Will POC make any difference?
A perspective on EID, CD4 and viral load.

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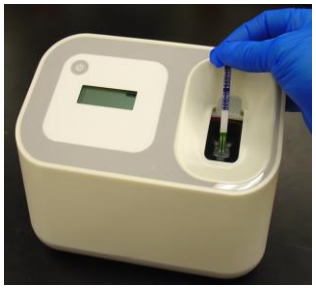
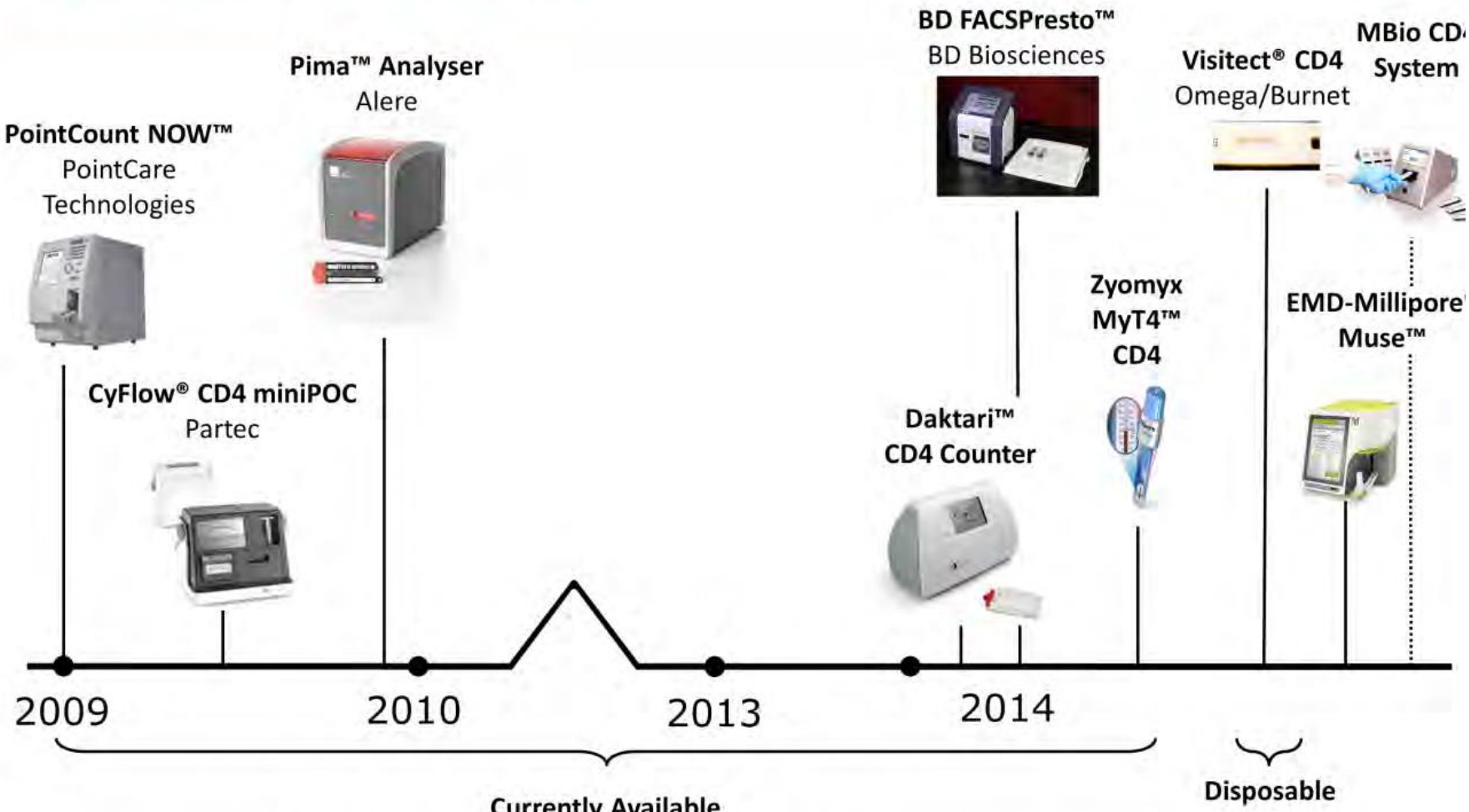
Automation has largely reduced complexity of viral load testing

- Lab-based tests are automated for sample extraction, target amplification and analysis

- Point-of-care tests, some of which will be imminently available, are completely automated “load-and-go” tests that include integrated sample processing but do often require plasma



