ACCESS CAMPAIGN
MEDECINS SANS FRONTIERES

HepHIV 2017
31 JANUARY-2 FEBRUARY · MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

NEW POINT-OF-CARE DIAGNOSTICS FOR HIV & HCV

Emmanuel Fajardo
HIV/HCV Diagnostics Advisor

Médecins Sans Frontières
(MSF) Access Campaign

OVERVIEW

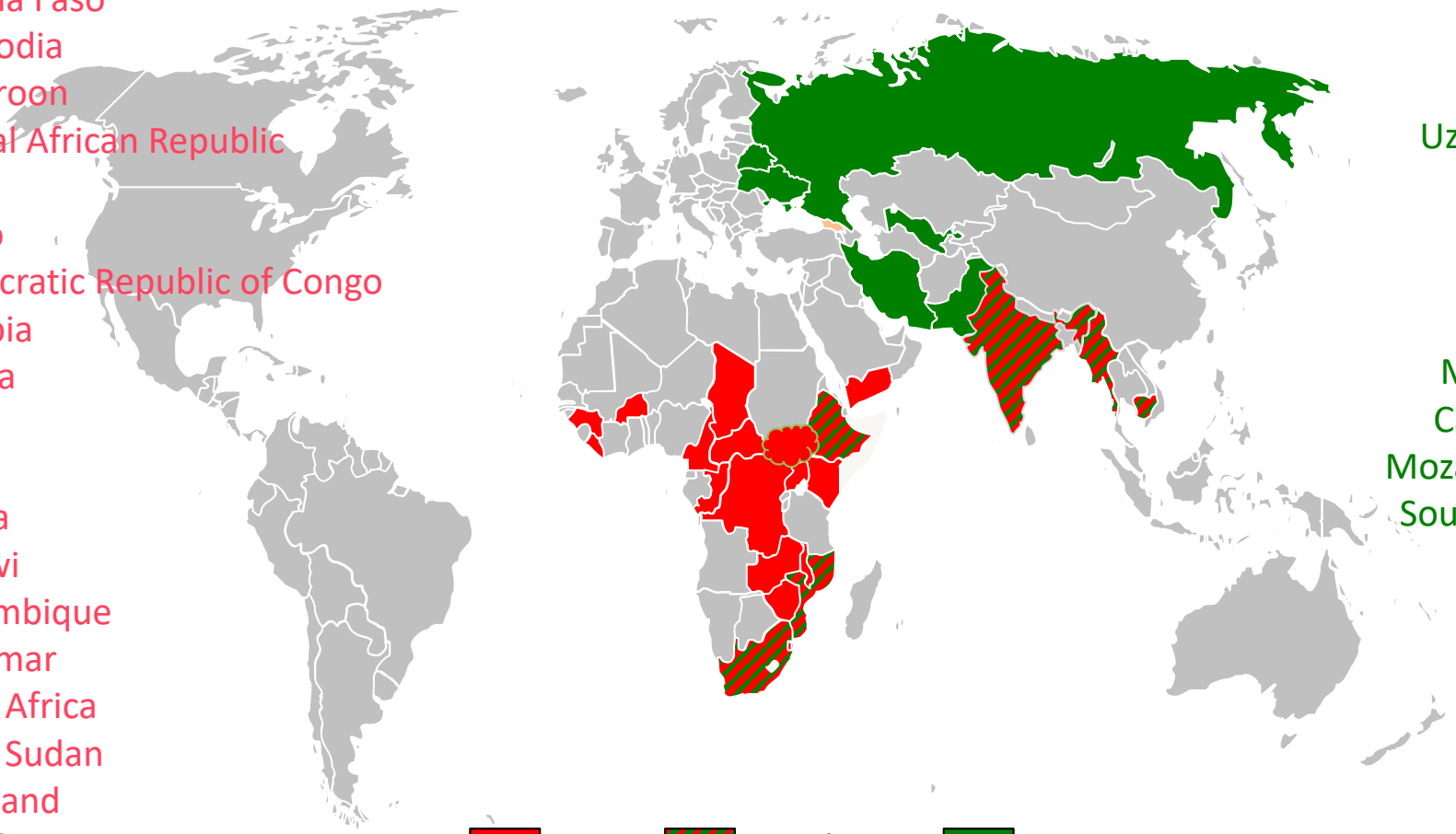
HepHIV 2017
31 JANUARY-2 FEBRUARY · MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

- MSF HIV and HCV Programmes
- New HIV Diagnostic Tools
- New HCV Diagnostic Tools
- POC Diagnostics in the pipeline
- Lessons learnt and key messages

MSF HIV & HCV Programmes

HepHIV 2017
31 JANUARY-2 FEBRUARY·MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

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



Russia
Ukraine
Uzbekistan
Belarus
Iran
Pakistan
India
Myanmar
Cambodia
Mozambique
South Africa

HIV HIV/HCV HCV

MSF currently provides HIV treatment to **247,000** people in 2015 in more than 20 countries and HCV treatment to >**1,200** people in 2016 in 11 countries


Models of care:
- Task-shifting
- Decentralization
- Integration of services
- Community-based approaches
MÉDECINS SANS FRONTIÈRES
DOCTORS WITHOUT BORDERS

