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Diagnostics Technology Landscape

SEMI-ANNUAL UPDATE

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Overview

The *HIV/AIDS Diagnostics Technology 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. 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 The material in this landscape was gathered by the author from publicly available information, published and unpublished reports and prospectuses, and interviews with developers and manufacturers.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 either because the supplier did not provide updates 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.)

A peer reviewed evaluation of the PointCare NOW™ platform was recently published.[1] The review 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]

The company concluded a method-comparison with the FACSCalibur (BD Biosciences) in March 2011 at the National Microbiology Reference Laboratory (NRL), Harare, Zimbabwe. The results from the NRL evaluation together with the results of an evaluation conducted at military clinics in Uganda and with clinical results from a study at Massachusetts General Hospital in 2012, have been submitted for peer review and are expected to be published in the near future.

CyFlow® miniPOC (Partec GmbH)

Starting in 2012, Partec has made available, both on its CyFlow Counter and miniPOC, a detailed instrument manual in video format. The manual covers instrument set-up and operation, instructions on how to perform the CD4 and CD4% assays, and basic maintenance instructions. This video can be selected from the on-screen menu, and operators can use it at any time.

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

Point-of-Care Testing Platforms

Daktari™ CD4 Counter (Daktari Diagnostics, Inc.)

Daktari reports that the Daktari™ system could be adapted to CD4 percentage, and future test cartridges for HIV viral load and other infectious diseases are also anticipated to run on the same platform. The company still anticipates market launch in 2013. The anticipated cost for the device is now $5,000, with per test cost still expected to be approximately $8.00, which may go lower with volume discounts.

MBio Diagnostics Systems (MBio Diagnostics® Inc.)

MBio Diagnostics® Inc. is developing robust and simple diagnostic systems for cellular analysis and multiplexed immunoassays in peripheral labs, clinics and at the point-of-care (POC). The systems combine one-step disposable cartridges and a reader, providing quantitative measurements and "lab-quality" results within the timeframe of a patient visit. This novel technology permits the use of a variety of assay formats (immunoassay, cellular analysis, nucleic acid testing) and sample types (blood, saliva, urine), giving MBio systems flexibility and a cost profile the company believes is appropriate to resource-limited settings for which the MBio systems have been specifically designed.

1 Bergeron M, Daneau G, Ding T, et al. Performance of the PointCare NOW system for CD4 counting in HIV patients based on five independent evaluations. PLoS ONE 2012; 7(8): e41166.
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/ml threshold.

MBio's current product pipeline consists of a CD4 cell-counting system and a multiplexed immunoassay system, the latter focused on HIV and opportunistic infections such as syphilis, viral hepatitis and tuberculosis.

The MBio CD4 system (pictured above) consists of a software-driven reader and single-use disposable cartridges to deliver absolute CD4 counts from finger stick or venous whole blood samples.

- ***Technology***: The instrument functions as a two color fluorescence imaging cytometer and delivers absolute CD4 counts based on immunostaining and direct cell counting.
- ***CD4 absolute count***: The initial product delivers absolute CD4 count. Future versions can be configured for CD4/CD8 ratio, CD4% and hemoglobin.
- ***Sample processing***: Capillary or venipuncture whole blood is loaded in one step directly into the cartridge.
- ***Cartridge***: The disposable cartridge is a robust, all-plastic design with no pumps, valves, or complex fluidic features.
- ***Biohazard and safety***: Blood and assay fluids stay on the sealed device, minimizing biohazard handling.
- ***Time-to-result:*** Turnaround time for a single sample is approximately 20 minutes; 15 to 20 minute sample incubation period in the cartridge and 3 minutes for reader processing.
- ***Sample throughput***: Cartridges can be processed in parallel (batch mode) using a separate cartridge rack with automatic timing. One operator with one system can process 10 samples per hour, or ~80 samples per day.

The MBio CD4 system includes an on-board computer for sample analysis, results management, internal quality control and event logs that can be exported in common and viewable file formats for data review. 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 multiple USB ports to support printers, external barcode readers and wireless adapters.

A first prototype version of the MBio CD4 system has been undergoing field testing on both capillary and venous blood samples at the Antiviral Research Center in San Diego, CA, USA. Pre-market field evaluations in sub-Saharan Africa are scheduled for late 2012 and early 2013. First regulatory approvals and in-country registration trials are scheduled for late 2013.

Visitect CD4 (Burnet Institute and Omega Diagnostics Ltd.)

Burnet Institute (Burnet) recently licensed its semi-quantitative CD4 technology to Omega Diagnostics Ltd. (UK). The test, which is now called the Visitect CD4, is expected to be available for commercial release in December 2012. At release, the cost of the test is expected to be about $5.00. The optional reader for the test, which has been developed by Axxin Ltd. (Australia), is expected to cost about $3,000, but may decline to below $2,000 over time. In addition to reading the results of the test, the reader also provides data storage and connectivity options, as well as real-time operating instructions for the tests.