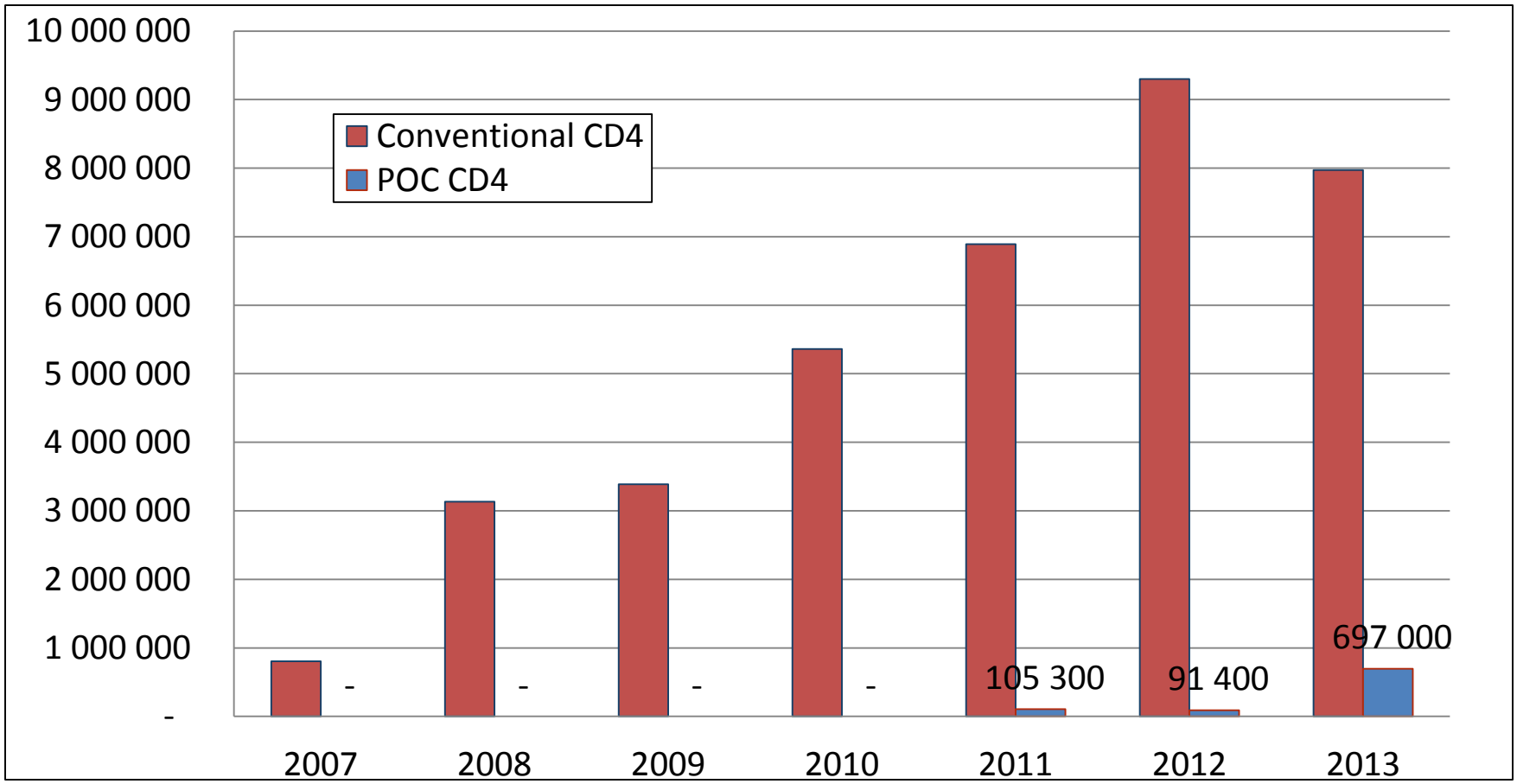
POC CD4 products: available and pipeline*



*Estimated as of May 2014 - timeline and sequence may change.

----No market launch date set by company.

11% Of CD4 Tests Delivered via SCMS Are POC Based (2013)



Ref: Jason Williams, SCMS

Country X: Example Of The PIMA POC Utilization (2012)

Total number of sites	269
Sites with "0" consumption	46
Sites with consumption ≤ 1/day	91
% of sites with 0 or consuming ≤1/day	34%
% of sites with access to referral lab	30%

Ref: Jason Williams, SCMS

POC viral load & EID products: available and pipeline*

SAMBA I VL
DDU/Cambridge

SAMBA EID
DDU/Cambridge

Alere q
Alere

ZIVA™
Cavidi

EOSCAPE HIV™
Wave 80 Biosciences

RT CPA HIV-1 Viral Load
Ustar

GeneXpert
Cepheid

Savanna Viral Load Platform
NWGHF

Liat™ Analyser
IQuum

Gene-RADAR
Nanobiosm

Micronics

LYNX HIV p24 Antigen
NWGHF

Truelab PCR
Molbio/bigTec

Viral Load Assay with BART Lumora

2013 2014 2015 2016

*Estimated as of May 2014 - timeline and sequence may change.

----No market launch date set by company.

MSF IMPLEMENTATION OF INFANT, VIRAL LOAD AND POC CD4 DIAGNOSTIC TOOLS

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Point-of-Care (POC) testing:

- MSF has implemented POC CD4 diagnostics**
- MSF is implementing or planning to implement POC VL / infant diagnostics

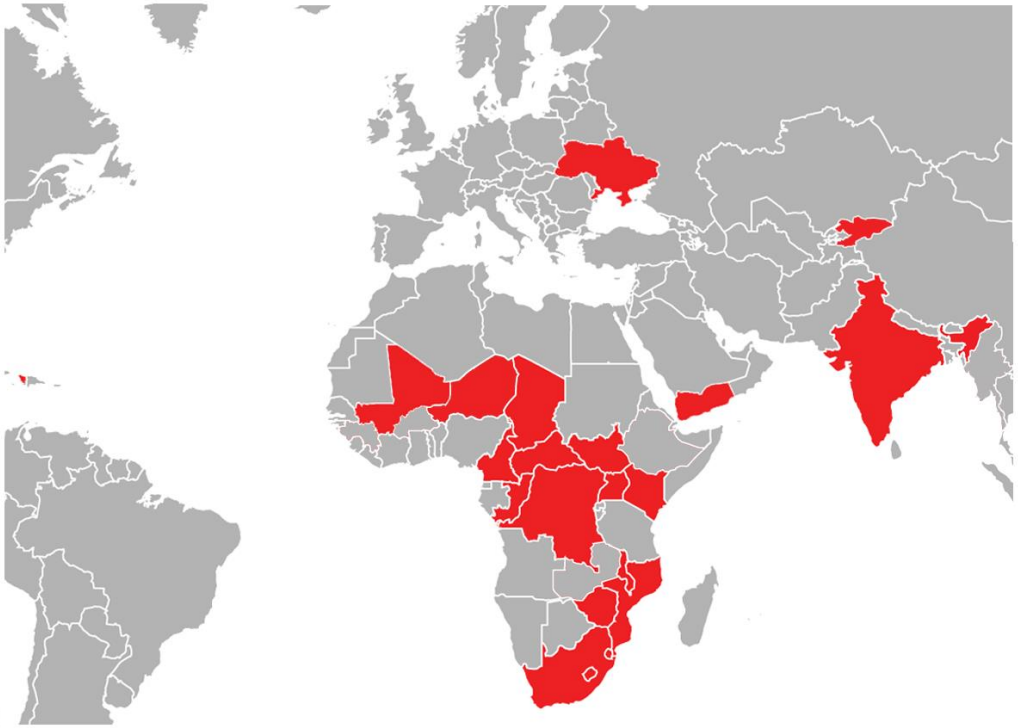
**Implementation in at least one MSF project in the country

