2011 HIV/AIDS DIAGNOSTIC TECHNOLOGY LANDSCAPE

SEMI-ANNUAL UPDATE

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Overview

The *HIV/AIDS Diagnostic Landscape* is published annually and is prepared as part of a broad and on-going effort to understand the technology landscape for HIV/AIDS. This document is a semi-annual update on the point-of-care (POC) technologies for CD4, viral load, and early infant diagnosis (EID) testing, as well as the diagnostic pipeline.

Methods

The *HIV/AIDS Diagnostic Landscape* is compiled by Maurine M. Murtagh with support from UNITAID. The material in this landscape was gathered by the author from publicly available information, published and unpublished reports and prospectuses, and interviews with developers and manufacturers. The updates in this document were provided by the developers of these diagnostic technologies. If technologies that appear in the *HIV/AIDS Diagnostic Landscape* do not appear in this update, it is either because the supplier did not provide one or indicated that there were none at this time.

CD4+ T-Cell Counting Technologies

Update on Point-of-Care CD4 Technologies in the Market

Point-of-Care Testing Platforms

PointCare NOW™ (PointCare Technologies Inc.)

PointCare reports that the reagents for the PointCare NOW™ CD4 system are heat stable to 42° Celsius for one year and can tolerate short periods of time at higher temperatures. The reagents do not require cold chain shipping and are not light sensitive. In addition, PointCare's heat stable Daily Check controls are included in the price of reagent kits.

With respect to evaluations of the performance of PointCare NOW, the company concluded a method-comparison with BD's FACSCalibur in March 2011 at the National Microbiology Reference Laboratory (NRL), Harare, Zimbabwe. The results from this evaluation in Zimbabwe as well as the results of an evaluation conducted at military clinics in Uganda are expected to be published in the near future.

Alere PIMA™ CD4 (Alere Inc.)

Alere is launching a USB connectivity module for PIMA™. In addition, the company is adding a power extender (i.e., a module with an extended battery life and adaptors for a variety of charging sources, including solar panels, car batteries, mains, etc.).

CyFlow® miniPOC (Partec GmbH)

Partec has lowered the price for the CyFlow® miniPOC. The company is currently offering a special point-of-care package (CyFlow® miniPOC, 5000 patient tests, 36-month full instrument warranty) with an effective instrument price of €3500 (~US$ 4980). The company notes that although independent, peer-reviewed data is not yet available on the CyFlow® miniPOC, the platform works on the same principles as the Partec CyFlow® Counter for which such studies are available.

Update on Point-of-Care CD4 Technologies in the Pipeline

Point-of-Care Testing Platforms

Daktari™ CD4 Counter (Daktari Diagnostics, Inc.)

Daktari™ now expects to begin clinical trials in the fourth quarter of 2011, with commercialization expected in the second quarter of 2012. Further, the price is expected to be US$ 1,000 (rather than US$ 800). The per test price is still expected to be approximately US$ 8.00, but volume discounts are expected to drive the price lower.

MBio™ Diagnostics CD4 system (MBio Diagnostics, Inc.)

The MBio™ Diagnostics CD4 system has been undergoing field testing on both capillary and venous blood samples since April 2011 at the Antiviral Research Center in San Diego, CA, USA, under the direction of MBio's clinical collaborators at the University of California, San Diego Medical Center. The company presented results from the initial system at the International AIDS Society meeting in Rome, Italy, in July 2011. Field evaluations in southern Africa are scheduled for autumn 2011.

As further development on the MBio system moves forward, the company has modified turnaround time for a single sample from 10 minutes to approximately 20 minutes (17 minutes in the cartridge and 3 minute instrument processing/read). The capacity of the device is 15 to 20 tests per hour, running cartridges in parallel. The laboratory protocol for venous or capillary whole blood currently uses a blood transfer device, a ready-to-use tube, and a cartridge. However, a point-of-care protocol with a single blood transfer device is in development. The MBio instrument automatically confirms sample and stain addition.

The MBio CD4 system in development now also includes an on-board computer for sample analysis, results management, and event logs. The user interface is an intuitive touchscreen with administrator-configurable settings such as user lockout/validation and QC scheduling. Cartridge barcodes will be read automatically, and the instrument will have a built-in Ethernet connection and multiple USB ports to support printers, external barcode readers, and wireless adapters.

Semi-quantitative CD4 test (Burnet Institute)

A second version of Burnet Institute's semi-quantitative CD4 test has been developed. The test measures whether a patient's CD4 is above or below a set threshold by the relative strength of the test and reference lines on a membrane in a lateral flow cartridge. While the first version of the device had a reference cutoff of 200 cells/µL, the newer version has a reference cutoff of 350 cells/µL. Testing of this newer version of the assay is currently ongoing in Australia.

Clinical trials of the POC test, which began in August 2011, are also currently underway in the United States, and trials of the POC test are planned to follow in Malawi in the fourth quarter of 2011. The product launch date continues to be contingent upon funding or partnering and results of clinical trials.

Point-of-Care Testing Platforms Added Since the Previous Edition

Since the release of the annual report, additional platforms have been introduced to the pipeline and are included in this semi-annual update.

CD4 Point of Care Technology (BD Biosciences)

BD Biosciences is developing an image-based counting technology suitable for resource-limited settings that will provide CD4 absolute count, %CD4, and haemoglobin (Hb) all on the same single-use disposable cartridge. Features of the automated device (Figure 1) include touch screen user interface, technician-

friendly operation, flexible workflow with high throughput, integrated micro-printer, battery or solar-powered capability, and data archive/transfer capabilities.