In response to WHO recommendations for treatment initiation, Burnet re-optimized the Visitect CD4 to change the primary reference cut-off from 200 CD4+ T-cells/µL (the original design level) to 350 CD4+ T-cells/µL. Evaluation of the prototype version of the test at the 350 CD4/µL cutoff at the Burnet and Alfred Hospital, Melbourne, has shown 97% sensitivity for samples below 350 CD4/µL and 80% specificity for samples above 350 CD4/µL (total n = 126). Clinical validation trials of the test are planned to follow in the UK, the United States, Kenya and South Africa in the last quarter of 2012.

BD FACSPresto™ (BD Biosciences)

The POC CD4 platform being developed by BD Biosciences, pictured below, will be called the BD FACSPresto™. Market launch is now expected in late 2013.

BD FACSPresto™ 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

To date, no POC viral load testing platforms have been launched. Below are updates on some of the products in the pipeline.

Liat™ Analyser (IQuum, Inc.)

IQuum reports that the turnaround time for the viral load assay on its Liat™ Analyser is now 30 – 35 minutes, and the limit of detection is less than 100 cp/mL. The Liat™ Analyser is now expected to be released in 2013.

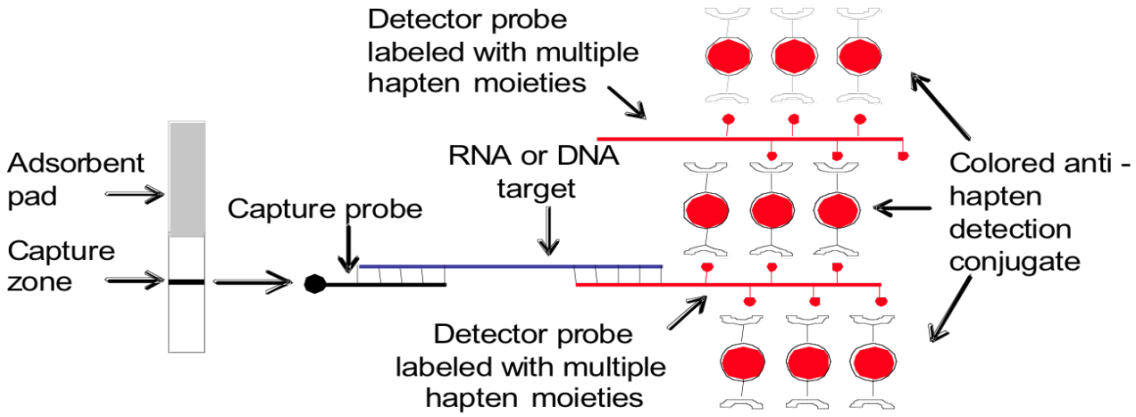
EOSCAPE-HIV™ HIV Rapid RNA Assay System (Wave 80 Biosciences)

Full scale validation and clinical testing of the Wave 80 EOSCAPE HIV-1 RNA test is now expected to begin in early 2013, followed by in-country testing for market launch later that year. Further expansion of the EOSCAPE assay platform includes development of assays for both TB and hepatitis.

SAMBA (Diagnostics for the Real World, Ltd.)

The **S**imple **AM**plification **B**ased **A**ssay (SAMBA) is being developed by a team led by Dr. Helen Lee, Director of the Diagnostics Development Unit (DDU) at University of Cambridge. Three NAT-based HIV assays are being developed: (i) a semi-quantitative test with a cutoff of 1,000 cp/mL for monitoring of ART (ii) a qualitative test based on plasma for detection of acute HIV infection during the window period before the appearance of antibodies and (iii) an EID test based on whole blood. The first SAMBA HIV assay to be launched will be the semi-quantitative viral load assay. The SAMBA system automates extraction and integrates amplification and detection into a bench-top analyser with amplification and detection taking place in a closed cartridge.

The SAMBA HIV test uses 200 µL of plasma for the semi-quantitative viral load assay, 500 µL of plasma for the qualitative acute infection assay and 100µL of whole blood for the EID assay. The sample preparation process is an aqueous-based method involving cell lysis and nucleic acid extraction using a solid phase. The amplification and detection process is integrated into a closed cartridge to prevent amplicon contamination and targets the LTR region of the genome. Amplification is based on both target and signal amplification (see below).



A capture probe is used to capture the target sequence, and a detection probe with multiple hapten labels is subsequently attached to the target sequence, enabling amplification of the signal to improve sensitivity and allow visual reading. The lattice structures, shown above, ensure visual detection of the RNA or DNA target, which can be visually read off of a test strip within 25 minutes. The test strip is based on a nitrocellulose membrane in a lateral flow format.