Laboratory-based testing:

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

Bangladesh
Cameroon
Central African Republic
Chad
Congo
Democratic Republic Congo*
Guinea
Haiti
India
Kenya
Kyrgyzstan#
Lesotho*
Malawi
Mali
Mozambique
Myanmar
South Africa
South Sudan
Swaziland
Uganda
Ukraine
Yemen
Zimbabwe

*MSF VL lab implementation planned
#MSF provides diagnostics but not treatment



MSF currently provides HIV treatment to people in 23 countries.

MSF 5-country survey

http://msfaccess.org/content/issue-brief-getting-undetectable-usage-hiv-viral-load-monitoring-five-countries

	India	Kenya	Malawi	South Africa	Zimbabwe
Number PLWHA (on ART)	2,085,008 (750,000)	1,646,012 (604,000)	1,129,768 (405,100)	6,070,751 (2,200,000)	1,368,128 (565,700)
VL tests 2013	6,000 - 7,000	53,000	37,000	2,400,000	30,000 - 48,000
Gov VL labs (machines)	9 (20)	7 (˜15)	5 (6)	17 (17)	1 (1)
Gov EID labs	7	7	5	9	1
EID TAT	sample transport: ≥3 days lab processing: 6 days result delivery: email to ART centre	2-4 weeks (>1 month in rural areas); some access to web-based results, SMS or SMS printers but mostly paper-based	3 weeks - 2 months; some access to SMS and SMS printers but mostly paper-based	1-10 weeks depending on geography; internet-based results possible otherwise SMS printers or hard copies	1-4 months
POC tests	none	100 Alere PIMA (not in operation)	125 Alere PIMA	A few in the Free State	>250 Alere PIMA
Interest in CD4 POC	yes, in specifically targeted areas only, based on difficulty of terrain and overload on ART centres only, limited to augment lab system	unsure	unsure, not if CD4 testing is phased out altogether	not currently (awaiting results from evaluation of Free State pilot)	yes, mainly due to quick turn around time and guaranteed results delivery
Interest in EID / VL POC	not currently, not prior to validation, only limited to augment lab system, depending on cost	not currently, although SAMBA is being evaluated by KEMRI; waiting for tests to become commercially available to gauge performance, usability and price	not currently (except for implementation of SAMBA by MSF); concerns about underuse, incorrect use and capacity for nurses to perform tests	not currently, although some products have been evaluated by the NHLS; possibly for infant diagnosis	not currently, although some products may be validated at the NMRL, and substantial interest to overcome lack of lab and sample transport capacity, and result delivery, including for infant diagnosis

MSF 5-country survey:
Access barriers to viral load testing and subsequent intervention

http://msfaccess.org/content/issue-brief-getting-undetectable-usage-hiv-viral-load-monitoring-five-countries

In most but not all countries:

- India: State AIDS Clinical Expert Panels (SACEPs) as “gate-keepers” for VL testing
- High cost
- Lack of funding
- Limited human resources (and training)
- Poor procurement management e.g. stock outs
- Lack of awareness among civil society, PLWHA, clinicians etc on importance of VL testing
- Geography and distance e.g. sample transport and results delivery
- Poor lab infrastructure and equipment maintenance
- No validation of DBS and POC tests
- Poor record keeping and patient tracking
- Poor follow-up on results and high patient loss to follow-up
- Unequal access within the same country e.g. urban versus rural
- Weak adherence counseling

POC versus DBS

MSF 5-country survey (http://msfaccess.org/content/issue-brief-getting-undetectable-usage-hiv-viral-load-monitoring-five-countries)

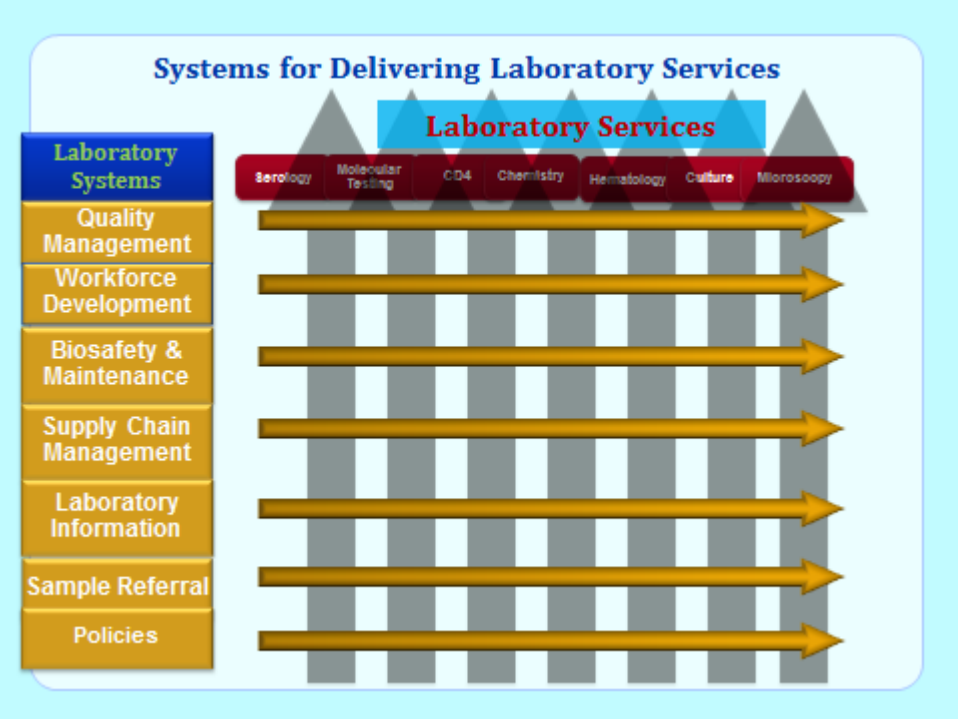
	India	Kenya	Malawi	South Africa	Zimbabwe
Use of DBS	only for infant diagnosis; needs validation for viral load use	yes, for infant diagnosis and viral load - although viral load is still controversial and requires further validation due to accuracy issues	yes, for infant diagnosis and, from 2014, for viral load (with a subsequent validation at 1,000 copies/ml)	only for infant diagnosis	yes, for both infant diagnosis and viral load