HIV CARE PATHWAY

HepHIV 2017
31 JANUARY-2 FEBRUARY · MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

Testing → **Staging** → **Eligibility** → **ART** → **Success**

HIV RDTs

40% unaware of their HIV status in 2015

diagnosed

ART initiation regardless of:
- WHO clinical stage
- Any CD4 count

Priority should be given to:
- WHO stage 3 and 4
- Patients with CD4 <350 cells/mm
- Screening of opportunistic infections such as TB, cryptococcus, etc (CD4<100)

virally suppressed

HIV SELF-TESTING
Point-of-care EID

Point-of-care CD4

DBS Viral load
Point-of-care VL

HIV SELF-TESTING WHO Guidelines 2016

HepHIV 2017
31 JANUARY-2 FEBRUARY · MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

http://www.who.int/hiv/pub/vct/hiv-self-testing-guidelines/en/

- HIVST should be offered as an additional approach to HIV testing services (strong recommendation, moderate quality of evidence)

Manufacturer Assay name	SENS	SPEC	Gen.	Specimen	Approval Status	Price Per Test (US$)
Autotest VIH (AAZ Labs, France)	100%	99.8%	2nd	Blood	CE	25-28 (to consumer)
INSTI HIV Self Test (Bioanalytical, Canada)	100%	99.8%	3rd*	Blood	CE	36 (to consumers)
Private Sector Version Biosure HIV Self Test (Biosure, UK)	99.7%	99.9%	2nd	Blood	CE	38-43 (to consumer)
Public Sector Version Biosure HIV Self Test (Biosure, UK)	99.7%	99.9%	2nd	Blood	CE	7.50–15 (to public sector)
OraQuick In-Home HIV Test (OraSure Technologies, USA)	100%	99.8%	2nd	Blood	Pending CE	NA
OraQuick In-Home HIV Test (OraSure Technologies, USA)	91.7%	99.9%	2nd	Oral	FDA	40 (to consumer)
OraQuick In-Home HIV Self-Test (OraSure Technologies, USA)	Available Upon Request	Available Upon Request	2nd	Oral	GF/ERPD	Available Upon Request

POC Early Infant Diagnosis

HepHIV 2017
31 JANUARY-2 FEBRUARY·MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

Alere Q
HIV-1/2 Detect

World Health Organization

Gold standard

AlereQ	Positive	Negative	Total
Positive	106	1	107
Negative	1	1776	1777
Total	107	1777	**1884**

Senstivity: 99.07% [95% CI: 95.4 – 99.9]
Specificity: 99.9% [95% CI: 99.7 – 100]

Cepheid Xper
HIV-1 Qual

World Health Organization

Gold standard

Xpert	Positive	Negative	Total
Positive	93	2	95
Negative	3	2500	2503
Total	96	2502	**2598**

Senstivity: 96.8% [95% CI: 91.7 – 99.2]
Specificity: 99.9% [95% CI: 99.7 – 99.9]

Point-of-care CD4

HepHIV 2017
31 JANUARY-2 FEBRUARY · MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

- A meta-analysis of the performance of the Pima CD4 for point-of-care CD4 testing (2015) https://www.ncbi.nlm.nih.gov/pubmed/26208867
- Performance of point-of-care CD4 testing technologies in resource-constrained settings: a systematic review and meta-analysis (2016) https://www.ncbi.nlm.nih.gov/pubmed/27769181
- POC CD4 Testing Improves Linkage to HIV Care and Timeliness of ART Initiation in a Public Health Approach: A Systematic Review and Meta-Analysis (2016) https://www.ncbi.nlm.nih.gov/pubmed/27175484

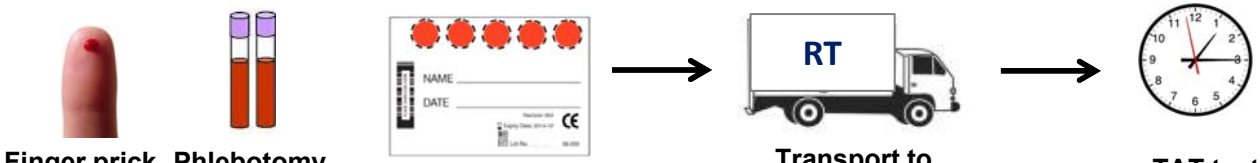
Pima POC CD4 (Alere)

BD FACSPresto (Becton Dickinson)

Visitect CD4 (Omega)

HIV DBS Viral Load

HepHIV 2017
31 JANUARY-2 FEBRUARY · MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care



Finger prick | Phlebotomy | Sample collection at field level | Transport to VL Lab | TAT test results

1. Roche (RUO)
2. Abbott
3. BioMerieux

Diagnostic Accuracy Study

Medicine®

OPEN

Sensitivity and specificity of dried blood spots for HIV-1 viral load quantification

A laboratory assessment of 3 commercial assays

World Health Organization

Pieter Pannus, MSc[a,*], Maarten Claus, BSc[a], Maria Mercedes Perez Gonzalez, MSc[b], Nathan Ford, FRCPE[c], Katrien Fransen, MSc[a]

Table 2

Sensitivity, specificity, false failures, and false successes for dried blood spot VL testing as compared to plasma VL testing.

