

# cobas b 101 system - performance evaluation

## *Study report from a multicenter evaluation of the new cobas b 101 system for the measurement of HbA1c and lipid panel*

### Introduction

The new **cobas b 101** system provides a point-of-care system for the measurement of HbA1c and lipid panel (total cholesterol (TC), triglycerides (TG), high density lipoprotein cholesterol (HDL), and calculated values for low density lipoprotein cholesterol (LDL), non-HDL, and a TC/HDL ratio). The main objective of the performance evaluation was to confirm the analytical performance of the system in the hands of healthcare professionals in a point-of-care environment.

### Method overview

The evaluation was carried out at two ISO-certified clinical laboratory sites: Barcelona, Spain and Zurich, Switzerland. The HbA1c evaluation was performed from March to August 2012, and the lipid panel from June to December, 2012. In this evaluation, the **cobas b 101** system was evaluated using both the HbA1c disc and the lipid panel disc for lot-to-lot reproducibility, precision according to CLSI EP5-A2 and method comparison. The **cobas c 501** as a module of **cobas**<sup>®</sup> 6000 analyzer series served as a reference system for the method comparison. Measurements were performed on the **cobas b 101** system by healthcare professionals and on the **cobas c 501** module by professional laboratory technicians. **Sample:** The measurements were performed with various blood samples: for HbA1c, capillary whole blood, venous EDTA whole blood and Li-heparin whole blood were used; for the lipid panel, capillary whole blood, venous EDTA whole blood and EDTA plasma were used. Samples were collected prospectively, and informed consent was obtained from all patients enrolled in the study. In total, 135 patients (71 male, 64 female) were recruited with a

HbA1c range from 4.1% to 13.6% HbA1c. 160 patients (84 male, 76 female) were recruited with lipid panel ranges: for TC from 1.9 – 12.63 mmol/L, for TG from 0.52 – 6.7 mmol/L and for HDL from 0.47 – 2.44 mmol/L. **Quantitative assessment.** All the data were analyzed using the WinCAEv tool. Statistical analysis of lot-to-lot reproducibility and method comparison data were evaluated using Passing-Bablok regression analysis. Precision experiments were analyzed by calculating the standard deviation (SD) and coefficient of variation (CV) between measurements. **Qualitative assessment.** Practicability and usability were qualitatively assessed by each site during the evaluation period.

### Key conclusions

All measurements evaluated with both the HbA1c disc and the lipid panel disc on the **cobas b 101** system met the pre-defined acceptance criteria for lot-to-lot reproducibility, precision and method comparison to the reference system (see Performance Evaluation Results below). The acceptance criteria for HbA1c were defined according to the National Glycohemoglobin Standardization Program (NGSP) guidelines as written prior to September 2012, as per the dates when the evaluation was carried out. Additional acceptance criteria were defined according to the Clinical and Laboratory Standards Institute (CLSI) guidelines and the National Cholesterol Education Program (NCEP) guidelines.

All sites confirmed the usability and practicability of the **cobas b 101** system and rated the system as convenient for use in a point-of-care environment.



## Evaluation results

### cobas b 101 and HbA1c disc:

#### Lot-to-lot reproducibility

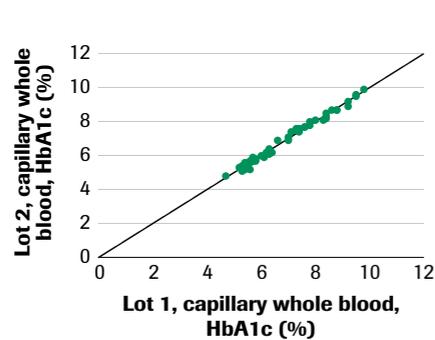
Guidelines from Roche internal development were used to define the acceptance criteria for lot-to-lot reproducibility.

For the concentration range of 4% to 9% HbA1c, a maximum 95% confidence interval (CI) of 0.5% HbA1c was considered acceptable.