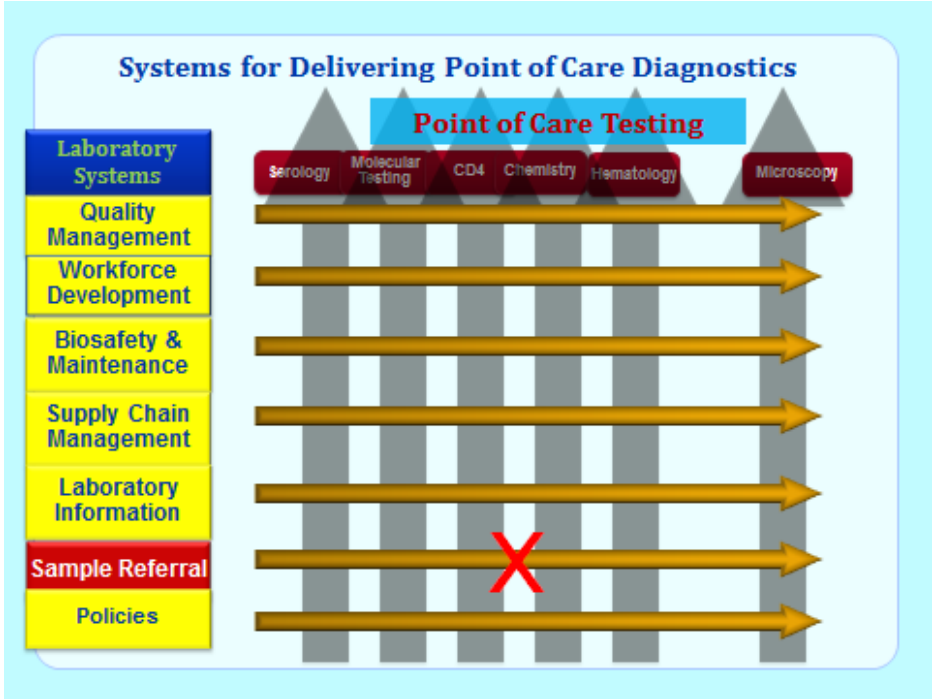
WHO: Implementing HIV VL Testing (July 2014) – Performance at 1000 copies/mL

Assay assessed	Sensitivity (mean %)	Specificity (mean %)	*n*
Abbott Molecular: Abbott RealTime HIV-1 (manual, m24sp and m2000sp) assays with m2000rt platform	95.24[a]	91.67[a]	1529
Biocentric: Generic HIV Charge Virale	94.86[a]	55.16[a]	531
bioMérieux: NucliSENS EasyQ® HIV-1 v2.0	84.37[a]	94.52[a]	1062
Roche Molecular Systems: COBAS® AmpliPrep/COBAS® TaqMan® HIV-1 Test, version 2.0 [free virus elution protocol]	81.02[b]	96.74[b]	229
HIV-1 RNA 1.0 Assay (kPCR)	90.97[a]	87.76[a]	144

Meta-analysis in press by Vojnov et al. (CHAI); Roche results by Carmona et al. (NHLS)

Laboratory Systems Approach vs Point of Care Diagnostics?

