

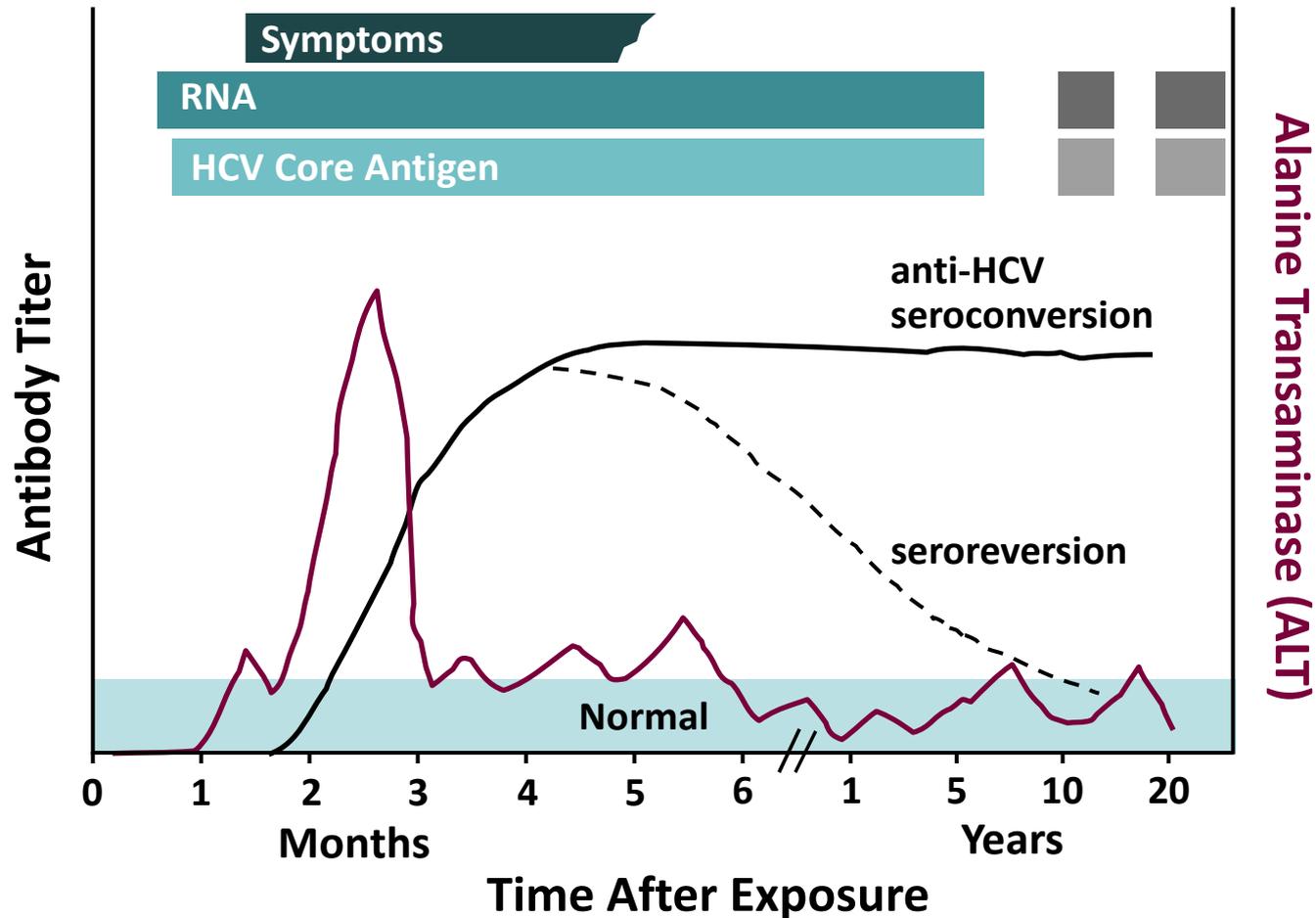
Performance of a CLIA-Waived Rapid Test for HCV Antibody

Stephen R. Lee PHD
Chief Science Officer
OraSure Technologies

Utility of a Rapid, Point-of-Care (POC) Test to Aid in Identification of HCV Infection