The sample is collected from the patient using a fingerstick or an EDTA tube. The cartridge is self-contained and is inserted by the operator into the device. After a short incubation period, detection takes place automatically and the result can be read immediately in a single, easy step. The new and innovative cartridge technology contains dried reagents and requires no-cold chain, which enables longer shelf life over a wide range of environmental conditions. Market launch is expected in late 2012.

Figure 1. POC CD4 Device from BD Biosciences. Photo source: BD Biosciences.

Viral Load Testing Technologies

Update on Point-of-Care Viral Load Technologies in the Pipeline

No POC viral load testing platforms have been launched yet. Below are updates on some of the products in the pipeline.

NAT system (Alere Inc.)

Alere Inc. has reported a number of technical improvements to its NAT system. The actual hands-on time for the device is expected to be approximately 1 minute (i.e., sample collection and loading of the cartridge onto the analyzer and subsequent reading of results and cartridge disposal). The company also notes that in addition to fingerstick blood, 25 µL of heelprick or venous blood can be used in the device. For venous blood, no metering is required onto the cartridge.

The NAT system will support wireless connectivity, and the device can be attached to a USB port for sample tracking, if desired by the user. Additionally, the system will be fully compatible with existing external quality assurance (EQA) programs. Finally, the company will be seeking regulatory approval for *in vitro* diagnostic use of the NAT system in the European Union (EU) (CE-IVD marking) and United States (US) Food and Drug Administration (FDA) clearance throughout 2012/2013.

Liat™ Analyzer (IQuum, Inc.)

The Liat™ Analyzer is an automated sample-to-result NAT platform that performs sample nucleic acid extraction, purification, reverse transcription, polymerase chain reaction (PCR) amplification, and real-time detection to detect and/or quantify pathogens. The Liat™ plant currently has assays developed and clinically validated for the detection of influenza H1N1 virus, as well as influenza A and B strains. An assay for Dengue virus is under development, and the platform can also accommodate HIV viral load testing, TB, and other disease categories.

As illustrated in Figure 2, the test procedure is straightforward and is a closed system, thus minimizing cross-contamination and biohazard risks.

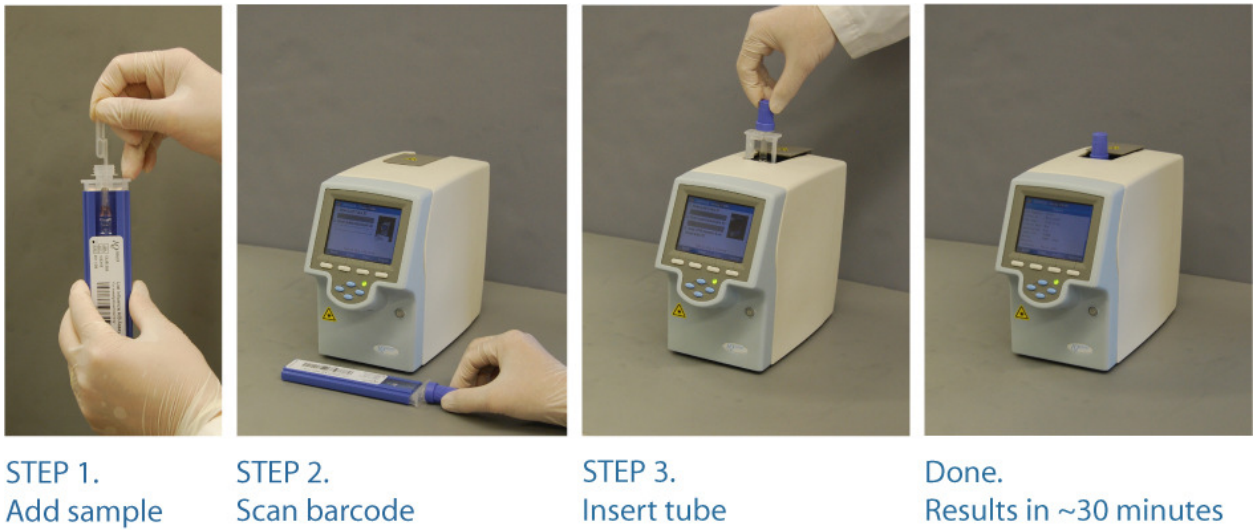


Figure 2. *Liat Analyzer. Photo source: IQuum, Inc.*

To aid the operator and provide reliable results, the Liat™ Analyzer incorporates a variety of intelligent and advanced features: barcode data entry avoids errors in sample or assay coding and on-screen prompts provide easy-to-follow directions to guide the operator through sample loading and tube insertion. Sample metering capabilities ensure that the correct volume of sample is used for the test, or outputs a warning if the sample volume is insufficient. A comprehensive set of sensors further monitors system operations in real-time and automatically recovers from errors or aborts the assay to prevent incorrect results from being reported. An internal control contained in each Liat tube is processed and detected with the sample to ensure the proper function of each step of the assay process. PCR curve pattern recognition and automated data interpretation provides results in plain English. The developer states that, collectively, these sophisticated features ensure the quality of results when testing is performed by minimally trained operators.

The company expects that the list price for the Liat Analyzer, which is currently US$ 25,000, may decrease for resource-limited settings. Susan A. Fiscus at the University of North Carolina at Chapel Hill has completed an evaluation similar to that previously conducted by Robert Coombs at the University of Washington, comparing the Liat Analyzer's viral load detection capabilities against the Roche COBAS® and the Abbott *m*2000 system. In both evaluations, the performance of the Liat device compared favorably to the predicate devices. A potential market launch for the Liat viral load assay is still possible in 2012.

