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HIV/AIDS

Diagnostics Technology Landscape

SEMI-ANNUAL UPDATE

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Glossary of terms and acronyms

AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
CE/CE-marking	A mark placed on products in the European Economic Area to indicate that a product conforms to the requirements of European Union directives (CE stands for Conformité Européenne [European Conformity])
DNA	Deoxyribonucleic acid
EDTA	Ethylenediaminetetraacetic acid (a potassium salt that is contained in blood collection tubes and is a strong anticoagulant)
EID	Early infant diagnosis
EQA	External quality assurance
HIV	Human immunodeficiency virus
IVD	In vitro diagnostics (tests that can detect diseases, conditions or infections)
PCR	Polymerase chain reaction
RNA	Ribonucleic acid
USAID	United States Agency for International Development
USB	Universal serial bus
WHO	World Health Organization

Overview

The *HIV/AIDS Diagnostics Technology Landscape* is published annually and is prepared as part of a broad and ongoing effort to understand the technology landscape for HIV/AIDS. This document is a semi-annual update on the technologies for CD4, viral load, and early infant diagnosis (EID) testing, as well as for the diagnostic pipeline. Previous editions and semi-annual updates of the *HIV/AIDS Diagnostics Technology Landscape* are available at:

http://www.unitaid.eu/resources/publications/technical-reports.

Methods

The *HIV/AIDS Diagnostics 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 The material in this landscape was gathered by the author from publicly available information, published and unpublished reports and prospectuses, and interviews with developers and manufacturers.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 Diagnostics Technology Landscape* do not appear in this update, it is because the supplier either did not provide updates or indicated that there were none available at this time.

CD4+ T-Cell counting technologies

Update on CD4 technologies in the market

Aquios CL™ *(Beckman Coulter, Inc.)*
Beckman Coulter now expects to launch its Aquios CL™ flow cytometry platform in 2014. The Aquios CL, which incorporates a technology called Load & Go™, is equipped with an automatic sample loader that utilizes cassettes to queue samples for preparation and analysis. Each cassette holds up to five specimen tubes, and up to eight cassettes can be loaded at one time for a total of 40 specimens. Cassettes can be continuously loaded and unloaded without interrupting the system's workflow.

Different specimen cassettes will be available to accommodate a variety of blood collection tubes. Towards the end of February 2014, Beckman Coulter will launch the Aquios CL with its Tetra panels, and later in 2014 the company plans to launch the system with PLG (PanLeucogating).

Update on point-of-care CD4 technologies in the market

Point-of-care testing platforms

PointCare NOW™ *(PointCare Technologies Inc.)*
The PointCare NOW™ system (pictured below) was developed by PointCare Technologies, Inc. specifically for decentralized and low-resource settings. This compact tabletop system measures CD4 absolute count and percentage (CD4%), white blood cell count and haemoglobin, as well as total count and percentage lymphocytes, monocytes, neutrophils and eosinophil. The system uses forward light scattering (rather than the fluorescent dyes used in some systems) to distinguish lymphocytes from white blood cells, and then uses a colloidal gold label[1] to change the natural light scatter characteristics of the CD4 subclass of lymphocytes in order to perform the CD4 enumeration.

The PointCare NOW instrument is considered to be robust due to its modular injection-moulded housings with few moving parts. The system has solid-state electronics and comes precalibrated from the factory, thus eliminating the need for calibration by the instrument operator. In addition, the system has the advantage of being fully automated. There are no manual sample preparation steps for pipetting, incubation and vortexing. The operator is able to take a capped phlebotomy blood-sample tube and, with the cap still in place, insert it into a receiving slot in the PointCare NOW instrument for analysis, thus eliminating operator contact with blood. The operator can, in fact, walk away from the instrument at this point in the process. Results are available in eight minutes.

1 The label consists of anti-CD4 antibodies coupled with nano-sized gold particles. The colloidal gold label technology is fully described in: Hansen P, Barry D, Restell A *et al*. Physics of a rapid CD4 lymphocyte count with colloidal gold. Cytometry. 2012; **81A**:222–231.

In September 2013, PointCare announced that it had validated a system of internal quality control using its proprietary heat-stable Daily Check controls that eliminate the need for external quality assurance (EQA) controls. PointCare reports that users find traditional EQA difficult to implement at the point of care due to the short shelf-life and temperature sensitivity of the controls. With a validated stability from 2°C to 42°C and a two-year shelf-life, Daily Checks offer a practical solution to performing quality control in remote settings at no additional cost to the user.

