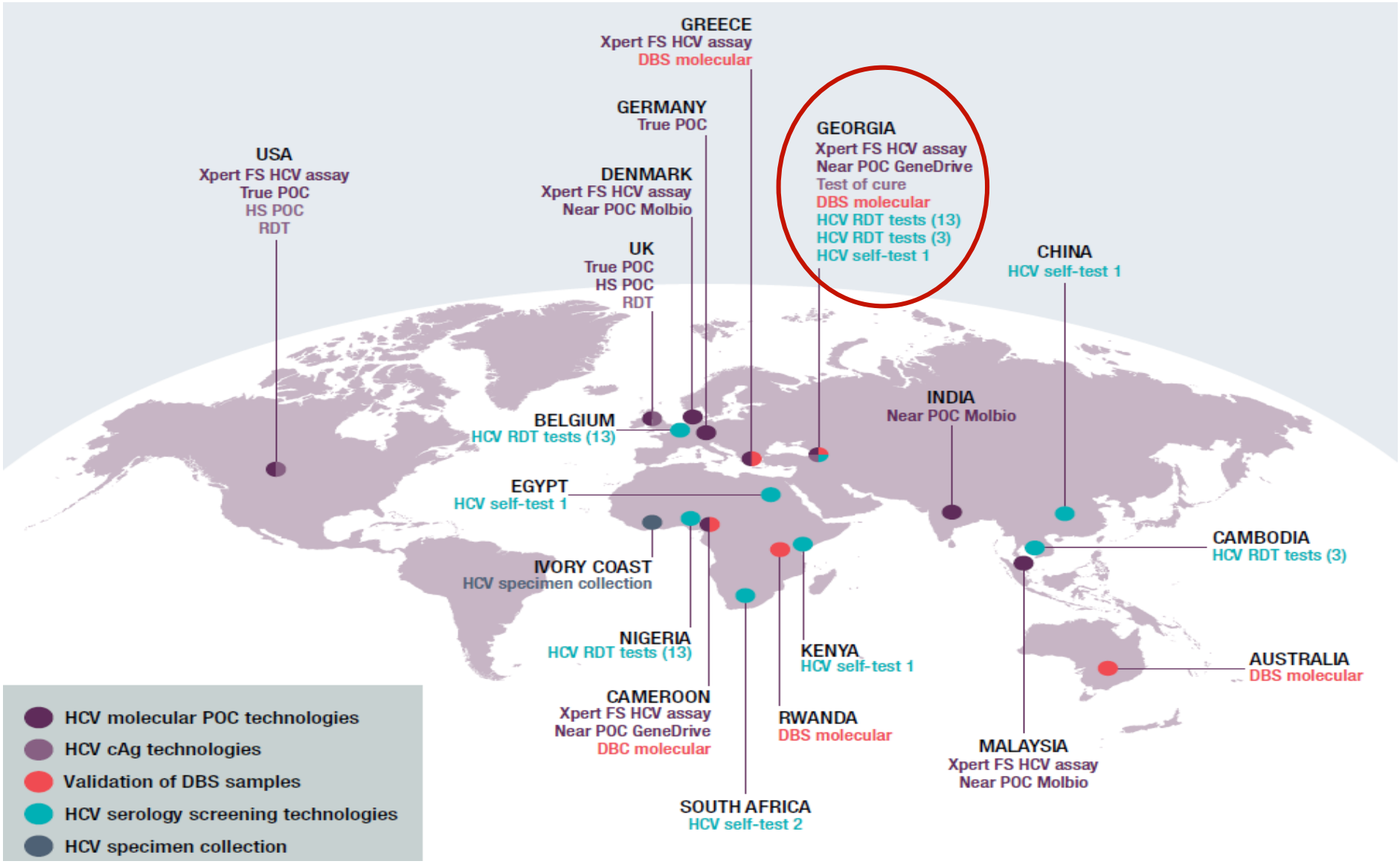
5th HEPATITIS C TECHNICAL ADVISORY GROUP