SAMBA (Diagnostics for the Real World)

An evaluation of the Simple Amplification Based Assay (SAMBA) platform was successfully conducted at the Chiradzulu District Hospital, a Médicens Sans Frontières (MSF) site, in Malawi this summer. Another evaluation, also at a MSF site, is currently underway in Arua, Uganda.

GeneXpert® System (Cepheid)

The Cepheid GeneXpert® System, which is a fully-automated and integrated system for PCR-based nucleic acid testing, currently has 11 FDA-cleared and 12 CE-IVD assays, including tests for enteroviral meningitis, methicillin-resistant staphylococcus aureus (MRSA), influenzas A and B, mycobacterium tuberculosis-resistance to rifampicin (MTB/RIF), and anthrax, among others. The projected release date for an HIV viral load assay is 2014.

Although it is not currently known what the price per cartridge will be for the viral load assay, the Foundation for New Innovative Diagnostics (FIND)-negotiated price of the GeneXpert® System (with four modules) for a high-burden, low-resource setting is approximately US$ 17,000; the current negotiated price per cartridge for MTB/RIF is about US$ 17. Cepheid agreed to a fixed price with the price decreasing based on increased sales.

The GeneXpert® System integrates and automates sample preparation, amplification, and detection in a single-use, self-contained microfluidic cartridge. All liquids and reagents can be prefilled so that only the sample itself needs to be added to the cartridge, greatly simplifying the pre-amplification process. GeneXpert® cartridges can handle a variety of sample volumes, which can increase the sensitivity of the assays.

Further, the GeneXpert® System is modular. Individual modules contain solid state circuitry that control temperature, pressure, rotation of the valve that moves the liquid between reservoirs, and the detection software. These individual modules are packaged in units of 1, 2, 4, 16, 48, or 80, and the latter two systems are fully automated, walk-away robotic instruments developed for high throughput laboratory applications. Additionally, the modules can be removed and replaced individually so that the entire system is not incapacitated if one module fails.

The GeneXpert® system is sufficiently simple that training can usually be completed within half a day. Further, although the system was designed to use AC power, it is currently being utilized in rural clinic sites using solar power. The GeneXpert® software comes pre-installed on a desktop or laptop computer and results can be displayed for each module in real time or uploaded via an Internet connection to a central database.

POC RT-PCR Testing Platform (Northwestern Global Health Foundation)

The Northwestern Global Health Foundation (NWGHF) is still on track, together with Quidel Corporation, to launch its POC rapid real-time polymerase chain reaction (RT-PCR) testing platform in 2013. An updated image of the planned device is shown in Figure 3.

Figure 3. NWGHF RT-PCR Testing Platform. Photo source: NWGHF.

Benchtop Analyzer (Advanced Liquid Logic, Inc.)

Advanced Liquid Logic's (ALL) benchtop analyzer is capable of performing a wide range of assay protocols, including PCR, immunoassays, and enzymatic activity assays. The company is currently developing a portable version of the analyzer. Although ALL does not have a viral load assay at this time, the scope of work under the company's US$ 5.2 million grant from the National Institute of Allergy and Infectious Diseases (NIAID) includes the development of a viral load assay.

HIV Quantitative Assay (BioHelix Corporation)

BioHelix recently submitted a proposal under the Small Business Innovation Research program to the National Institutes of Health (NIH) in which the company proposed to develop a low-price HIV quantitative assay. BioHelix received a fundable score on this grant proposal, a final funding decision is expected in November 2011.

With respect to the company's isothermal nucleic acid amplification platform, a multicenter clinical trial on its assay for genital and oral herpes has been completed and the results have been submitted to the US FDA for clearance.

Early Infant Diagnostics

Update on Point-of-Care EID Technologies in the Pipeline

No POC testing platforms dedicated to early infant diagnosis (EID) have been launched yet. Below are updates on some of the products in the pipeline.

Ultrasensitive p24 Antigen Rapid Lateral Flow Assay for EID (NWGHF)

Clinical and field trials of the NWGHF ultrasensitive p24 antigen rapid lateral flow assay for EID at the point of care are still expected to be conducted in 2011, with availability of the device in late 2011 or early 2012. An updated image of the device is shown in Figure 4.

Figure 4. NWGHF EID Platform. Photo source: NWGHF.

The assay procedure now requires collecting 80µL of heelstick blood from the infant, but sample preparation steps are unchanged. Waiting time for visual read out of a test result has increased slightly to 30 minutes with total assay duration of about 40 minutes.

The price of the processor device is now expected to be between US$ 400 and US$ 700, and the per-test price is expected to range from US$ 7 to US$ 15.

Qualitative EID Assay (Micronics, Inc.)

Micronics, Inc., which was recently acquired by Sony Corporation, has been funded to develop a qualitative EID assay. The company is now planning clinical validation of the first assay in 2012 rather than 2011.