The PointCare NOW system is a medium- to low-throughput platform that can handle some 50 samples per day and is appropriate in settings with that level of volume. The system is closed and requires the use of PointCare reagents. The cost of the PointCare NOW instrument is about US$ 25 000. The price of reagents, which includes PointCare's heat-stable Daily Check controls, is approximately US$ 10 per test.

A peer-reviewed evaluation of the PointCare NOW™ platform was published in 2012. The evaluation found that the instrument had low sensitivity in adults, misclassifying 53% and 61% of patients at the 350 and 200 cells/µL thresholds, respectively. While sensitivity was better for children, the authors concluded that the sample size was not large enough to draw a conclusion.[2] In March 2011 PointCare concluded a method comparison with the BD FACSCalibur from BD Biosciences at the National Microbiology Reference Laboratory in Harare, Zimbabwe. The results of this evaluation are expected to be published online in the Journal of AIDS and Clinical Research.[3]

Update on CD4 technologies in the pipeline

BD FACSClearCount *(BD Biosciences)*
BD does not expect to launch its FACSClearCount platform before 2015.

Update on point-of-care CD4 technologies in the pipeline

Point-of-care testing platforms

BD FACSPresto™ *(BD Biosciences)*
The market launch for the BD FACSPresto™ (pictured below) is now expected in early 2014.

2 Sensitivity to identify children in need of ART using a 25% CD4 threshold was 90% and sensitivity was 100% using a 750 CD4 cells/mm^3 threshold.
3 Gumbo P, Chideme M, Mangwanya D, *et al*. Analysis of bias and ART enrollment for a point-of-care CD4/CD4% analyzer. *J AIDS Clin Res. 2013;* **4**: 247. doi: 10.4172/2155-6113.1000247.

EMD Millipore® Muse™ *(Merck)*
EMD Millipore® is poised to introduce a new platform, the Muse™ cell analyser (pictured below), for its CD4/CD4% assay. The Muse cell analyser uses patent-pending, miniaturized fluorescent detection and microcapillary technology to provide accurate, precise and quantitative cell analysis. The microcapillary and miniaturized options of the system take up about one-tenth of the space of typical cytometers, and the laser-based fluorescence detection can evaluate up to three cellular parameters, as compared to two parameters for imaging-based systems.

The Muse cell analyser is easy to use. The primary skills required are pipetting and operating the software on the analyser. The Muse requires only 10µL of patient sample. Sample preparation requires two simple dilutions and two 15-minute incubations. The operator loads the CD4/CD4% reagents on the Muse Auto CD4/CD4% system and then follows easy guided menus on the Muse touchscreen. Results, which are displayed in both graphical and statistical formats, are provided within 2–4 minutes.

The Muse Auto CD4/CD4% system will have two power sources. In the clinic laboratory, the Muse system can be plugged into an uninterruptible power supply. However, for portability, the Muse system offers an optional battery pack that will provide hours of operation.

The cost of the Muse Auto CD4/CD4% system is expected to be approximately €10 000, and the price per test is expected to be € 2.00. EMD Millipore will obtain CE-IVD marking for the Muse system.

Daktari™ CD4 counter *(Daktari Diagnostics, Inc.)*
Daktari reports that independent validation studies on the Daktari™ CD4 system, which is expected to be CE-IVD marked in December 2013, are currently underway in four countries in eastern and southern Africa. It is anticipated that the system will be commercially available in the second quarter of 2014.

MBio Diagnostics CD4 system *(MBio Diagnostics® Inc.)*
At MBio Diagnostics, each product in development is a diagnostic system combining an easy-to-use, software-driven portable reader with single-use disposable cartridges. Initial product development has focused on the rapid diagnosis of complex infectious disease, including HIV and hepatitis.

In 2014, MBio Diagnostics will commercialize its first product, the MBio CD4 system. Requiring a small blood sample of 15 µL, the MBio system will provide an absolute CD4 count in about 25 minutes. MBio Diagnostics received ISO 13485 certification in June 2013.

The immunofluorescence approach is both simple and robust. The novel design capitalizes on the robustness and low cost of modern consumer electronic components, such as cell phone cameras and DVD lasers. The core technologies facilitate an elegant, low-cost, disposable cartridge manufactured via select automation.

MBio reports that its CD4 system (pictured above) offers the following benefits in either near-patient settings or in the clinic.