Based on an assessment with the WHO International standard HIV RNA genotype panel containing 400 cp/mL, the SAMBA assay was able to detect all HIV-1 subtypes.

The SAMBA semi-quantitative viral load test was successfully evaluated on clinical samples from St. Thomas Hospital and Royal London Hospital and conducted at two Médecins Sans Frontières (MSF) sites (Chiradzulu,

Malawi and Arua, Uganda) in a total 488 HIV patients. The company reports that overall concordance between SAMBA and the Roche COBAS® TaqMan v2.0 was 97%.

The SAMBA qualitative acute infection assay using plasma has been evaluated in-house using 416 clinical samples from the Royal London Hospital and compared to the Roche COBAS® TaqMan v1.0 in a blinded fashion. Samples with discrepant results were tested by the Abbott RealTi*m*e HIV-1 assay. Using both the Roche and Abbott viral load assays as combined gold standards, the company reports that the SAMBA qualitative HIV assay was able to detect all samples with viral load greater than 100 cp/mL and showed a sensitivity of 98.5% and a specificity of 100%.

The SAMBA EID assay has been evaluated in-house using HIV positive or negative adult whole blood clinical samples in a blinded comparison with DBS testing using the Roche Amplicor v1.5 assay and the Ampliprep/TaqMan carried out by two laboratories in Zambia and Uganda. Discrepant samples were further tested by the Royal London Hospital using a multiple gene-based in-house PCR. Per the company, SAMBA was more sensitive than Roche and showed good reproducibility. However, evaluation in the field using infant blood is required and will take place in Uganda and Malawi upon receiving ethics approval.

Currently, the total assay time is 2 hours for the SAMBA EID and acute infection assays and 90 minutes for the semi-quantitative viral load assay. SAMBA is suitable for use at district hospital level or large clinics in sub-Saharan Africa. Diagnostics for the Real World, Ltd, the spinout company of DDU located in California, is the manufacturer of the SAMBA system.

The expected market release dates for the SAMA assays are as follows: viral load assay, first quarter of 2013; acute infection assay, second quarter of 2013; and EID assay, third quarter of 2013. There is currently no pricing information available from the company.

GeneXpert® System (Cepheid)

Effective August 6, 2012, PEPFAR, USAID, UNITAID and the Bill & Melinda Gates Foundation announced an agreement to reduce the cost of the GeneXpert MTB/RIF cartridges from $16.86 to $9.98 in 145 high-burden and developing countries (HBDCs).

The projected release date for the HIV viral load assay on the GeneXpert System is now anticipated to be in early 2014.

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

The Northwestern Global Health Foundation (NWGHF) in collaboration with Quidel Corporation is developing a POC rapid RT-PCR testing platform that will be both easy to use and low cost. The product design calls for a small device (pictured below) that can process multiple samples at a time with test results in 60-90 minutes. The system will incorporate internal controls. The proposed viral load assay could be run off of whole blood from fingerstick or venipuncture, achieving a limit of detection of between 200 to 1,000 copies/mL, depending on sample volume.

The device will run on AC power, but will come equipped with a back-up battery in the event of power loss. No specific cost data is currently available, but NWGHF indicates that pricing is anticipated to be competitive with CD4 testing.

NWGHF/Quidel expect to launch this product in 2014.

HIV Quantitative Assay (BioHelix Corporation)

BioHelix has received a two-year SBIR grant from the NIAID to develop a quantitative HIV RNA assay based on its isothermal HDA amplification technology and a portable fluorescence analyzer which is capable of monitoring fluorescent signals in real-time. Pursuant to the SBIR grant, BioHelix will collaborate with Dr. Jeanne Jordan at George Washington University to develop a low-cost HIV viral load test for use at the POC in resource-limited settings.