TAG Meeting

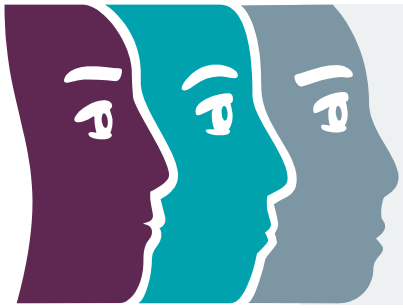
EVALUATION STUDY OF HCV RAPID DIAGNOSTIC TESTS (RDTS), DRY BLOOD SPOTS FOR HCV RNA TESTING, AND THE GENEDRIVE® HCV ID KIT IN GEORGIA

Maia Alkhazashvili
NCDC

Output 1 projects, trials, studies



Unitaid
Innovation in Global Health



HCV Rapid Diagnostic Test Evaluation Studies

Evaluation studies of HCV rapid diagnostic tests

Study I

Laboratory evaluation of 13 HCV RDTs on archived plasma samples
(60% of samples HIV co-infected)

Aim: Evaluate which HCV RDTs meet the World Health Organization criteria

Study sites and sample origins:

Georgia
Cambodia
Nigeria
Belgium

Timeframe: Oct 2018 – March 2019

Study II

Field evaluation of 3 HCV RDTs on freshly collected whole blood, plasma and serum samples

Aim: Generate data for HCV RDT World Health Organization pre-qualification application

Study sites:

Georgia
Cambodia

Timeframe: Aug 2019 - ongoing

World Health Organization HCV RDT criteria

An HCV RDT receiving WHO pre-qualification should have….

- ≥ 98% sensitivity
- ≥ 97% specificity
- <5% operational variation

Study I: Archived sample evaluation of 13 RDTs
SETUP

Study design

- Retrospective cross-sectional study using archived plasma samples to evaluate 13 RDTs against a reference standard
- Total sample numbers in statistical analysis: 1'500

HCV+ve 648 (264 HIV co-infected)
HCV-ve 852 (646 HIV co-infected)

Study partners

samples per county

- National Centre for Disease Control, 354 samples, 24% Tbilisi, Georgia
- Nigerian Institute for Medical Research, 568 sample, 38% Lagos, Nigeria
- Sihanouk Hospital Centre of HOPE, 458 sample, 31% Phnom Penh, Cambodia (tested in Belgium)
- Institute of Tropical Medicine, Antwerp, 120 sample, 8% Belgium

RDTs evaluated

Test name	Manufacturer
Standard Q HCV Ab	SD Biosensor
HCV Antibody Test	Artron Laboratories
HCV-Ab Rapid Test	Beijing Wantai
Rapid Anti-HCV Test	InTec
First Response HCV	Premiere Medical Corp.
Signal HCV Ver 3.0	Arkray healthcare
TRI DOT HCV	J. Mitra & Co
HCV-only Antibody Test	Biosynex SA
SD Bioline HCV	Abbott Diagnostics
OraQuick HCV	OraSure
Prototype HCV Antibody Test*	bioLytical
Prototype DPP HCV*	Chembio Diagnostic
Prototype CareStart HCV*	Access Bio