- ***Accuracy, precision, and quality***. Peer-reviewed studies document minimal Bland-Altman bias, good linearity along the clinical range, and a low rate of misclassification for two common antiretroviral therapy (ART) thresholds – 350 and 500 cells/mm.[4] The MBio CD4 reader utilizes several quality control features on every run to ensure a high-quality assay. The MBio CD4 system is also compatible with several EQA standards, including UK NEQAS and Streck.
- ***Simplicity of use***. Initial usability assessments demonstrate that novice users can master the core workflow in less than 10 minutes. The CD4 reader offers an icon-based graphical user interface. The CD4 cartridge contains heat-stable dried reagents, eliminating the need for "cold chain" transportation of external fluid-based reagents. The CD4 cartridge also accepts either capillary or venous whole blood.
- ***Robustness***. The MBio platform has been utilized in research applications in 12 different locations worldwide. Over 99% of all tests have delivered a quantifiable result. The CD4 cartridge offers a simple design, free of pumps and microfluidics.
- ***Efficiency***. By utilizing an external rack (not shown above) to control the 20-minute incubation period, the throughput of the CD4 reader can be optimized. The CD4 reader requires only three minutes to analyse each sample. As a result, in optimal conditions, operators can process 15–20 units per hour with a single instrument. This level of productivity makes the MBio CD4 reader a cost-efficient technology for use in most clinics. For less frequent operation, the time required to generate the result for one sample is less than 25 minutes.
- ***Connectivity***. The MBio CD system includes integrated Ethernet, four USB ports, and wireless connectivity. Operators can easily export up to 20 000 test results to a mass storage device.

The pipeline for MBio Diagnostics is full. In addition to the CD4 assay, products include immunoassays for HIV and opportunistic infections such as syphilis, viral hepatitis and tuberculosis.

4 Logan, C, Givens M, Ives, JT *et al*. Performance evaluation of the MBio diagnostics point-of-care CD4 counter. *J Immunol Methods*. 2012; **387**: 107–113.

Visitect® CD4 *(Burnet Institute and Omega Diagnostics Ltd.)*
Omega has developed a smartphone app for the Visitect CD4 assay. The app uses the camera in the telephone to read the test result, and a software application provides interpretation and interface to an external laboratory information management system or cloud database.

The company now expects clinical trials of the Visitect CD4 to begin in Africa in the first quarter of 2014, with the commercial launch to follow.

Zyomyx CD4 test *(Zyomyx, Inc. and Mylan Inc.)*
Zyomyx recently finalized an exclusive agreement with Mylan Inc, which will be responsible for distributing their CD4 test in developing countries. The Zyomyx CD4 test, a fully quantitative CD4 readout in a service-free point-of-care format, is still expected to be commercially available before the end of 2013.

Viral load testing technologies

Update on point-of-care viral load technologies in the pipeline

Only one point-of-care testing platform for viral load has been launched to date – i.e., the SAMBA. Below are updates on the SAMBA and on viral load platform products in the pipeline.

SAMBA *(Diagnostics for the Real World, Ltd.)*
Following launch and implementation of the SAMBA viral load assay in two clinics in Malawi in early 2013, Médecins Sans Frontières began implementing the test in the Arua district hospital in Uganda in mid-September 2013.

EOSCAPE-HIV™ rapid RNA assay system *(Wave 80 Biosciences)*
Wave 80 reports that it has recently added two new features to its HIV rapid RNA assay: (i) an internal plasma separation step for the applied fingerstick sample and (ii) a fast isothermal amplification step to extend detection to ~400 copies/mL. Wave 80's device also includes an internal amplification control that corresponds to a 1000 copies/mL detection threshold. This allows semi-quantitative assessment of specimens (above/below) at a threshold of 1000 copies/mL without the need for external calibration. Nonetheless, the entire assay process will still be completed within 50 minutes.

Because of these adjustments to the Wave 80 assay, the company does not expect to finalize the product's design until the end of 2013. The product will be commercially available in 2014, and Wave 80 is currently putting its ISO production facilities into place to support the product launch.

Truelab™ Real Time micro PCR system *(Molbio Diagnostics Pvt. Ltd. [A Tulip Group – Bigtec labs partnership])*
The HIV viral load assay from Truelab™ is now expected to be launched in the second quarter of 2014. The assay is currently undergoing laboratory-based trials in India.

GeneXpert® system *(Cepheid)*
The Cepheid GeneXpert® System HIV viral load assays are on track to be launched commercially in 2014. The quantitative HIV-1 assay using plasma and the qualitative HIV-1 assay using either whole blood or dried blood spots are expected to be CE-IVD marked at launch.

LYNX viral load test and platform *(Northwestern Global Health Foundation)*
The LYNX viral load test and platform (pictured below), which is being developed by the Northwestern Global Health Foundation (NWGHF) in collaboration with Quidel Corporation, is now expected to be launched in 2015. The platform can accommodate 13 tests in an eight-hour day and is easy to use. The LYNX viral load platform is expected to cost US$ 12 000, with reagent costs of US$ 10 per test.