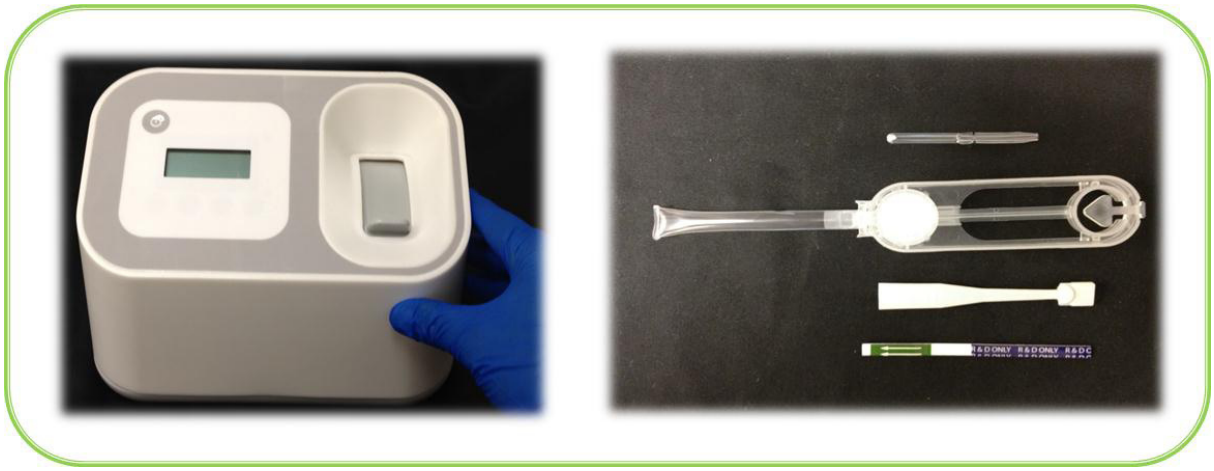
Early Infant Diagnostics

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

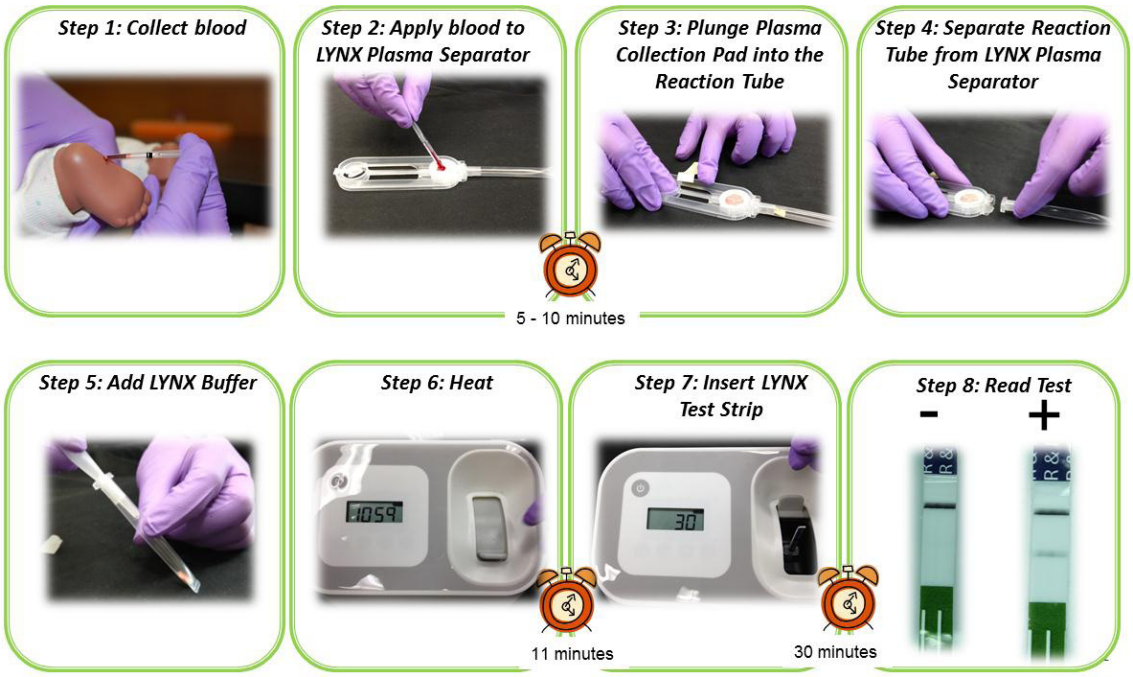
To date, no POC testing platforms dedicated to early infant diagnosis (EID) have been launched. Below are updates on some of the products in the pipeline.

LYNX HIV p24 Antigen Test (NWGHF)

NWGHF is developing an ultrasensitive p24 antigen rapid lateral flow assay for use at the point of patient care. The technology (pictured below), LYNX, involves not only a lateral flow strip that detects HIV p24 antigen, but pre-analytical devices for separating plasma from heel-stick blood and disrupting immune complexes that would interfere with immunoassays. NWGHF has demonstrated proof of principle of the test.



The assay procedure involves collecting about 80µL of heel-stick blood from the infant using a capillary tube; separating plasma from the sample; adding buffer to the sample and pretreating it with "heat shock" in a small, battery-powered processor device; inserting the rapid test strip into the device; and waiting approximately 40 minutes to read the result. The total assay duration is about 45 – 50 minutes. An illustration of the procedure is pictured below.



Note that, similar to other rapid tests, if only the top line appears (the control line only), the test is negative and the infant has not been infected with HIV. If both lines appear (the control line and the test line), the test is positive and the infant has been infected with HIV. If the top line does not appear, the test is invalid and must be re-run.

In early testing, the assay has shown about 95% sensitivity and 99% specificity. The price of the processor device is expected to be between $700 and $900 and the per-test cost is expected to range from $7 to $15. Clinical and field trials on the assay commenced in 2012, with availability expected in 2013.

