Cambridge Consultants

Cost assessment of Cepheid's Xpert® HIV-1 Viral Load assay technology platform

Addendum to *Cost assessments of HIV viral load assay technology platforms: final report (P1646-P-008)*

Médecins Sans Frontières

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27 November 2015

P1646-P-014 v1.0

MSF asked Cambridge Consultants to conduct a cost assessment of the *Xpert® HIV-1 Viral Load* cartridge, in line with an approach used in a previous analysis

- In 2013, Médecins Sans Frontières ("MSF") asked Cambridge Consultants to assess the relative cost per HIV viral load test based on different technology platforms employed
- We conducted a four-step approach, which involved a review of exemplar products and parameters to form the basis of a relative cost assessment; systems used in reference labs and POC assays were assessed
- The key findings of the cost analysis, including methodology, exemplar products studies and assumptions, are described in our final report, entitled *Cost assessments of HIV viral load assay technology platforms*
  - Document reference P1646-P-008, dated 8th November 2013
- In 2015, MSF asked Cambridge Consultants to carry out a cost analysis of the Xpert® HIV-1 Viral Load cartridge, manufactured by Cepheid Inc (Sunnyvale, CA), to augment its understanding of the field
  - Scope of analysis as per *Offer letter for proposed approach to conduct diagnostics work programmes*, document reference S4998-L-048, dated 6th March 2015
- The cost analysis should include an assessment of key cost parameters of the cartridge, including reagent chemistries, packaging, manufacturing and intellectual property rights / licensing considerations
- MSF request quantitation of the above cost parameters to derive a 'cost per test' estimate of the cartridge, using methodologies and assumptions which are in line with the approach used in our previous analysis
- The purpose of this addendum is to present a summary of the key findings of our cost analysis of Xpert® HIV-1 Viral Load cartridge; a cost analysis of the Xpert® HIV-1 Qual cartridge is also described
- Please note these slides should be read in conjunction with P1646-P-008

The Xpert® HIV-1 Viral Load cartridge enables the test process including RNA extraction, purification, reverse transcription and copy number quantitation

Xpert® HIV-1 Viral Load (Cepheid Inc)	
Intended use	• Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR)-based assay, performed on Cepheid's proprietary GeneXpert® instrument system, for in vitro quantitation of HIV-1 in human plasma from HIV-1 infected individuals over the range of 40 to 10,000,000 copies/mL
Assay description	• The GenXpert® system automates and integrates sample preparation, nucleic acid extraction, target amplification and detection of the target sequence in samples using RT-PCR • The assay cartridge includes reagents for the detection of HIV-1 RNA in specimens, including two internal controls used for quantitation of HIV-1 RNA
Size	• Single test per disposable cartridge (1 test per run)
Test kit composition	• Test kit consists of a disposable cartridge containing all reagents required for nucleic acid isolation, sample processing, amplification and detection
Cost per test(1)	• US$19.10(1)

Xpert HIV-1 Viral Load Test

Image shows disposable cartridge which contains all reagents to perform assay processing and amplification. Signal detection performed on GeneXpert Instrument systems

(1) Source: *Virology prices* (dated 19th February 2015). Reference is a PowerPoint slide, received from MSF, comprising prices for a range of Cepheid Xpert® test cartridges. 'At Launch' price point for Xpert® HIV-1 Viral Load cartridge is chosen as reference point for this analysis

The Xpert® HIV-1 Viral Load cartridge is proposed to work across the full assay workflow except for the sample extraction step