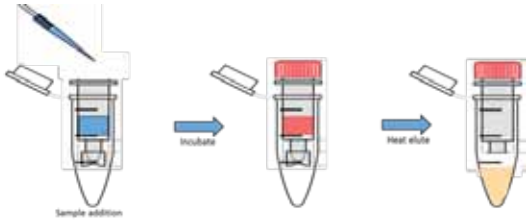
Viral load assay using BART (Bioluminescent Assay in Real Time) technology *(Lumora Ltd.)*
Lumora has developed an assay system, from extraction to result, that will enable a minimally-trained user to perform viral load assays in a nonspecialist laboratory or clinic setting.

Lumora's Stem Primer technology has facilitated the development of a fully-inclusive HIV viral load test utilizing the isothermal LAMP (loop-mediated amplification) technology.

The company believes that ease of sample preparation and processing is key to the success of any assay system, and Lumora's pursuit of simplicity and robustness has led to the development of two novel and proprietary approaches

1. Heat elution for whole blood and dried blood spot; and
2. Bead-based viral extraction from whole blood or plasma.

Whole blood and dried blood spots
Through the utilization of Lumora's proprietary heat elution sample preparation technology, it is possible to extract a sample from whole blood or dried blood spots in 10 minutes using only a heating block and Lumora sample preparation kits. The processed sample can then be added directly to freeze-dried amplification reagents.



Viral extraction kit for whole blood or plasma
Lumora's novel manual three-step viral extraction technology allows nucleic acid to be extracted from whole blood or plasma in 20 minutes. The processed sample can then be added directly to freeze-dried amplification reagents.

The first-generation assays with either heat elution or manual sample extraction are now ready to license, and Lumora is seeking a partner to commercialize this product. Lumora anticipates that the assay can be in the market within six months of securing a commercial partnership.

Fully integrated device

The simplicity and robustness of the manual viral sample extraction chemistry enables the development of a second-generation assay that is that is fully integrated (i.e. "sample in, result out"). As this development continues, it will not be limited to HIV viral load but will have access to the menu of tests that Lumora is developing.

The second-generation assays with viral extraction technology are still being developed, and Lumora is seeking partners to commercialize this product. The company anticipates that the assay can be in the market within 12 months of securing a commercial partnership.

RT CPA HIV-1 viral load test *(Ustar Biotechnologies)*
Ustar is now actively working on the development of its viral load assay with completion and launch expected in the 2016–2017.

Gene-RADAR® platform *(Nanobiosym®, Inc.)*
Nanobiosym® was recently awarded grants from USAID and Grand Challenges Canada under the programme Saving Lives at Birth: A Grand Challenge for Development. The grants are for the design and implementation of a pilot trial in Rwanda for viral load testing using the Gene-RADAR® platform.

Most recently, Nanobiosym® received the grand prize in a nano-sensing competition sponsored by the XPrize Foundation and Nokia. Nanobiosym was selected from a pool of 26 competing teams from seven countries for the US$ 525 000 award.

HIV quantitative assay *(BioHelix Corporation)*
In May 2013, BioHelix Corporation was acquired by Quidel Corporation. As a result of the acquisition, the BioHelix viral load assay development project is no longer active.

Advanced liquid logic

On 23 July 2013, Illumina, Inc. acquired Advanced Liquid Logic, Inc. It is not known at this time whether Illumina will continue to pursue the development of a viral load assay.

Early infant diagnostics

Update on point-of-care EID technologies in the pipeline

To date, no point-of-care testing platforms dedicated to early infant diagnosis (EID) have been launched. Below are updates on one of the products in the pipeline.

LYNX HIV p24 antigen assay *(NWGHF)*
The price of the LYNX HIV p24 antigen processor device is now expected to be in the range US$ 700–2000 depending on volume; the per-test cost, which is expected to range from US$ 7 to US$ 15, will also be dependent on volume. Clinical and field trials on the assay commenced in 2013, with availability expected in late 2013/early 2014.

APPENDIX 1: Operational characteristics of CD4, viral load, and early infant diagnosis platforms

Note: Only tables that have been updated from the June 2013 *HIV Diagnostics Technology Landscape* are included here. For a comprehensive catalogue of tables, please see the June 2013 report at:

http://unitaid.org/en/resources/publications/technical-reports.