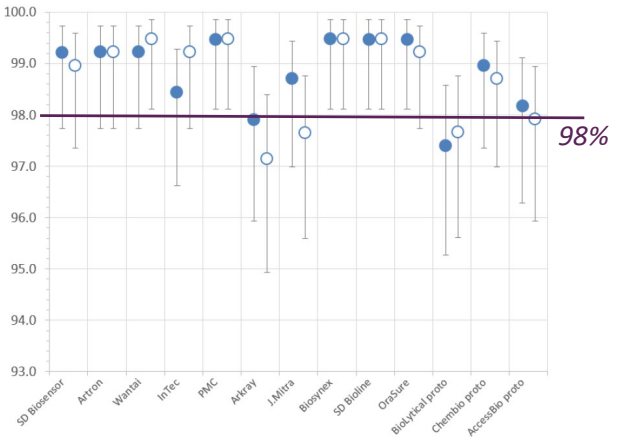
*under development

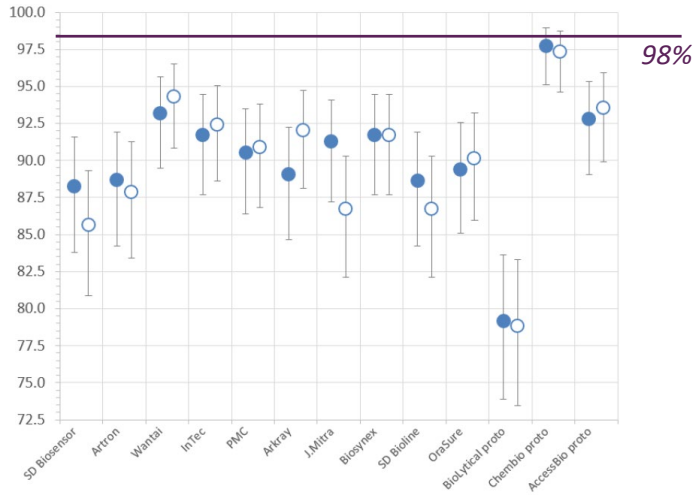
Study I: Archived sample evaluation of 13 RDTs
RESULTS

HCV-only

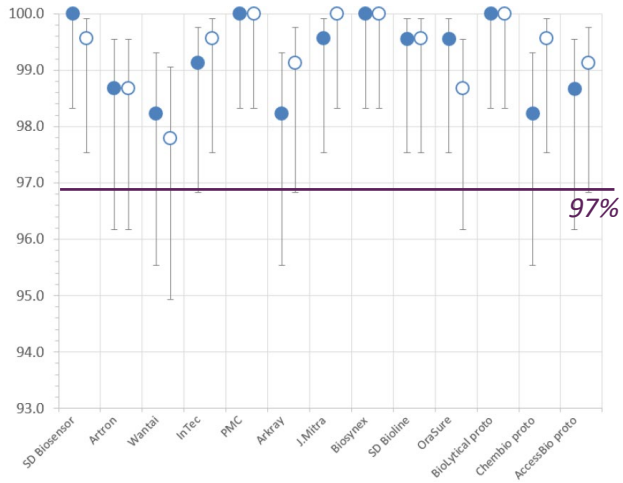
HCV/HIV co-infected

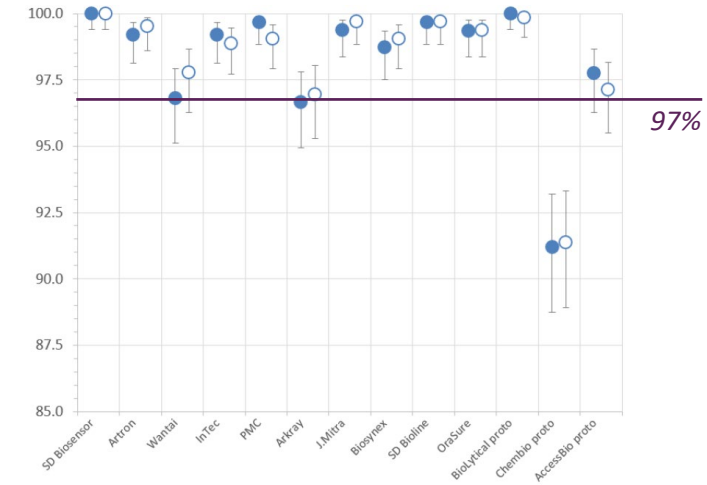
Sensitivity





Specificity





● Lot 1 ○ Lot 2

- Majority of RDTs met WHO criteria in HCV-only samples
- RDT sensitivity was below WHO criteria in HIV co-infected samples
- Further evaluation showed that false negative were mostly found in samples without detectable viral load
- All RDTs met WHO operational criteria (data not shown)

Study II: Fresh sample evaluation on 3 HCV RDTs
SETUP

Study design

- Prospective cross-sectional study on fresh whole blood, plasma and serum samples to evaluate 3 RDTs against a WHO-PQed RDT and a reference method
- Total sample numbers : 1'540 HCV+ve 440
  HCV-ve 1'100

RDTs under evaluation

Test name	Manufacturer
HCV-Ab Rapid Test	Beijing Wantai
First Response HCV	Premiere Medical Corp.
Prototype CareStart HCV*	Access Bio