APPENDIX 1: Operational Characteristics of CD4, Viral Load, and Early Infant Diagnosis Platforms[1]

Point-of-Care CD4 Technologies in the Market

PointCareNOW™	
Type of technology	Desk top, flow cytometer
Output	Absolute and percentage CD4 counts, WBC, hemoglobin concentration, total and percentage lymphocytes, monocytes count and monocyte %, neutrophil count %, eosinophil count and eosinophil%
Turnaround time	8 Minutes
Capacity	50 samples per day
Throughput per technician / per day	~40-50 samples per technician/day; no batching capabilities; walk-away operation.
Sample needed and stability	40 µL whole blood collected in 2 mL vacuum K2 EDTA anticoagulant tubes provided by PointCare; system will accept 3 and 4 mL tubes as well. Sample is stable for 8 hours from time of draw.
Sample preparation and protocol complexity	No sample preparation steps. (i) Draw venous blood into PointCare-supplied tube; (ii) scan sample ID with barcode reader; (iii) insert unopened sample into instrument slot and press "run" button.
Reagent stability	Reagents are stable for 12 months from date of manufacture when stored at 2° to 42°C (30° to 108 ° F) transient exposure (shipping delay or temperature excursion) of 10 days at 50° C (122°F).
Price/test	About US$ 10.00 per test, including Daily Check ™ controls
Price/instrument	~ US$ 25,000
Regulatory status	FDA cleared (CLIA moderate-complexity rating); CE-IVD marked
Physical dimensions (cytometer only) (W x H x D)	Width: 25 cm Height: 35cm Depth: 34 cm
Weight	12kg (~26.5 lbs) (cytometer only)
Third-party supplies	All phlebotomy supplies provided in CD4*NOW*™ Reagent Kit 100
Electric power requirements	Uninterruptable Power Supply (UPS) - 110 V or 220 V, 60W; portable battery power system available, solar charge system available
Environmental requirements	Temperature: 18° to 34°C (64° to 93° F) Humidity: < 80% Maximum altitude: N/A
Data station	Dedicated CPU integrated into instrument, up to 8000 results can be stored on the instrument (unlimited patient records transferable to USB). Menu languages: English, French, Spanish and Portuguese. Indonesian under development.
Monitor	LED color touch screen integrated into instrument
Printer	Separate printed (prints on non-thermal paper)
Bar-code scanner	Available in Customer Installation Package from PointCare
Training	Moderate level of training (2-3 days) required
Maintenance	Instrument is optional with a light source and tubes; should therefore undergo routine preventive maintenance by (i) operator and (ii) vendor technician. In case of breakdown vendor-trained technician required to repair.
Internal QC	PointCare provides heat stable, synthetic, bead-based reagents (Daily Check ™ controls); Controls are stable at 2° - 42° C (36° to 108° F) for 6 months from date of manufacture.
External QA	Yes
Infrastructure requirements	Technology can be used at central, regional, district and some well-developed primary sites with dedicated laboratory facilities and technicians.

[1] Only tables that have been updated are included here. For a comprehensive catalog of tables, please see UNITAID Technical Report: HIV/AIDS Diagnostic Landscape, July 2011. Available at: http://www.unitaid.eu/images/marketdynamics/publications/unitaid_md_technical_report_diagnostics_landscape_web.pdf. Accessed on 14 October 2011.

Alere Pima™ Analyzer and Alere CD4 Test	
Type of technology	Portable bench-top, fixed volume cytometer
Output	Absolute CD4 counts only
Turnaround time	18-20 minutes
Capacity	Maximum of ~20 samples per day
Throughput per technician / per day	~20 Samples per technician/day; no batching capabilities; walk-away operation
Sample needed and stability	25 µL of capillary (fingerstick) blood wicked directly into the sample collector contained in the Pima catridge or 25 µL of venous blood collected in EDTA anti-coagulant tube. Cartridge must be inserted and tested within 5 minutes of sample application. When using venous blood, sample is stable for 36 hours from time of draw.
Sample preparation and protocol complexity	No sample preparation is required. For capacity blood: (i)lancet finger (ii) wipe away first drops and apply following blood drops to cartridge; (iii) close cartridge; (iv) insert cartridge into analyzer; (v) analysis starts automatically; (vi) enter patient ID data; (vii) read result from LED screen; (viii) print result
Reagent stability	Freeze-dried reagents require no refrigeration. Stable for 12 months at 2^{o} to 30^{o}C
Price/test	~US$ 6 per test
Price/instrument	~US$ 5,500
Regulatory status	CE-IVD marked, FDA-approval expected in 2011
Physical dimensions (cytometer only) (L x H x D)	Length: 22 cm (8.7") Height: 16 cm (6.3") Depth: 13 cm (5.1")
Weight	2.54kg (~5.6 lbs) (instrument only)
Third-party supplies	For venous samples: volumetric or transfer pipette. For capillary samples: sterile lancets, alcohol swabs, dry swabs (also available from Alere).
Electric power requirements	100-240 V (A/C) at 47-63 Hz mains power Analyzer contains on-board rechargeable battery. Power extender is available (module with an extended battery life and adaptors for a variety of charging sources, including solar panels, car batteries, mains power, etc.)
Environmental requirements	Operating Temperature: 10^{o} to 40^{o}C (50^{o} to 104^{o}F) Humidity: N/A; no directly sunlight; keep dry Maximum altitude: N/A
Data station	Dedication CPU integrated into instrument; approximately 1,000 test results can be stored on the instrument archive; results can be downloaded via USB. There is also a USB connectivity module. Potential to install an SMS chip to transmit results or internal calibration data.
Monitor	LED mono-color screen integrated into instrument.
Printer	Separate printer (prints on thermal paper); battery powered (L 95mm x W 93mm x H 66mm, weight: ~350 grams, including thermal paper roll.)
Bar-code scanner	Integrated into instrument for test cartridges only
Training	Minimal training required. Lay person can be trained in less than half a day. Primary skill required is for correct lancet blood draw.
Maintenance	Analyzer contains an integrated camera and computer that might be susceptible to damage if dropped. If damaged, low cost and portability of the device allows for direct swap-out replacement rather than on-site repair.
Internal QC	Extensive internal controls: sample volume control; reagent control; automatic control of cartridge expiry date; internal process controls; and automatic test identification.
External QA	TBD whether it will be compatible with EQA programs; the cartridge cannot be retested to confirm results.
Infrastructure requirements	May be used at all levels of health facility, including health centres or in mobile facilities.
User interface	16-button keypad