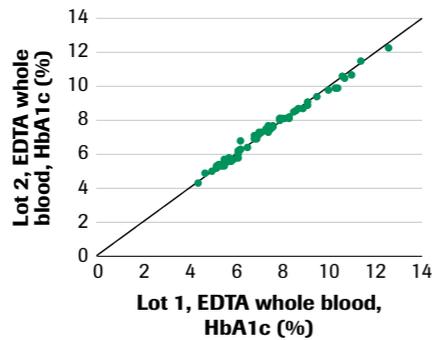
Sample type	N	Mean deviation	Lower 95% CI (%)	Upper 95% CI (%)	Acceptance criterion (%)
Capillary WB	60	0.01	-0.27	0.30	0.50
EDTA WB	70	0.00	-0.36	0.36	0.50
Li-heparin WB	41	-0.02	-0.30	0.26	0.50

Table 1: Lot-to-lot comparison of HbA1c disc. Measurements were made on the cobas b 101 system at the site in Barcelona. For analysis of all sample types, results obtained with Lot 1 were used as the reference values and results from Lot 2 as the comparator values. "WB" is whole blood.

(a)  $y = 1.0x + 0.0$ ;  $r = 0.9944$ ;  $N = 60$



(b)  $y = 1.0x + 0.0$ ;  $r = 0.9956$ ;  $N = 70$



(c)  $y = 1.0x + 0.0$ ;  $r = 0.9946$ ;  $N = 41$

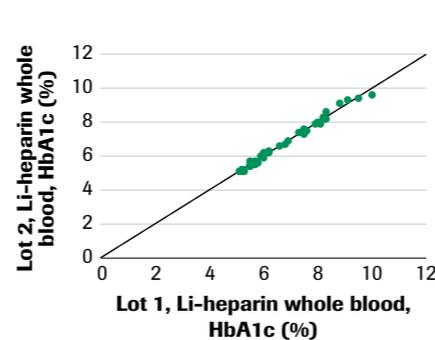


Figure 1 a, b, c: Linear regression analysis of lot-to-lot comparison of HbA1c disc. Passing-Bablok regression analysis was performed for comparison of Lot 1 and Lot 2 with each sample type: capillary whole blood (a), EDTA whole blood (b), and Li-heparin whole blood (c).

All lot-to-lot measurements fall within the specified criteria of a 95% CI of 0.5% for the concentration range 4% to 9% HbA1c. For this reason, the two lots can be considered equivalent and only data from one lot will be shown for the precision and method comparison results below.

## Precision

Intermediate precision and repeatability of the cobas b 101 system were measured according to CLSI EP5-A2 guidelines using four patient sample pools (A, B, C and D) with HbA1c in four concentrations: below medical decision level (5%), at medical decision level (6.5%), above medical decision level (8%), and significantly above medical decision level (12%). In addition, cobas b 101 system controls covering two concentration ranges were used to assess the precision. Control level 1 contains the concentration range 4.3% to 6.5% HbA1c, and control level 2 contains the concentration range 7.4% to 11.2% HbA1c. Acceptance criteria were specified according to the CLSI guidelines for two ranges of HbA1c: for HbA1c  $\leq 5.5\%$ , the SD should be used to assess precision, and an SD of  $\leq 0.22\%$  is specified as acceptable; for HbA1c  $> 5.5\%$ , the CV should be used to assess precision, and a CV of  $\leq 4\%$  is specified as acceptable.

Specimen	Mean % HbA1c	Intermediate SD*	Intermediate CV* (%)	Repeatability SD*	Repeatability CV* (%)
Sample A	5.2	0.141	-	0.120	-
Sample B	6.2	-	2.4	-	2.0
Sample C	8.1	-	2.4	-	1.5
Sample D	13.0	-	1.4	-	1.1
Control level 1	5.6	-	1.9	-	1.7
Control level 2	9.9	-	2.0	-	1.3

\*according to the CLSI guidelines acceptance criteria, either SD or CV is shown.

Table 2: HbA1c disc precision. Measurements were performed on the cobas b 101 system over 21 days at the site in Barcelona by using EDTA whole blood. A total of 84 measurements were made.

Table 2 demonstrates that the precision measurements for all control samples are within the SD and CV ranges defined in the acceptance criteria.