*under development

Study partners

participants per county

- National Centre for Disease Control, 770 sample, 50% Tbilisi, Georgia
- Sihanouk Hospital Centre of HOPE, 770 sample, 50% Phnom Penh, Cambodia (tested in Belgium)

Currently recruited 511 participants

Currently recruited 457 participants

Study II: Fresh sample evaluation on 3 HCV RDTs
INTERIM RESULTS Georgia

- Two RDTs show promising performance to meet WHO criteria for sensitivity and specificity in freshly collected samples
- One RDT has a weaker performance in specificity in this limited preliminary sample set
- Final results expected in early 2020

Conclusions

- Independent performance evaluations are important to verify RDT performance in samples from a range of different regions and with HIV co-infection
- Many RDTs have the potential to meet WHO PQ criteria in archived plasma samples
- Performance evaluations in freshly collected in whole blood, serum and plasma are important to reflect expected field performance of HCV RDTs

Multicenter clinical trial to assess the performance of centralized assays for hepatitis C virus RNA detection from Dried Blood Spot (DBS) samples

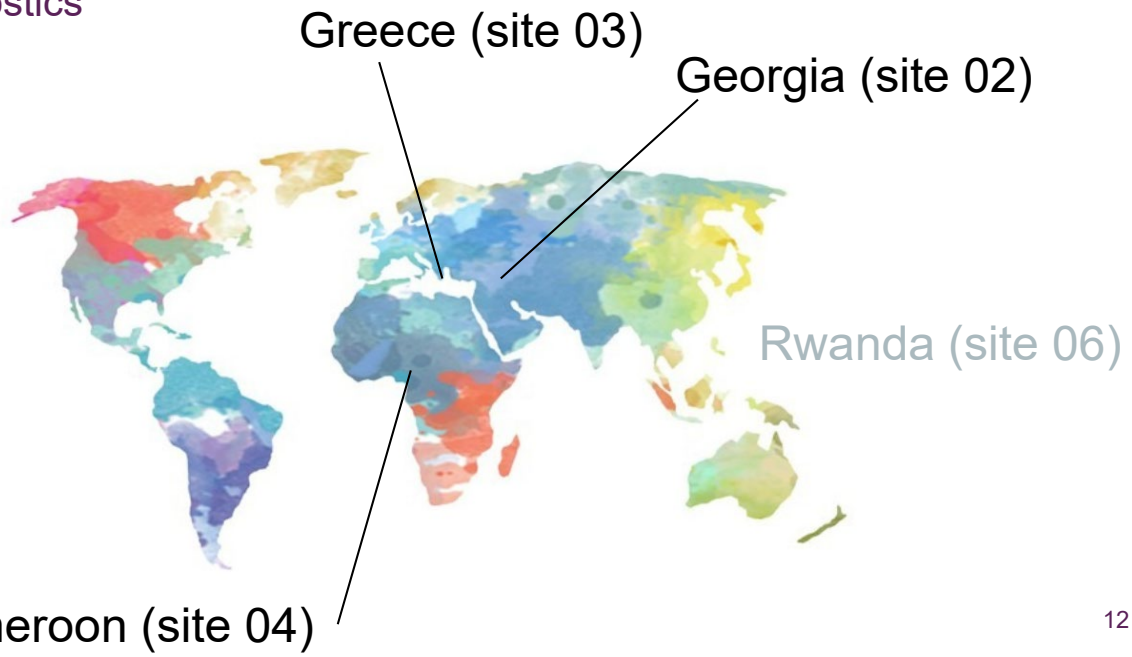
Prospective cross-sectional multicentre diagnostic accuracy study

- **Multicenter clinical trial to assess the performance of centralized assays for hepatitis C virus RNA detection from Dried Blood Spot (DBS) samples**

  Protocol Number 8160-2/1

- Evaluate performance of centralised HCV VL on DBS/PSC and paired plasma

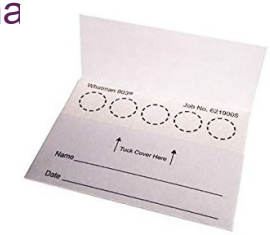
- To facilitate WHO PQ for HCV VL testing on plasma and DBS/PSC and increase global HCV diagnostics



