentiated. When companies provided cost per test result in a different manner, the components of these test results are specified. FCA prices were requested, but price per test result is displayed on tables according to the incoterm provided by the manufacturer.*

4. VOLUME-BASED AND TIERED PRICING

Companies were requested to provide details on their volume-based and/or tiered pricing schemes. Some companies requested that interested parties contact them directly for more information on possible volume-based or tiered pricing.

5. MAINTENANCE, TRAINING AND WARRANTY INFORMATION

The details and pricing information provided by manufacturers has been incorporated into the maintenance, training, and warranty tables.

6. CONTACT INFORMATION

When provided by companies, contact information is given. This information enables interested parties to contact the companies directly for more detailed pricing information and to place orders.

***For more information on Incoterms, please refer to the Glossary.**

POINT-OF-CARE CD4
ALERE

01 | TECHNICAL INFORMATION

Company	Alere	**Product**	Pima Analyzer
Assay type	Fixed volume cytometry	**Mean time between failures**	Proprietary
Technological Set-up	Portable bench-top, fixed volume cytometer	**Transport and storage (include fridge required)**	Freeze-dried reagents require no refrigeration; Stable for 12 months at 2 – 30°C
Sample preparation	No sample preparation required	**Fridge at -80°C required?**	No
T-cell specific?	Yes, T-cells identified using CD3 & CD4	**Shelf life (each item in the kit)**	12 months
Time to Result	18–20 minutes	**Technical skill required for laboratory staff**	Minimal
Throughput	1 sample per run, 24 samples/day	**Laboratory set-up**	None required
Sample type	Capillary, venous	**Waste disposal requirements**	Proprietary
Sample volume	25µL	**Applicable settings**	N/A
Kit components	Only the instrument and the CD4 cartridge are required. Optional accessories available (see pricing table)	**Regulatory approval**	WHO PQ, CE-IVD
Kit sizes	25 & 100	**Connectivity options for mobile health & electronic access**	Yes
Components required outside the kit (i.e. buffers)	None, FS Kit optional, Printer paper if using the optional printer	**Battery Powered**	Yes on board with the option of an extra external battery with the solar solution
Controls	Extensive internal controls, sample volume control, reagent control, automatic control of cartridge expiry date, internal process controls, automatic test identification; Low & Normal daily control Cartridge; Can work with some EQA samples and process controls	**Solar**	Yes
Equipment required	None	**Polyvalency**	N/A

02 | PRICING

Instrument		Reference number	Reference number	Cartridge/reagents	
Pima Analyzer	1 Pima Analyzer	260300003	260100100	Pima CD4 100X Cartridge kit	100 Pima CD4 foil sealed test cartridges: 1 PIMA CD4 Product insert
	1 Power transformer		260100025	Pima CD4 2 5X Cartridge kit	25 Pima CD4 foil sealed test cartridges: 1 PIMA CD4 Product insert
	1 EU power cable		260400199	Fingerprick Sample Collection Kit for 100 Pima CD4 tests	4 units of safety lancets (x28)
	1 PIMA Analyzer User Guide				4 units of gauze swabs (x25)
	1 PIMA Bead standard (260400011)				1 unit of alcoholic swabs (x100)
Alere Pima Instrument & Accessory Pack	1 Pima Analyzer	260300004			4 units of plasters (x26)
	1 Power transformer				1 safety-lancet user guide
	1 EU power cable		260400009	Pima Printer Paper I	10 Rolls Thermal Paper, non-adhesive
	1 PIMA Analyzer User Guide		260400010	Pima Printer Paper 2	10 Rolls Thermal Paper, adhesive
	1 PIMA Bead standard (260400011) 1 PIMA Bag (260400001) 1 Pima Printer (260400007) 1 Connectivity Pack 1 (260400015)		260400011	Pima Bead Std	1 Normal cartridge
					1 Low cartridge
					1 Pima Bead standard User Guide

Instrument Accessories		Reference number	Cost (US$) EXW	Reference number	Cartridge/ reagents		Cost (US$) EXW
260400001	Pima Instrument Bag	1 Pima Analyzer Bag		260400011	Pima Bead Std	1 Low cartridge	
260400007	Pima Printer	1 Pima Printer				1 Pima Bead standard User GuideC	
		1 Pima Printer User Guide					
		1 Roll Thermal Paper I, coated, non-adhesive					
260400015	Pima Connectivity Pack 1	1 Pima Connectivity Pack 1 User Manual					
260400040	Alere Solar Solution	1 Solar Panel 1 Power Pack (260400015) 1 User Manual					
260400017	Alere Power Pack	1 Power Pack 1 User Manual					
		Cost per instrument	**$6,000 – $12,000**			**Cost per test result**	**$6 – $12**

1. These prices are for illustration value only and need to be negotiated in the different regions of the world with the local business unit.
2. Alere have a programme with special pricing for low-income countries in response to the HIV epidemic; please enquire with the local business unit.

03 | TIERED AND VOLUME-BASED PRICING | No Information Provided

04 | MAINTENANCE, WARRANTY & TRAINING

	Description
Warranty	Alere now offer a 2-year warranty. Customers can negotiate an extended warranty from Alere in the different regions of the world. Several options are available from local organisations.
Maintenance	The instrument does not require any preventative maintenance.

05 | CONTACT INFO

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POINT-OF-CARE CD4
BURNET OMEGA

01 | TECHNICAL INFORMATION

Company	Burnet Institute/Omega Diagnostics	**Product**	Semi-quantitative CD4 Test/Visitect CD4
Assay type	Lateral Flow	**Transport and Storage**	Transport at ambient temperature
Technological Set-up	Lateral Flow Point-of-Care Test	**Freezing at -80°C required?**	No
Sample preparation	None	**Shelf life (each item in the kit)**	18 months from production date
T-cell specific?	Yes	**Technical skill**	Minimal training required, primary skill required is for fingerprick
Time to Result	40 minutes	**Laboratory Set-Up**	None
Throughput	120 samples/day	**Waste disposal requirements**	According to local regulations
Sample type	Fingerprick, capillary and venous (EDTA)	**Applicable settings**	Field-based – no laboratory infrastructure required
Kit sizes	25 cassettes	**Regulatory approval**	CE Mark in process; US FDA in the future
Controls	Procedural control included in test format	**Connectivity options for mobile health & electronic access**	Test visually read; Optional instrument has data storage capacity and PC connectivity
Equipment required	Lateral flow strip		
Mean time between failures	N/A	**Polyvalency**	N/A

02 | PRICING

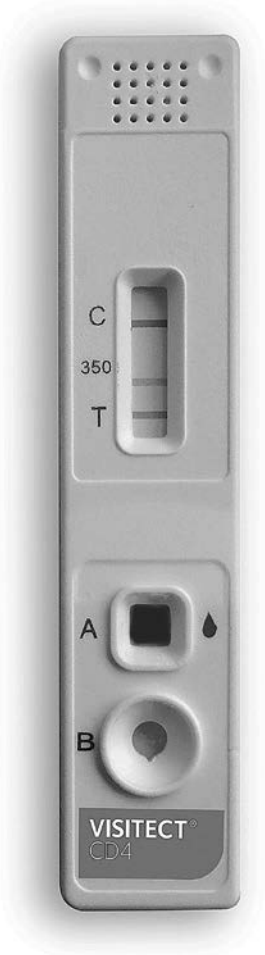
Instrument	Reference number	Cost (US$) EXW	Cartridge/reagents	Reference number	Cost (US$) FCA
Reader (optional) (40 minutes, 120 samples/ technician/day)	OD286	$3,000/unit	Lateral flow strip (25 tests per kit)	OD266	$125
				Cost per test result	$5
Transport details	Airfreight: FCA Glasgow – at cost, no mark up.				

03 | TIERED AND VOLUME-BASED PRICING

No volume-based or economic tier-based pricing. $5 test price based on optimal manufacturing capacity. Subsequently, Burnet Omega offers a single unit price per test to ensure maximum benefit for all recipient countries, regardless of size, depending on committed volume commitments.

04 | MAINTENANCE, WARRANTY & TRAINING

	Description
Leasing or reagent rental for instruments	N/A
Installation	No requirements for the test. (Optional Reader requires installation/ training of less than 2 hours).
Training	Training will be provided. Training aids and 'train the trainer' local workshops are provided by Omega in the country of use. Local costs such as transportation and living expenses to be handled by the recipient.
Maintenance	Optional instrument is maintenance-free. Swap-out if required if still within 12 month warranty period.
Length(s) of warranty and additional costs for an extended warranty	No warranty or long-term maintenance costs.
Warranty components	N/A