- Despite significant evolution in the quality of laboratory based tests for HCV, the majority of HCV infection remains undiagnosed
- Prevalent, undiagnosed chronic HCV infection represents a major future healthcare burden¹
- Availability of a rapid, non-instrumented POC test will increase opportunities for diagnosis through increased testing outside of laboratory settings
- Recent improvements in efficacy and reduced treatment duration are expected to increase the number of patients initiating therapy
- Continued improvement in available therapies will mean increased diagnoses will be an important factor in reducing future morbidity and mortality associated with HCV

Natural History of Hepatitis C Virus Infection



OraQuick[®] HCV Rapid Antibody Test Device



A Simple Test Procedure Utilizing All Sample Types

COLLECT

TEST

Oral Fluid



**Venipuncture
Whole Blood**



Serum / Plasma



**Fingerstick
Whole Blood**



MIX



OraQuick® HCV Rapid Antibody Test Devices Matrix Specificity and Sensitivity* (95% CIs)

Matrix	Specificity (n=450)	Sensitivity (n=122)
Oral Fluid	100% (99.2 – 100%)	99.2% (95.5 – 100%)
Venous Whole Blood	100% (99.2 – 100%)	100% (97.0 – 100%)
Fingerstick Blood	100% (99.2 – 100%)	100% (97.0 – 100%)
Plasma	99.8% (98.8 – 100%)	100% (97.0 – 100%)
Serum	99.8% (98.8 – 100%)	100% (97.0 – 100%)

Agreement of OraQuick® HCV Results with HCV Serostatus in a Population at Risk of HCV or with Signs and/or Symptoms of Hepatitis

OraQuick® HCV Rapid Antibody Test Results	Subject HCV Infected Status		
	Positive	Negative	Unable to Determine Infected Status ⁺
Positive	708	3	11
Negative	11*	923	4
Invalid	0	0	0

* Six (6) of the eleven (11) were negative for HCV RNA by PCR
⁺ Subjects with EIA Reactive or Equivocal results, RIBA® Indeterminate, and PCR Negative were classified as “unable to determine status” (excluded from calculation of test performance here)

Rapid test agreement with HCV positive status= 708/719= 98.5% (97.3-99.2%)
 Rapid test agreement with HCV negative status= 923/926= 99.7% (99.1-99.9%)

Supplemental Laboratory Test Results for At Risk Individuals Reactive in the OraQuick® HCV Test

Number of OraQuick® HCV Reactive Results	RIBA® Results		
	Positive	Indeterminate	Negative
722^	690	29*	2

* Eighteen (18) of the RIBA® indeterminate results were positive for HCV RNA
^ One (1) reactive subject by OraQuick® HCV did not have RIBA and PCR completed.

708/722 (98%) OraQuick® HCV reactive subjects were positive by lab testing

Seroconversion Sensitivity

OraQuick[®] HCV seroconversion results compared to FDA-approved EIA were as follows:

	Days to Evidence of HCV Infection		
	OraQuick [®] HCV Rapid Antibody Test	FDA-Approved anti-HCV EIA	Difference (OraQuick-EIA)
	Time to Detection	Time to Detection	
Average	59.2	62.7	-3.6 (-5.9 to -1.2)

OraQuick[®] rapid HCV test was able to detect antibodies earlier than the approved EIA in 9 of 18 seroconversion panels and by an overall average of 3.6 days (CIs = 1.2 to 5.9 days earlier)

Agreement of OraQuick® HCV Results with HCV Serostatus in a Population (N=606) at Unknown Risk for HCV

OraQuick® HCV Rapid Antibody Test Results	Subject HCV Infected Status		
	Positive	Negative	Unable to Determine Infected Status [^]
Positive	21	1	0
Negative	0	582	2*
Invalid	0	0	0

[^] Subjects excluded from calculation of rapid test performance here.