Manufacturers and platforms

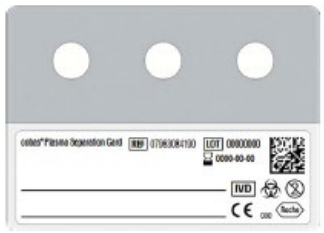
Abbott Molecular, USA

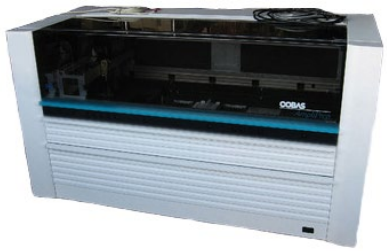
Abbott M2000 (DBS) All clinical sites, NRL Australia for plasma



Roche Diagnostics, Switzerland

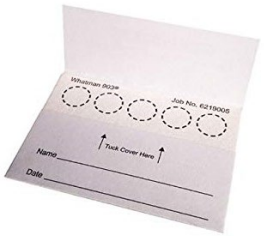
COBAS® AmpliPrep/COBAS® TaqMan® (DBS) and
Roche cobas® 4800/6800 (PSC and DBS) NRL Australia





Hologic, USA

Hologic Panther (DBS) NRL Australia

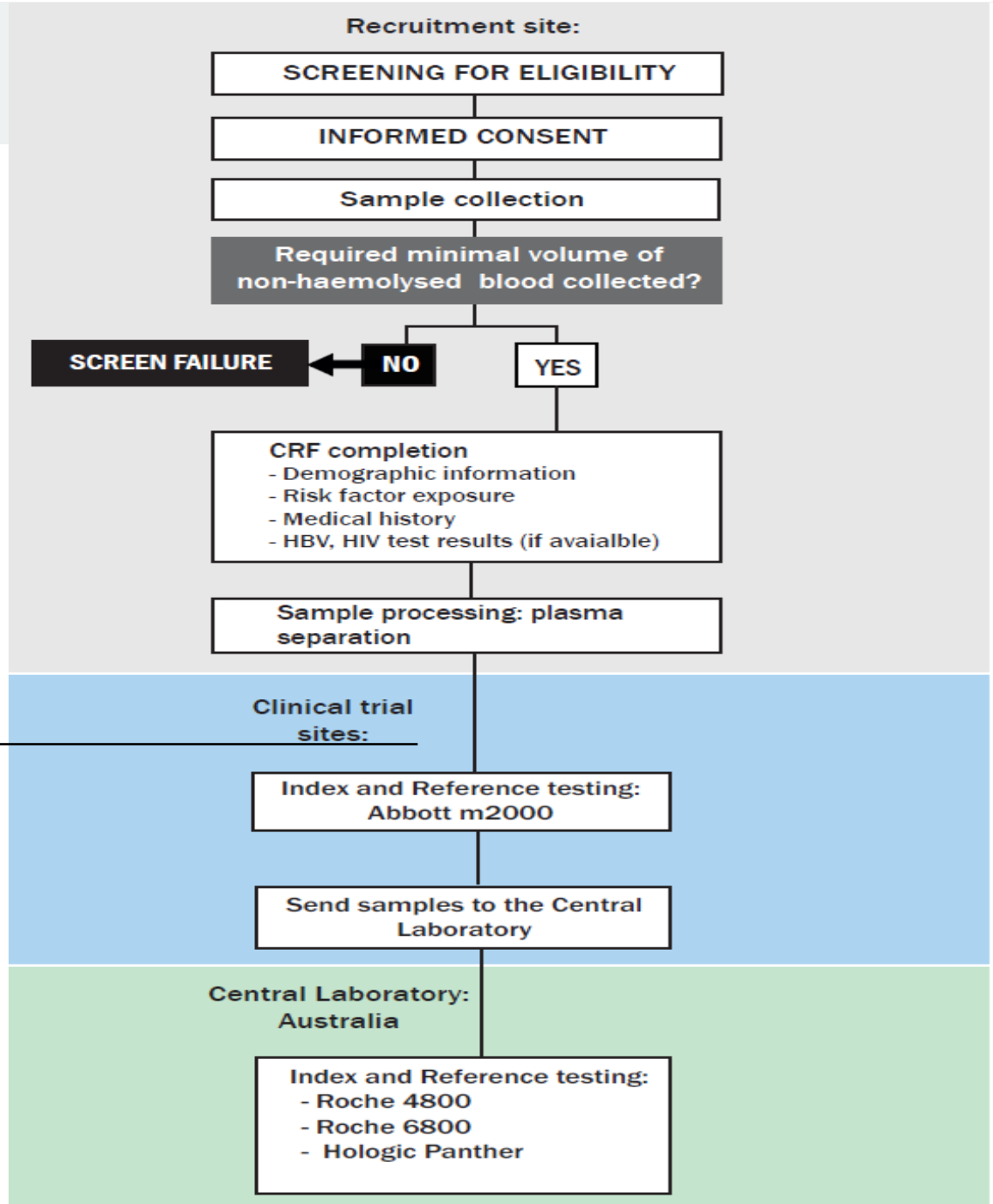


Objectives

- **Primary Objective:**
  - To evaluate the performance of centralized HCV viral load (VL) assays from DBS and/or PSC specimens, against HCV VL test used as a standard of care at the clinical site

- **Secondary objectives:**
  - To evaluate the performance of centralized HCV VL assays from DBS and/or PSC specimens against the same assay performed from a paired plasma specimen
  - To assess the operational characteristics of centralized HCV VL assays, including invalid and indeterminate rate, throughput, number of steps, time-to-result
  - *For Central Laboratory only*: to evaluate the performance of three centralized HCV VL assays from plasma specimens against the performance of Roche cobas® 6800 HCV VL assay