Point-of-care CD4 technologies in the pipeline

EMD Millipore® Muse™ Auto CD4/CD4% System	
Type of technology	Small, bench-top, flow cytometer
Output	Absolute and percentage CD4 counts
Turnaround time	2-4 minutes, after two 15-minute incubations
Capacity	Approximately 16 samples per day
Throughput per technician/ per day	16 samples per technician per eight-hour day
Sample needed and stability	10 µL whole blood collected in EDTA anticoagulant
Sample preparation and protocol complexity	Process: (i) add reagents to tube; (ii) add 10 µL of blood from patient; (iii) incubate for 15 minutes; (iv) add lyse solution; (v) incubate sample for 15 minutes in darkness; (iv) sample is run on the instrument.
Reagent stability	Reagents must be stored at 2-8°C (36-46°F); reagents are shipped with 12 months of shelf-life.
Price/test	~€2.00 per test for CD4/CD4%, regardless of volume
Price/instrument	Approximately €10 000
Regulatory status	CE-IVD marking is being sought.
Physical dimensions (cytometer only) (W x H x D)	Width: 20.62 cm (8.12 inches) Height: 22.07 cm (8.69 inches) Depth: 28.22 cm (11.11 inches)
Weight	5.94 kg (13.1 lbs)
Third-party supplies	Refrigerator, vortex and pipettor
Electric power requirements	100–240 VAC, 50–60 HZ, 80 W; or optional battery pack
Environmental requirements	Temperature: 15–35°C (59-95°F) Humidity: 10–90% Maximum altitude: N/A
Data station	Dedicated CPU is integrated into the instrument; results can be downloaded via USB.
Monitor	Colour touch screen is integrated into the instrument.
Printer	Not included
Barcode scanner	No
Training	Less than one day of training is required
Maintenance	Routine preventative maintenance required. If damaged, device will be sent to a regional repair laboratory. Repair and return of device should be effected within one week.
Internal quality control	Extensive internal controls include reagent control, automatic control of cartridge expiry date, internal process controls.
External quality assurance	TBD
Infrastructure requirements	Can be used at all levels of health facility, including health centres and mobile facilities.

N/A: not available.
TBD: to be decided.

MBio CD4 system	
Type of technology	A point-of-care, fully-automated diagnostics instrument with single-use, self-contained cartridges that contain heat-stable dried reagents
Output	Absolute CD4 count (quantitative). Future releases will provide haemoglobin and percentage CD4.
Turnaround time	~23 minutes, including a room-temperature incubation period of 20 minutes which is controlled by the CD4 rack, followed by a three-minute analysis by the CD4 reader. The read window is 100 minutes after the incubation period.
Capacity	15–20 tests per hour per instrument
Throughput per technician/ per day	More than 100 samples per day per instrument, assuming a workday
Sample needed and stability	~10–15 µL of capillary (by fingerstick) or venous whole blood
Sample preparation and protocol complexity	Complexity comparable to that of CLIA-waived diagnostic instruments in the USA. No buffers or liquid reagents are necessary. Only one incubation period is required.
Reagent stability	The lyophilized reagents on the cartridge do not require cold chain transportation or storage. CD4 cartridges can be stored in the package between 2°C and 40°C for 12 months at 70% relative humidity.
Price/test	US$ 6 per test (estimated), with volume discounts
Price/instrument	Less than US$ 5000 per system; reagent rental or leasing plans are available.
Regulatory status	CE-IVD mark anticipated in late 2013
Physical dimensions (cytometer only) (W x H x D)	Length: 25 cm (~10 inches) Width: 15 cm (~6 inches) Height: 17 cm (~7 inches)
Weight	2.5 kg (5.5 lbs)
Third-party supplies	Sterile lancets (for capillary blood samples), alcohol swabs, dry swabs, gauze, band-aid
Electric power requirements	Rechargeable battery operation (eight hours) or plug in to electricity supply (100–220 VAC)
Environmental requirements	Operating temperature: 15–35°C Humidity: 5-95%, non-condensing Maximum altitude: 4000 metres (~6900 feet)
Data station	On-board computer for sample analysis, results management and event logs. Instrument will have a built-in ethernet connection and multiple USB ports to support printers, external barcode readers.
Monitor	Integrated touchscreen interface has administrator-configurable settings such as user lockout, validation and quality control scheduling. Predominantly icon-driven.
Printer	External USB printer
Barcode scanner	Internal barcode reader captures cartridge information. Capable of supporting an external barcode reader.
Training	Formal training can be achieved in one day. Basic competency can be acquired in 10 minutes.
Maintenance	No routine maintenance or service; system replacement via depot/distributor.
Internal quality control	Internal quality control on every cartridge for multiple parameters, including sample volume, reagent quality, lot expiry, etc.
External quality assurance	Compatible with pre-identified, third-party external quality assurance materials.
Infrastructure requirements	None provided that environmental requirements are met.