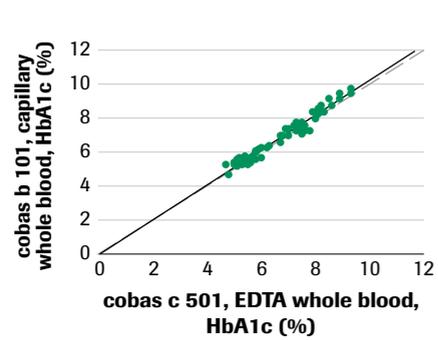
## Method comparison

The performance of the cobas b 101 system with the HbA1c test was compared to the cobas c 501 module with the Tina-quant HbA1c Gen. 3 reagent, which is a certified method for HbA1c measurement. As a control, a reference set of eight IFCC (International Federation of Clinical Chemistry) standards was measured before and after the method comparison experiments. The statistical analysis of the correlation results were performed according to NGSP guidelines by calculating the mean deviation and the  $\pm 2$  SD intervals (95% CI). The acceptance criteria based on these guidelines specify a 95% CI of less than 0.75% HbA1c in the concentration range 4% to 10% HbA1c. In addition, Passing-Bablok linear regression analysis was performed yielding the slope, intercept, and Pearson's r values for each sample type (Table 3, Figure 2a, b, c).

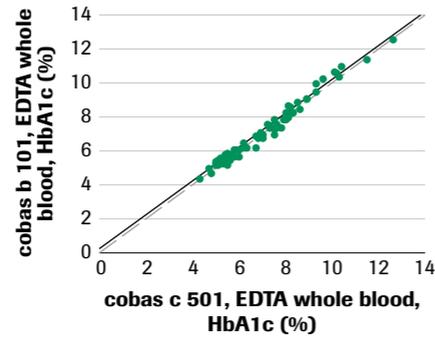
cobas b 101 sample type	N	Mean deviation	Min (%)	Max (%)	Lower 95% CI	Upper 95% CI	Acceptance criterion	Slope	Intercept	Pearson's r
capillary WB	60	0.18	4.7	9.3	-0.34	0.70	0.75	1.03	-0.08	0.9818
EDTA WB	70	0.12	4.3	12.6	-0.26	0.50	0.75	1.00	0.10	0.9900
Li-heparin WB	40	0.09	4.7	9.3	-0.35	0.52	0.75	1.00	0.10	0.9867

Table 3: Method comparison with HbA1c disc. Measurements made on the cobas b 101 system using the HbA1c disc were compared with measurements made on the cobas c 501 module (reference system) at the site in Barcelona. For all cobas c 501 measurements, the sample type used was EDTA whole blood. "WB" is whole blood.

(a) — Identity ( $x = y$ ); — Regression;  
 $y = 1.034x - 0.081$ ;  $r = 0.9818$ ;  $N = 60$



(b) — Identity ( $x = y$ ); — Regression;  
 $y = 1.0x + 0.1$ ;  $r = 0.9900$ ;  $N = 70$



(c) — Identity ( $x = y$ ); — Regression;  
 $y = 1.0x + 0.1$ ;  $r = 0.9867$ ;  $N = 40$

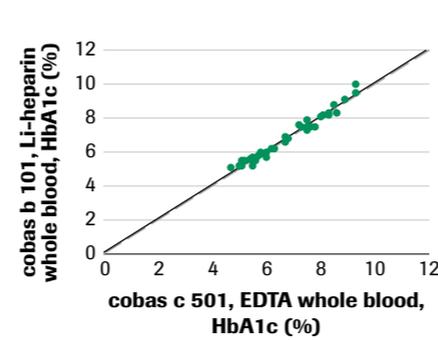


Figure 2 a, b, c: Linear regression analysis of method comparison with HbA1c disc. Passing-Bablok regression analysis was performed for comparison of the cobas b 101 system against the cobas c 501 module as reference with each sample type: capillary whole blood (a), EDTA whole blood (b) and Li-heparin whole blood (c). Only EDTA whole blood was used in the cobas c 501 module for all comparisons.

The acceptance criteria based on pre-September 2012 NGSP guidelines specify a 95% CI of less than 0.75% HbA1c in the concentration range 4% to 10% HbA1c. Table 3 and Figures 2a, b and c demonstrate that the method comparison 95% CI values for the **cobas b 101** system compared to the reference **cobas c 501** module fully satisfy these criteria.