05 | CONTACT INFO

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POINT-OF-CARE CD4 PARTEC

01 | TECHNICAL INFORMATION

Company	Partec	**Product**	CyFlow miniPOC
Assay type	The CyFlow miniPOC is based on the cell enumeration "gold standard" technology flow cytometry. In each sample run, the absolute CD4, the CD4%, and the total lymphocyte count (TLC) are produced.	**Controls**	Controls are already included in the Partec miniPOC CD4% reagent kit (order no. 05-8409-d)
Technological Set-up	The CyFlow miniPOC features the Partec alignFree technology. Dedicated installation or a complex technological set-up of the unit is therefore usually not required	**Equipment required**	Additional equipment not required
Sample preparation	20µl EDTA blood is transferred into the ready-to-use CD4/CD45 dry mAb reagent tube and shaken by hand for approximately 3 seconds, then stored in the dark for 15 minutes (during this incubation time, a large number of samples can be processed in batches in parallel). The ready-to-use prefilled buffer solution "Buffer 1" is added (no pipetting required). Prior to analysis, the ready-to-use prefilled buffer solution "Buffer 2" is added (no pipetting required). The sample is transferred into the plastic disposable syringe (no pipetting required) which is placed at the sample port of the device, and analysis is started. The result of the measurement is automatically displayed and stored on the hard disk drive of the instrument as well as printed by the built-in thermo transfer printer	**Mean time between failures**	> 5 years
		Transport and Storage	The reagent kits supplied by Partec for the CyFlow miniPOC can be transported and stored at 2-8°C in cold chain / refrigerator or at 10-35°C
		Freezing at -80°C required?	No
		Shelf life (each item in the kit)	The reagent kits supplied by Partec for the CyFlow miniPOC have a shelf life of 6 months
		Technical skill	Nurse or lab technician
		Laboratory Set-Up	Clean desk or table
T-cell specific?	Yes: CD4/CD45 mAb – fluorochrome conjugate based assay	**Waste disposal requirements**	None
Time to Result	40–70 seconds	**Applicable settings**	Technology can be used at all levels of the health system, including central, regional, district and mobile labs, and some primary sites
Throughput	200–250 patients/day	**Regulatory approval**	EU CE-IVD
Sample type	Fingerprick, venous	**Connectivity options for mobile health & electronic access**	The following are already available: large data storage: > 20,000 data sets, USB port, e.g. for easy patient data transfer, built-in thermal printer. A connection system via a GSM module will be available for data transfer starting from second quarter of 2013
Kit sizes	20 CD4absolute/CD4% tests per unit	**Polyvalency**	No

02 | PRICING

Instrument	Reference number	Cost (US$) EXW	Reagents kits	Reference number	EXW (US$)
CyFlow miniPOC (15 minutes incubation; 40–70 seconds/test with a maximum of 250 samples/d)	CY-S-3033	$9,246	Partec miniPOC CD4% count kit-dry	05-8049-d	$78
Transportation bag for CyFlow miniPOC	CY-S-3091	$420	sample tubes pre-filled with lyophilized CD4/CD45 mAb reagents (20)		
Portable Rechargeable battery pack for CyFlow miniPOC	CY-S-3095	$247	sample tubes pre-filled with Buffer 1 (20)		
Solar Panel + battery pack for CyFlow miniPOC	CY-S-3097	$767	sample tubes pre-filled with Buffer 2 (20)		
Partec Control Blood	05-8993		Controls: 5 sample tubes pre-filled with Count Check Beads green – dry (QC material)		
			Controls: 5 sample tubes pre-filled with Rehydration Solution		
			Consumables: 1 sheath fluid container and 2 bottles Sheath Fluid (each 250mL)		
			Consumables: 1 roll thermo printer paper		
			Consumables: Cleaning Solution (2 x 5mL), Decontamination Solution (5mL), 40 syringes, 20 pipette tips (2-200µl)		
			Eppendorf pipette 20µl fix (for transferring 20µl of blood sample)	1 x 04-6-1023	
			Vacuette blood collection set, 100 pcs, including 1 manual	1 x 04-6-2040	
			Sample tubes rack for CyFlow miniPOC	1 x 04-2000-03	
			Hypochlorite Solution (250mL)	1 x 04-4012	
			Cost per test result*		**$3.90**

*Includes consumables.

03 | TIERED AND VOLUME-BASED PRICING

Instrument	Income levels (according to the World Bank Classification of Economies)		
Pricing range	**Upper**	**Middle**	**Lower**
CyFlow miniPOC (CY-S-3033)	$11,557.00	$9,245.60	$9,245.60

For bulk procurements, Partec can offer significant discounts.

Continued overleaf

Point-of-Care CD4 – Partec continued

04 | MAINTENANCE, WARRANTY & TRAINING

	Description	Cost (US$) (FCA)
Leasing or reagent rental for instruments	Purchase and instrument swaps are available. Instrument swaps can always be offered by Partec. In each country with CyFlow miniPOC placements, a suitable quantity of backup units will be safely available at Partec subsidiaries/offices and Partec distributors. A minimum of 10% of the total quantity of placed instruments will be kept as back-up units in the specific inventory for utmost rapid exchange/ swap on demand. Additionally, leasing options can be inquired at Partec. Reagent rental options are offered by Partec and can be inquired based on quantity of CyFlow miniPOC instruments and quantity of patient tests performed per site within a year.	
Installation	The CyFlow miniPOC software provides all the information for set-up, user training and maintenance, and contains a built-in operation and maintenance training video which can be seen on the colour TFT screen of the instrument. Bench-aids combining pictures and text are provided for ensuring adherence to SOP daily. Furthermore, dedicated training eWebinars will be available online on the internet (starting from April 2013). If requested, installation and on-site training can be optionally offered at remote testing sites by Partec on demand. Also, centralised training programmes and training seminars are available on demand.	
Training	CyFlow miniPOC device contains a built-in operation and maintenance training video which can be seen on the colour TFT screen of the instrument. On request, installation and user training can be offered locally by Partec.	
Maintenance	Service/maintenance: Based on the wide experience of Partec from placements of more than 1,800 CyFlow CD4 instruments in 100 countries, it can be confirmed that the usual response time for service/maintenance will be not more than two working days under normal conditions. Depending on very specific factors, longer response times may be possible, e.g. due to very difficult travel planning and travel performance in countries like Somalia, South Sudan, eventually difficult or time-consuming visa procedures, etc. For any support, service or maintenance inquiry, both the responsible local service provider (Partec subsidiary/office or distributor) and Partec Support center should be contacted.	Besides regular warranty coverage, preventive maintenance contracts can be offered by Partec at four different levels starting at a cost of $1,891.50 per year. For instrument bulk procurements and maintenance contracts covering multiple sites in a country or region, Partec is offering discounts on the annual contract fees. This depends on the target region, the quantity of instruments to be covered with the contract, and the geographical distribution of the covered instruments in the region or country.
Length(s) of warranty and additional costs for an extended warranty	2-year warranty (3rd-year warranty optionally available on request)	
Warranty components		Partec provides a special package for CyFlow miniPOC unit + 5,000 CD4abs/CD4% tests, plus a 3-year warranty, at EUR 23,000. Volume discounts are possible.
Turnkey option	1 CyFlow miniPOC unit plus 5,000 CD4abs/CD4% tests plus 3 years warranty. The turnkey option includes installation/training.	Total net cost of $29,900 (effective cost/test: $5.98). Delivery costs are excluded; package price is net EXW.

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LAB-BASED VIRAL LOAD
ABBOTT

01 | TECHNICAL INFORMATION

Company	Abbott	**Product**	RealTime HIV-1 assay
Assay type	RT PCR with fluorescence detection	**Mean time between failures**	Unknown
Technological Set-up	Manual or automated options, closed system		
Extraction method/ sample preparation	Manual or automated (m24sp or m2000sp)	**Transport and Storage**	Store reagents, calibrators A+B, and controls at -10°C
Linear Range	40–10,000,000 copies/mL	**Freezing at -80°C required?**	No
Target	HIV-1 RNA polymerase	**Shelf life (each item in the kit)**	18 months
HIV-1, HIV-2, Subtypes	HIV-1: Group M (A-H, CRF01_AE, CRF02_AG), Group O, Group N	**Technical Skill**	Medium-highly trained; precision pipetting required at low volumes
Time to Result	5–7 hours	**Laboratory Set-Up**	Specialised: 2–3 dedicated areas are required
Throughput	21–93 samples/run; 48-288 samples/day	**Waste disposal requirements**	Unknown
Sample type	Plasma, DBS (RUO)	**Applicable settings**	Highly-resourced settings
Sample volume	200µL – 1mL	**Regulatory approval**	WHO PQ, CE-IVD, US-FDA-IVD, Cananda-IVD, TGA (plasma)
Kit sizes	96 tests (4 x 24 tests/pack)	**Connectivity options for mobile health & electronic access**	Unknown
Controls	Internal control; negative, low positive and high positive controls		
Equipment required	Sample preparation: m24sp or m2000sp	**Polyvalency**	HIV DNA kit for infant diagnosis, Hepatitis B&C, HPV, CT/NG, CMV, MRSA
	Amplification and detection: m2000rt		

Continued overleaf

Lab-based Viral Load – Abbott continued

02 | PRICING

Instrument	Reference number	Cost (US$) EXW	Reagents kits	Reference number	Cost (US$) EXW	Not included in kit, but required	Reference number
Sample preparation			**Manual sample preparation**			**Automatic sample preparation**	
m24sp	3N06-01	$90,000	Manual sample preparation startup	02N28-03	$6,000	**RealTime System consumables (m24sp and m2000)**	
m2000sp	9K14-090	$120,000	**Automatic sample preparation**			Disposable Tips (DiTis): 1mL (2304 Tips)	04J71-10
Amplification and detection			RealTime System consumables (m24sp and m2000)			Disposable Tips (DiTis): 200µL (2304 Tips)	04J71-17
m2000 Real Time System	07K25-001	$38,000	mSample Preparation Systems RNA (4x24 Preps) (viral load)	04J70-24		5mL Reaction Vessles (2000 Vessles)	04J71-20
			mSample Preparation Systems DNA (4x24 Preps) (infant diagnosis)	06K12-24		200mL Reagent Vessles (90 Vessels)	04J71-60
			Amplification and detection			96 Deep Well Plates (32 Plates)	04J71-30
			Abbott RealTime HIV-1 Amplification Reagent Kit [96 Assays (4 packs x 24 assays)]	06L18-090		96-Well Optical Reaction Plates (20 Plates)	04J71-70
			Abbott RealTime HIV-1 Control Kit (8 Low Positive, 8 High Positive, 8 Negative)	06L18-080		Optical Adhesive Covers (100 Covers)	04J71-75
			Abbott RealTime HIV-1 Calibrator Kit (12 Cal A, 12 Cal B, 4 Complete Calibration Sets)	06L18-070		Master Mix Tubes/Caps (150 Tubes/Caps)	04J71-80
						Splash Free Support Base (5 each)	09K31-01
						mSystems Wrench (1 each)	01N71-01
						Additional for m24sp	
						1.4mL Internal Control Vial	03N19-01
						1.4mL Internal Control Vial Cap	03N20-01
						Optical Calibration Kit (1 each)	04J71-93
						Abbott RealTime HIV-1 Application CD-ROM	06L83-001
			Cost per test result*		**$15-70**		

*Inclusive of all items to run assay: amplification, extraction, controls, calibrators, but does not include consumables.
Note: all prices are estimates provided by Abbott.