Point-of-care viral load technologies in the pipeline

Truelab™ real-time micro PCR system	
Type of technology	Nucleic acid amplification test (real-time PCR)
Output	HIV-1 RNA level (quantitative)
Turnaround time	60 minutes (from sample to result)
Capacity	One chip per processing unit (company plans a four-chip version)
Throughput per technician/ per day	About 12 per eight-hour day (about 50 with four-chip version)
Sample needed and stability	100µL plasma for viral load or 100µL of blood for screening. Sample must be processed immediately on collection or stored at -20°C. Alternatively, for transport, 100µL of the specimen may be transferred to a tube to which 500µL of lysis reagent has been pre-added.
Sample preparation and protocol complexity	The extraction process currently involves multiple pipetting steps that require operator interventions, including adding reagents, aspirating liquid, adding buffer, etc. (An automatic sample preparation is expected to be introduced soon). Once extracted, the nucleic acid is dispensed into a chip that is inserted into the PCR analyser, and the thermal cycling and analysis take place automatically within the analyser.
Reagent stability	Reagents are ready to use, shelf-stable for one year when stored at 2–30°C and for three months at temperatures up to 40°C.
Price/test	US$ 15
Price/instrument	US$ 8000 (includes sample preparation, PCR analyser, printer, pipettes)
Regulatory status	Manufacturing facility is ISO 13485 and ISO 9001 certified. The Indian test manufacturing licence has been obtained and the registration process is under way.
Physical dimensions (analyser only) (L x H x D)	Length: 21 cm (8.27 inches) Width: 14 cm (5.5 inches) Height: 10.9 cm (4.29 inches)
Weight	0 .9 kg (~ 2 lbs)
Third-party supplies	Powder-free disposable gloves, waste disposal container with lid, sterile lancets, alcohol swabs, dry swabs
Electric power requirements	Continuous power supply not required. Rechargeable lithium ion battery pack (7.5V, 2200mAh) provides for over eight hours of back-up on a full charge.
Environmental requirements	Operating temperature: 15–~35°C Humidity: 10-80% Maximum altitude: N/A
Data station	Dedicated CPU integrated into instrument; approximately 5000 test results can be stored on the instrument archive. Supports wireless connectivity (Wi-Fi, Bluetooth, GPRS).
Monitor	Integrated touchscreen 3.2-inch (8.13 cm) colour monitor; touchscreen interface; power on/off switches on analyser unit.
Printer	External 2-inch (5.08 cm) Bluetooth thermal printer
Barcode scanner	No
Training	2–3 hours, high school diploma or equivalent
Maintenance	Yearly contract, warranty one year
Internal quality control	Full process internal control that validates the sample preparation and PCR
External quality assurance	Universal control kit containing. Positive and negative controls must be ordered separately. Positive and negative controls should be run from time to time. It is advised to run controls under the following circumstances: (i) whenever a new shipment of test kits is received; (ii) when opening a new test kit lot; and (iii) by each new user prior to performing testing on a clinical specimen.
Infrastructure requirements	None
User interface	Continuous power supply not required. Rechargeable lithium ion battery pack (7.5V, 2200mAh) provides for over eight hours of back-up on a full charge.

Cross-priming amplification: Ustar RT CPA HIV-1 viral load test	
Type of technology	Nucleic acid amplification – isothermal cross-priming amplification
Output	Viral cps/mL of blood (dynamic range of 1000 to 20 000 cps/mL)
Turnaround time	<1 hour
Capacity	12 tests plus four controls
Throughput per technician/ per day	>36 tests
Sample needed and stability	50–100µL of whole blood finger stick; or 1mL of venous blood
Sample preparation and protocol complexity	No more than 3-5 steps from sample to result
Reagent stability	Stable for 24 months at 0-40˚C, 90% humidity, including transport stress (48 hours with fluctuations up to 50˚C and down to 0˚C).
Price/test	US$ 3-5 per test (ex-works)
Price/instrument	<US$ 5000
Regulatory status	Under development
Physical dimensions (W x H x D)	Width: TBD Height: TBD Depth: TBD
Weight	<2 kg (<4.4 lbs)
Third-party supplies	None
Electric power requirements	110–220V AC current or DC power with rechargeable battery lasting eight hours.
Environmental requirements	Temperature: 15–40°C Humidity: No requirement Maximum altitude: >2000 metres (6500 feet)
Peripherals/supporting instrumentation	None
Barcode Scanner	TBD
Training	Approximately half a day
Maintenance	System is swapped for a new one upon malfunction.
Internal quality control	Internal amplification control; fluorescent control ensures probes are working.
External quality assurance	Three quantitative standards and one negative control
Infrastructure requirements	Intermittent power, bench to store instrument, incineration for medical waste

TBD: to be decided.