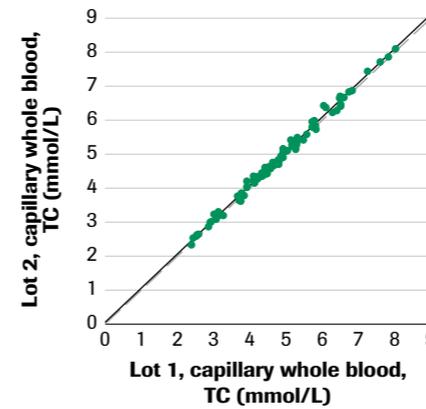
#### cobas b 101 and lipid panel disc: Lot-to-lot reproducibility

A comparison between two disc lots (Lot 1 and Lot 2) was performed for the three lipid parameters: total cholesterol (TC), triglycerides (TG), and high density lipoprotein cholesterol (HDL). Samples used for the comparison were capillary whole blood, EDTA whole blood and EDTA plasma. For each parameter, the acceptable mean bias was defined according to Roche internal development guidelines as follows: TC,  $\leq 3\%$ ; TG,  $\leq 5\%$ ; HDL,  $\leq 5\%$ . The bias was also calculated at two medically relevant decision values, referred to in Table 4 as “Bias 1” and “Bias 2”, for each parameter as follows (TC: 5.18 mmol/L and 6.19 mmol/L; TG: 1.7 mmol/L and 2.25 mmol/L; HDL: 1.04 mmol/L and 1.55 mmol/L).

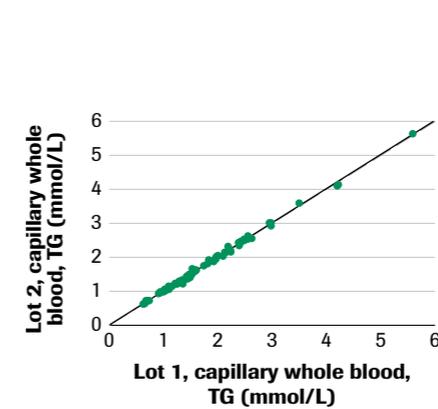
Sample type	Test	N	Min (mmol/L)	Max (mmol/L)	Slope	Intercept	Pearson's r	Mean Bias %	Bias 1 %	Bias 2 %	CV %
Capillary WB	TC	87	2.38	8.02	1.01	0.00	0.9970	0.61	0.7	0.7	1.57
	TG	69	0.61	5.58	1.01	0.01	0.9984	1.07	1.1	0.9	3.17
	HDL	81	0.46	2.38	1.05	-0.05	0.9952	1.24	0.5	1.9	2.78
EDTA WB	TC	85	2.38	7.61	1.02	-0.06	0.9970	0.53	0.9	1.1	1.57
	TG	84	0.61	5.43	1.00	0.01	0.9995	0.60	0.6	0.4	3.17
	HDL	79	0.47	2.44	1.07	-0.07	0.9958	1.39	0.6	2.8	2.78
EDTA Plasma	TC	93	1.92	10.81	1.01	-0.05	0.9988	-0.10	-0.1	0.1	1.67
	TG	91	0.54	5.77	1.00	0.00	0.9996	0.20	0.0	0.0	1.19
	HDL	82	0.47	2.39	1.06	-0.06	0.9973	0.90	0.6	2.5	2.57

Table 4: Lot-to-lot comparison of lipid panel disc. Measurements were made on the cobas b 101 system at the site in Zurich. For analysis of all sample types, results obtained with Lot 1 were used as the reference values and results from Lot 2 as the comparator values. Results from Passing-Bablok regression analysis are reported (slope, intercept, Pearson's r). “WB” is whole blood.

(a) — Identity ( $x = y$ ); — Regression;  
 $y = 1.007x + 0.001$ ;  $r = 0.9970$ ;  $N = 87$



(b) — Identity ( $x = y$ ); — Regression;  
 $y = 1.005x + 0.012$ ;  $r = 0.9984$ ;  $N = 69$



(c) — Identity ( $x = y$ ); — Regression;  
 $y = 1.048x - 0.045$ ;  $r = 0.9952$ ;  $N = 81$

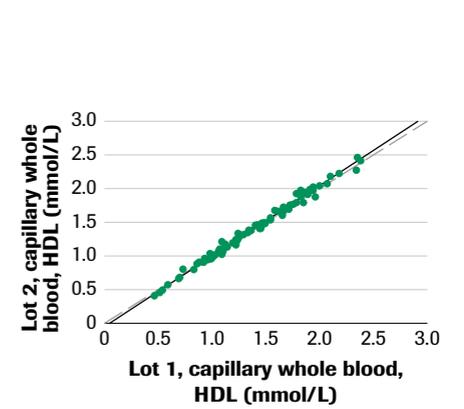


Figure 3 a, b, c: Linear regression analysis of lot-to-lot comparison of lipid panel disc. Passing-Bablok regression analysis was performed for comparison of Lot 1 and Lot 2 with capillary whole blood for each lipid parameter: TC(a), TG (b), and HDL (c).