	Roche CAP/CTM HIV-1 v2.0% (95% CI)	Abbott RealTime HIV-1 test % (95% CI)	bioMérieux NucliSENS EasyQ HIV-1 v2.0% (95% CI)
Sensitivity	80.8 (73.3–86.7)	76.0 (68.1–82.5)	76.7 (68.9–83.1)
Specificity	87.3 (79.9–92.3)	89.7 (82.7–94.2)	92.9 (86.5–96.5)
False failures	11.9 (7.2–18.9)	10.5 (5.9–17.6)	7.4 (3.7–14.0)
False successes	20.3 (14.1–28.2)	23.6 (17.2–31.4)	22.5 (16.3–30.2)

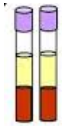
CAP/CTM = COBAS AmpliPrep/COBAS TaqMan, CI = confidence interval, VL = viral load.

Near-POC HIV Viral Load

HepHIV 2017
31 JANUARY-2 FEBRUARY·MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

EDTA whole blood

centrifuge



plasma

1. GeneXpert VL

CE

2. SAMBA-1 VL

CE

3. ExaViri VL

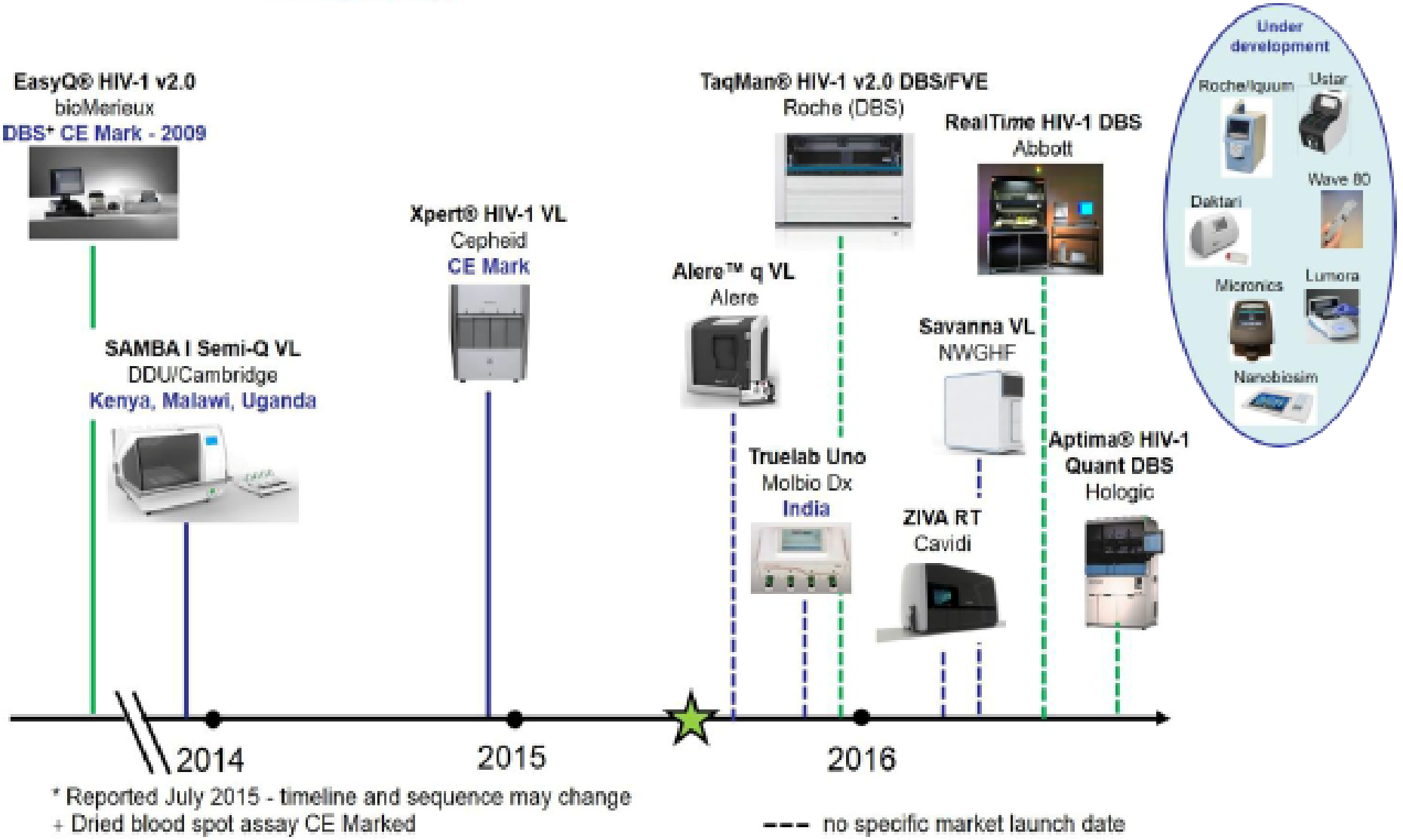
CE

True POC VL (in the pipeline)