Partec CyFlow® miniPOC	
Type of technology	Portable and compact flow cytometer
Output	Absolute and percentage CD4 counts
Turnaround time	Set-up time: < 5minutes; Blood preparation time: 15 minutes; Run time: 70 seconds (1 minute, 10 seconds)
Capacity	Up to 250 tests/day
Throughput per technician/per day	N/A
Sample needed and stability	20 µL of whole blood collected in EDTA anticoagulant
Sample preparation and protocol complexity	Process for dry reagents only: (i) add 20 µL of fresh, whole EDTA blood to Partec CD4 tube containing dry reagents; (ii) incubate 10 minutes at room temperature in the dark; (iii) add 820 µL of prefilled buffer from syringe to tube; (iv) shake tube; (v) refill volume from sample tube into syringe; (vi) attach syringe to CyFlow miniPOC.
Reagent stability	Dry reagents may be stored at room temperature and have a maximum shelf life of 12 months.
Price/test	€1.75 (~US$ 2.40) per test for absolute CD4 and €2.50 (~US$ 3.40) for CD4 percentage, regardless of volume
Price/instrument	~ US$ 12,790. Partec offers a point-of-care package (i.e. reagents for 5,000 tests; 36-month instrument warranty) with an effective instrument price of US$ 4,980.
Regulatory status	CE-IVD marked
Physical dimensions (cytometer only) (W x H x D)	Width: 36.8 cm Height: 24.3 cm Depth: 18.6 cm
Weight	< 5 kg (~11 lbs)
Third-party supplies	Syringe, sterile lancets, alcohol swabs, dry swabs, gauze, bandage
Electric power requirements	100 – 240 VAC or 12V DC power (car battery) 50 – 60 Hz
Environmental requirements	Operating temperature: N/A Humidity: N/A Maximum altitude: N/A
Data station	Dedicated Intel® Atom™ CPU integrated into the instrument; Windows™-based analysis software.
Monitor	5.7”-colour touch screen integrated into the instrument.
Printer	Dedicated thermal printer integrated into the instrument.
Bar-code scanner	No
Training	Moderate level of training is required given the sample handling requirements.
Maintenance	Routine preventative maintenance required. In the event of breakdown, a vendor-trained technician is required to repair the instrument.
Internal QC	Supports internal QC.
External QA	Compatible with CD4 EQA programs.
Infrastructure requirements	Technology is suited for use at primary health centres and remote areas, but may also be used in central, regional, district, and mobile labs.

Point-of-Care CD4 Technologies in the Pipeline

Daktari™ CD4 Counter	
Type of technology	Small, portable device that uses cartridge microfluidic-based system to selectively capture CD4 cells in whole blood and to count them by measurement of electrical sensing.
Output	Absolute CD4 counts only
Turnaround time	8 minutes
Capacity	~40 – 50 samples/day
Throughput per technician/per day	~40 – 50 samples per technician/day; no batching capabilities; walk-away operation.
Sample needed and stability	16 µL of capillary (fingerstick) blood applied to the Daktari cartridge.
Sample preparation and protocol complexity	No manual sample preparation is required. Protocol: (i) lancet finger; (ii) apply blood drop to cartridge; (iii) insert into CD4 counter; (iv) press "Start"; (v) read the result from the LCD screen.
Reagent stability	Dried reagents require no refrigeration.
Price/test	US$ 8/test (estimated), but may be lower with volume discounts
Price/instrument	US$ 1,000 (estimated)
Regulatory status	TBD
Physical dimensions (cytometer only) (W x H x D)	Width: 22.9 cm Height: 17.8 cm Depth: 12.7 cm
Weight	2.5 kg (~5.5 lbs)
Third-party supplies	Sterile lancets for capillary blood samples, alcohol swabs, dry swabs, gauze, bandages
Electric power requirements	Regular AC with long-life rechargeable battery self-contained in the device.
Environmental requirements	Operating temperature: TBD Humidity: TBD Maximum altitude: TBD
Data station	Daktari is developing a model that will include a data management system and will contain a keypad user interface. It will also have a back-end data package built into the device.
Monitor	LCD screen integrated into the instrument. Results are stored on the instrument and may be automatically uploaded to a remote server for analysis.
Printer	None
Bar-code scanner	No
Training	Minimal training is required. A lay person can be trained in less than 90 minutes (1 hour, 30 minutes). Primary skill required is for correct lancet blood draw.
Maintenance	Device uses lasers rather than optics and may be less prone to damage. If damaged, depending on the cost of the instrument, it might be possible to swap-out a replacement device rather than repair the damaged instrument on-site.
Internal QC	TBD
External QA	TBD whether it will be compatible with EQA programs; the cartridge cannot be retested to confirm results.
Infrastructure requirements	May be used at all levels of health facility, including health centres or in mobile facilities.