Qualitative EID Assay (Micronics, Inc.)

Micronics has a number of tests in development, including an assay for Shiga toxin-producing E-coli, and the company is now planning clinical validation of the first assay in 2012. Micronics has also been funded to develop qualitative assays for each of HIV, HHV and HCV; however, the company still has no current plans for a quantitative viral load assay.

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

Note: Only tables that have been updated from the June 2012 *HIV Diagnostics Technology Landscape* are included here. For a comprehensive catalog of tables, please see the June 2012 report: http://www.unitaid.eu/images/marketdynamics/publications/UNITAID-HIV_Diagnostics_Landscape-2nd_edition.pdf.

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	10 minutes
Capacity	~40 – 50 samples per day
Throughput per technician/ per day	~40 to 50 samples per technician per day; no batching capabilities; walk-away operation.
Sample needed and stability	16 µL of capillary (fingerstick) blood applied to Daktari cartridge.
Sample preparation and protocol complexity	No manual sample preparation required. Protocol: (i) lancet finger; (ii) apply blood drop to cartridge; (iii) insert into CD4 counter; (iv) press "start"; (v) read result from LCD screen or printout.
Reagent stability	Dried reagents require no refrigeration. Stable to 50°C in preliminary studies.
Cost/test	$8.00 per test (estimated), but may be lower with volume discounts
Cost/instrument	<$5,000 (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)
3rd party supplies	Sterile lancets (for capillary blood samples), alcohol swabs, dry swabs, gauze, bandaid

Daktari™ CD4 Counter (2)	
Electric Power Requirements	Regular AC. Long-life rechargeable battery self-contained in device which can operate for up to 3 days on a single battery charge.
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 instrument. Results stored on instrument and can be downloaded, if needed, and can be automatically uploaded to a remote server for analysis.
Printer	Daktari will offer a USB printer accessory for printed results.
Bar-code Scanner	TBD
Training	Minimal training required. Lay person can be trained in less than 90 minutes. Primary skill required is for correct lancet blood draw.
Maintenance	The device does not use lasers, but rather employs an electronic system and may be less prone to damage. If damaged, the company plans to swap-out the device rather than repair it on-site.
Internal QC	Internal QC of instrument performed with each assay run; internal QC of cartridge with each run includes checks on sensors, assay protocol, and key reagents. No calibration required. Instrument will also perform QC of capillary blood draw and inform user if fingerstick is inadequate prior to running assay.
External QA	TBD whether compatible with CD4 EQA programs; cartridge cannot be retested to confirm results.
Infrastructure Requirements	Can be used at all levels of health facility, including health centers or in mobile facilities.

MBio CD4 system	
Type of Technology	Small, portable instrument with disposable, self-contained sample cartridges; measurement is by fluorescence imaging cytometry with on-board immunostaining and direct cell counting.
Output	First product delivers absolute CD4 count. Future versions can be configured for CD4/ CD8 ratio, CD4%, Hb, etc.
Turnaround time	~20 minutes (15 to 20 minutes in cartridge and 3 minute instrument read time). Multiple cartridges can be processed in parallel.
Capacity	10 tests per hour, manually running cartridges in parallel.
Throughput per technician/ per day	~80 samples per technician per 8 hour day.
Sample needed and stability	~10 µL of capillary (fingerstick) or venous whole blood
Sample preparation and protocol complexity	One-step whole blood transfer to cartridge. Cartridge incubation on rack with automatic timing. Manual cartridge insertion into reader.
Reagent stability	Target requirement: capable of being stored in package between 2° and 40°C for 18 months at 70% relative humidity.
Cost/test	$6.50/test (estimated); volume discounts
Cost/instrument	Less than $5,000 per system
Regulatory Status	Plan to obtain CE-IVD mark and other approvals as necessary.
Physical dimensions	Length: 25 cm (~10")
(cytometer only)	Width: 15 cm (~6")
(LxWxH)	Height: 17 cm (~7")
Weight	3.0 kg (~6.6 lbs)
3rd party supplies	Sterile lancets (for capillary blood samples), alcohol swabs, dry swabs, gauze, bandaid.