GeneXpert Omni

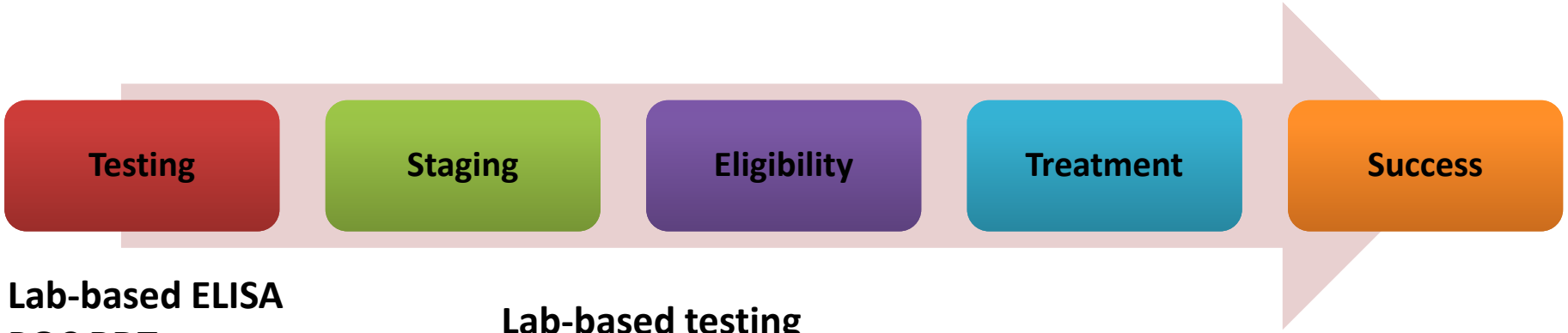
SAMBA II

Appendix 4: Point-of-care (POC) viral load (VL) technologies in the pipeline



HCV CARE PATHWAY

HepHIV 2017
31 JANUARY-2 FEBRUARY·MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care



Lab-based ELISA
POC RDTs
RNA molecular

Most people unaware of their HCV status
75% in HIC
99% in LMIC

- HCV RDT
- HCV SELF-TESTING
- HCV core Ag
- Point-of-care RNA
- Dried Blood Spot

Lab-based testing
- Genotyping
- Fibrosis staging
- Renal function tests
- Liver function tests
- Co-morbidities (HIV, HBV, TB)

- DBS genotyping
- POC creatinine
- POC ALT
- POC hemoglobin
- POC WBC Diif
- POC Multi-disease

Lab-based RNA testing (qualit or quant)
Lab-based core Ag

- Point-of-care RNA
- Dried Blood Spot

Monitoring simplification

HepHIV 2017
31 JANUARY-2 FEBRUARY·MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

TABLE 8.4 Framework for the frequency of monitoring patients undergoing HCV therapy based on type of regimen

Time	DAA alone			DAA + ribavirin			DAA + pegylated interferon + ribavirin			
	FBC, renal, liver function	Adher-ence, side-effects	HCV RNA	FBC, renal, liver functions	Adher-ence, side-effects	HCV RNA	FBC, creat-inine, ALT	Thyroid function	Adher-ence, side-effects	HCV RNA
Baseline	X		X	X		X	X	X		X
Week 1				X	X		X		X	
Week 2				X	X		X		X	
Week 4	X	X		X	X		X		X	
Week 8				X	X		X		X	
Week 12				X	X		X	X	X	
Week 12 after end of treat-ment			X	X		X	X	X		X
Week 24 after end of treat-ment										X

ALT: alanine aminotrar direct-acting antiviral; FBC: full blood count

Source: WHO Guidelines for the screening, care and treatment of persons with chronic HCV infection 2016

HCV Rapid Tests

HepHIV 2017
31 JANUARY-2 FEBRUARY·MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