Test kit impact

Xpert HIV-1 Viral Load assay self contained disposable assay cartridge

Self-contained cartridge comprising all required reagents

Test workflow

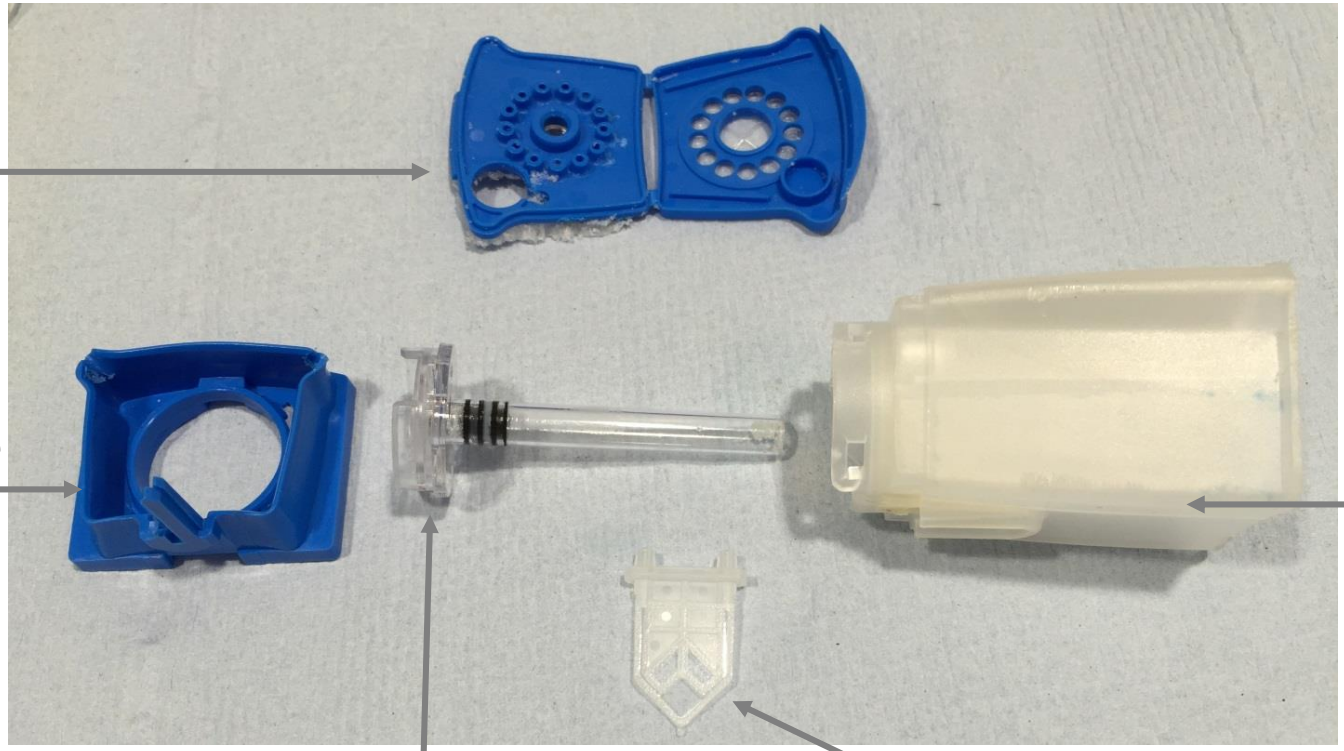
- Sample extraction
- **Nucleic acid isolation**
- **Sample processing**
- **Target amplification**
- **Target detection**

Instrumentation requirements

The GeneXpert system II analyser[1]

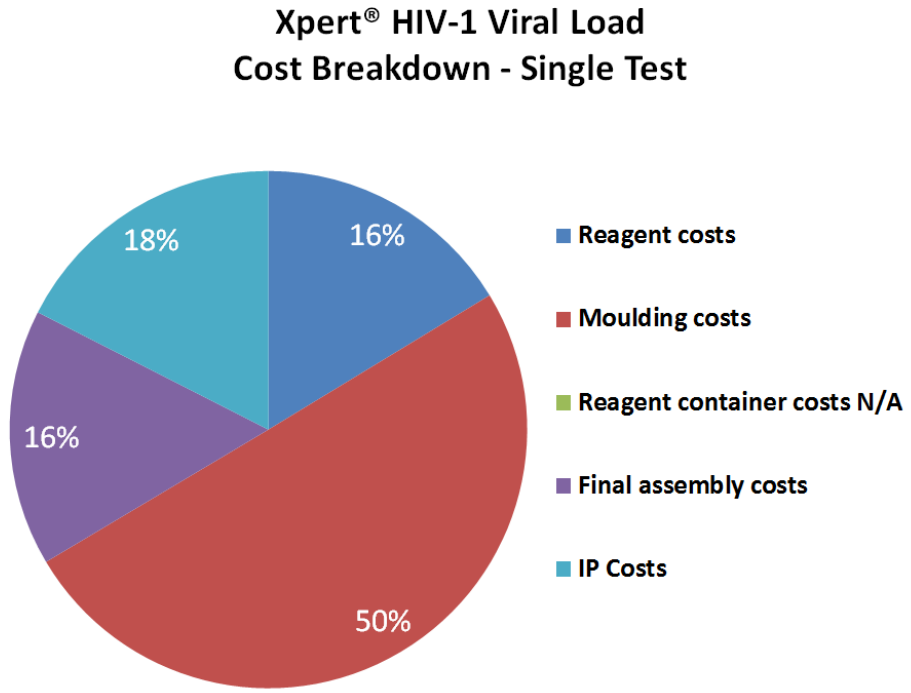
[1] Test instrument requirements not included in relative cost assessment; provided for illustrative purposes only