MBio CD4 system	
Type of technology	Small, portable device that is a two-colour fluorescence imaging cytometer that uses immunostaining and direct cell counting. The system uses disposable, self-contained fluidic cartridges.
Output	Absolute CD4 counts only; could be configured for other stain combinations.
Turnaround time	20 minutes (17 minutes in the cartridge and 3 minutes for instrument processing and reading). Cartridges may be processed in parallel.
Capacity	15 – 20 tests/hour running cartridges in parallel.
Throughput per technician/per day	~100 – 160 samples per technician per 8 hour day.
Sample needed and stability	10 µL of capillary (fingerstick) blood; may also use venipuncture.
Sample preparation and protocol complexity	Current laboratory protocol for venous or capillary whole blood uses a blood transfer device, ready-to-use tube, and a cartridge. A point-of-care protocol with a single blood transfer device is in development.
Reagent stability	N/A; the company has not released reagent stability data.
Price/test	TBD
Price/instrument	Not available from the company.
Regulatory status	TBD
Physical dimensions (cytometer only) (L x W x H)	Length: 38.0 cm (15”) Width: 19 cm (7.5”) Height: 15.0 cm (5.9”)
Weight	3 kg (~6.6 lbs)
Third-party supplies	Sterile lancets for capillary blood samples, alcohol swabs, dry swabs, gauze, bandages
Electric power requirements	Battery powered
Environmental requirements	Operating temperature: TBD Humidity: TBD Maximum altitude: TBD
Data station	On-board computer for sample analysis, results management, and event logs. The instrument will have a built-in Ethernet connection and multiple USB ports to support printers, external bar-code readers, and wireless adapters.
Monitor	LCD screen integrated into the instrument and includes a touchscreen interface with administrator-configurable settings, such as user lockout/validation and QC scheduling.
Printer	Not internal to the device.
Bar-code scanner	Yes. Cartridge bar-codes will be read automatically.
Training	Minimal training is required. A lay person can be trained in less than 90 minutes (1 hour, 30 minutes). Primary skill required is for correct lancet blood draw.
Maintenance	The device is non-optical and should be less prone to damage. If damaged, low cost and portability of the instrument may allow direct swap-out replacement rather than on-site repair.
Internal QC	TBD
External QA	TBD whether it will be compatible with EQA programs; the cartridge cannot be retested to confirm results.
Infrastructure requirements	May be used at all levels of health facility, including health centres or in mobile facilities.

Point-of-Care Viral Load Technologies in the Pipeline

Alere NAT System (Viral Load)

Type of technology	Portable bench-top, NAT-based purification, amplification, and detection system for total HIV RNA.
Output	Quantitative HIV-1 and HIV-2 RNA viral load measurement
Turnaround time	About 30 – 60 minutes
Capacity	Maximum of ~10 samples/day
Throughput per technician/per day	~10 samples per technician/day; no batching capabilities; walk-away operation
Sample needed and stability	25 µL of capillary (fingerstick) blood wicked directly into the sample collector contained in the dedicated cartridge. Alternatively, 25 µL of heelprick or venous blood can be used in the device. For venous blood, no metering is required onto the cartridge. Cartridge containing sample can be stored and shipped, if needed, as sample is expected to be stable for weeks.
Sample preparation and protocol complexity	No sample preparation required. For capillary blood: (i) lancet finger; (ii) wick whole blood directly into the cartridge; (iii) close the cartridge; (iv) insert the cartridge into the analyzer; (v) enter operator and sample ID; (vi) analysis begins automatically; (vii) remove the cartridge from the analyzer and dispose of it; and (viii) read the results from the screen. Hands-on time is expected to be ~1 minute.
Reagent stability	Freeze-dried reagents require no refrigeration. Stable for 12 months at 2 to 30° C
Price/test	TBD
Price/instrument	TBD
Regulatory status	Alere is seeking regulatory approval for EU CE-IVD marking and US FDA approval in 2012/2013.
Physical dimensions (analyzer only) (L x H x D)	Length: 28 cm (11”) Height: 17 cm (6.7”) Depth: 17 cm (6.7”)
Weight	< 5 kg (< 11 lbs)
Third-party supplies	For capillary samples: sterile lancets, alcohol swabs, dry swabs (also available from Alere).
Electric power requirements	Analyzer contains on-board rechargeable battery that provides a full work day (at least 8 hours) of operation.
Environmental requirements	Operating temperature: 15°to 40° C (59° to 104° F) Humidity: < 90% relative humidity Maximum altitude: N/A (Permissible atmospheric pressure: 850 to 1100 hPa.)
Data station	Dedicated CPU integrated into the instrument; approximately 5,000 test results may be stored on the instrument archive; results may be downloaded via USB. Potential to install an SMS chip to transmit results or internal calibration data. Will support wireless connectivity and the device can be attached to a USB port for sample tracking, if desired by the user.
Monitor	Colour touch screen integrated into the instrument.
Printer	Separate printer (prints on thermal paper); battery powered. (L 95mm x W 93mm x 66mm; weight: ~350 grams, including thermal paper roll.)
Bar-code scanner	Integrated into the instrument for test cartridges only.
Training	Minimal training is required. A lay person can be trained in less than half a day. Primary skill required is for correct lancet blood draw.
Maintenance	If damaged, low cost and portability of the device allows for direct swap-out replacement rather than onsite repair.
Internal QC	Yes
External QA	Will be fully-compatible with existing EQA programs.
Infrastructure requirements	May be used at all levels of a health facility, including in health centres or in mobile facilities.
User interface	Touch screen colour display to enter patient information, view results, adjust settings, download results, and navigate system software.