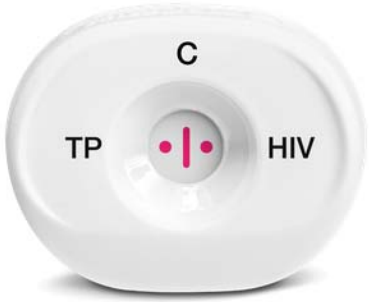
No.	Test name	Manufacturer	Country	Certification
1	ACON HCV Test	ACON Laboratory	USA	Discontinued
2	Axion HCV Card	Axion Diagnostics	Germany	**CE-marked**
3	DIAGNOSE HCV BI-DOT	J. Mitra & Co Pvt. Ltd	India	Local (DCGI)
4	HCV Tri-Dot	J. Mitra & Co Pvt. Ltd	India	Local (DCGI) **WHO evaluated 2001**
5	HCV Rapid Test Bioeasy	Bioeasy Diagnostica (Standard Diagnostics)	Brazil	Cancelled by ANVISA
6	Chembio DPP HCV Test	Chembio Diagnostics Systems, Inc	USA	Not in the market
7	Core HCV Test	Core Diagnostics	UK	No CE-marked
8	ImmunoFlow HCV	Core Diagnostics	UK	**CE-marked**
9	Hepa-Scan HCV card test	Bhat Biotech	India	**CE-marked**
10	Instant-view HCV	Alfa Scientific Deasigns Inc	USA	
11	One Step HCV Rapid Test	Inter-chemical Ltd	China	
12	Toyo anti-HCV test	Turklab	Turkey	**CE-marked**
13	Serocard HCV	Trinity Biotech ple	Ireland	Discontinued WHO evaluated
14	Signal HCV	SPAN Diagnostics Ltd	India	**CE-marked**
15	ABON HCV Ab Test	ABON Biopharm (Hangzhou) Ltd	China	**CE-marked**
16	Accu-Tell Rapid Anti-HCV Test	AccuBio Tech Co., Ltd	USA	
17	HCVTOP	BioSynex	France	**CE-marked**
18	Anti-HCV Rapid Test	Autobio Diagnostics Co., Ltd	China	
19	Advanced Quality One Step HCV Test	Bionike Inc	USA	**WHO Evaluated 2001**
20	Diaquick HCV Cassette	Dialab	Austria	**CE-marked**
21	Genedia HCV Rapid	Green Cross Life Science Corp	South Korea	
22	Hexagon HCV	HUMAN Diagnostics	Germany	No CE-marked
23	Advanced Quality Rapid Anti-HCV Test	Intec PRODUCTS, Inc	China	
24	Hepatitis C Virus (HCV) Antibody Assay Kit	Sichuan Maccura Biotechnology Co., Ltd.	China	
25	Miriad Rapid HBV/HIV/HCV Antobody Test	MedMira Laboratories	Canada	
26	HCV-SPOT	MP Diagnostics	Singapore	
27	ASSURE HCV Rapid Test	MP Diagnostics	Singapore	
28	MultiSure HCV Antibody Test	MP Diagnostics	Singapore	
29	HCV Rapid Test Kit	newScen Coast Bio-Pharmaceutical	China	
30	OraQuick HCV Rapid Antibody Test	OraSure Technologies, Inc	USA	**FDA-approved; CE-marked**
31	SM-HCV Rapid Test	SEROMed Labor Spezialitaten	Germany	
32	SD Bioline HCV	Standard Diagnostics, Inc	South Korea	**WHO-prequalified**
33	Imuno-Rapido HCV	WAMA Diagnostica	Brazil	
34	One Step HCV Test	Guangzhou Wondfo Biotech Co., Ltd.	China	
35	HCVSCAN	EY Laboratories, Inc	USA	

FDA APPROVED CE

World Health Organization

Multi-disease Rapid Tests

Multiplo HBc/HIV/HCV
(MedMira, Canada)



Multiplo TP/HIV
(MedMira, Canada)

SD Bioline HIV/Syphilis Duo
(Standard Diagnostics, Korea)

World Health Organization

Dried Blood Spots

HepHIV 2017
31 JANUARY-2 FEBRUARY · MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

- **HCV Ab**:
  - Sensitivity 98% (CI95% 94-99)
  - Specificity 99% (CI95% 97-100)
  - Positive likelihood ratio 171
  - Negative likelihood ratio 0.02
- **HBV sAg**:
  - Sensitivity 96.6% (CI95% 92-98.6)
  - Specificity 99.9% (CI95% 97.6-100)
  - Positive likelihood ratio 49.16
  - Negative likelihood ratio 0.06

- **HCV RNA**:
  - Sensitivity 96.0% (CI95% 93.4-97.6)
  - Specificity 97.7% (CI95% 94.7-99.0)
  - Positive likelihood ratio 171
  - Negative likelihood ratio 0.02
- **HBV DNA**:
  - Sensitivity 96% (CI95% 90-98)
  - Specificity 99% (CI95% 54-100)
  - Positive likelihood ratio 304
  - Negative likelihood ratio 0.04

- To **mimick real world conditions**, further info is needed when DBS are stored outside of the cold chain under conditions of higher temperatures and humidity and for up to 1 month

- **Manufacturers should validate DBS** as a sample type, provide protocols to end-users and submit for WHO PQ and regulatory approval