* Specimens had a non-evolving (indeterminate) antibody pattern with persistent absence of HCV RNA in 2 tests 6 months apart

21/22 subjects (95%) of OraQuick® reactive subjects were positive by lab tests
 Agreement with negative HCV status= 582/583= 99.8% (99.1-100%)

Requirements for CLIA Waiver

- FDA has set very stringent requirements for approval of a CLIA waiver for rapid tests
- Demonstration of equal clinical sensitivity and specificity in untrained users
- Demonstration of a limit of detection (lowest level of antibody detected 95% of the time) equal to laboratory assays
- Reliable reproduction of that limit of detection (LOD) in untrained users
- CLIA studies conducted in users without laboratory training, no prior experience of the test and no verbal instruction
 - Users provided only product labeling and associated educational material

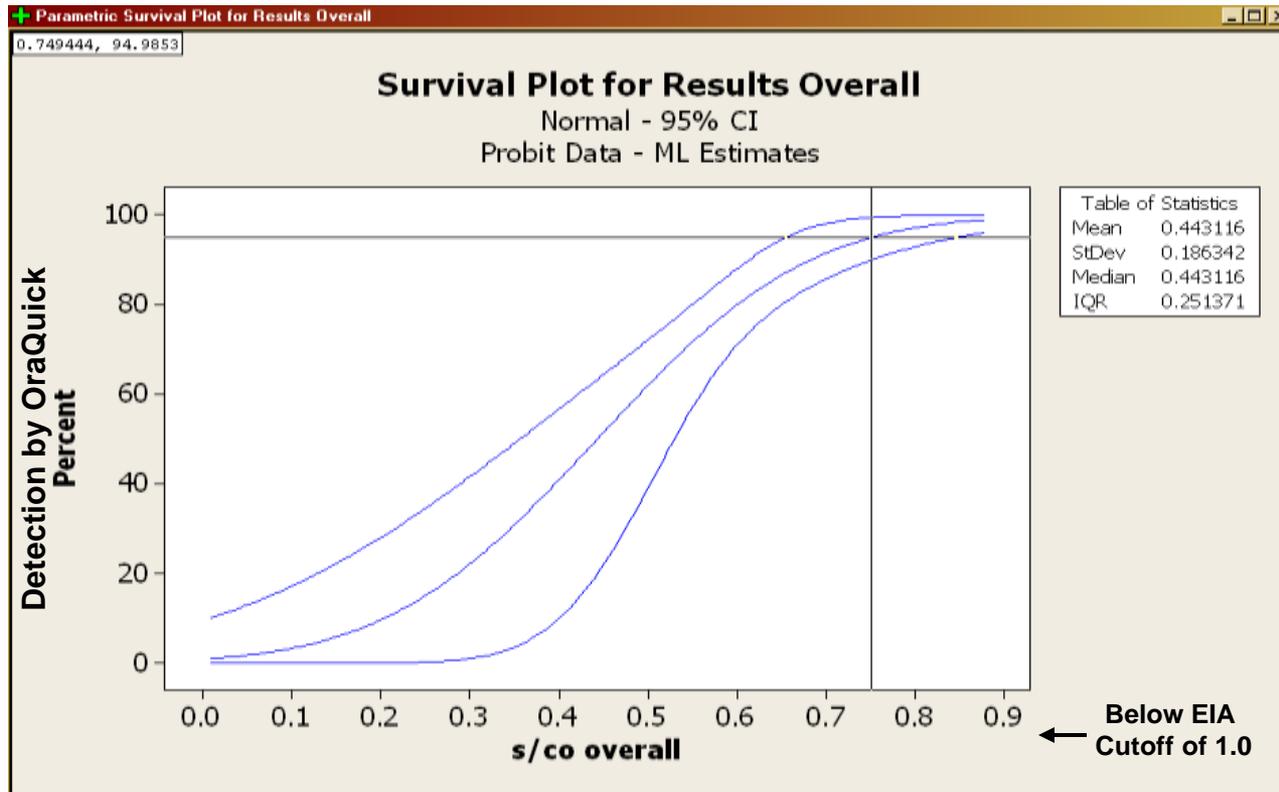
OraQuick® HCV Rapid Antibody Test Results by Untrained Users in Fingerstick Whole Blood: Comparison with HCV Serostatus