MBio CD4 System (2)	
Electric Power Requirements	Rechargeable battery operation (8 hours) or plug-in to electrical supply (100 to 220 VAC)
Environmental Requirements	• Operating Temperature: 15-35°C • Humidity: 5% - 95%, non-condensing • Maximum altitude: 2,000 meters
Data Station and Reports	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 and wireless adapters. Data reports, including QC, are available for off-line analysis or transfer.
Monitor	Integrated touchscreen interface with administrator-configurable settings such as user lockout/validation and QC scheduling. Predominantly icon-driven.
Printer	External USB printer.
Bar-code Scanner	Internal barcode reader captures cartridge information. Capable of supporting an external barcode reader.
Training	Minimal training required: less than one day training, minimally skilled staff. Primary skill required is for correct fingerstick blood draw.
Maintenance	No routine maintenance or service; system replacement via depot/distributor swap-out
Internal QC	Internal QC on every cartridge for multiple parameters, including sample addition, reagent quality, lot expiration, etc.
External QA	Compatible with pre-identified, third-party external QC materials.
Infrastructure Requirements	Minimal infrastructure – no water requirements; access to power for battery recharge. Target settings are clinic / health post and peripheral labs.

Visitect CD4	
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	
Throughput per technician/ per day	~120 samples per technician per 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 whole blood to Well A of test strip using MicroSafe pipette, wait 3 minutes; (iii) add 1 drop of supplied buffer to Well A and allow sample to run for 17 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
Cost/test	$5.00 per test (estimated)
Cost/reader	$3,000 for reader (eventual price estimated $2,000). 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 of reader	390 g (~14 oz)
3rd party supplies	Sterile lancets (for capillary blood samples), alcohol swabs, dry swabs, gauze, bandage

Visitect CD4 (2)	
Electric Power Requirements	None for cartridge; reader 12V DC via adapter (110-240V), optional battery pack.
Environmental Requirements	• Operating Temperature: TBD • Humidity: TBD • Maximum altitude: TBD
Data Station	None (reader stores most recent 1,000 tests; downloadable via USB/ethernet)
Monitor	None (reader 2.4 inch color touch screen)
Printer	None (reader can support printing)
Bar-code Scanner	Yes (optional on reader)
Training	Minimal training required. Lay person can be trained in less than 120 minutes. Primary skill required is for correct lancet blood draw, and for visual test reading (automated with reader). Reader provides on-board training instructions (can be used in instruction/assay run mode, or read-only for batched tests).
Maintenance	Test is disposable and does not require service/maintenance; reader is expected to be robust and will be swapped out if it fails.
Internal QC	None (Reader has internal QC)
External QA	TBD
Infrastructure Requirements	Can be used at all levels of health facility, including health centers or in mobile facilities.

BD FACSPresto™	
Type of Technology	Small, bench-top, fixed volume cytometer
Output	Absolute CD4, CD4% and Hb
Turnaround time	2 -5 minutes (once optimized); plus incubation of cartridge (20 minutes)
Capacity	Maximum of ~25 - 30 samples per day
Throughput per technician/ per day	~25 samples per technician per day; [batching] capabilities; walk-away operation.
Sample needed and stability	~ 20 µL of capillary (fingerstick) blood wicked directly into BD cartridge or ~ 20µL of venous blood collected in EDTA anti-coagulant tube. Cartridge must be inserted and tested within a few hours of sample application.
Sample preparation and protocol complexity	No sample preparation required. For capillary blood: (i) lancet finger; (ii) apply blood drops to cartridge; (iii) close cartridge; (iv) incubate cartridge; (v) insert cartridge into analyzer; (vi) press "start"; (vii) read result from LED screen; (viii) print result
Reagent stability	Dried reagents require no refrigeration. Shelf life: (on-going study)
Cost/test	~ $__ per test
Cost/instrument	~ $_____
Regulatory Status	Will be CE-IVD marked, FDA-approval will follow.
Physical dimensions (cytometer only) (L x H x D)	Length: ~ 26 cm (10.2") Height: ~ 30 cm (11.6") Depth: ~ 25 cm (9.8")
Weight	~ 5 kg (~ 11lbs) (instrument only)
3rd party supplies	For venous samples: volumetric or transfer pipette For capillary samples: sterile lancets, alcohol swabs, dry swabs (also available from BD)

BD FACSPresto™ (2)	
Electric Power Requirements	100 to 240 V (A/C) at 47 – 63 Hz mains power Analyser contains on-board rechargeable battery. Can be charged with cigarette lighter.
Environmental Requirements	• Operating Temperature: (*on-going study*) • Humidity: (*on-going study*) • Maximum altitude: (*on-going study*)
Data Station	Dedicated CPU integrated into instrument; approximately 1,000 test results can be stored on the instrument archive; results can be downloaded via USB. The USB port also can be used to support an external blue tooth or GPRS/GSM module to communicate with SMS printer or the port would be developed but not enabled, providing an option for wireless to be enabled post launch. Potential to install an SMS chip to transmit results or internal calibration data.
Monitor	LED multi-color screen integrated into instrument
Printer	On board printer (prints on thermal paper);
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	Analyser contains an integrated camera and microscope that might be susceptible to damage if dropped. If damaged, low cost and portability of device allows for direct swap-out replacement rather than on-site repair.
Internal QC	Yes. Instrument will check itself each day and each cartridge will have onboard QC.
External QA	TBD whether compatible with CD4 EQA programs; cartridge cannot be retested to confirm results.
Infrastructure Requirements	Can be used at all levels of health facility, including health centers or in mobile facilities.
User interface	Touch screen keyboard on the device