Overall trial flow



SUBSTUDY

Georgia, Cameroon

200UL of plasma: POC HCV Test

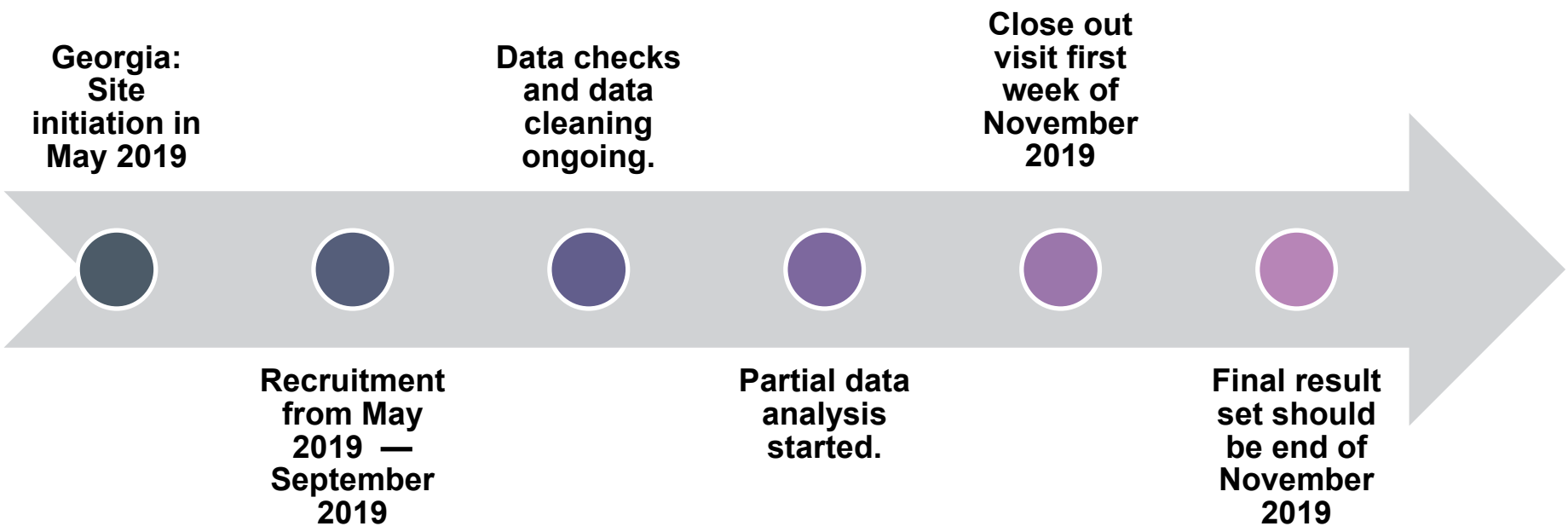
Eligibility criteria – Population group

- **HCV SEROPOS: Individuals at risk of having HCV infection based on documented positive HCV serology test results**
  - Reached the age of an adult as defined in Georgia
  - Able to understand the trial and provide informed consent
  - Documented positive results of HCV serology test
- **HCV RISK: Individuals at risk of having HCV infection based on past and/or current exposure to risk factors**
  - Reached the age of an adult as defined in Georgia
  - Able to understand the trial and provide informed consent
  - Past and/or current exposure to one of the high-risk factors as defined by WHO and CDC guidelines
