

Comparative Clinical Evaluation of the cobas TaqScreen MPX Test with the COBAS AmpliScreen HIV-1 v1.5, HCV v.2.0, and HBV Tests Using High Risk Population and Seropositive Specimens

Yosh Ohhashi, Anuradha Pai, Harkanwal Halait, and Rainer Ziermann

Roche Molecular Systems, Pleasanton, CA

BACKGROUND

The **cobas**® TaqScreen MPX Test is a single-assay, multiplex blood screening test for use with the **cobas** s 201 system. The test is the first to detect nucleic acid from HIV-2 and from HIV-1 Group O, mainly found among individuals in Africa, but recently detected in Europe and the US. Additionally, the real-time PCR-based MPX test also simultaneously detects nucleic acid from HIV-1 Group M, as well as hepatitis C and hepatitis B viruses. This test received US FDA licensure on December 30, 2008. An extensive comparative performance evaluation with the COBAS® AmpliScreen blood screening tests for HIV-1, HCV, and HBV on clinically relevant samples was conducted.

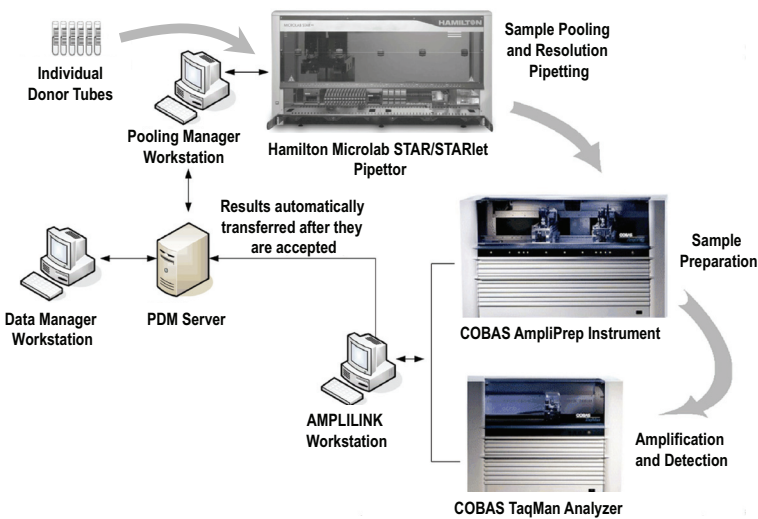
AIMS

The primary studies reported here had the following goals: samples collected from individuals identified at high risk for infection with either HIV, HCV, and/or HBV were tested and analyzed for concordance of the two different assay platforms; specimens confirmed to be seropositive for HIV, HCV, and/or HBV were tested to determine the clinical sensitivity of the TaqScreen MPX Test.

METHODS

Approximately 1,500 plasma specimens from a high risk population and approximately 2,400 seropositive specimens were tested neat and diluted (1:6 for TaqScreen MPX Test and 1:24 for COBAS® AmpliScreen tests) on both platforms. Dilutions were prepared to simulate minipools according to the recommended uses of the different assays. High risk samples were tested at four external trial sites and seropositive samples at six external trial sites with the **cobas**® TaqScreen MPX Test with two lots of reagents. The COBAS® AmpliScreen tests were run at one external site and at Roche Molecular Systems.

Work Flow



Principles of the Procedure

cobas s 201 system is based on 4 major processes:

1. Automated Specimen Pooling and Control Pipetting using the HAMILTON Microlab® STAR IVD Pipettor
2. Automated Specimen Preparation using the COBAS® AmpliPrep Instrument
3. Automated Amplification of Nucleic Acid and Real Time Detection of PCR products using the COBAS® TaqMan Analyzer
4. Automated Data Management using the Pooling and Data Management (PDM) Software