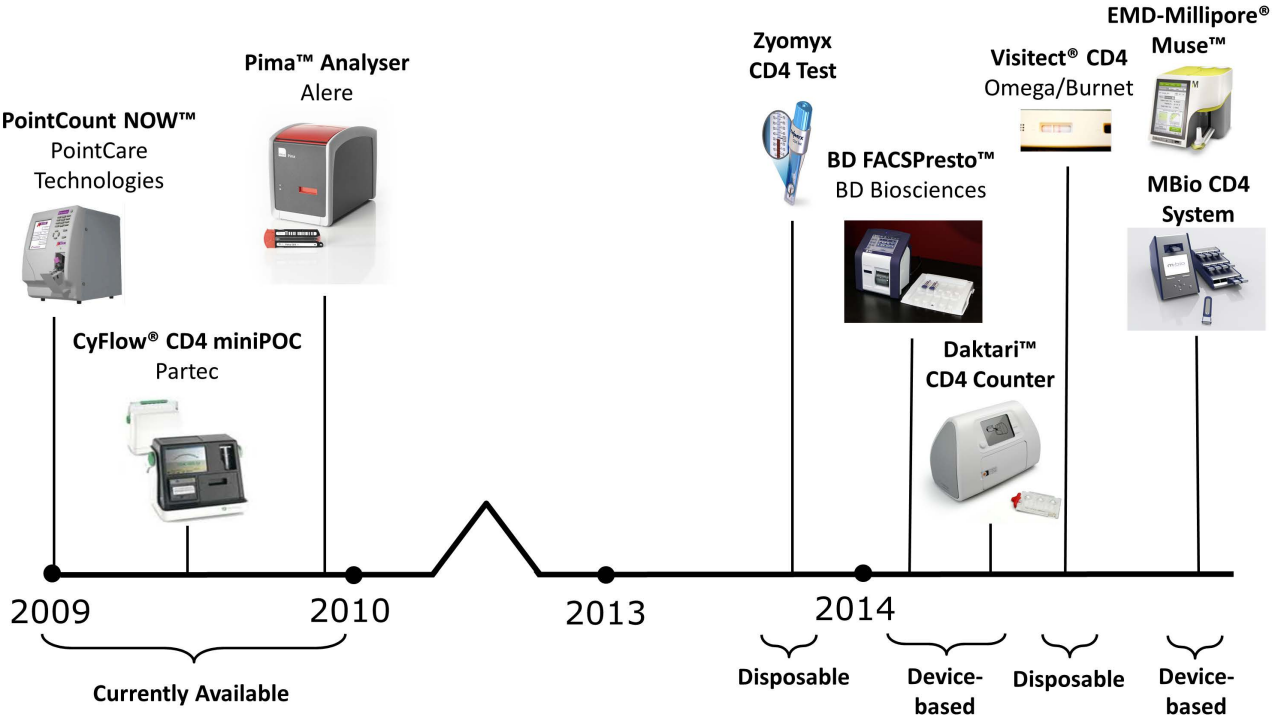
Point-of-care early infant diagnosis technologies in the pipeline

NWGHF p24 antigen rapid lateral flow assay	
Type of technology	A bench-top automated cartridge-based system that extracts amplifies and detects nucleic acid targets for IVD applications.
Output	Quantitative HIV-1
Turnaround time	~60-90 minutes
Capacity	The processor will accommodate 13 tests per eight-hour workday.
Throughput per technician/ per day	13 tests per eight-hour workday
Sample needed and stability	To achieve 1000 copies per mL of plasma, ~150 µL of whole blood will be converted into plasma with simple sample preparation materials provided by NWGHF.
Sample preparation and protocol complexity	(i) Add sample to mini-cartridge; (ii) close sample port and cap to seal mini-cartridge; (iii) place the mini-cartridge in the sample preparation device for 2–3 minutes; (iv) remove mini-cartridge from sample preparation device and attach to cartridge; (v) place the cartridge on the loading/unloading position on the system; (vi) read the results on the screen.
Reagent stability	The shelf-life of the assay kit is expected to be 12–18 months at 30-40°C, 70-90% humidity.
Price/test	<US$ 10 per test
Price/instrument	<US$ 12 000
Regulatory status	TBD
Physical dimensions (cytometer only) (W x H x D)	TBD
Weight	TBD
Third-party supplies	Blood collection supplies
Electric power requirements	The processor is powered by an external power transformer that connects to either an AC or DC power cable connected to an AC or DC power socket in the clinic or laboratory. A fully-charged battery will process the cartridges in the processor.
Environmental requirements	No cold chain or humidity control is required for shipping and transport.
Data station	An internal EDGE/3G modem is provided on request.
Monitor	Integrated into the instrument
Printer	Optional
Barcode scanner	Optional
Training	Minimal training required; the primary skill required is correct lancet blood draw.
Maintenance	Minimal maintenance
Internal quality control	Yes
External quality assurance	Will be fully compatible with existing external quality assurance programmes.
Infrastructure requirements	Can be used at all levels of health facility, including health centres and mobile facilities.
User interface	Onboard display