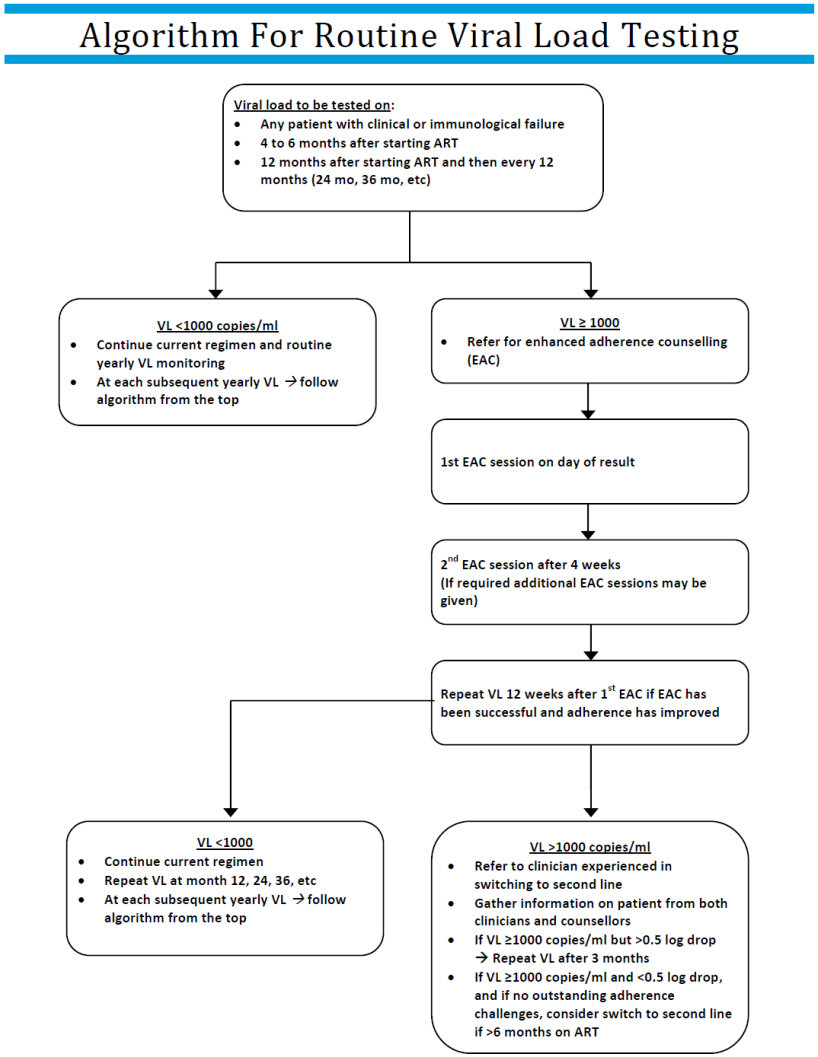




Need to Strengthen Functional Tiered Laboratory Health Systems and Networks

Ref: John Nkengasong (CDC)

Beyond the lab:
preparing the clinicians with a new VL algorithm



Early Viral Load
Zimbabwe Month 3
Malawi Month 6

Frequency of Viral Load
Zimbabwe Month 12 then yearly
Malawi 2 yearly

CD4 Tx monitoring
Zimbabwe : Stopped
Malawi : Never started

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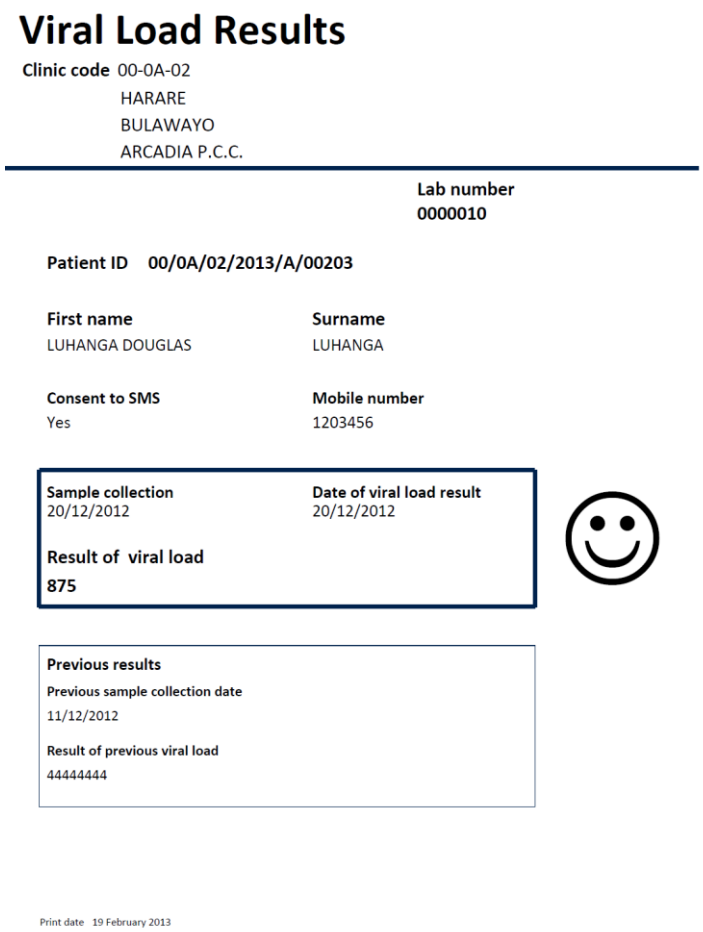
Acting on the result: training and supervision is essential



Viral Load Results

Clinic code 00-0A-02
HARARE
BULAWAYO
ARCADIA P.C.C.

Lab number
0000010

Patient ID **00/0A/02/2013/A/00203**

First name
LUHANGA DOUGLAS

Surname
LUHANGA

Consent to SMS
Yes

Mobile number
1203456

Sample collection
20/12/2012

Date of viral load result
20/12/2012

Result of viral load
875

Previous results

Previous sample collection date
11/12/2012

Result of previous viral load
44444444

Print date 19 February 2013

- **Flagging of results**
- **Person in clinic delegated to be responsible for filing**
- **Automatically generated lists of results from VL database per clinic sent as well as individual results- highlighting those with VL > 1000 copies/ml**
- **Easy lookup in database**
- **VL SMS result delivery of >1000 copies to the clinics: plan to SMS all results to patients**

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Task shifting point-of-care testing to alleviate HR shortages

In Malawi, MSF is investigating whether point-of-care testing can be task-shifted to lay workers (PIMA, SAMBA*)

In Swaziland, MSF has set up “mini-labs” at clinics, where lay workers have been trained to perform point-of-care testing (RDTs, PIMA, HemoCue, Reflotron)

*Performance data on the SAMBA may be found at: Ritchie et al., *J Clin Microbiol*, 2014

Barriers to implementation of task shifting include:

- **Professional protectionism** – where doctors feel that their many years of training count, and not just anyone can do their work. Nurses too feel that their profession is being invaded by nursing aides. As a result, community health workers are not embracing task shifting.
- **Professional boundaries and regulations** – while the regulatory environment in some countries is permissive of task shifting, the cadre has no legal protection for additional tasks if anything was to go wrong.
- **Poor salaries and working conditions** – most doctors are not willing to be deployed to rural areas and the public sector, where the impact of the shortage is most felt. Task shifting is therefore still seen as a government ploy to avoid paying the right people to do their rightful jobs.
- **Perceived focus on HIV and AIDS** - task shifting tends to be viewed as another HIV and AIDS initiative, and hence a challenge that will weaken the health systems.
- **Prohibitive policies and laws** – some countries still have outdated policies or laws that prevent lower level cadres from carrying out particular tasks.