03 | TIERED AND VOLUME-BASED PRICING | No Information Provided

04 | MAINTENANCE, WARRANTY & TRAINING | No Information Provided

05 | CONTACT INFO

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LAB-BASED VIRAL LOAD
BIOCENTRIC

01 | TECHNICAL INFORMATION

Company	Biocentric	**Product**	Generic HIV viral load assay
Assay type	RT PCR with fluorescence detection	**Mean time between failures**	Unknown
Technological Set-up	Manual or automated options, open system	**Transport and Storage**	Store reagents at -20°C for short periods
Extraction method/ sample preparation	Manual (Qiagen spin column) or automated (NorDiag Arrow)	**Freezing at -80°C required?**	No
Target	HIV-1 RNA LTR (long terminal repeat)	**Shelf life (each item in the kit)**	12 months
HIV-1, HIV-2, Subtypes	HIV-1: Group M (B and non-B subtypes including CRF)	**Technical Skill**	Medium-highly trained, precision pipetting required at low volumes
Linear Range	Standard: 300 – 50,000,000 copies/mL; ultrasensitive 40 – 50,000,000 copies/mL	**Laboratory Set-Up**	Specialised, 2–3 dedicated areas are ideal but a single room protocol may be used (with a lab hood and optional thermal plate sealer)
Time to Result	3 hours, including RNA isolation		
Throughput	min 1, max 96 samples/run; 192 samples/day		
Sample type	Plasma, DBS 3,000–5,000 copies/mL (RUO)	**Waste disposal requirements**	Waste for biohazard material
Sample volume	Standard 200µL; ultrasensitive 500µL – 1,200µL	**Applicable settings**	Developing countries, low- to medium-resourced settings
Kit sizes	220 or 440 tests	**Regulatory approval**	Commercialised but currently RUO (WHO PQ and CE mark in process)
Controls	Provided, along with standards in the assay	**Connectivity options for mobile health & electronic access**	Yes, connectivity to database
Equipment required	Sample preparation: Nordiag arrow (for automatic extraction)	**Polyvalency**	Same instrumentation may be used for other tests but Biocentric do not currently provide other test kits (other than the Generic HIV DNA assay for infant diagnosis)
	Amplification & detection: any Real Time thermocycler [e.g. CFX96 Touch Real-Time PCR Detection System (Bio-Rad)]		

Continued overleaf

02 | PRICING

Instrument	Reference number	Cost (US$) EXW	Cost (US$) FCA	Reagents kits	Reference number	Cost (US$) EXW	Not included in kit, but required	Reference number	Cost (US$) FCA
Extraction/sample preparation				**Extraction/sample preparation**			**Extraction/sample preparation**		
Manual				**Manual**			**Manual**		
Qiagen manual extraction using QIAamp Viral RNA mini kit (20 samples at a time /45 minutes to result)	52904 or 52906	contact Qiagen	contact Qiagen	QIAamp viral RNA kit (250)			Qiagen		
Automatic				QIAamp Mini Spin Columns			1. Ethanol (96–100%)		
NorDiag Arrow (12 samples per run/45 minutes to result)	8.31.01	$15,275	$15,581	1. Collection Tubes (2mL)			2. 1.5mL microcentrifuge tubes		
Amplification and detection				2. Buffer AVL	52906	$1,105	3. Sterile, RNase-free pipette tips (pipette tips with aerosol barriers for preventing cross-contamination are recommended)		
CFX96 Touch Real-Time PCR Detection System (Bio-Rad)	185-5196	$39,000	$39,325	3. Buffer AW1 (concentrate)			4. Collection tubes (1.5 and 2.0mL) (Qiagen) (for manual extraction)		
Assay, extractor & thermocycler			$54,581	4. Buffer AW2 (concentrate)			5. Microcentrifuge (with rotor for 1.5mL and 2mL tubes)		
				5. Buffer AVE					
				6. Carrier RNA (poly A)					
				7. Handbook					
				Automatic			**Automatic extraction**		
				Arrow Viral NA test (96 preps)			Arrow Viral NA items		
				1. Magnetic Bead in Storage Buffer (1x500µL) >25% surface coated magnetic beads, >50% MQ H2O, <0.005% Sodium azide			1. Proteinase K (100mg/mL)		
				2. Lysis solution (1x800µL) 40-70% GITC, <10% salt solution, <50% detergent			2. Sample tubes		
				3. Wash Solution I (1x1700µL) 20-35% GITC, <5% salt solution, <25% detergent, 50% Isopropanol	12.08.02	$715	3. Elution tubes (optional brand)		
				4. Wash Solution II (1X1200µL) 40-70% EtOH			4. Piercing tool		free
				5. Elution buffer (1x400µL) <12 mM Tris			Gloves	405-002-100	$51.61
				6. Isopropanol (1x1300µL)			Pipettes with filter tips		
				7. MQ H^2O (2x2500µL)			5. Commercial liquid household bleach, 5.25% hypochlorite solutions or equivalent for sterilisation of instrument		240.50
				8. 98 pumps					
				9. 96 tips					
				10. 1 instructions for use					
				Amplification and detection			**Amplification & detection**		
				220 Generic HIV viral load assay			Bio-Rad items		
				1. Primers			Bio-Rad microplates (50)	HSP-9655	$240.50
				2. Probes	TR001-250	$2,171	Plate sealers		$1,950
				3. Enzyme mix			Sarstedt screw cap microtubes (1,000)	72.692.405	$175.50
				4. Standards					
				5. Controls					
				440 Generic HIV viral load assay	TR001-440	$3,796			
				Cost per test result* (manual)		**$13**			
				Cost per test result* (automatic)		**$16**			

*Includes consumables.

03 | TIERED AND VOLUME-BASED PRICING

No Information Provided

04 | MAINTENANCE, WARRANTY & TRAINING

	Description	Cost (US$) (FCA)
Leasing or reagent rental for instruments	None.	
Installation	Takes 1 day; see turnkey option.	
Training	Takes 3 days.	
Maintenance	Full maintenance needs to be renewed each year.	
Length(s) of warranty and additional costs for an extended warranty	Not provided.	
Warranty components	Not provided.	
Turnkey option	Turnkey option including 2 Arrows and all disposables (includes everything to make a lab operational), not counting transport of goods, no minimum number of assays.	$78,000

05 | CONTACT INFO

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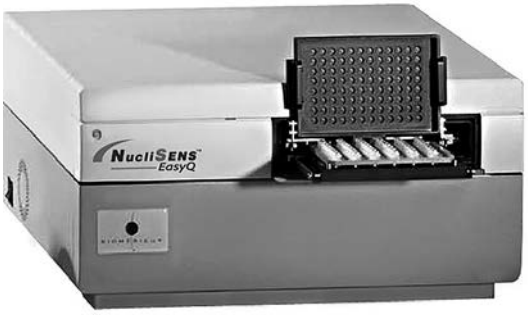
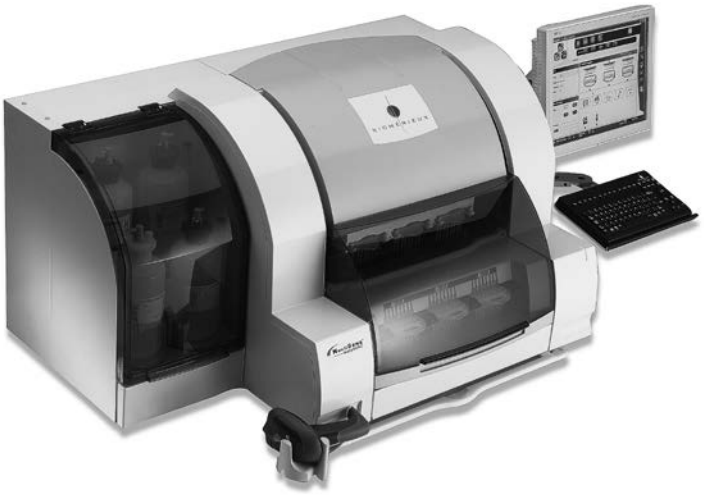
LAB-BASED VIRAL LOAD
bioMÉRIEUX