- **HCV TREAT: Individuals diagnosed with chronic HCV infection who initiated or completed the anti-HCV treatment with direct acting antivirals (DAA) presenting at the clinical site for treatment monitoring or test of cure (i.e. sustained virological response)**
  - Reached the age of an adult as defined in Georgia
  - Able to understand the trial and provide informed consent
  - Initiated on DAA treatment (regardless the type of a DAA regimen) within 12 months prior to the enrolment to the trial

Sample Size

	Georgia	Cameroon	Rwanda	Greece
HCV RNA Pos	**120**	100	100	100
HCV RNA Neg	**150**	150	100	120
Total participants	**270**	250	200	220

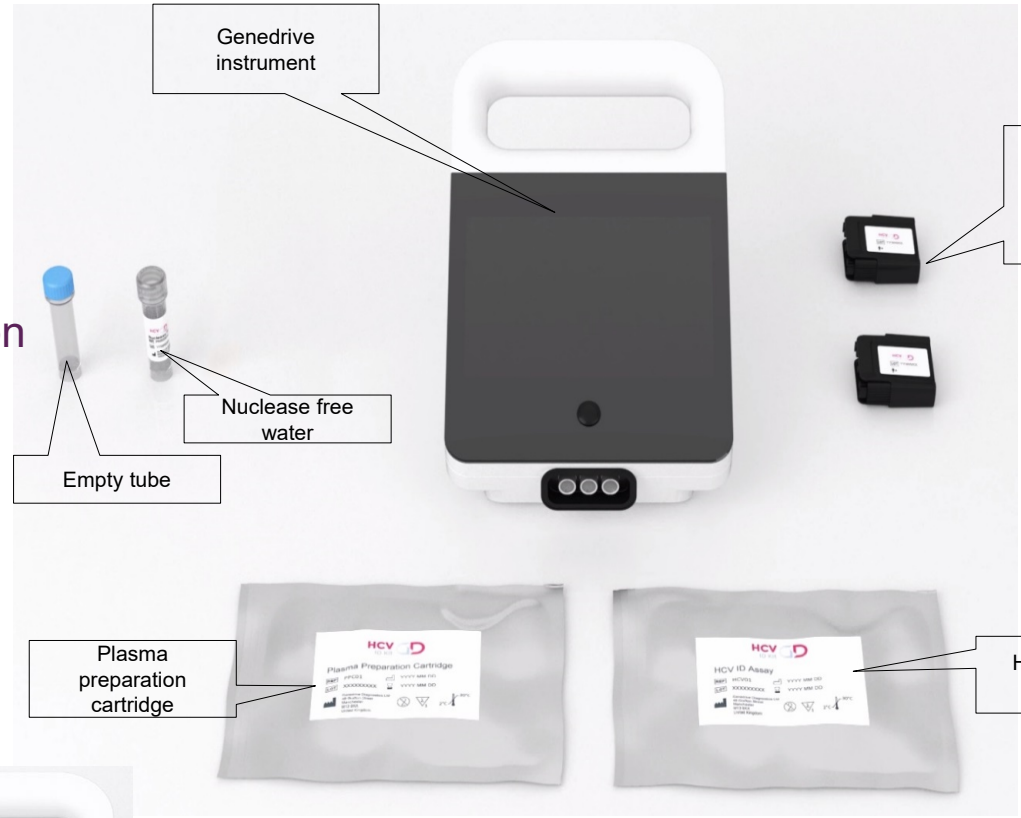
Progress Timeline



Genedrive® HCV ID kit in Georgia

Genedrive

- CE-IVD certification
  4th September 2017
- Portable, simple platform
- Qualitative nucleic acid detection
- Uses 30μL of plasma
- Result available in 90 minutes
- Run Positive and negative plasma control daily