OraQuick® HCV Rapid Antibody Test Results	Subject HCV Infected Status		
	Positive*	Negative	Unable to Determine Infected Status ⁺
Positive	129	3	3
Negative	1	526	2
Invalid	0	0	0

*One (1) subject excluded due to inconsistent laboratory results.
⁺Subjects excluded from calculation of rapid test performance here

Rapid test agreement with HCV positive status= $129/130 = 99.2\%$ (95.8-100%)
 Rapid test agreement with HCV negative status= $526/529 = 99.4\%$ (98.4-99.9%)

Analytical Sensitivity of the OraQuick[®] HCV Test Compared to Laboratory EIA



Limit of Detection (LoD*) of OraQuick[®] HCV is lower than laboratory EIA (0.75 S/C)

*LoD determined as the lowest level of antibody (EIA S/C) which the OraQuick test could detect 95% of the time. Testing conducted using multiple lots, across multiple days and operators

Summary of Blinded Panel Member Testing Results by Trained and Untrained Users

Testing Sites (No.)	Specimen Type		
	Negative	LoD*	Low Positive
Trained (1)	29/30 (96.7%)	28/29 (96.6%)	30/30 (100%)
Untrained (4)	88/89 (98.9%)	87/89 (97.8%)	89/90 (98.9%)

*Limit of detection determined as level of antibody detected with 95% reliability
Corresponded to 0.75 S/C (Abbott AxSym)

Sensitivities and Specificities in Each Specimen Type for the OraQuick® HCV Rapid Antibody Test*- CE Approved Claims

Matrix	Sensitivity ^a		Specificity ^a	
	TP	Proportion (95% CI ^b)	TN	Proportion (95% CI ^b)
Serum	756/757	99.9% (99.3%, 100.0%)	1422/1423	99.9% (99.6%, 100.0%)
Plasma	755/756	99.9% (99.3%, 100.0%)	1420/1422	99.9% (99.5%, 100.0%)
Venipuncture	753/755	99.7% (99.9%, 100.0%)	1421/1423	99.9% (99.5%, 100.0%)
Fingerstick	752/754	99.7% (99.0%, 100.0%)	1421/1422	99.9% (99.6%, 100.0%)
Oral Fluid	739/753	98.1%* (96.9%, 99.0%)	1418/1423	99.6% (99.2%, 99.9%)

Abbreviations: TP = true positive; TN = true negative; CI = confidence interval

^a Sensitivity and specificity are calculated based on the HCV-infected or not HCV-infected samples with valid OraQuick® Rapid HCV Antibody Test result.

^b The two-sided 95% exact CI of sensitivity is calculated using the exact method (Clopper-Pearson) by PROC FREQ with options BINOMIAL, EXACT, and ALPHA=0.05.

*Of the 12 specimens that were FN in oral fluid alone, only 4 (0.5%) were PCR positive

OraQuick[®] HCV Test- Regulatory Status

- CE approved in December 2009 for use with 5 specimen types
- Approved for sale in US for use with fingerstick or venous blood
- Product launched worldwide with 18 months dating
- CLIA waiver for use with fingerstick and venous blood recently approved by FDA

OraQuick[®] Rapid HCV Test- Summary

- The OraQuick[®] HCV Rapid Antibody Test appears highly suitable for identification of HCV infection in at-risk individuals
- Sensitivity and specificity are highly comparable to laboratory-based tests
- Analytical sensitivity and clinical performance were virtually identical in trained and untrained users
- Positive predictive value was high even in relatively low prevalence populations
- Performance of the OraQuick[®] HCV Rapid Antibody Test has been verified in independent published studies^{1,2,3}
- Availability of a rapid test may facilitate increase testing for HCV and be an important public health tool in raising awareness⁴
- Increased identification of prevalent infection may require expanded definition of HCV risk⁵

1. Smith BD et al. (2011) JID 204: 825-831

2. Smith BD et al. (2011) CID 53: 780-786

3. Dobnick A et al (2011) AJPH 101: 2151-2155

4. Agehemo A & Colombo M (2011) Gastroenterol. 140: 1347-49

5. Rein DS et al. (2011) Ann Intern Med In press

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