Ref: Sagie Pillay (NHLS)

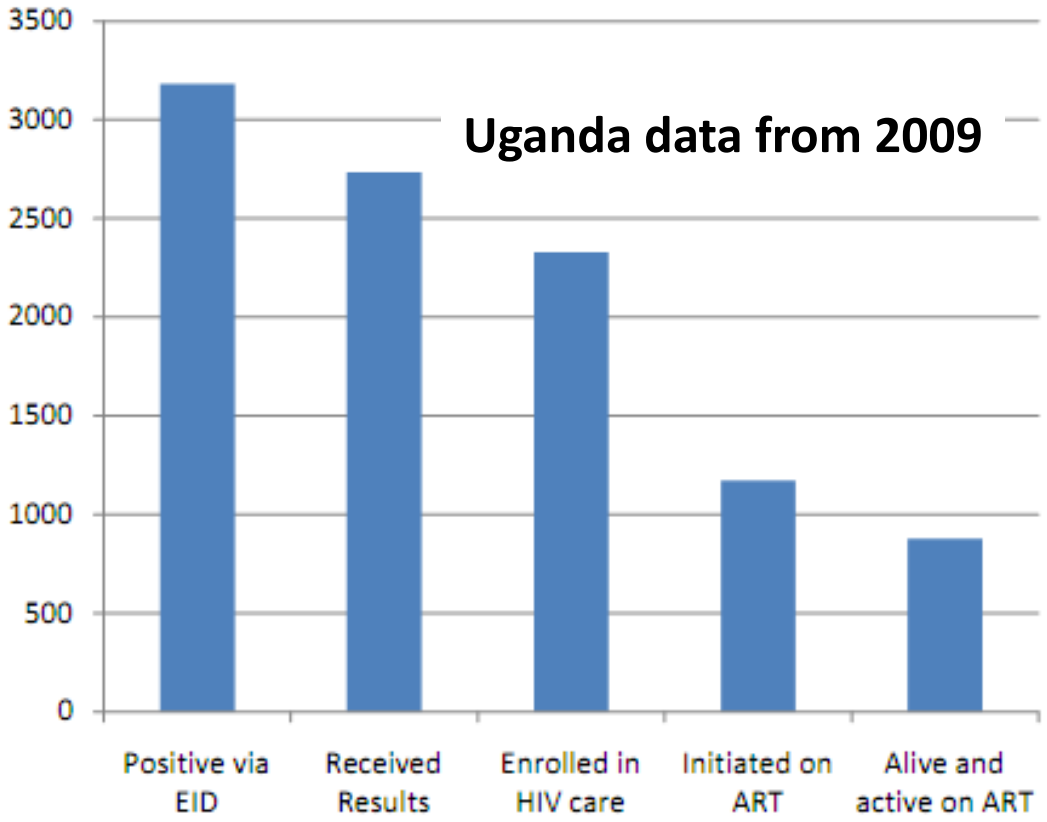
How can the laboratory improve access to testing and treatment?

- New POC staff cadres need to be defined
- Regulatory barriers for these new professionals need to be overcome
- Improve transport infrastructure and telecommunications can make access to centralized laboratories more attainable, reducing the burden on the nurse for POC
- Lab personnel can provide support in areas of training and quality assurance (at site or through remote connectivity)

Ref: Sagie Pillay (NHLS)

Can POC testing decrease LTFU?

For infants, rates of LTFU are quite significant – in a 4 country review by UNICEF almost ¾ of all positive infants were not on treatment at 1 year



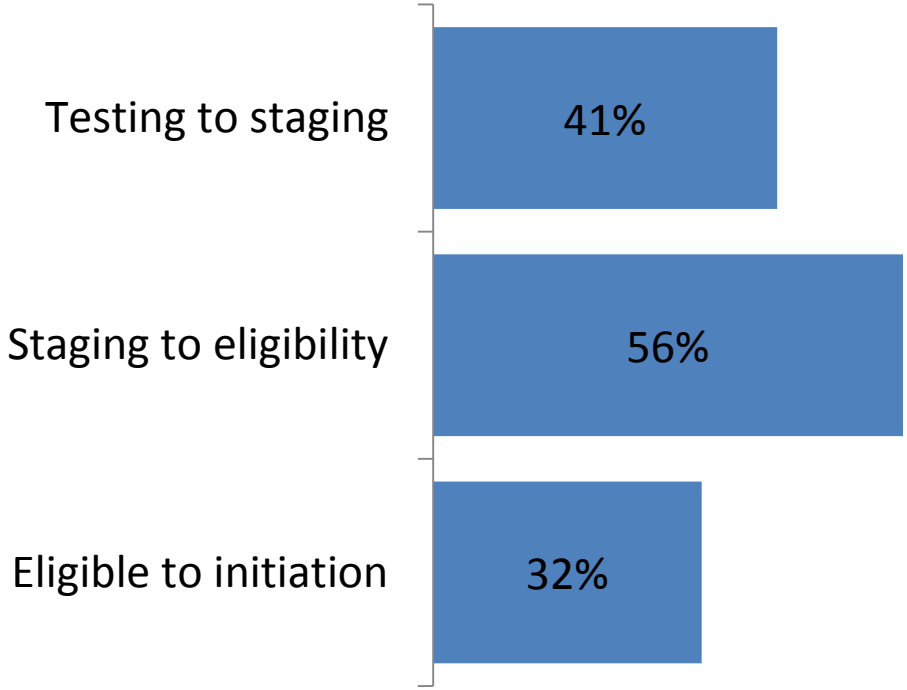
Greatest loss point is between a positive test and the return of results where as much as 51% of infants are lost.