Prospective diagnostic accuracy study

- **Prospective evaluation of the Genedrive® HCV ID kit in Georgia and Cameroon**

  Protocol Number 8160-2/1

Objectives:

- To evaluate the sensitivity and specificity, negative predictive value and positive predictive value of the Genedrive® HCV ID kit for the detection of HCV

- To assess the usability of the Genedrive® HCV ID kit in a real-life settings

Prospective diagnostic accuracy study

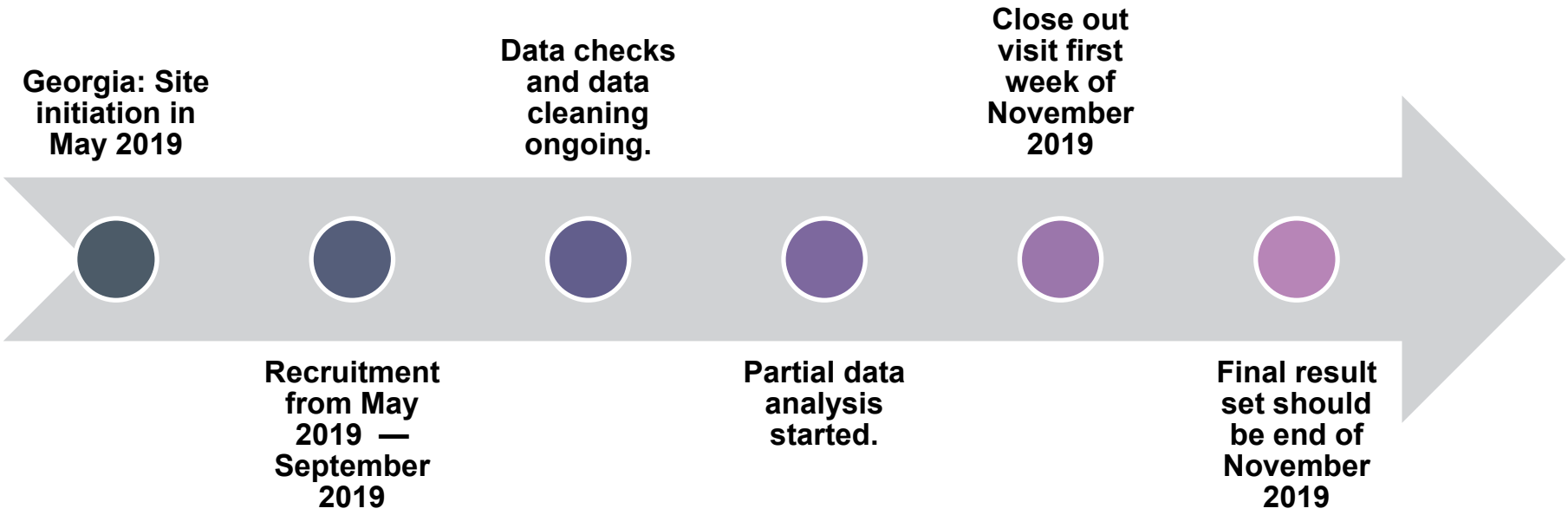
	Georgia	Cameroon
HCV RNA detectable	120	100
HCV RNA non-detectable	150	52
Total	270	152

Subjects who consented to participate in the Parent Trial were invited to participate in this substudy.

The performance of the Genedrive will be measured against the results of Abbott RealTi*me* HCV VL assay obtained in the Parent Trial.

Procedure	Day 1	End of the study
Informed consent	X	
HCV RNA testing on Genedrive® Instrument	X	
Genedrive® usability questionnaire, error rate review		X

Progress Timeline as at November 2019



Acknowledgements

- FIND
- NCDC/Lugar Center
- Hepa+
- Center of Mental Health and Prevention of Addiction
- ALL participants