ANALYTICAL SENSITIVITY

LODs for target viruses

Analyte	Standard	Units	Average 95% LOD	95% Lower Limit	95% Upper Limit
HIV-1 Group M	Roche Secondary Standard	IU/mL	49	42.4	58.1
HIV-1 Group O	Roche Primary Standard	Copies/mL	89	56	217
HIV-2	Roche Primary Standard	Copies/mL	59.3	51.9	69.7
HCV	WHO Second International Standard	IU/mL	11	7.0	21.7
HBV	WHO International Standard	IU/mL	3.8	3.3	4.4

ASSAY COMPARISON

High Risk Population

Specimens from a high risk population, which included individuals at risk for infection with HIV, HCV, and/or HBV due to injection drug use, multiple sexual partners, diagnosis of a STD (other than HIV or HBV), recipient of blood, blood component or transplant and dialysis were tested with both the **cobas**® TaqScreen MPX Test and the licensed COBAS® AmpliScreen Tests (COBAS® AmpliScreen HIV-1 Test v1.5, COBAS® AmpliScreen HCV Test v2.0, and COBAS® AmpliScreen HBV Test).

1,256 high risk specimens were tested neat with the **cobas**® TaqScreen MPX Test and neat using the Standard Specimen Processing Procedure with the COBAS® AmpliScreen Tests. 1,284 high risk specimens were tested diluted 1:6 with the **cobas**® TaqScreen MPX Test and diluted 1:24 using the Multiprep Specimen Processing Procedure with the COBAS® AmpliScreen Tests.

Concordance of the cobas® TaqScreen MPX Test with the Combined COBAS® AmpliScreen Test Results in a High Risk Population

Assay	Sample	Total Tested	COBAS® AmpliScreen Test* Positive		COBAS® AmpliScreen Test** Negative		Concordance (%)
			MPX Reactive	MPX Non-Reactive	MPX Reactive	MPX Non-Reactive	
Combined COBAS® AmpliScreen Tests	Neat	1,251****	376	30	34	811	94.9
	Diluted***	1,283°	364	42	54	823	92.5

*Positive with one or more of the licensed COBAS® AmpliScreen Tests

**Negative with all three licensed COBAS® AmpliScreen Tests

***Tested diluted 1:6 with MPX Test and diluted 1:24 with COBAS® AmpliScreen Tests

**** There were 11 HIV-1/HCV/HBV co-infected specimens, 37 HIV-1/HCV co-infected specimens, 20 HCV/HBV co-infected specimens and 7 HIV-1/HBV co-infected specimens in this population

° There were 2 HIV-1/HCV/HBV co-infected specimens, 33 HIV-1/HCV co-infected specimens, 12 HCV/HBV co-infected specimens and 8 HIV-1/HBV co-infected specimens in this population

- 94.9% concordance was shown between the **cobas**® TaqScreen MPX Test and the licensed COBAS® AmpliScreen Tests for the neat HIV-1, HCV and HBV high risk population.
- 92.5% concordance was shown between the **cobas**® TaqScreen MPX Test and the licensed COBAS® AmpliScreen Tests for the diluted HIV-1, HCV and HBV high risk population.

CLINICAL SENSITIVITY

Seropositive Population – HIV-1, HCV and HBV

HIV-1, HCV and HBV confirmed seropositive specimens were purchased from commercial vendors and were tested at six external clinical sites with two lots of reagents.

2,042 specimens were tested neat with the **cobas**® TaqScreen MPX Test and were also tested neat using the Standard Specimen Processing Procedure with the COBAS® AmpliScreen Tests. 2,090 specimens were tested diluted 1:6 with the **cobas**® TaqScreen MPX Test and were also diluted 1:24 and tested using the Multiprep Specimen Processing Procedure with the COBAS® AmpliScreen Tests.