Slide Ref: Shaffiq Essajee (CHAI)

Source: Chatterjee et al. BMC Public Health, 2011

Also…

Average rates of LTFU at various points along the continuum from Testing to Treatment

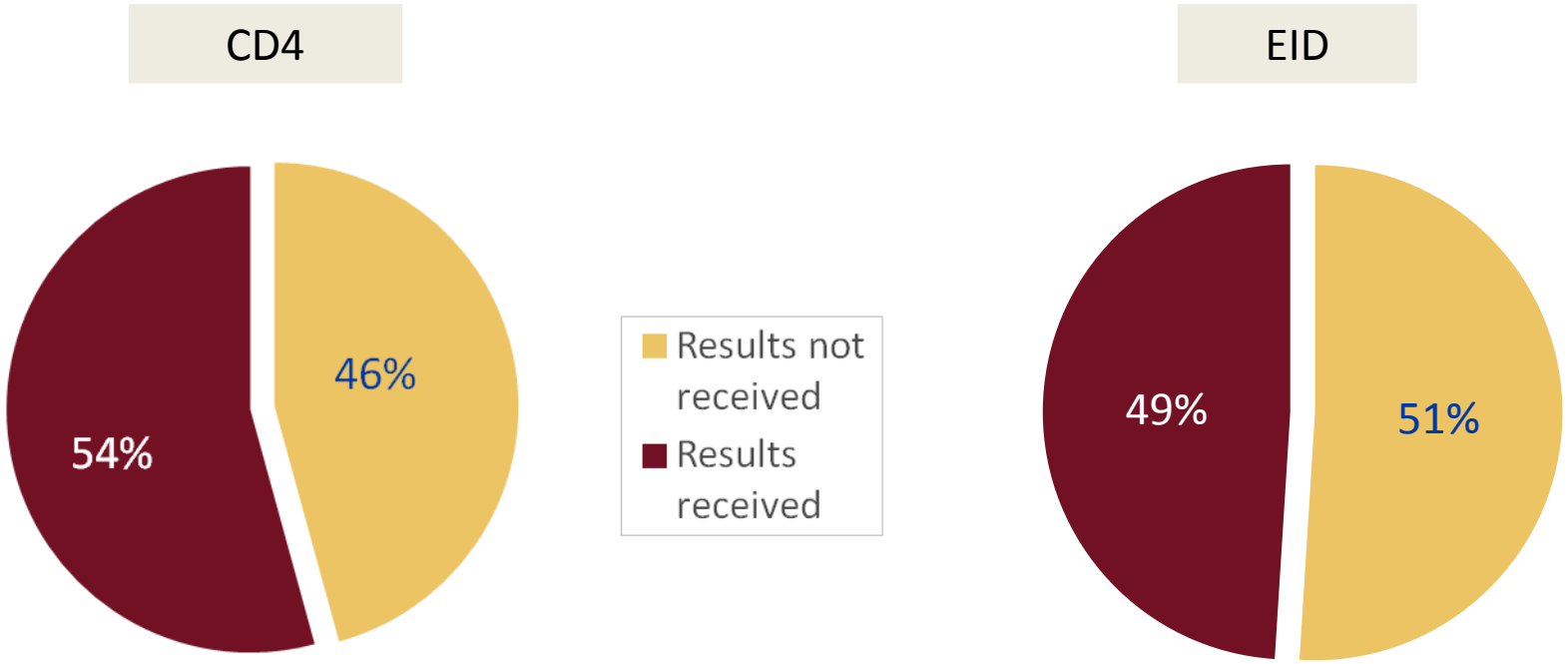


Large meta-anlysis found that overall only 1/3 of people who test HIV+ and are eligible are ultimately started on treatment

Slide Ref: Shaffiq Essajee (CHAI)

Source: Rosen and Fox Plos Med (2011)

Many tests are performed but results are never delivered to patients



Ref: National volumes for Mozambique, Malawi and South Africa based on CHAI data

In Mozambique, POC CD4 testing decreased LTFU

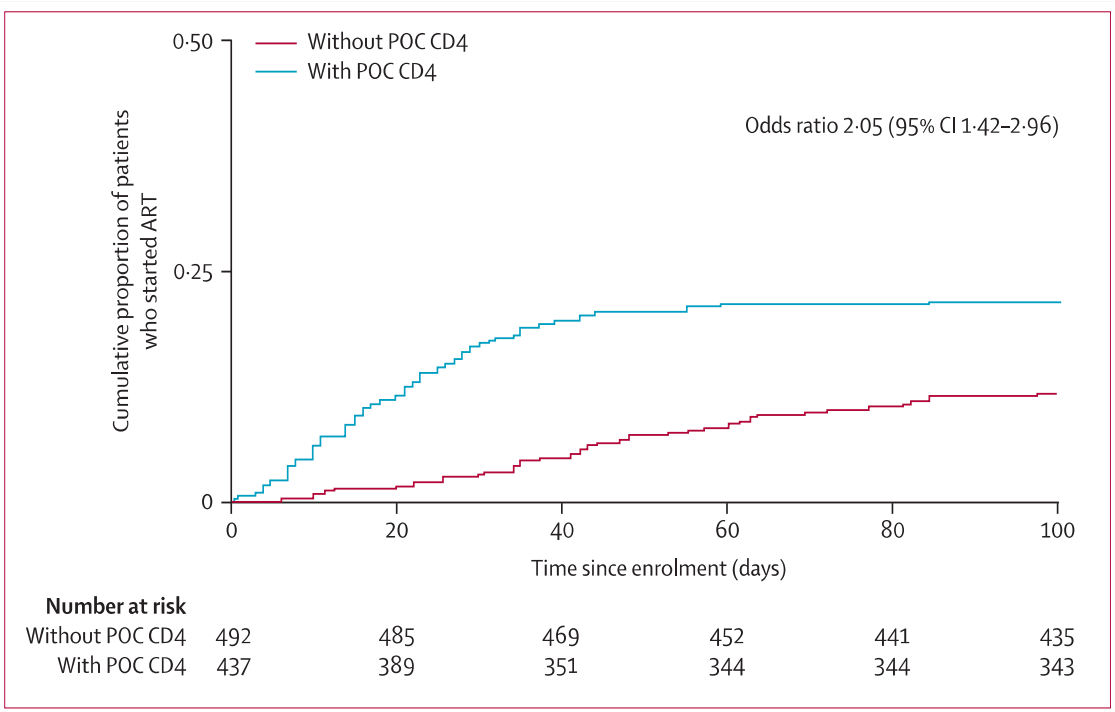


Figure 2: **Kaplan–Meier estimate of time from enrolment into HIV care to initiation of antiretroviral therapy before and after the use of POC CD4 for immunological staging at primary health care clinics (p=0·0001)**
ART=antiretroviral therapy. POC CD4=point-of-care CD4 cell count.