Source: Lange et al, ESCMID & unpublished

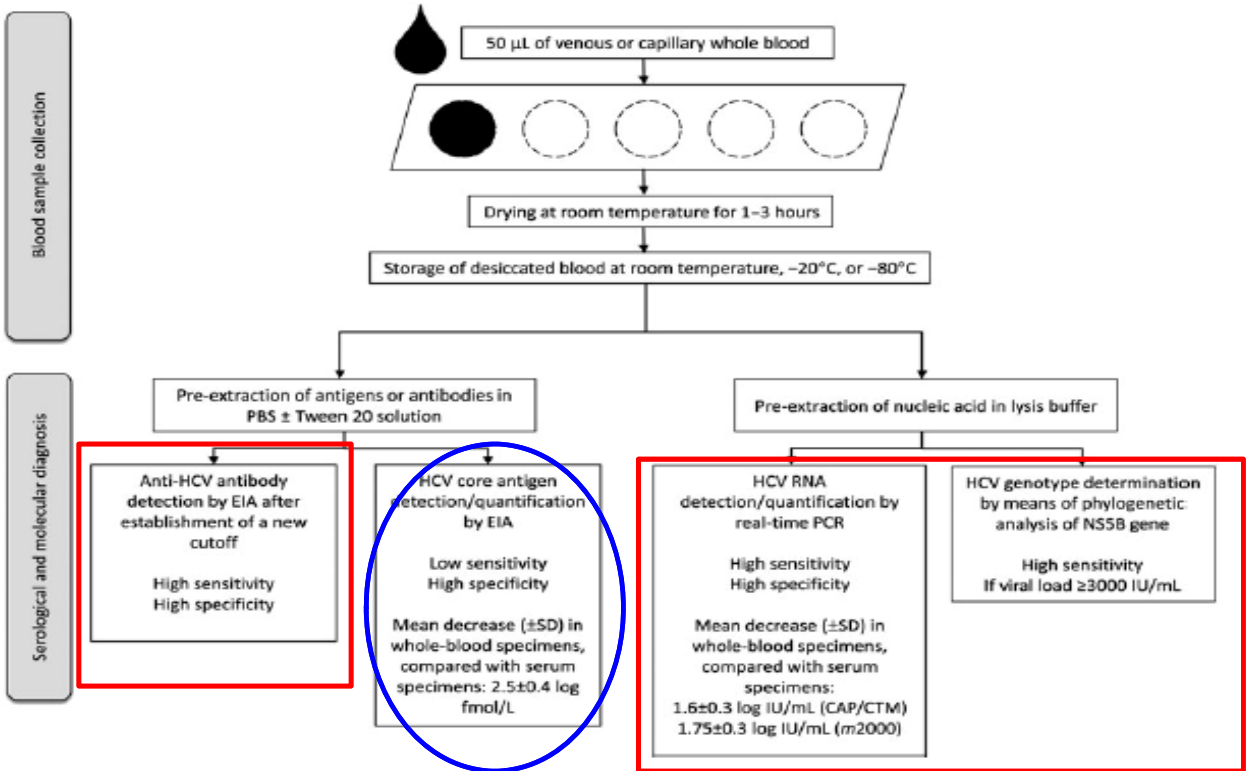
The Journal of Infectious Diseases

MAJOR ARTICLE

Dried Blood Spots: A Tool to Ensure Broad Access to Hepatitis C Screening, Diagnosis, and Treatment Monitoring

Alexandre Soulier,[1,4] Lila Poiteau,[1,4] Isabelle Rosa,[5] Christophe Hézode,[2,4] Françoise Roudot-Thoraval,[3,4] Jean-Michel Pawlotsky,[1,4] and Stéphane Chevaliez[1,4]

[1]National Reference Center for Viral Hepatitis B, C, and Delta, Department of Virology, [2]Department of Hepatology and Gastroenterology, [3]Department of Public Health, Hôpital Henri Mondor, Université Paris-Est, [4]INSERM U955, and [5]Department of Hepatology and Gastroenterology, Centre Hospitalier Intercommunal de Créteil, France



HCVcAg vs RNA

HepHIV 2017
31 JANUARY-2 FEBRUARY · MALTA

Annals of Internal Medicine

REVIEW

Hepatitis C Core Antigen Testing for Diagnosis of Hepatitis C Virus Infection

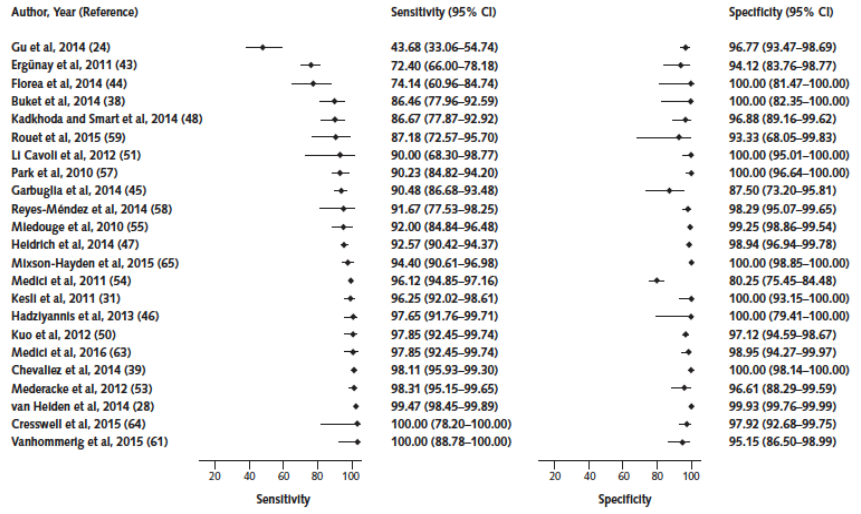
A Systematic Review and Meta-analysis

J. Morgan Freiman, MD; Trang M. Tran, BA; Samuel G. Schumacher, MSc, PhD; Laura F. White, PhD; Stefano Ongarello, PhD; Jennifer Cohn, MD, MPH; Philippa J. Easterbrook, MD, MPH; Benjamin P. Linas, MD, MPH; and Claudia M. Denkinger, MD, PhD

HCV core Ag assays can perform with **high sensitivity** (>90%) and **specificity** (>98%) **compared with RNA assays**

HCV core Ag can conceivably reach a lower cost (based on cost of goods analysis); <10USD

Figure 1. Forest plot of Abbott ARCHITECT's sensitivity and specificity for the diagnosis of active HCV infection compared with NAT for all samples, regardless of anti-HCV status.