Clinical Sensitivity of the cobas® TaqScreen MPX Test for HIV-1 Group M, HCV and HBV Confirmed Seropositive Specimens – Comparison to the Licensed COBAS® AmpliScreen Test Results

TaqScreen MPX Test	Sample	Total Tested #	MPX Reactive	Clinical Sensitivity (%)	95% CI
Neat	All	1,767**	1,744	98.7	98.1 – 99.2
	HIV-1 Group M	582	569	97.8	96.2 – 98.8
	HCV	818	810	99.0	98.1 – 99.6
Diluted*	All	1,618***	1,584	97.9	97.1 – 98.5
	HIV-1 Group M	461	441	95.7	93.4 – 97.3
	HCV	797	789	99.0	98.0 – 99.6
HBV	All	367	365	99.5	98.0 – 99.9
	HBV	360	354	98.3	96.4 – 99.4

Number of specimens with valid MPX results and positive with one or more COBAS® AmpliScreen Tests

* Tested diluted 1:6 with MPX Test and diluted 1:24 with COBAS® AmpliScreen Tests

** There were 6 HIV-1/HCV/HBV co-infected specimens, 37 HIV-1/HCV co-infected specimens, 116 HCV/HBV co-infected specimens and 106 HIV-1/HBV co-infected specimens in this population

*** There were 6 HIV-1/HCV/HBV co-infected specimens, 9 HIV-1/HCV co-infected specimens, 101 HCV/HBV co-infected specimens and 66 HIV-1/HBV co-infected specimens in this population

CLINICAL SENSITIVITY

HIV-1 Group O

	Total	MPX Reactive	MPX Non-reactive	Sensitivity	95% C.I.	
HIV-1 Group O (Neat)	5	4*	0	100.0%	82.4%	100.0%
HIV-1 Group O (1:6 Diluted)	22	19**	3***	100.0%	82.4%	100.0%

* One of the 5 specimens was invalid on initial testing with insufficient volume for a repeat test

** There was 1 HIV-1 Group O/HIV-1 Group M co-infected specimen (as shown by positive HIV-1 Group M serology and sequence analysis), 1 HIV-1 Group O/HCV co-infected specimen (as shown by positive results with the COBAS® AmpliScreen HCV Test, v2.0), and 1 HIV-1 Group O/HBV co-infected specimen (as shown by positive results with the COBAS® AmpliScreen HBV Test)

*** All 3 non-reactive specimens had undetectable HIV-1 viral load (<60 copies/mL) using the Abbott Real Time HIV-1 Test (Research Use Only) and were excluded from the sensitivity analysis

HIV-2

	Total	Alternate NAT Positive	MPX Reactive	MPX Non-reactive	Sensitivity	95% C.I.	
HIV-2 (Neat)	200	43**	43	0	100.0%	91.8%	100.0%
HIV-2 (1:6 Diluted)	200	43*	40	3	93.0%*	80.9%	98.5%

* HIV-2 NAT RNA quantification test (Research Use Only) developed by Dr. Florence Damond (Hopital Bichat Claude Bernard, Paris, France) and was run on neat specimens only

** One HIV-2 specimen had a viral load of 117 copies/mL and was reactive for 5 out of 8 replicates when tested neat with the **cobas**® TaqScreen MPX Test

GENOTYPE INCLUSIVITY

The performance of the **cobas**® TaqScreen MPX Test was determined on the subtypes of HIV-1 Group M, HIV-1 Group O, HIV-1 Group N and HIV-2, and the genotypes of HCV and HBV (see table). At 3X LOD all replicates of genotype specimens were detected at 100%.

Virus	Genotype
HIV-1 Group M	A, AE, AG, B, C, D, F, G, H, J
HBV	A, B, C, D, E, F, G, H
HCV	1a, 1b, 2, 2a, 2a/c, 2b, 3a, 3a/b, 4, 4a, 4b/4c, 4h, 5, 5a, 6, 6a

CLINICAL SPECIFICITY

99.98% (based on 72,281 blood donations tested)

CONCLUSIONS

These data show very good analytical and clinical performance of the **cobas**® TaqScreen MPX Test. There is also high concordance between this assay and the COBAS® AmpliScreen tests when analyzing specimens obtained from a high risk population and the data demonstrate excellent clinical sensitivity of the **cobas**® TaqScreen MPX Test when testing confirmed seropositive specimens. In conclusion, these studies support the **cobas**® TaqScreen MPX Test's proven performance characteristics as a comprehensive multiplex blood screening assay.