01 | TECHNICAL INFORMATION

Company	bioMérieux	**Product**	NucliSENS EasyQ HIV-1 v2.0
Assay type	Real time NASBA Isothermal signal amplification Detection with molecular beacons	**Mean time between failures**	Easy MAG: 384 days; EasyQ: 5 years
Technological set-up for extraction	Semi or automated closed system (MiniMAG or Easy MAG). Extraction eluate can be used on other platforms	**Transport**	Transport should be studied on a case by case basis depending the incoterm and product
Technological set up for amplification, detection	semi Automated closed system (EasyQ)	**Storage**	2–8°C amplification reagents; 2–30°C extraction reagents (buffers 1, 2 and lysis buffer); 2–8°C Buffer 3 and magnetic silica
Target	HIV-1 RNA gag	**Fridge at -80°C required?**	Not required unless EDTA plasma samples are stored for more than 1 month; in this case samples should be placed at -70°C and remain stable for maximum 1 year
HIV-1, HIV-2, Subtypes	HIV-1 group M (A-J), HIV-1 CRF (CRF01_AE, CRF02_AG and others)	**Shelf life (each item in the kit)**	Extraction and lysis buffers Easy MAG, Magnetic silica, Easy MAG and Easy Q disposable, Strip plates Greiner: > 7 months Extraction Magnetic reagent MiniMAG: > 4 months Micro tubes 1,5mL, NucliSENS EASY Q HIV V2O Kit: > 5 months
Linear Range	25–10,000,000 copies/mL	**Technical Skill**	Medium-highly trained, precision pipetting required at low volumes
Time to Result	2.5–3 hours including extraction	**Laboratory Set-Up**	Specialised; 2–3 dedicated areas required
Throughput	MiniMAG: Up to 144 specimens/day (6 runs of 21, 2 MiniMAG at the same time); Easy MAG: Up to 168 extractions per shift – Lysis on board workflow / Up to 240 extractions – Lysis in tube workflow; EasyQ: Up to 192 samples (4 runs of 48)	**Waste disposal requirements**	Container for solid waste, container for liquid waste, waste plastic bags
Sample Type	Plasma, serum, DBS on EDTA and capillary blood, body fluids	**Applicable Settings**	Technology can be used at regional / central level or national reference (or comparable) laboratories; Access to decentralised settings via DBS
Sample Volume	100µL, 500µL, 1mL of plasma and any other interim quantity	**Regulatory Approval**	WHO PQ, CE IVD, (plasma and EDTA + capillary DBS)
Kit sizes	NucliSENS Easy Q HIV-1 V2 Ref 285033; Kit contains 48 tests	**Connectivity options for mobile health & electronic access**	Can be linked with LIS using NucliSENtral, an integrated software system that can link Nuclisens Easy MAG and NucliSENS EasyQ to a Laboratory Information System
Controls	Internal controls		
Equipment required	Extraction: miniMAG (semi-automated), Easy MAG (automated)	**Polyvalency**	Yes, other kits available on Nuclisens platform: Enterovirus, HPV, HSV, KPC, MRSA
	Amplification & detection: Easy Q		

02 | PRICING

Instrument	Catalogue number	Cost (US$) EXW	Reagents kits	Catalogue number	Cost (US$) EXW	Not included in kit, but required	Catalogue number
Extraction (only one required)			**Extraction (only one required)**			**Extraction (only one required)**	
Semi-automated			**miniMAG (semi-automated)**			**miniMAG**	
miniMAG (12 extractions/run)	4700015	$9,000.00	NucliSENS lysis buffer 2mL (48 tests)	200292		Micro tubes 1.5mL (500 tubes & 500 caps)	200294
Automated			NucliSENS Magnetic Extraction Reagents (48 tests)	200293		Centrifuge 1500g for Lysis buffer tube 15mL	
Easy MAG (48 extractions/run)	4700014	$49,000.00	**Easy MAG (automated)**			Thermo Shaker for 1.5mL microtubes (Eppendorf)	5350 000.013
Keyboard AZ	280154		Extraction Buffer 1 (4 x 1 litre)	280130		Highly recommended: vacuum pump with intermediate recipient for eluant (IBS Integra biosciences)	158320
Keyboard QW	280155		Extraction Buffer 2 (4 x 1 litre)	280131		Vortex	
Easy MAG Biohit Adapter – US	280147		Extraction Buffer 3 (storage 2–8°C) (4 x 1 litre)	280132		ELISA microplates	
Easy MAG Biohit Adapter – AU	280148		Magnetic Silica (384 extractions)	280133		Rack for 15mL tubes	
Easy MAG Biohit Adapter – EU	280149		Lysis Buffer (4 x 1 litre)	280134		Rack for 1.5mL tubes	
Easy MAGBiohit Adapter – JP	280150		Disposables (48 x 8 tests)	280135		Pipette 10 to 100µL	
Easy MAG Biohit Adapter – UK	280151		NucliSENS lysis buffer 2mL tubes (48 tests)	200292		Pipette 20 to 200µL	
Amplification and detection			**Amplification and detection**			Pipette 100 to 1000µL	
Easy Q (48 extractions/run)	4700016	$95,000.00	NucliSENS EasyQ HIV-1 V2.0 (48 tests)	285033		Non filtered tips for vacuum	
Strip centrifuge (220v)	285056	$1,500.00				Filtered tips 10–100µL	
UPS converters UPS APC 1500 VA EU	413647	$1,200.00				Filtered tips 20–200µL	
Printer LEXMARK E360DN 230V	93621	$320.00				Filtered tips 100–1000µL	
bioMérieux DBS Puncher**	411 022	$2,000.00				Detergent	1075552500
						Additional materials for Easy MAG	
						Filter tips for multichannel bioHIT (10 X 96 tips)	280146
						Easy MAG disposables (48 X 8 tests)	280135
						Strip plate (Greiner) (100 X 96wells)	278303
						Amplification and detection	
						Additional materials for the EasyQ	
						8-Tube Strips (125 X 8 tests)	285048
						8-Tube Caps (125 X 8 tests)	285051
						DBS materials**	
						Whatman 903 paper example: Protein Saver	10531018
						Plastic zip lock bags (for storage)	10548232
						Dessicant packs without indicator (for storage)	10548234
						Humidity indicator	
						Roller mixer	SRT6
			Cost per test result*		**$23.40**		

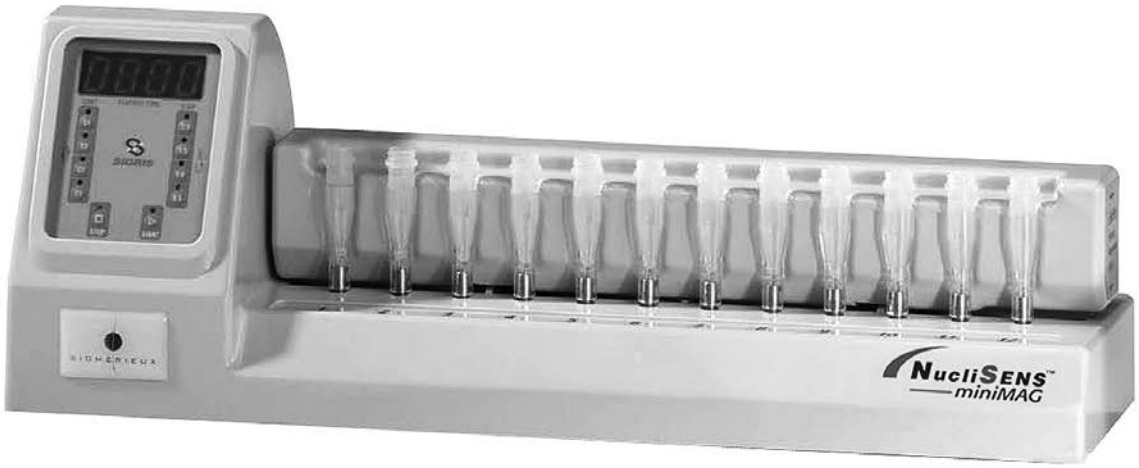
Note: all prices are approximate.
*Includes reagent kit and disposables (extraction, amplification, detection).
** bioMérieux DBS puncher recommended, but other DBS punchers can be used.

Continued overleaf

Lab-based Viral Load – bioMérieux continued

03 | TIERED AND VOLUME-BASED PRICING

No Information Provided



04 | MAINTENANCE, WARRANTY & TRAINING

Item	Description
Leasing or reagent rental for instruments	These options can be considered on a case-by-case basis.
Installation	Included in the EXW price of the equipment.
Training	Training of two people maximum in the laboratory during three days maximum is included in the price of equipment. Please contact bioMérieux if you require any additional personnel. Travel expenses are included.
Maintenance	Preventive and corrective maintenance is provided by the bioMérieux legal representative in the country of destination, following bioMérieux procedures and recommendations. Warranty extensions will be considered on a case-by-case basis.
Length(s) of warranty and additional costs for an extended warranty	A warranty period of 15 months is included in the instrument price, from the date of shipping by the bioMérieux International Delivery Centre in Saint Vulbas, France. Warranty extensions will be considered on a case-by-case basis.
Warranty components	The bioMérieux warranty covers the instrument, parts and labour, for a period of 15 months from the shipping date of the bioMérieux International Delivery Centre in Saint Vulbas, France. Disposable and replacement items with a normal life expectancy of less than one year such as, but not limited to, batteries, lamps and tubing, are excluded from this warranty.

05 | CONTACT INFO

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LAB-BASED VIRAL LOAD
CAVIDI

01 | TECHNICAL INFORMATION

Company	Cavidi	**Product**	ExaVir Load
Assay type	ELISA of reverse transcriptase activity using colorimetric detection	**Controls**	RT activity control included; positive, negative plasma control not included
Technological Set-up	Not fully automated but closed system	**Equipment required**	Microplate reader with A405 filter, incubator (33°C), freezer (-20°C), end-over-end mixing table
Extraction method/ sample preparation	N/A	**Mean time between failures**	No equipment failures recorded to date
Target	Reverse transcriptase activity	**Transport and Storage**	Transport and store frozen, -14 to -25°C
HIV-1, HIV-2, Subtypes	HIV-1 (all subtypes) and HIV-2; Type- and subtype independent	**Fridge at -80°C required**	No
Linear Range	~200–600,000 RNA copies/mL equivalent	**Shelf life (each item in the kit)**	Two years at delivery
Time to Result	48 hours (including 5 hours of hands-on time)	**Technical Skill**	Low-moderate training required; precision pipetting required
Throughput	30 samples/run = 30–60 samples/2day or <180/week	**Laboratory Set-Up**	Not-specialised, single work area; freezing required
Sample type	Plasma	**Waste disposal requirements**	Follow local SOPs for hazardous waste handling
Sample volume	1mL	**Applicable settings**	Technology can be used at central, regional, and district hospitals, and some well developed primary hospitals
Kit components	Reagents and consumables	**Regulatory approval**	CE-IVD marked
Kit sizes	30 samples + 2 controls /kit	**Connectivity options for mobile health & electronic access**	N/A
Components required outside the kit (i.e. buffers)	Purified water	**Polyvalency**	None