In Figure 3a, b and c, regression graphs are shown for the capillary blood samples only. Refer to Table 4 for results from EDTA whole blood and EDTA plasma (graphs available upon request). All mean biases for the lot-to-lot measurements fall within the specified criteria for each parameter: TC,  $\leq 3\%$ ; TG,  $\leq 5\%$ ; HDL,  $\leq 5\%$ . For this reason, the two lots can be considered equivalent and only data from one lot will be shown for the precision and method comparison results below.

### Precision

Intermediate precision and repeatability of the **cobas b 101** system were evaluated according to CLSI EP5-A2 guidelines using two control samples covering both normal and pathological concentration ranges for all three lipid parameters. Acceptance criteria were specified according to the CLSI guidelines for two ranges of each parameter. For TC with a concentration of  $\leq 3.1$  mmol/L, the criteria is an SD  $\leq 0.093$  mmol/L; for concentration  $> 3.1$  mmol/L, the criteria is CV  $\leq 3\%$ . For TG with a concentration of  $\leq 1.37$  mmol/L, the criteria is an SD  $\leq 0.069$  mmol/L; for concentration  $> 1.37$  mmol/L, the criteria is CV  $\leq 5\%$ . For HDL with a concentration of  $\leq 1.09$  mmol/L, the criteria is an SD  $\leq 0.044$  mmol/L; for concentration  $> 1.09$  mmol/L, the criteria is CV  $\leq 4\%$ .

Sample	Test	Min (mmol/L)	Max (mmol/L)	Mean (mmol/L)	Intermediate precision SD*	Intermediate precision CV* (%)	Repeatability SD*	Repeatability CV* (%)
Control Level 1	TC	3.59	3.96	3.82	-	1.6	-	1.4
	TG	1.07	1.15	1.11	0.014	-	0.014	-
	HDL	0.99	1.16	1.08	0.035	-	0.034	-
Control Level 2	TC	6.69	7.23	7.03	-	1.8	-	1.8
	TG	4.40	4.57	4.49	-	0.8	-	0.7
	HDL	1.64	1.87	1.77	-	2.5	-	2.2

\*according to the CLSI guidelines acceptance criteria, either SD or CV is shown.

Table 5: Lipid panel disc precision. Measurements were performed on the **cobas b 101** system over 21 days at the Zurich site using standard control samples with two concentration ranges. A total of 84 measurements were made. All units are in mmol/L, unless otherwise indicated.

Table 5 demonstrates that the intermediate precision and repeatability measurements for both of the control sample levels fall within the SD or CV ranges defined, satisfying the acceptance criteria.

### Method comparison

The performance of the **cobas b 101** system with the lipid panel test was compared to the **cobas c 501** module for TC, TG, and HDL measurement. As a control, measurements were performed with NIST (National Institute of Standards and Technology) standards (two different concentration levels for TC and TG, no material for HDL was available) before and after the method comparison experiments. Both prospective and residual patient samples were used in the experiments. The acceptance criteria were defined according to the NCEP and CDC (Cholesterol Disease Control) guidelines and are summarized in Table 6. Statistical analysis of the correlation results was performed according to the NCEP guidelines including calculation of the mean deviation over all measurements, the bias at two medically relevant decision values (TC: 5.18 mmol/L and 6.19 mmol/L; TG: 1.7 mmol/L and 2.25 mmol/L; HDL: 1.04 mmol/L and 1.55 mmol/L), and the total error (TE). Calculation of the TE was performed as follows: TE (%) = Mean Bias (%) + 1.96 x CV (%). In addition, Passing-Bablok regression analysis was performed yielding the slope, intercept, and Pearson's r values for each sample type (Table 7, Figure 4a, b, c).