Disassembly of the Cepheid Xpert® HIV-1 Viral Load cartridge demonstrates five moulding assemblies, each requiring individual tooling and moulding processes



Our cost estimate for the Xpert® HIV-1 Viral Load Test assay is US$10.91 per test; principal cost is attributable to cartridge mouldings and assembly

Assay cost analysis	
Product cost	**US$10.91**
Principal cost parameters	• Majority of assay cost is attributable to cartridge mouldings and associated overheads • Nominal IPR licensing costs of 10% price per test have been assumed(1)
Manufacturing complexity	• High
Additional costs to complete test workflow	• None; cartridge comprises all reagents and packaging required for sample preparation thought to detection
Transportation requirements	• Requires storage at 2-8ºC(2)



See P1646-SSHT-004 for detailed cost breakdown by cost parameter

(1) The package insert references use of Armored RNA®, a patented technology jointly developed by Asuragen Inc. and Cenetron Diagnostics, LLC, which we have assumed will incur a nominal royalty of 10% price per test result

(2) Xpert® HIV-1 Viral Load package insert (Ref. GXHIV-VL-CE-10, December 2014)

Cepheid's Xpert® HIV-1 Qual cartridge provides a NAAT-based test for qualitative detection of viral RNA and pro-viral DNA

	Xpert® HIV-1 Qual (Cepheid Inc)
Intended use	• RT-PCR-derived assay, performed on Cepheid's proprietary GeneXpert® system, for in vitro qualitative HIV-1 detection from whole blood sample
Assay description	• The GenXpert® system automates and integrates sample preparation, nucleic acid extraction and amplification, and detection of the target sequence in samples using RT-PCR. • Cartridge includes reagents for the detection of HIV-1 total nucleic acids in specimens as well as an internal control to ensure adequate processing of the target and to monitor the presence of inhibitor(s) in the RT and PCR reactions. • Probe Check Control verifies reagent rehydration, PCR tube filling in the cartridge, probe integrity, and dye stability.
Size	• Single test per disposable cartridge (1 test per run)
Test kit composition	• Disposable cartridge containing all reagents necessary for sample processing (cell lysis, amplification target capture, real-time amplification and fluorescence detection)
Price per test(1)	• US$19.90(1)

Xpert HIV-1 Qual

Image shows disposable cartridge which contains all reagents to perform assay processing and amplification. Signal detection performed on GeneXpert Instrument systems (not pictured)

(1) Source: *Virology prices* (dated 19th February 2015). Reference is a PowerPoint slide, received from MSF, comprising prices for a range of Cepheid Xpert® test cartridges. 'At Launch' price point for Xpert® HIV-1 Qual cartridge is chosen as reference point for this analysis

Our analysis of the Xpert® HIV-1 Qual cartridge indicates a similar cost per test to the Xpert® HIV-1 Viral Load cartridge

- Our analysis of the Xpert® HIV-1 Qual cartridge demonstrates very similar system architecture and chemistry to the Xpert® HIV-1 Viral Load cartridge
  - Disassembly of the Xpert® HIV-1 Qual cartridge indicates five moulding assemblies as per Xpert® HIV-1 Viral Load cartridge; there is a slight difference in cuvette assembly design but this is not considered to change moulding/assembly process
  - High level analysis of the cartridge chemistry – according to the Xpert® HIV-1 Qual cartridge package insert(1) – indicates similar overall reagents
  - Package insert also references Armored RNA® (Asuragen Inc. and Cenetron Diagnostics, LLC), which we assumed will incur a nominal 10% royalty payment
- As a result we have assumed that the cost per test of the Xpert® HIV-1 Qual cartridge is similar to the Xpert® HIV-1 Viral Load cartridge

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