Liat™ Analyzer	
Type of technology	Portable bench-top, real-time PCR
Output	Viral Load (limit of detection ~50 cp/mL)
Turnaround time	30 – 55 minutes, depending on the limit of the detection set (30 minutes for 500/1000 cp/mL)
Capacity	~8 – 15 samples/day, depending on the limit of detection
Throughput per technician/per day	~8 – 15 samples per technician/day; no batching capabilities on the device
Sample needed and stability	200 µL of plasma or 10 – 50 µL of fingerstick blood wicked directly into the Liat tube.
Sample preparation and protocol complexity	No sample preparations required, if using capillary blood. For capillary blood: (i) lancet finger; (ii) apply blood drops to the Liat tube; (iii) scan the tube's bar code on the device; (iv) insert the tube into the Liat analyzer; (v) start the device.
Reagent stability	Reagents expected to be shipped with an expiration date of at least 6 months; reagents must be stored at approximately 4° C (39.2° F).
Price/test	TBD
Price/instrument	~US$ 25,000, but may be priced lower for resource-limited settings.
Regulatory status	TBD
Physical dimensions (W x H x D)	Width: 4" Height: 7" Depth: 7"
Weight	3.46 kg (~8 lbs)
Third-party supplies	For capillary samples: sterile lancets, alcohol swabs, dry swabs.
Electric power requirements	AC or battery powered
Environmental requirements	Operating temperature: 15°to 30° C (59° to 86° F) Humidity: N/A Maximum altitude: N/A
Data station	Dedicated CPU integrated into the instrument; approximately 10,000 test results may be stored on the instrument archive; results may be downloaded via USB.
Monitor	LED colour screen integrated into the instrument.
Printer	No printer provided.
Bar-code scanner	Integrated into the instrument for tubes only.
Training	Minimal training is required. A lay person can be trained in 60 minutes (1 hour). Primary skill required is for correct lancet blood draw.
Maintenance	Analyzer contains an internal optical system and controls that could be damaged. On-site service/maintenance is required.
Internal QC	Extensive internal controls: sample volume control; internal process controls; and more.
External QA	TBD whether it will be compatible with EQA programs; the cartridge cannot be retested to confirm results.
Infrastructure requirements	May be used at all levels in a health facility, including in health centres or in mobile facilities.
User interface	7-button keypad

Point-of-Care Testing Platforms Added Since the Previous Edition

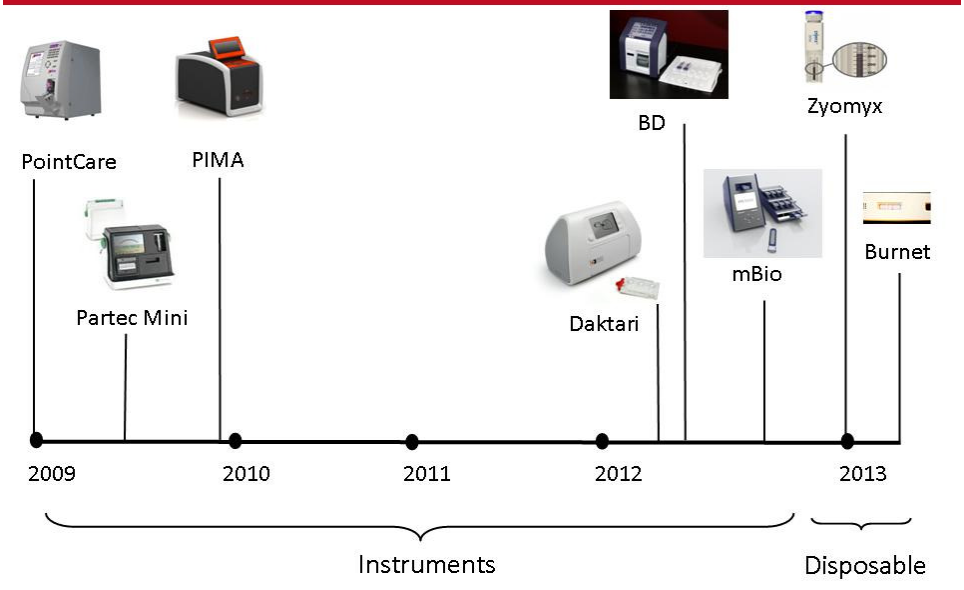
Burnet Institute CD4 Counter	
Type of technology	Disposable cartridge containing test strip (lateral flow) that measures CD4 proteins on T cells qualitatively (above and below 350 cells/µL
Output	Absolute CD4 counts only
Turnaround time	~40 minutes, including incubation
Capacity	Not available
Throughput per technician/per day	~120 samples per technician/day; batching capabilities (up to ~10/technician)
Sample needed and stability	40 µL of capillary (fingerstick) blood, or peripheral blood into EDTA anticoagulant
Sample preparation and protocol complexity	Protocol: (i) lancet finger; (ii) add who blood to Well A of test strip using MicroSafe pipette; (iii) add 1 drop of supplied buffer to Well A and allow sample to run for 18 minutes; (iv) add 3 drops of buffer to Well B of test strip; (v) wait for 20 minutes; (vi) read results.
Reagent stability	> 6 months at 40° C
Price/test	US$ 2/test (estimated)
Price/instrument	US$ 1,200 for the reader (eventual price estimated: US$ 400). Note that tests can also be read by eye.
Regulatory status	TBD
Physical dimensions of reader (W x H x D)	Width: 12 cm (4.7”) Height: 8.5 cm (3.3”) Depth: 7.7 cm (3”)
Weight	390 g (~14 oz)
Third-party supplies	Sterile lancets for capillary blood samples, alcohol swabs, dry swabs, gauze, bandages
Electric power requirements	None for the cartridge; reader requires 12V DC via adapter (110-240V); optional battery pack.
Environmental requirements	Operating temperature: TBD Humidity: TBD Maximum altitude: TBD
Data station	None. The reader stores the most recent 1,000 tests; downloadable via USB / Ethernet).
Monitor	None. The reader is a ~6.1 cm (2.4”) colour touch screen.
Printer	None. The reader can support printing.
Bar-code scanner	Yes. (Optional on the reader.)
Training	Minimal training is required. A lay person can be trained in less than 120 minutes (2 hours). Primary skill required is for correct lancet blood draw and visual test reading (automated with the reader). The reader provides on-board training instructions and can be used in instruction/assay run mode, or in read-only for batched tests.
Maintenance	The test is disposable and does not require service or maintenance. The reader is expected to be robust and may be swapped out if it fails.
Internal QC	None. The reader has internal QC.
External QA	TBD
Infrastructure Requirements	May be used at all levels of the health facility, including in health centers or in mobile facilities.