Parameter/Test	Mean Bias	Bias 1	Bias 2	TE
TC	$\leq 3\%$	$\leq 3\%$	$\leq 3\%$	$< 8.9\%$
TG	$\leq 5\%$	$\leq 5\%$	$\leq 5\%$	$< 15\%$
HDL	$\leq 5\%$	$\leq 5\%$	$\leq 5\%$	$< 13\%$

Table 6: Summary of acceptance criteria for method comparison of lipid panel disc.

cobas b 101 sample type	Test	N	Min (mmol/L)	Max (mmol/L)	Slope	Intercept	Pearson's r	Mean Bias %	Bias 1 %	Bias 2 %	CV %	TE
Capillary WB	TC	68	2.88	7.72	1.03	-0.18	0.9906	-0.54	-0.5	0.1	1.66	2.71
	TG	61	0.53	4.57	1.01	0.02	0.9909	3.88	2.5	2.2	1.39	6.60
	HDL	67	0.78	2.70	0.93	0.12	0.9748	2.06	4.4	0.7	2.30	6.57
EDTA WB	TC	69	2.88	7.72	1.00	-0.10	0.9930	-1.94	-1.9	-1.6	1.55	1.10
	TG	67	0.52	4.57	1.00	0.00	0.9937	0.13	0.0	0.0	1.38	2.83
	HDL	68	0.78	2.42	0.92	0.10	0.9806	-0.15	1.6	-1.5	2.08	3.93
EDTA Plasma	TC	100	1.90	12.63	1.00	-0.11	0.9942	-2.53	-2.1	-1.8	1.65	0.70
	TG	89	0.52	6.77	0.99	0.01	0.9939	-0.17	-0.6	-0.7	1.28	2.34
	HDL	85	0.49	2.42	0.98	0.01	0.9817	-0.50	-0.4	-0.8	2.17	3.75

Table 7: Method comparison with lipid panel disc. Measurements made on the **cobas b 101** system using the lipid panel disc were compared with the measurements made on the **cobas c 501** module (reference system) at the site in Barcelona. For all measurements on the **cobas c 501**, the sample type was Li-heparin plasma. "WB" is whole blood.

(a) — Identity ( $x = y$ ); — Regression;  $y = 1.029x - 0.175$ ;  $r = 0.9906$ ;  $N = 68$       (b) — Identity ( $x = y$ ); — Regression;  $y = 1.014x + 0.018$ ;  $r = 0.9909$ ;  $N = 61$       (c) — Identity ( $x = y$ ); — Regression;  $y = 0.933x + 0.115$ ;  $r = 0.9748$ ;  $N = 67$

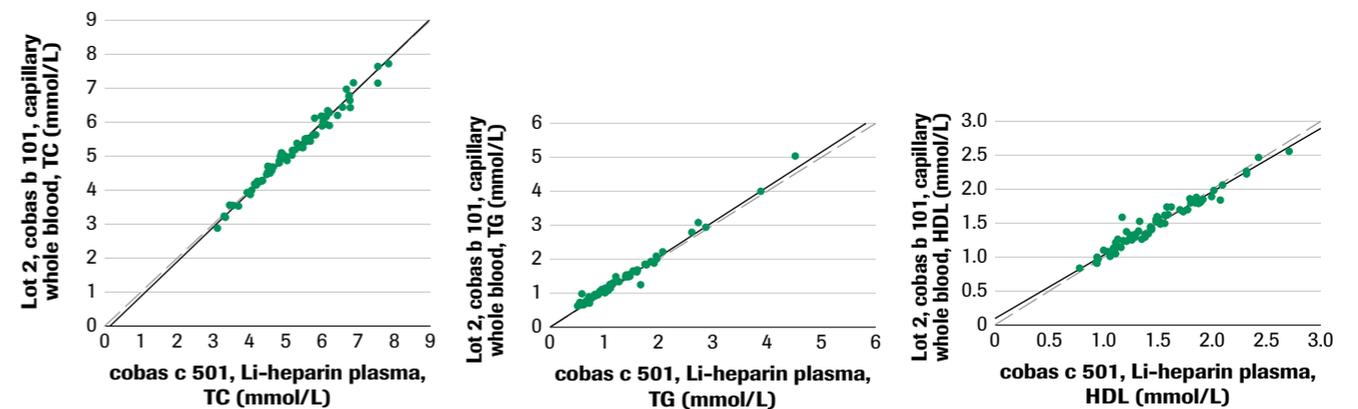


Figure 4 a, b, c: Linear regression analysis of method comparison with lipid panel disc. Passing-Bablok regression analysis was performed for comparison of the **cobas b 101** system versus the **cobas c 501** module as reference with capillary whole blood for the three lipid parameters: TC (a), TG (b) and HDL (c). Li-heparin plasma was used on the **cobas c 501** module for all comparisons.

Table 7 demonstrates that the method comparison mean bias, the bias at the two medically relevant decision values and the total error satisfy the acceptance criteria determined according to the NCEP and CDC guidelines as specified in Table 6.