Abbott ARCHITECT = Abbott ARCHITECT HCV Ag assay; Ag = antigen; anti-HCV = antibody to hepatitis C virus; HCV = hepatitis C virus; NAT = nucleic acid testing.

POC HCVcAg

HepHIV 2017
31 JANUARY-2 FEBRUARY · MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

Daktari's Approach to HCV Testing

Robust Instrument
Designed to work anywhere

Data Management
Built-in global SIM
Secure, encrypted global transmission

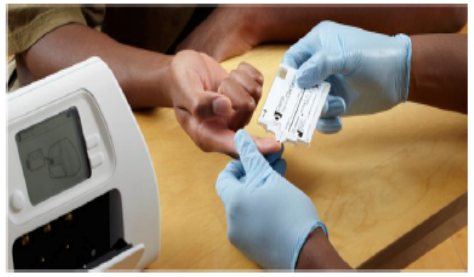
Electrochemical Assays
Sensitive detection in 30 minutes

Microfluidic Sample Handling
Whole blood
No sample preparation, minimal training

Integrated Reagent Storage
Self-contained, long shelf life in extreme environments

Characteristic	Performance
Sample type	Capillary or venous WB
Time to Result	<30 Minutes
Limit of Detection	≤1,000 IU/ml (equiv. to 10 fM cAg)
Specificity	>98%
Regulatory	CLIA-waived, WHO PQ
Connectivity	Integrated, full export capabilities through SystemOne solution