Point-of-Care Early Infant Diagnosis Technologies in the Pipeline

NWGHF p24 Antigen Rapid Lateral Flow Assay (EID)	
Type of technology	p24 antigen assay for EID
Output	Detection of HIV infection
Turnaround time	40 minutes, including blood draw and sample preparation (30 minutes for readout only)
Capacity	1 sample tested sequentially
Throughput per technician/per day	~16 samples per day
Sample needed and stability	~80 µL of blood from the infant's heel.
Sample preparation and protocol complexity	(i) Prick the infant's heel and collect the blood; (ii) separate the plasma from the red blood cells; (iii) add buffer and heat; (iv) insert the test strip into the heat block, and wait 20 minutes; (v) read the test.
Reagent stability	Reagents should be stored from 2° - 37° C; reagent kit shelf life is likely to be 12 months at launch but will try to improve this to 18 or 24 months.
Price/test	Estimated to be US$ 7 to US$ 15/test
Price/instrument	~US$ 400 to US$ 700 for the device
Regulatory status	TBD
Physical dimensions (cytometer only) (W x H x D)	Width: Not available Height: Not available Depth: Not available
Weight	Not available
Third-party supplies	Sterile lancets for blood samples, alcohol swabs, dry swabs, gauze, bandages
Electric power requirements	The heat block is battery powered.
Environmental requirements	Operating temperature: TBD Humidity: TBD Maximum altitude: TBD
Data station	None
Monitor	None
Printer	No printer provided.
Bar-code scanner	None
Training	Minimal training is required. Primary skill required is for correct lancet blood draw.
Maintenance	The test is disposable. The heat block is expected to last 2 years with original battery life. The life of the device may be extended to 5 years, if the battery is changed.
Internal QC	Yes
External QA	TBD whether it will be compatible with EQA programs; the cartridge cannot be retested to confirm results.
Infrastructure requirements	May be used at all levels in a health facility, including in health centres or in mobile facilities.
User interface	Not available.

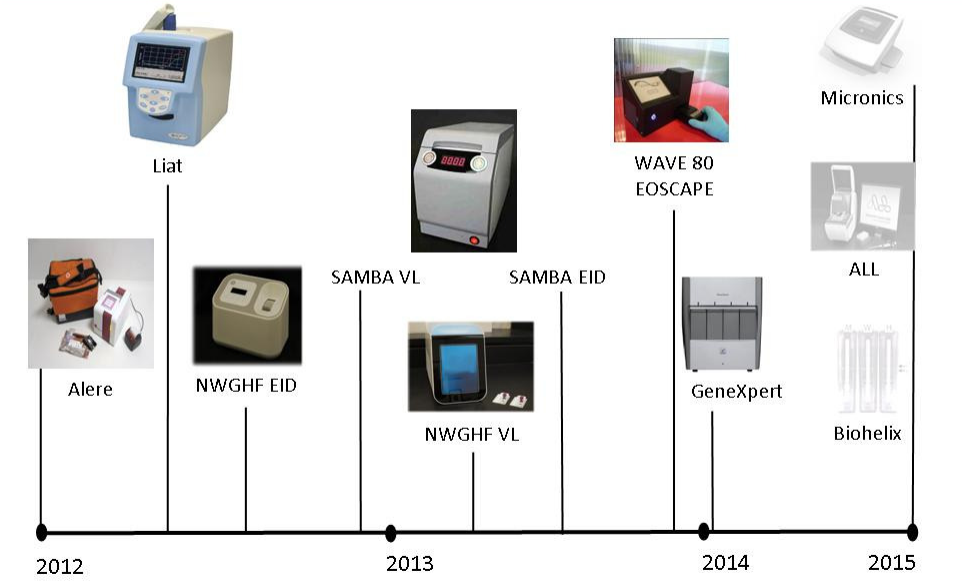
APPENDIX 2: Point-of-Care CD4, Viral Load, and EID Technologies in the Pipeline

Point-of-Care CD4 Technologies in the Pipeline*



*Estimated; timeline and sequence may change.

Point-of-Care Viral Load and EID Technologies in the Pipeline*



*Estimated; timeline and sequence may change.

APPENDIX 3: Glossary of Terms and Acronyms

CE / CE-marking	A mark placed on products in the European Economic Area that indicates the product conforms with requirements of EU directives. CE stands for Conformité Européenne (European Conformity).
EDTA	Ethylenediaminetetraacetic acid, or EDTA, is a potassium salt that is contained in blood collection tubes and is a strong anticoagulant.
EID	Early infant diagnosis
FDA	Food and Drug Administration (U.S.)
FIND	Foundation for Innovative New Diagnostics
IVD	*In vitro* diagnostics, which are tests that can detect diseases, conditions or infections.
NAT / NAAT	Nucleic acid test (NAT) or nucleic acid amplification test (NAAT) is a biochemical test used to detect a virus or bacteria.
NIAID	National Institute of Allergy and Infectious Diseases (U.S.)
NIH	National Institutes of Health (U.S.)
POC	Point-of-care / point-of-care
WHO	World Health Organization