Point-of-Care Viral Load Technologies in the Pipeline

SAMBA Analyzer	
Type of Technology	Isothermal target/signal amplification and visual detection; separate extraction
Output	Qualitative for EID (limit of detection ~400 cp/mL RNA with 100µL of whole blood, also detects DNA) and acute infection detection (limit of detection ~100 cp/mL with 500µL of plasma) and semi-quantitative viral load test for ART monitoring (1,000 cp/mL cutoff with 200µL of plasma)
Turnaround time	90 to 120 minutes depending on the assay
Capacity	6 samples per run
Throughput per technician/ per day	24 for EID or acute infection tests; 36 for viral load, assuming 6.5 hour/working day
Sample needed and stability	200µL (plasma) for viral load test, 500µL (plasma) for acute infection test or 100µL (whole blood) for EID test; sample stable at room temperature for 6-8 hours
Sample preparation and protocol complexity	Simple, pre-loaded disposable cartridges containing all required liquid or dry reagents
Reagent stability	Transport stability: up to 55°C for one month. Reagents do not require cold-chain storage and to date are stable up to 37oC for 1 year
Cost/test	TBD
Cost/instrument	TBD
Regulatory Status	Regulatory approval obtained in Malawi for viral load assay
Physical dimensions (W x H x D)	TBD
Weight	TBD
3rd party supplies	NA

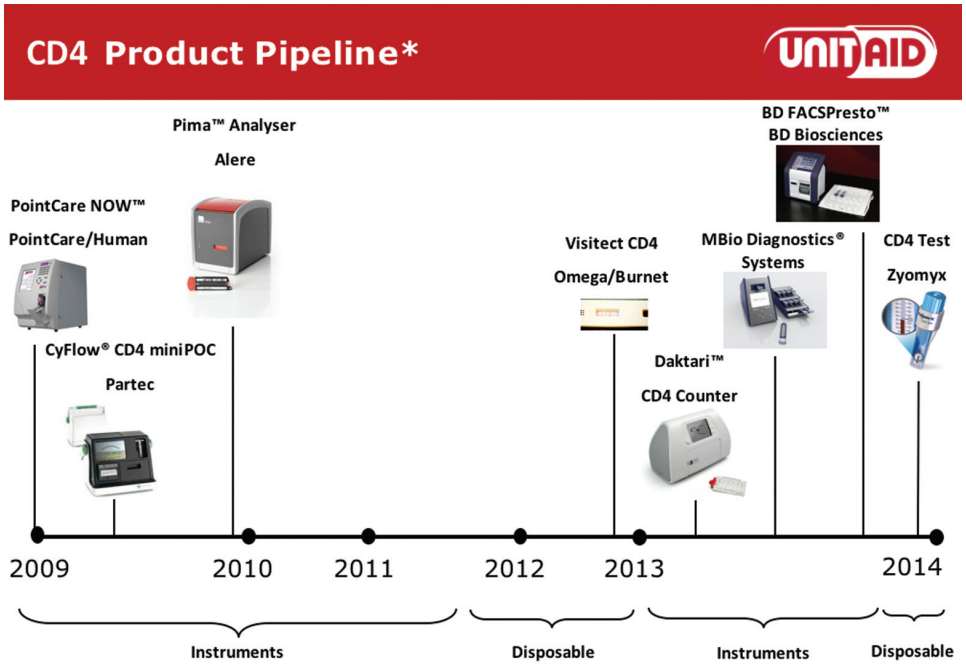
SAMBA Analyzer (2)	
Electric Power Requirements	AC powered (100-240V); can be battery powered to complete the run
Environmental Requirements	• Operating Temperature: 10 – 37°C • Humidity: up to 95% • Maximum altitude: N/A
Data Station	None
Monitor	Small screen integrated into instrument
Printer	No printer provided
Bar-code Scanner	None
Training	Minimal training required
Maintenance	No maintenance required. Swap-out if needed.
Internal QC	Synthetic non-target nucleic acid internal controls
External QA	Freeze-dried EQA panel provided consisting of negative and a range of positive samples
Infrastructure Requirements	Can be used at health facility levels, including health centers and mobile facilities
User interface	Touch screen