Continued overleaf

Lab-based Viral Load – Cavidi continued

02 | PRICING

Instrument	Catalogue number	Cost (US$) FCA	Reagents & consumables	Catalogue number	Cost (US$) FCA	Not included in kit, but required
Sample box with lid			EXAVIR Load Kit (includes reagents & consumables)	55011	$360 - $750 per kit (30 tests plus 2 controls)	One-in house positive control
Buffer dispenser			**Reagents**			One-in house negative control
Column holder			1 Sample Additive (Reconst. to 4mL)			Purified water
Waste collector			1 Separation Gel (36mL)			General disinfectant
Collector tube rack			1 Gel Buffer 1 conc. (120mL)			ELISA-plate reader with A_{405} filter
Lysate collector			1 Gel Buffer 2 conc. (21mL)			Incubator set at 33°C
Rack containing 96 storage tubes	59311 (230 V)		1 Lysis Buffer (24mL)			Freezer set at -14 to -25°C
3L wash buckets	59310 (110 V)		1 Lysis Buffer Additive (Reconst. to 24mL)			End-over-end mixing table
Container, 5L			1 RT Reaction Plate (96 wells)			Vortex
Waste container			1 RT Reaction Buffer (12.5mL)			Single channel pipettes 100–1,000µL
Vacuum pump			1 RT Reaction Components (Reconst. to 4mL)			Multi-channel pippettes 30–200µL
Vacuum tubing			1 Dilution Buffer (24mL)			Reservoirs for multi-channel pipettes
Plastic bottles, 250mL and 2L			1 Dilution Buffer Additive (Reconst. to 24mL)			Pipette filter tips (1,000µL)
CD with ExaVir Load Analyzer software			1 HIV-1 rRT Standard (Reconst. to 6mL)			Pipette tips (200µL)
			1 Plate Wash Buffer conc. (80mL)			25mL bottle/tube
			1 RT Product Tracer (Reconst. to 12mL)			Absorbing paper
			1 Product Tracer Dissolvent (12.5mL)			Plastic Pasteur pipettes
			1 Substrate Tablet (15mg)			Computer with Microsoft Excel and Adobe Reader
			1 Substrate Buffer (30mL)			
			1 HIV-1 rRT Standard Sheet			
			Consumables			
			32 Plasma Processing Tubes with separate caps			
			32 Columns			
			48 Storage Tubes			
			2 Pieces of Adhesive Tape			
			1 Plastic lid for 96-well plate			
			Rubber bands			
Instrumentation total		**$4,500**	**Cost per test result***		**$12 – $25**	

*Includes consumables and reagents.

03 | TIERED AND VOLUME-BASED PRICING | No Information Provided

04 | MAINTENANCE, WARRANTY & TRAINING

Item	Description	Approximate Costs (US$) FCA
Leasing or reagent rental for instruments	Purchase, leasing and reagent rental options can be offered.	Offered and negotiated upon request.
Insurance for instrumentation	None provided.	
Installation		Wherever we have representation, we do installation free of charge. If it is a new market for Cavidi, only travel costs are charged (can also be negotiated).
Training	Training takes 4-5 days. Up to the lab how many people to include.	Only travel costs are charged.
Maintenance	The ExaVir Load instrument only requires disinfection and washing. Maintenance of the microplate reader, while not part of our equipment supply, may be offered by the Cavidi local representative.	Cost varies depending on make of reader and country, and will be provided upon request.
Warranty components	None provided.	
Turnkey option	None provided.	

05 | CONTACT INFO

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LAB-BASED VIRAL LOAD
QIAGEN

01 | TECHNICAL INFORMATION

Company	Qiagen	**Product**	artus HI Virus RG/QS-RGQ RT-PCR
Assay type	RT PCR with fluorescence detection	**Equipment required**	Rotor-Gene Q, Vortex mixer, Benchtop centrifuge
Technological Set-up	Semi-automated or automated, closed system	**Mean time between failures**	Not provided
Extraction method/ sample preparation	Manual (QIAamp DSP Virus Kit) or automated (QS-RGQ)	**Transport and Storage**	Store the artus HI Virus-1 RG RT-PCR Kit at -20°C, with some variation by reagent
Target	HIV-1 RNA LTR	**Fridge at -80°C required**	No
HIV-1, HIV-2, Subtypes	HIV-1: Group M (A-H)	**Shelf life (each item in the kit)**	All reagents are stable until the expiration date stated on the label
Linear Range	RG: 60-50,000,000 copies/mL; QS-RGQ: 45–45,000,000 (LOD 34 c/mL)	**Technical Skill**	Medium-highly trained, precision pipetting required at low volumes
Time to Result	5–6 hours (per 24 reactions)	**Laboratory Set-Up**	Specialised: RG 3; QS-RGQ: 2 dedicated areas are required
Throughput	Up to 67 samples/run	**Waste disposal requirements**	Not provided
Sample type	Plasma	**Applicable settings**	Highly resourced settings
Sample volume	RG: 500µL; QS-RGQ: 1,000µL	**Regulatory approval**	CE-IVD
Kit sizes	24 or 72 reactions	**Connectivity options for mobile health & electronic access**	None provided
Controls	Internal control; standard supplied at 4 different concentrations	**Polyvalency**	HBV, CMV, EBV, C. trachomatis, M. tuberculosis

02 | PRICING

Instrument	Reference number	Cost (US$) EXW	Reagents kits	Reference number	Cost (US$) EXW	Not included in kit, but required	Reference number
Extraction/sample preparation			**Extraction/sample preparation**			**Extraction/sample preparation**	
QIAsymphony SP	9001297		**Manual extraction**			QIAsymphony SP instrument	9001297
QIAsymphony AS	9001301		QIAamp DSP Virus Kit (50 preps)	60704 (50 preps)		QIAsymphony AS instrument	9001301
QIAsymphony Cabinet SP/AS	9020246		QIAamp MinElute Columns			**Amplification and detection**	
Amplification and detection			Buffers			Rotor-Gene Q software version 2.1, or higher	
Rotor-Gene Q MDx 5plex HRM platform	9001580		Reagents			Optional: Rotor-Gene Assay Manager version 1.0, or higher	
Inclusive instrumentation package			Tubes			**Other materials**	
QIAsymphony RGQ system (includes QIAsymphony SP, QIAsymphony AS, Rotor-Gene Q MDx 5plex HRM, required accessories and consumables)	9001850		Column extenders			Pipettes (adjustable) and sterile pipette tips with filters	
			VacConnectors			Vortex mixer	
			Multilanguage handbook			Benchtop centrifuge with rotor for 2mL reaction tubes, capable of centrifugation at 6800 x g	
			Automated extraction				
			QIAsymphony DSP Virus/Pathogen Midi Kit	937055 (96 samples)			
			2 reagent cartridges				
			Enzyme racks				
			Accessories				
			Amplification and detection				
			Manual				
			artus HI Virus-1 RG RT-PCR Kit (24) CE				
			2 Masters	4513263 (24 reactions)			
			4 Quantitation standards				
			Internal control				
			Water (PCR)				
			Automated				
			artus HI Virus-1 QS-RGQ Kit (24 reactions)	4513363 (24 reactions)			
			HI Virus-1 RG Master A (4 x 144µl)				
			HI Virus-1 RG Master B (4 x 216µl)				
			HI Virus-1 RG QS 1 (1x 104 IU/µl) 200µl				
			HI Virus-1 RG QS 2 (1x 103 IU/µl) 200µl				
			HI Virus-1 RG QS 3 (1x 102 IU/µl) 200µl				
			HI Virus-1 RG QS 4 (1x 101 IU/µl) 200µl				
			HI Virus-1 RG IC (internal control) 1000µL				
			Water (PCR grade) 1000µl				
			Handbook				
			artus HI Virus-1 QS-RGQ Kit (72 reactions)	4513366 (72 reactions)			
			Cost per test result*		**$16–$35 per test***		

Note: Prices will vary considerably depending on quantities, infrastructure and support required plus special negotiations.
*Includes extraction, controls, reagents and consumables.

Continued overleaf

Lab-based Viral Load – Qiagen continued

03 | TIERED AND VOLUME-BASED PRICING

No Information Provided

04 | MAINTENANCE, WARRANTY & TRAINING

	Description
Leasing or reagent rental for instruments	Available on a case-by-case basis, purchase, reagent rental.
Insurance for instrumentation	Not provided.
Installation	Not provided.
Training	Not provided.
Maintenance	Not provided.
Warranty components	Not provided.
Turnkey option	Not provided.