TBD: to be decided.

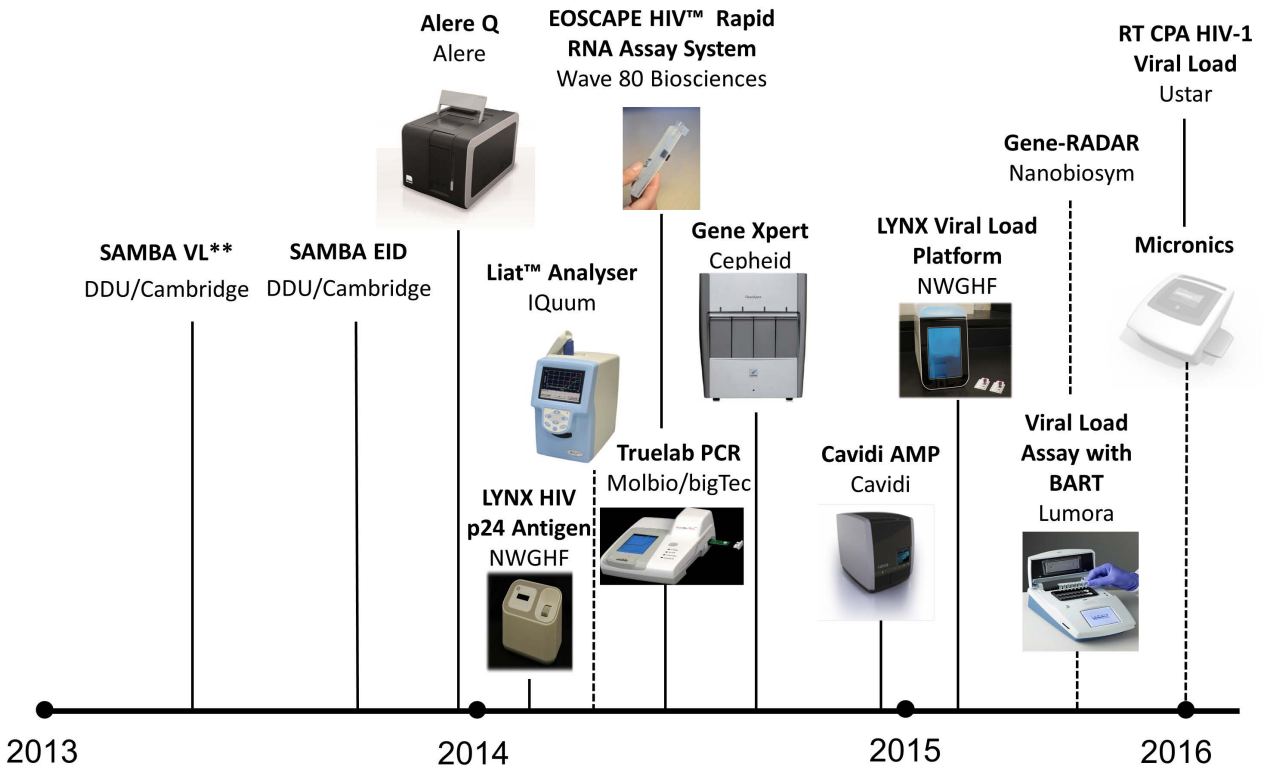
APPENDIX 2:
Point-of-care CD4, viral load, and EID technologies in the pipeline

POC CD4 products: available & pipeline*



*Estimated as of October 2013 - timeline and sequence may change.

POC viral load & EID products: available and pipeline*



*Estimated as of October 2013 - timeline and sequence may change. ---- No market launch date set by company.
**Available in limited release.