- LTFU between CD4 staging and Rx initiation fell from 64 to 33%
- Proportion starting ART doubled 12 to 22%
- Median time to ART start fell by half

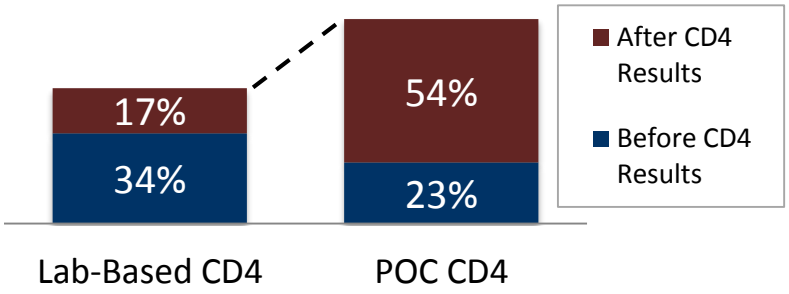
Ref: Jani et al., *Lancet,* 2011

POC CD4 has now been widely implemented and many pilot programs showed marked reduction in LTFU and incl in initiations

Malawi[2]

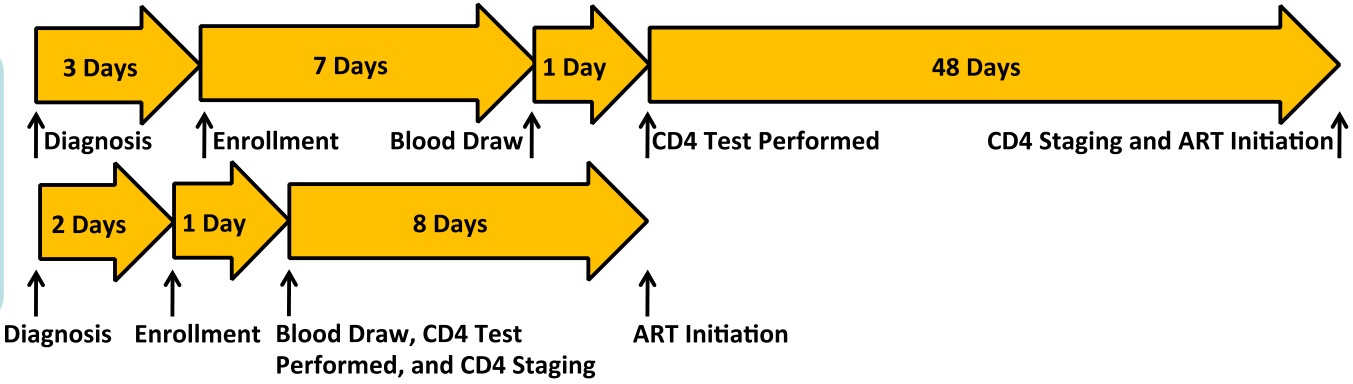
- **PMTCT LTFU:** PMTCT initiation during pregnancy increase from 51 to 78%
- **Time to CD4 result:** time from CD4 blood draw to result reduced from 11 to 0 days

PMTCT Initiation in Malawi using POC CD4 vs. Lab-based tests



Uganda[1]

- **Time to ART initiation:** Reduced from 59 to 11 days



Source: [1]MOH Uganda; [2]MOH Malawi

Slide Ref: Shaffiq Essajee (CHAI)

The Alere Q is one of the VL / EID PoC platforms that is at the more proximal end of the pipeline

Specifications

- Battery Operated, no cold-chain needed
- No sample preparation. Direct sampling
- Processing time: 45 minutes
- Results stored in the device or printed out
- Internal modem for connectivity
- Capillary whole blood EID read outs

Slide Ref: Shaffiq Essajee (CHAI)

When used for EID, the Alere Q had an overall agreement of more than 99% compared with the reference Roche technology

- Total of 827 HIV-exposed infants were enrolled and tested on both the Alere Q and the Roche reference technology.
- 60% were tested between 1-2 months of age.
- Only 2 discordant samples were found.

		Conventional Results	
		Positives	Negatives
POC NAT Results	Positives	64	1
	Negatives	1	761

Overall agreement	95% C.I.	Positive percent agreement	95% C.I.	Negative percent agreement	95% C.I.
99.8%	99.1 - 100%	98.5%	95.5 - 100%	99.9%	99.3 - 100%

Cohen's Kappa	95% C.I.	McNemar's Test	p-value
0.981	0.960 - 1.000	0.500	0.480

Sensitivity of the Alere Q was 98.5%, specificity was 99.9%

Ref: Jani et al., *J Acquir Immune Defic Syndr,* 2014

Slide Ref: Shaffiq Essajee (CHAI)

MSF lessons learnt

- Assess your context to establish what sample type and platform will be feasible
- Training of clinicians and counsellors essential
- Having the viral load test is not a magic bullet
- Supervision is essential using your Laboratory and M and E tools
- **Empower the patient to ask for and be able to act on their viral load result**
- **More information: http://msfaccess.org/undetectable**

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Thank you — Ngiyabonga — Enkosi — Ke a leboga — Dankie

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http://www.fixthepatentlaws.org/