05 | CONTACT INFO

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LAB-BASED VIRAL LOAD
ROCHE

01 | TECHNICAL INFORMATION

Company	Roche	**Product**	COBAS Ampliprep/COBAS TaqMan HIV-1 monitor version 2.0
Assay type	RT PCR using detection by FRET	**Equipment required**	COBAS AmpliPrep plus COBAS TaqMan 48 or Analyzer (96)
			Docking station – to dock CAP to CTM96
Technological Set-up	Fully automated, closed system		For DBS application: a Thermomixer compact is required (package insert)
Extraction method/ sample preparation	Automated (docked and undocked options)	**Mean time between failures**	Cobas Ampliprep (114 days between failures)
			Cobas Taqman Analyzer (96) (236 days between failures)
			Cobas TaqMan 48 (850 days between failures)
Target	HIV-1 RNA gag and LTR	**Transport and Storage**	Refrigeration required 2 to 8°C
HIV-1, HIV-2, Subtypes	HIV-1: Group M (A-H), group O	**Fridge at -80°C required**	No
Linear Range	20–10,000,000 copies/mL	**Shelf life (each item in the kit)**	Average 6 months
Time to Result	5–8 hours	**Technical Skill**	Medium-highly trained, precision pipetting required
Throughput	Taqman 48 (21 samples/run; 20–100 tests/day); Taqman 96 (63 samples/run; 100–250 tests/day)	**Laboratory Set-Up**	Specialised; 1 dedicated area required for Cobas Ampliprep Cobas Taqman 96 with docking station. Preferably 2 dedicated areas for Cobas Ampliprep Cobas TaqMan 48 option.
Sample type	Plasma, DBS (RUO)	**Waste disposal requirements**	According to the regulations for each country
Sample volume	200µl–1mL plasma; 1 DBS (60–70µl)	**Applicable settings**	Medium to highly-resourced settings
Kit sizes	48 tests	**Regulatory approval**	WHO-PQ, CE-IVD, US-FDA-IVD, Canada-IVD, Japan-IVD (plasma)
Controls	Internal; 4 sets of controls per kit consisting of a Negative, Low Positive, High Positive Controls	**Connectivity options for mobile health & electronic access**	Yes, laboratory information systems connectivity and interface to mobile systems available
		Polyvalency	HIV DNA kit for infant diagnosis, Hepatitis B&C, M. tuberculosis, Clamydia, CMV

Continued overleaf

Lab-based Viral Load – Roche continued

02 | PRICING

Instrument	Catalogue number	Cost (US$) CPT*	Turnkey	Reagents kits	Catalogue number	Cost (US$) CPT
Sample preparation				**Sample preparation**		
Cobas Ampliprep (72 samples/run)	3051315001	$80,000 - $100,000		Tube-K Box of 12x96/Cob.TaqMan	3137082001	
Amplification and detection				SPU of 12x24/Cob.AmpliP	3755525001	
Cobas TaqMan 48 Analyzer Taqman 48 (21 samples/run; 20–100 tests/day)	3279332001	$40,000 – $50,000	$180,000 – 200,000	Tube-S Box of 12x24/Cob. AmpliP	3137040001	
Cobas TaqMan96 Analyzer with docking station Taqman 96 (63 samples/run; 100–250 tests/day)	3121453001	$100,000 – $110,000	$240,000 – $260,000	Tip-K 1,2 mm ID Box of 12 x36	3287343001	
				COBAS AMPLIPREP / COBAS TAQMAN Wash Reagent	3587797190	
				For DBS, additional reagent	5035970190	
				1000µl micro-pipette tips		
				Amplification and detection		
				KIT CAP-G/CTM HIV-1 V2.0 EXPT-IVD	5212294190	
				HIV-1 v2.0 CS1 1 x 48 Tests (HIV-1 Magnetic Glass Particles Reagent Cassette)		
				HIV-1 v2.0 CS2 1 x 48 Tests (HIV-1 Lysis Reagent Cassette)		
				HIV-1 v2.0 CS3 1 x 48 Tests (HIV-1 Multi-Reagent Cassette containing: Protease & Elution Buffer)		
				HIV-1 v2.0 CS4 1 x 48 Tests (HIV-1 Test-Specific Reagent Cassette containing: Quantitative standard, Master Mix, Manganese 2+)		
				HIV-1 H(+)C, v2.0 4 x 1.0mL (HIV-1 High Positive Control, v2.0)		
				HIV-1 L(+)C, v2.0 4 x 1.0mL (HIV-1 Low Positive Control, v2.0)		
				CTM (–) C 4 x 1.0mL (COBAS TaqMan Negative Control (Human Plasma))		
				Cost per test result*	**This applies to all LDCs or countries in SSA with high HIV burdens**	**$11–25**

The agent is able to charge an additional commission within a specific price range that has been agreed by Roche for any international public health initiative. The price commission is usually country, location, and infrastructure-dependent and also depends on the support required for the distributor in the region.
*Prices provided include consumables and are all CPT unless insurance is required, in which case prices are CIF.

03 | TIERED AND VOLUME-BASED PRICING

	Income levels*	
Pricing range	**Low***	**Other**
TaqMan HIV-1 Monitor test 2.0	$11–25	$35–90
Cost per result (CPT)	LDC: $11–25	

*"Low-income" includes includes all countries in sub-Saharan Africa (SSA) and selected low-income countries in Asia-Pacific and Latin America and Central America; other refers only to sub-Saharan Africa. Pricing is volume-based and Roche negotiates with individual funders/donors/governments depending on the scale of the programme. The pricing provided is broadly what is known in the public domain but remains negotiable depending on the envisaged scale of the programme.

04 | MAINTENANCE, WARRANTY & TRAINING

	Description	Cost (US$) (CPT)
Leasing or reagent rental for instruments	Outright purchase, leasing and rental are available dependent on contractual volume commitment with mitigating risk assessment.	Equipment price range is variable depending on choice of 1) outright instrument purchase 2) reagent rental or 3) volume dependant tiered pricing option.
Installation	A turnkey laboratory solution is offered inclusive of Roche equipment, third-party equipment, implementation, training and 3 year service and support.	Incorporated as part of turnkey laboratory.
Training		Incorporated as part of turnkey laboratory.
Maintenance	Year 1: Full warranty covered by Roche; Year 2: Comprehensive service contracts are offered by locally trained contractors/distributors in country. Negotiated fee based on preventative maintenance and call outs.	Tiered pricing based on volume. Variable by disease burden and by UN income classification.
Length(s) of warranty and additional costs for an extended warranty	12 months from installation date.	
Turnkey option	Roche equipment, third party equipment, implementation, training (on-site and off-site) and 3 year service and support. This is customisable according to current laboratory infrastructure.	

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LAB-BASED VIRAL LOAD
SIEMENS (VERSANT bDNA)

01 | TECHNICAL INFORMATION

Company	Siemens	**Product**	VERSANT HIV-1 RNA 3.0 Assay (bDNA)
Assay type	Branched-DNA (bDNA), a signal amplification using ELISA-format with chemiluminescent detection	**Controls**	No internal controls; negative, low positive and high positive controls
Technological Set-up	Semi-automated	**Equipment required**	VERSANT 440 Molecular System. Centrifuge, heat block or water bath.
Extraction method/ sample preparation	No extraction of nucleic acids required	**Mean time between failures**	Not provided
Target	HIV-1 RNA pol	**Transport and Storage**	Refrigeration required, 2–8°C: assay box A; down to -80°C: assay box B
HIV-1, HIV-2, Subtypes	HIV-1: Group M (A-G)	**Fridge at -80°C required**	Yes
Linear Range	50–500,000 copies/mL	**Shelf life (each item in the kit)**	12 months (expanding to 18)
Time to Result	Up to 22 hours for a full plate run (96 test)	**Technical Skill**	Molecular practices expertise needed. Easy-of-Use technology
Throughput	12–168 patient samples/run	**Laboratory Set-Up**	Single room technology
Sample type	Plasma	**Waste disposal requirements**	Not stipulated
Sample volume	1mL	**Applicable Settings (national hospital/provincial or regional/ district or primary/government community health center)**	Highly resourced settings
Kit components	VERSANT HIV-1 RNA 3.0 Assay (bDNA) Box A + Box B 96 Tests + 2 set of Standards and Controls (10327028)	**Regulatory approval**	CE-IVD, US-FDA-IVD
Kit sizes	96 test/kit	**Connectivity options for mobile health and electronic databases**	LIS Interface capability
Components required outside the kit (i.e. buffers)	Only plastic consumables	**Polyvalency**	Hepatitis B&C

02 | PRICING

Instrument	Catalogue number	Cost (US$) EXW	Reagents kits (reference number)	Catalogue number	Cost (US$) EXW	Not included in kit, but required	Catalogue number
VERSANT 440 system	02104561		VERSANT HIV bDNA 3.0 Assay	7826476		Reagent Tube 0,5mL	09741478
						Reagent Tube 30mL	06635146
						Reagent Tube 4,5mL	05661712
Cost per instrument		**$55,400**	**Cost per test result***		**$36 – 72**		

*Includes all items to run assay: amplification, extraction, controls, calibrators.
Note: all prices listed are estimates from the UNITAID HIV/AIDS diagnostics technology landscape - 2nd edition (June 2012)[73]

03 | TIERED AND VOLUME-BASED PRICING | No Information Provided

04 | MAINTENANCE, WARRANTY & TRAINING | No Information Provided

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LAB-BASED VIRAL LOAD
SIEMENS (VERSANT kPCR)

01 | TECHNICAL INFORMATION

Company	Siemens	**Product**	VERSANT HIV-1 RNA 1.0 Assay (kPCR)
Assay type	Kinetic PCR	**Controls**	Internal controls; negative, low positive and high positive controls
Technological Set-up	Fully automated, closed system	**Equipment required**	VERSANT kPCR molecular system
Extraction method/ sample preparation	Automated using proprietary beads	**Mean time between failures**	N/A
Target	HIV-1 RNA pol	**Transport and Storage**	Refrigeration required. VERSANT HIV-1 RNA (kPCR) Kit, Box 1 (10375763) -30°/-10°C; VERSANT HIV-1 RNA (kPCR) Kit, Box 2 (10375764) -90/-60°C; VERSANT Sample Preparation 1.0 Reagents Kit (Box 1 + Box 2) (10472144); Box 1: 15/30°C; Box 2: 2/8°C
HIV-1, HIV-2, Subtypes	HIV-1: group M (A-H, CRF01_AE, CRF02_AG), Group O	**Fridge at -80°C required**	Yes
Linear Range	37–11,000,000 copies/mL	**Shelf life (each item in the kit)**	12 months
Time to Result	up to 6 hours for a full plate run (96 tests)	**Technical Skill**	Molecular practices expertise required. Easy-of-Use having a low impact on users.
Throughput	89 patient samples/run, 178 patient samples/shift	**Laboratory Set-Up**	System concept supports either 1- or 2-room technologies
Sample type	Plasma	**Waste disposal requirements**	Not stipulated
Sample volume	500µL plasma	**Applicable Settings**	Highly-resourced settings
Kit components	VERSANT HIV-1 RNA (kPCR) Kit, IVDD Box 1 & 2 and VERSANT Sample Preparation 1.0 Reagents Kit (Box 1 + Box 2)	**Regulatory approval**	CE-IVD Directive 98/79/EC
Kit sizes	96 test/kit	**Connectivity options for mobile health and electronic databases**	LIS Interface capability
Components required outside the kit (i.e. buffers)	Plastic consumables (e.g. tips, plates)	**Polyvalency**	Hepatitis B&C, CT/GC