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

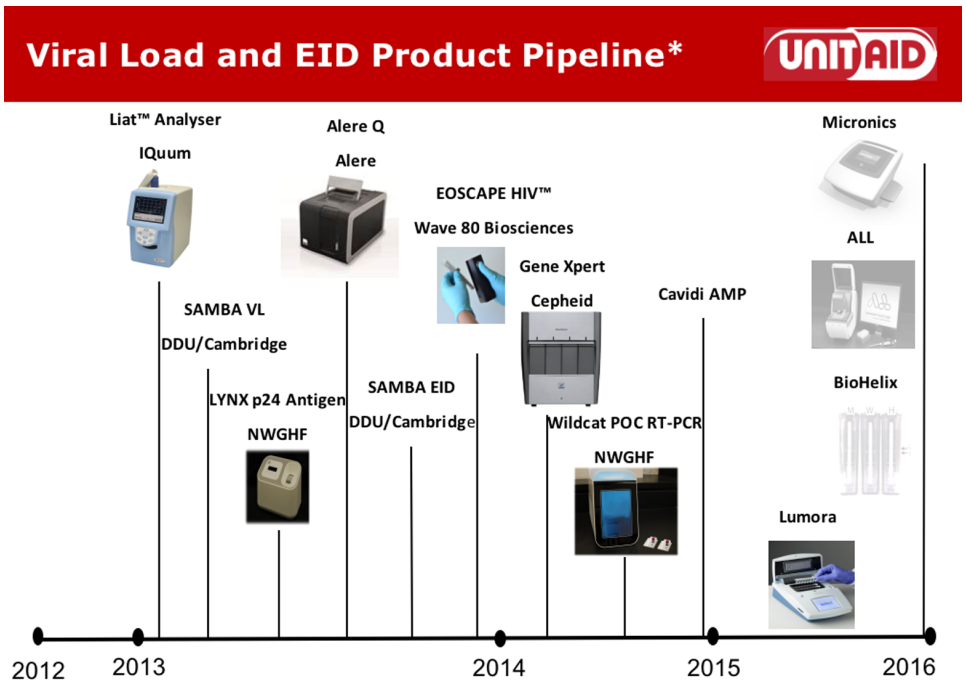
NWGHF LYNX HIV P24 Antigen Test (EID)	
Type of Technology	p24 Antigen Assay for EID
Output	Detection of HIV infection
Turnaround time	40 minutes, including blood draw and sample preparation (30 minutes for readout only)
Capacity	1 sample tested sequentially
Throughput per technician/ per day	~16 samples per day
Sample needed and stability	~80 µL of blood from the infant's heel
Sample preparation and protocol complexity	(i) Prick infant's heel and collect blood; (ii) separate plasma from red blood cells; (iii) add buffer and heat; (iv) insert test strip into heat block and wait 30 minutes; (v) read test.
Reagent stability	TBD
Cost/test	Estimated to be: $7 to $15 per test
Cost/instrument	~$700 - 900 for device
Regulatory Status	TBD
Physical dimensions (W x H x D)	Width: 202mm (~8 inches) Height: 156mm (6.1 inches) Depth: 134mm (5.3 inches)
Weight	1.7 kg (~3.7 lbs)
3rd party supplies	Sterile lancets (for blood samples); alcohol swabs, dry swabs, gauze, bandage

NWGHF LYNX HIV P24 Antigen Test (EID) (2)	
Electric Power Requirements	Heat block is battery powered
Environmental Requirements	TBD
Data Station	Internal 3G modem provided upon request
Monitor	None
Printer	No printer provided
Bar-code Scanner	None
Training	Minimal training required; primary skill required is for correct lancet blood draw.
Maintenance	Test is disposable; heat block is expected to last 2 years with original battery; life can be extended to 5 years if battery is swapped out.
Internal QC	Yes
External QA	TBD whether compatible with EQA programs; cartridge cannot be retested to confirm results.
Infrastructure Requirements	Can be used at all levels of health facility, including health centers or in mobile facilities.
User interface	Display with timer and battery indicator

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



*Estimated as of October 2012 - timeline and sequence may change



*Estimated as of October 2012 - timeline and sequence may change

APPENDIX 3:
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 that indicates the product conforms with requirements of EU directives. CE stands for Conformité Européenne (European Conformity).
DBS	Dried blood spot
DNA	Deoxyribonucleic acid
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.)
IVD	*In vitro* diagnostics, which are tests that can detect diseases, conditions or infections.
MTB	mycobacterium tuberculosis
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.)
PCR	Polymerase chain reaction
PEPFAR	President's Emergency Plan for AIDS Relief
POC	Point-of-care / point-of-care
RIF	rifampicin (rifampin)
RNA	Ribonucleic acid
SBIR	Small Business Innovation Research
UPS	Uninterruptible power supply
USAID	United States Agency for International Development
USB	Universal serial bus
WHO	World Health Organization

UNITAID Secretariat
World Health Organization
Avenue Appia 20
CH-1211 Geneva 27
Switzerland
T +41 22 791 55 03
F +41 22 791 48 90
unitaid@who.int
www.unitaid.eu

UNITAID is hosted and administered by the World Health Organization