From Patient to Result In Two Steps



1. Collect blood

2. Insert card – Results in 30 minutes

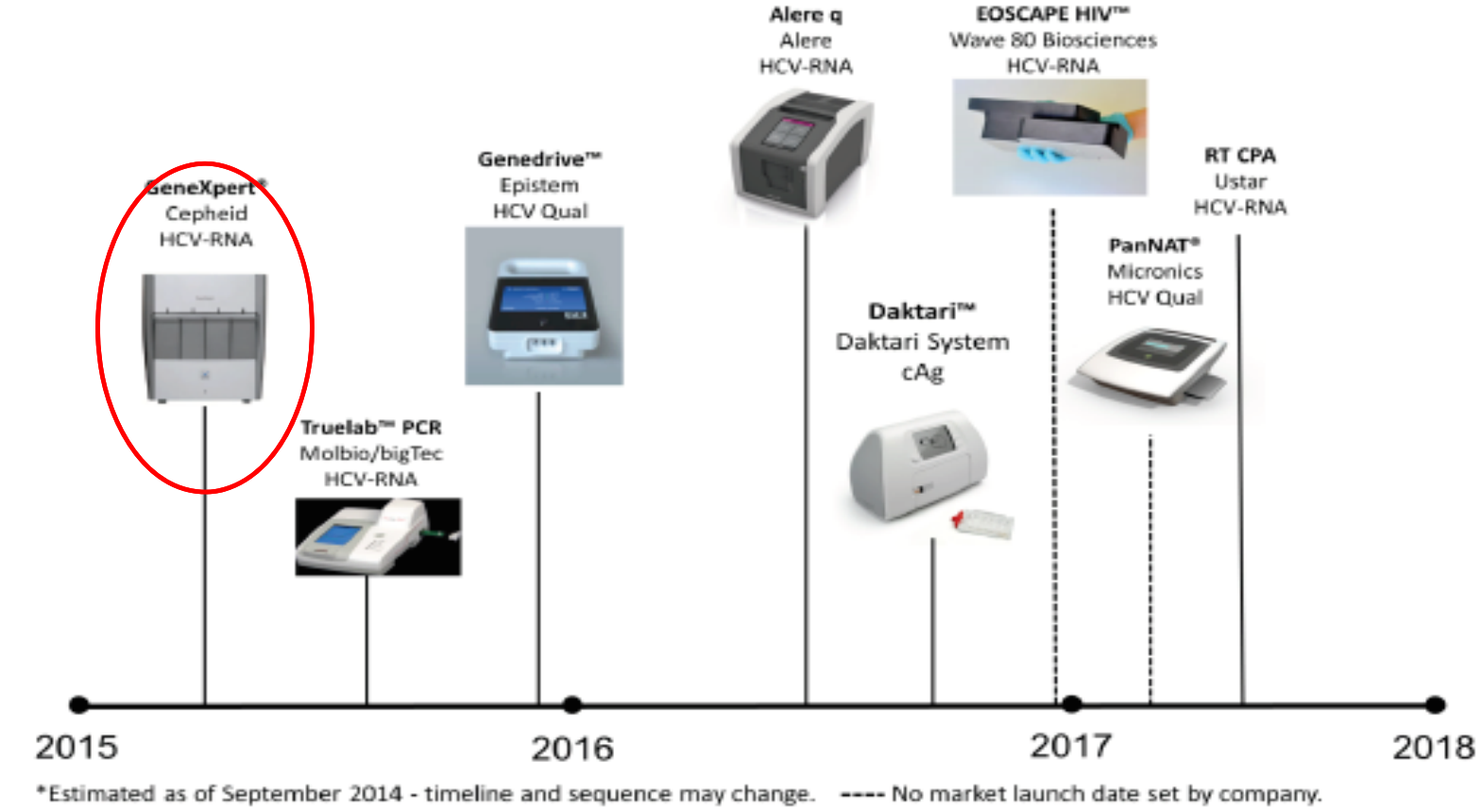
Commercial launch in late 2018

Source: Betsy Wonderly, Daktari

HCV RNA POC

Appendix 2: Pipeline for point-of-care diagnostics

Hepatitis C virus point-of-care diagnosis and treatment monitoring platforms: pipeline*



*Estimated as of September 2014 - timeline and sequence may change. ---- No market launch date set by company.

Source: http://unitaid.org/images/marketdynamics/publications/UNITAID-HCV_Diagnostic_Landscape-1st_edition.pdf

Xpert HCV Viral Load

HepHIV 2017
31 JANUARY-2 FEBRUARY · MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

Test features

Intended use:	Monitoring antiviral therapy
Target:	5' UTR
Genotypes:	1 – 6
Type of result:	Quantitative (IU/ml)
Linear range:	10 – 100,000,000 IU/ml
Nucleic acid detection:	RNA
Sample type:	Plasma or serum
Sample volume:	1 ml
Time to results:	105 minutes
Cartridge storage:	2 – 28°C
Cartridge shelf-life:	9 months
Regulatory approval	CE-IVD marked; WHO PQ (in process)
Price (HBDC):	$17.10

Detected: xx IU/ml
Detected: $1x10^8$ IU/ml
Detected: <10 IU/ml
Not detected
Invalid
Error
No result

Xpert HCV Viral Load Performance by independent studies

HepHIV 2017
31 JANUARY-2 FEBRUARY·MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

Author	Year	Country	Reference assay	Sample type	Sample size	Population	Design	Correlation	Se	Sp	Bias	Precision	Invalid
McHugh	2015	UK, USA, FR, BE	Abbott	Plasma, serum	607	HCV+	Retrospective	r = 0.989	97.9 %	100%	NR	NR	3.5%
Rahamat	2015	Netherlands	Roche	Plasma	42	HCV+	Retrospective	r = 0.910	100%	100%	5%: >1Log	NR	NR
Weismann	2015	Germany	Abbott	Plasma	n=12 ↑VL	HCV+	Retrospective	NR	NR	NR	**0.30 Log**	NR	NR
					n=10 ±VL	HCV+	Retrospective	NR	NR	NR	**0.10 Log**	NR	NR
					n=17 ↓VL	HCV+	Retrospective	NR	NR	NR	**0.03 Log**	NR	NR
					n=11 TND	HCV+	Retrospective	NR	NR	82%	**0.79 Log**	NR	NR
Grebely	2016	Australia	Abbott	Plasma	166	PWID	Prospective	NR	100%	99.1 %	NR	NR	NR
Grebely	2016	Australia	Abbott	Fingerprick	162	PWID	Prospective	NR	96%	98.2 %	NR	NR	NR
Maleska	2016	France	Roche	Plasma	20	HCV+	Retrospective	r = 0.984	NR	NR	**-0.31 Log**	CV=28%	NR

Lessons Learnt and Key messages

HepHIV 2017
31 JANUARY-2 FEBRUARY · MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

- **Delay in HCV screening** due to lack of in-country policy, guidelines and programmes
- **Unknown quality of serological screening** where countries use cheaper RDTs of unknown manufacturing quality and performance; **HIV co-infection** may cause false positives (polyclonal) and false negatives (immunosuppression)
- **DAAs are allowing for diagnostic simplification and decentralisation** but guidelines and models of care are still very conservative
- **Delay in access to DAA treatment in countries due to slow registration** and companies having no incentive to apply for WHO prequalification (no donor purchasing of drugs therefore no quality policy – same for Dx) means delay in implementing HCV programming overall
- **Reliance on external stakeholders and political will but no dedicated international funding available**; preferential pricing normally not extended to MICs, and LMICs are struggling to pay everything domestically, means manufacturers are not convinced of a viable market
- **Price of diagnostics**, particularly in MIC remains a challenge!
  - Increased procurement by large, classical donors will provide incentive for quality RDTs
  - Large procurers can also facilitate pooled procurement, increased volumes and competition for price reductions
  - Countries should strengthen their quality policies for diagnostics in general (tender systems should be based on quality and performance, not just price)
  - Ramping up of country HCV programmes will lead to price reductions due to increased volumes and competition
- **Advocacy**
  - Ramped up advocacy is needed for increased awareness for importance of HCV testing & funding

THANK YOU

HepHIV 2017
31 JANUARY-2 FEBRUARY · MALTA
HIV and Viral Hepatitis: Challenges of Timely Testing and Care

Acknowledgement: Teri Roberts, Diagnostics Advisor at the MSF Access Campaign