02 | PRICING

Instrument	Catalogue number	Cost (US$) EXW	Reagents kits (reference number)	Catalogue number	Cost (US$) EXW	Not included in kit, but required	Catalogue number
Sample preparation			**Sample preparation**			Disposable Tips 1mL Filtered (8 X 480 tips per case)	06635759
kPCR Sample Prep Sub-system	10282928		VERSANT Sample Preparation 1.0 Reagents Box 1	4801677		Disposable Tips 300µl Filtered (12 X 480 tips per case)	06635767
			VERSANT Sample Preparation 1.0 Reagents Box 2	4801675		Sample Prep Reagent Trough Kit per 20 Sleeves of 6 Containers	10489008
Amplification and detection			**Amplification and detection**			Ultra Clear Cap Strips (120 strips of 8)	06653439
kPCR Amp/ Detect Instrument	10282939		Versant HIV-1 RNA (kPCR) Kit, IVDD Box 1	10375763		96 Deep Well Plate 2mL (case of 60 plates)	06691055
kPCR SW Installation kit	10813498		Versant HIV-1 RNA (kPCR) Kit, IVDD Box 2	10375764		PCR Plates Bar coded (25 per)	06653412
BACK-UPS 1500VA	10638181					Bag Waste Bio Hazard (200 per)	06635856
kPCR AD Workstation	10702393						
kPCR SP Workstation	10702391						
Mini Plate Spinner	10484522						
			Cost per test for reagents		**$43.25–57.70**		
			Cost per test for sample preparation materials		**$10.80–14.40**		
Cost per instrument		**$166,200–221,600**	**Cost per test result***		**$54.05–72.10**		

*Includes all items to run assay: amplification, extraction, controls, calibrators.
Note: all prices listed are estimates from the UNITAID HIV/AIDS diagnostics technology landscape – 2nd edition (June 2012)[73]

03 | TIERED AND VOLUME-BASED PRICING | No Information Provided

04 | MAINTENANCE, WARRANTY & TRAINING | No Information Provided

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POINT-OF-CARE VIRAL LOAD
NORTHWESTERN GLOBAL HEALTH FOUNDATION (p24 Antigen Test for infant diagnosis)

01 | TECHNICAL INFORMATION

Company	Northwestern Global Health Foundation (NWGHF)	**Product**	LYNX HIV p24 Antigen Test
Assay type	Heat-denatured, immunochromographic test	**Equipment required**	LYNX HIV p24 Antigen Test Processor
Technological Set-up	Portable, POC device; 1 sample tested sequentially; fully automated and closed system; no batching capability; no maintenance	**Mean time between failures**	5 years, assuming a battery switch at year 2 or 3
Extraction method/ sample preparation	N/A	**Transport and Storage**	No refrigeration required
Target	p24 (core protein)	**Fridge at -80°C required**	No
HIV-1, HIV-2, Subtypes	TBD	**Shelf life (each item in the kit)**	TBD
Linear Range	Visually read test; Limit of detection > 50pg/mL	**Technical Skill**	Minimally trained
Time to Result	45–50 minutes	**Laboratory Set-Up**	Laboratory not required; heat block is battery powered (battery lasts 3 years)
Throughput	12 samples/day	**Waste disposal requirements**	Test waste disposal necessary
Sample type	Capillary blood	**Applicable settings**	Decentralised facilities including mobile clinics, RLS
Sample volume	~80µL (heelstick)	**Regulatory approval**	TBD
Kit sizes	10	**Connectivity options for mobile health & electronic access**	Yes
		Polyvalency	Anticipated
Controls	Internal control; lateral flow device cannot be retested	**If Pipeline - confirm 1launch date**	The LYNX HIV p24 test is expected to begin independent evaluation in second quarter of 2013. Pending a successful independent evaluation, the test will be made commercially available in late 2013

02 | PRICING

Instrument	Reference number	Cost (US$) EXW	Cartridge/reagents	Reference number	Cost (US$) EXW
LYNX HIV p24 Antigen Test Processor (1 test/run, 45–50 min/run)	TBD	$700–900	LYNX-HIV p24 Antigen Test	TBD	
			Blood Collection Tube (12)		
Battery & AC adapter		Included in device	LYNX Plasma Separator (10)		
Cellular modem	TBD	$200	LYNX Buffer (10)		
			LYNX Test Strip (10)		
			Package Insert (1)		
			Gloves (20)		
			Lancet (10)		
			Alcohol Swab (10)		
			Gauze (10)		
			Cost per test kit (10 tests)		**$65–150**
Instrumentation costs		**$900-1,100**	**Cost per test result**		**$6.50–15.00**

Shipping cost widely varies depending on the size of the order as well as by the region for delivery. The use of a third party distributor to be determined.

03 | TIERED AND VOLUME-BASED PRICING

LYNX HIV p24 Antigen Test Processor		Each LYNX HIV p24 Antigen Test Kit	
Volume	**Price per device**	**Volume**	**Price per device**
100	$900	25,000	$15
250	$800	50,000	$10
1, 000	$700	100,000	$9
		500,000	$6.50

Tiered pricing anticipated based on volume, but not economic tier.

04 | MAINTENANCE, WARRANTY & TRAINING

	Description	Cost (US$) (CPT)
Leasing or reagent rental for instruments	Leasing, lease to buy option, and reagent rental options anticipated.	
Installation	N/A	TBD
Training	NWGHF recommends a 'train the trainer' model, whereby several 'super-users' are selected by the customer to perform further training in the field. Training materials will be provided by NWGHF for these purposes.	$1,000 per training.
Maintenance	NWGHF plans to offer a 1–2 year warranty for the Processor. If the instrument breaks down within that year, NWGHF plans to have the local distributor swap out the instrument, rather than perform on-site service and maintenance.	N/A
Length(s) of warranty and additional costs for an extended warranty	NWGHF plans to offer a 1–2 year warranty for the Processor.	
Warranty components	If the instrument breaks down, NWGHF plans to have the local distributor swap out the instrument, rrather than perform on-site service and maintenance.	
Turnkey option	A total installation package for the LYNX HIV p24 Antigen Test (that would contain necessary instruments, training, installation and maintenance, as appropriate) is anticipated to be offered.	

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POINT-OF-CARE VIRAL LOAD
NORTHWESTERN GLOBAL HEALTH FOUNDATION (VL Test Kit)

01 | TECHNICAL INFORMATION

Company	Northwestern Global Health Foundation	**Product**	LYNX HIV Viral Load Test Kit and sample processor
Assay type	Quantitative detection of HIV viral load	**Equipment required**	Processor and mini-centrifuge (for plasma separation)
Technological Set-up	Portable device; multiple samples via random access; fully automated and closed system; no maintenance	**Mean time between failures**	Target is 10,000 tests per instrument bay
Extraction method/ sample preparation	N/A	**Transport and Storage**	No refrigeration required
Target	N/A	**Fridge at -80°C required**	No
HIV-1, HIV-2, Subtypes	HIV-1	**Shelf life (each item in the kit)**	TBD
Linear Range	200 to 1,000,000 copies/mL, depending on sample input volume	**Technical Skill**	Minimally trained
Time to Result	60–90 minutes	**Laboratory Set-Up**	Laboratory not required; The processor is powered by an external power transformer that connects to either an AC or DC power cable that connects to an AC or DC power socket in the clinic or laboratory. A fully charged battery shall complete the cartridges in the processor
Throughput	8-96 tests/day, the processor will accommodate a range of throughput requirements based on the setting	**Waste disposal requirements**	Test waste disposal necessary
Sample type	Fingerprick , venous	**Applicable settings**	Decentralised facilities including mobile clinics and resource-limited settings
Sample volume	~150µL of whole blood to achieve 1,000 copies/mL plasma	**Regulatory approval**	TBD
Kit sizes	TBD	**Connectivity options for mobile health & electronic access**	Yes
		Polyvalency	No
Controls	There will be internal quality controls in each cartridge	**If Pipeline - confirm launch date**	The test will be made commercially available in late 2014 or early 2015

02 | PRICING

Instrument	Reference number	Cost (US$) EXW	Cartridge/reagents	Reference number	Cost (US$) EXW	Compatability
Device	TBD	Varies based on Configuration. Smallest configuration is <$12,000	Tests	TBD	<$10 per test result	The cartridge is compatible with Virology Quality Assurance (VQA) and United Kingdom National External Quality Assessment Service (NEQAS)

Shipping cost widely varies depending on the size of the order as well as by the region for delivery. Third-party distributor to be determined.

03 | TIERED AND VOLUME-BASED PRICING

Tiered pricing anticipated based on volume, but not economic tier.

04 | MAINTENANCE, WARRANTY & TRAINING

	Description	Cost (US$) (CPT)
Leasing or reagent rental for instruments	Leasing, lease to buy, or a rental reagent option.	The cost of the instrument can be absorbed in the test kit price.
Installation	Not provided.	
Training	Not provided.	
Maintenance	Not provided.	
Length(s) of warranty and additional costs for an extended warranty	NWGHF plans to offer a 1- 2 year warranty for the processor.	
Warranty components	If the instrument breaks down, NWGHF plans to have the local distributor swap out the instrument, rather than perform on-site service and maintenance.	
Turnkey option	Total installation package for the LYNX HIV Viral Load Test Kit and sample processor (that would contain necessary instruments, training, installation and maintenance, as appropriate) will be offered.	

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GLOSSARY AND ABBREVIATIONS

INCOTERM GLOSSARY

Incoterms are an internationally recognised collection of terms that specify the responsibility of the buyer and seller in a purchase.[83] The terms used in this report include the following:

EXW (Ex works): Where the seller is responsible for the product, the export packing, and the monitoring and labelling.

FCA (Free carrier): Where the seller is responsible for the product, the export packing, the monitoring and labelling, and the export clearance (including licences, EEI/AES).

CPT (Carriage paid to): Where the seller is responsible for the product, the export packing, the monitoring and labelling, and the export clearance (including licences, EEI/AES), freight forwarder documentation fees, inland freight to main carrier, original terminal charges, vessel loading charges, ocean/air freight, and nominate export forwarder.

CIF (Cost, insurance, and freight): Where the seller is responsible for the product, the export packing, the monitoring and labelling, and the export clearance (including licences, EEI/AES), freight forwarder documentation fees, inland freight to main carrier, original terminal charges, vessel loading charges, ocean/air freight, nominate export forwarder, and marine insurance.

In general, companies specify the port to which the product will be delivered. When provided by the companies, the ports of delivery were indicated in the product tables.

AIDS: Acquired Immunodeficiency Syndrome.

ART: Antiretroviral treatment.

ARV: Antiretroviral medicine to treat HIV/AIDS.

CD4 count: The absolute number of CD4 positive T lymphocytes (lymphocytes are CD3 positive immune cells) in the blood. CD4 count is measured in cells per microliter (cells/µL) of blood; equivalent to cells per cubic millimetre (cells/mm3). A normal, healthy value for a CD4 count is usually above 500 cells/µL.

CD4 percentage: The percentage of CD4 positive versus CD3 positive lymphocytes in the blood. A normal, healthy value for a CD4% is usually above 29%. Since CD4 counts can vary naturally from day to day, CD4% is a more accurate measurement of the health of the immune system. Children under the age of five years should be tested using CD4% because the number lymphocytes can be higher in children and therefore using CD4% is more accurate.

CDC: Centers for Disease Control and Prevention in the US.

CE: Conformite Europeenne. Europe's regulatory agency for medical drugs and devices.

Clinical: Based on signs, symptoms, morbidities and diseases.

CMV: Cytomegalovirus.

CRF: Circulating Recombinant Form.

CT/NG or CT/GC: Chlamydia trachomatis and Neisseria gonorrhoeae.

DBS: Dried blood spot. A spot of blood that is preserved on filter paper through a process of desiccation.

DNA: Deoxyribonucleic acid. The genetic material of living organisms.

DRM: Drug resistance mutation. Genetic mutations of the HIV genome that result in resistance to antiretroviral drugs so that viral replication is no longer suppressed.

EBV: Epstein–Barr virus.

EID: Early infant diagnosis. According to current WHO guidelines, the first diagnostic test should be performed by a virological test when the infant is six weeks of age.

ELISA: Enzyme-linked immunosorbent assay.

FDA: Food and Drug Administration. The US FDA is the USA's regulatory agency for medical drugs and devices.

FRET: Fluorescence resonance energy transfer.

FS: Fingerstick, also termed fingerprick. A lancet is used to prick or cut the fingertip to get a drop of capillary blood.

GMP: Good Manufacturing Practice. A production and testing practice that helps to ensure a quality product.

HBV and HCV: Hepatitis B virus and hepatitis C virus.

HIV: Human Immunodeficiency Virus. There are two types of HIV, HIV-1 and HIV-2. HIV-1 is more widespread and more virulent.

HPV: Human papillomavirus.

Immunologic: Based on the measurement of the immune system (e.g. for HIV the CD4 count or percentage and the change in the CD4 count or percentage over time). Clinico-immunological monitoring is based on both clinical and immunological measurement.

IVD: In vitro diagnostic.

kPCR: Kinetic polymerase chain reaction.

LDC: Least-Developed Countries, according to the United Nations classification.

LTR: Long terminal repeat. A conserved region of the HIV genome that is repeated on both ends.

mAb: Monoclonal antibody. A type of mono-specific antibody that binds to only one antigen.

MRSA: Methicillin-resistant Staphylococcus aureus.

NASBA: Nucleic Acid Sequence Based Amplification.

N/A: Not applicable.

PMTCT: Prevention of mother-to-child transmission. Providing treatment to mothers who are HIV-positive and their infants to prevent vertical infection in utero, intra-partum and post-partum.

POC: Point-of-care.

RLS: Resource-limited settings.

RNA: Ribonucleic acid. Similar to DNA but is used to transmit information from DNA (transcription) to proteins (translation).

RT: Reverse transcriptase. An enzyme than transcribes DNA into RNA.

rt-PCR or q-PCR: Real-time or quantitative polymerase chain reaction. A form of PCR that is quantitative.

RUO: Research use only. Usually in connection with the fact that a product has not yet received FDA regulatory approval.

Serologic: Based on the measurement of antibodies in the blood.

SOP: Standard operating procedure.

TB: Tuberculosis. A disease caused by the pathogen Mycobacterium tuberculosis. MDR- and XDR-TB are multidrug-resistant and extensively drug-resistant TB, respectively.

TBD: To be determined.

TGA: Therapeutic Goods Administration. Australia's regulatory agency for medical drugs and devices.

UNITAID: UNITAID is a global health initiative in great part financed by a solidarity levy on airline tickets. UNITAID uses innovative financing to increase funding for greater access to treatments and diagnostics for HIV/AIDS, malaria and tuberculosis in low-income countries. It is hosted and administered by WHO.

Virologic: Based on the measurement of the virus or a component of the virus (e.g. for HIV, p24 or RNA).

VL: Viral load.

VLT: Viral load test.

WHO: World Health Organization.

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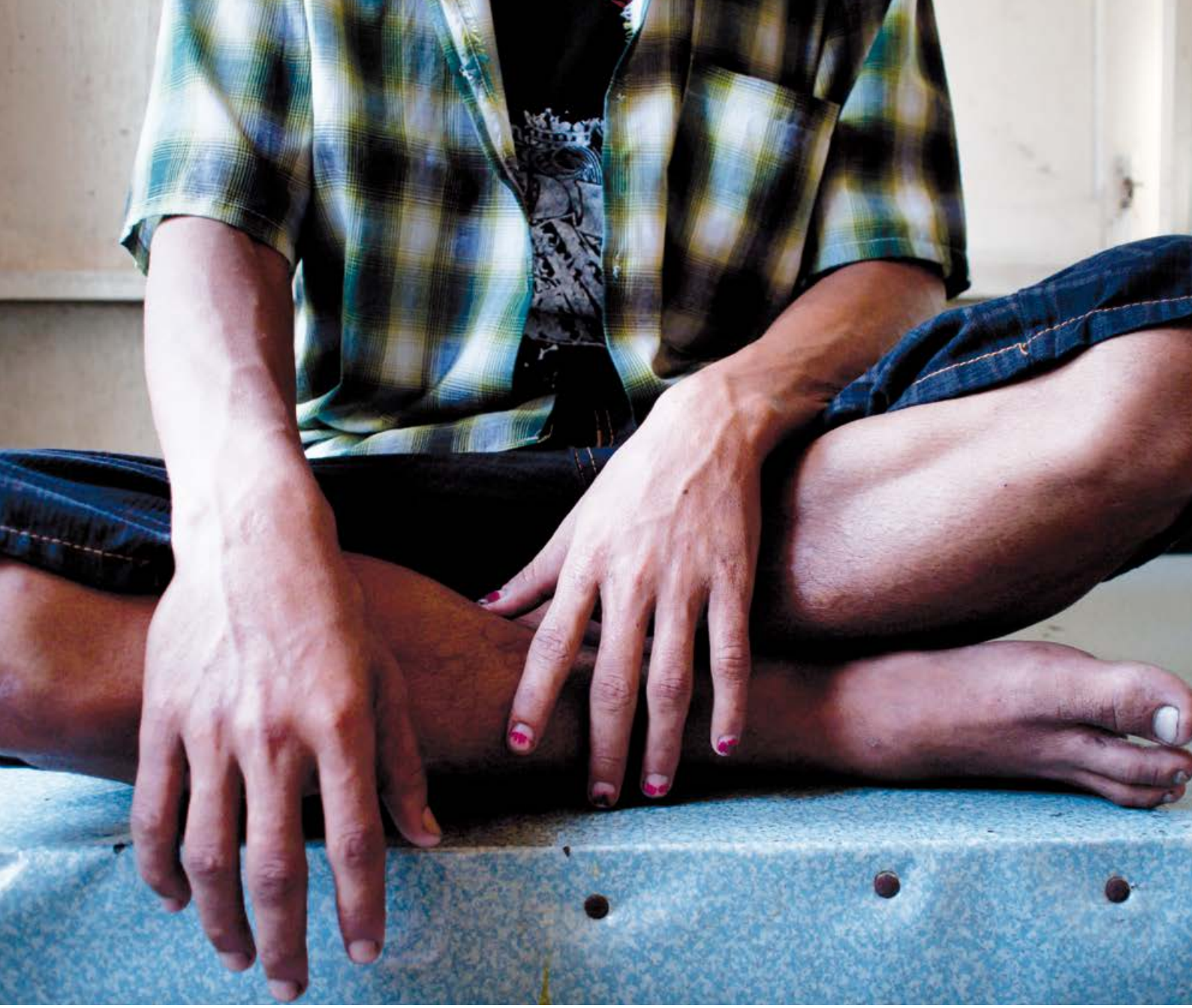

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