APPLICATION REPORT

Interference Study
Version 1

cobas u 601 Urine Analyzer
cobas u Pack

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Analytical Performance Characteristics cobas u601 Urine Analyzer: Interference Study

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Interference Study **cobas u** Pack

Introduction:

Interference Studies for **cobas u** Pack on the **cobas u** 601 urine analyzer were performed to assess the effect of 34 therapeutic drugs and endogenous substances on the results obtained on **cobas u** 601 urine analyzer. For this study three cassette lots were measured on one **cobas u** 601 instrument.

Protocol:

Each analyte was tested in two concentrations: negative/normal range (a1) and the first positive range (a2).

The first positive range samples were prepared by spiking a pooled analyte negative urine (0-native urine) from apparent healthy donors without medication with the following substances: Blood Standard (ERY), Pathological Leucocyte positive urine (LEU), Sodium-Nitrite for Nitrite (NIT), Human Serum Albumin (PRO), Acetic Acid-Li-salt (KET), Glucose Monohydrate (GLU), Urobilinogen (UBG) and unconjugated Bilirubin (BIL).

The concentrations for the first positive range are listed below:

ERY	10 Ery/µL
LEU	25 Leu/µL
NIT	0.1 mg/dL
PRO	25 mg/dL
GLU	50 mg/dL
KET	5 mg/dL
UBG	1 mg/dL
BIL	1.6 mg/dL

Then each pharmaceutical compound /endogenous substance was spiked in two concentrations (c1, c2) into the samples a1 and a2. The potentially interfering substances were evaluated in the concentrations presented below:

Therapeutic drug	**Interferent c1: at least 5-fold maximal daily dosage [mg/L]**	**Interferent c2: Maximal daily dosage under medication [mg/L]**
Acetaminophen	3000	500
N-Acetyl-Cysteine	200	100
Ascorbic acid	4000	400
Cefoxitin	12000	2000
Gentamycin Sulfate	400	80
Ibuprofen	2500	500
Levodopa	1250	250
Methyldopa	2000	200
Ofloxacin	900	100
Phenazopyridine	300	50
Salicyl uric acid	6000	100
Tetracycline	500	100
Amoxicillin	10000	2000
Cetirizine	66.6	13.3
Cotrimoxazol	6000	1200
Lisinopril	133.3	26.6
Levothyroxine	1.0	0.2
Amlodipin Besylat	33.3	6.6
Hydrochlorothiazide	333	66.6
Furosemide	3333	666
Hydroxychloroquine	1333	266
Cyclosporine A	80	16

Endogenous substances	**Interferent c1: High pathological value [mg/L]**	**Interferent c2: Intermediate value (4-40% of c1) [mg/L]**
Hemoglobin	750	300
Ammonium	25000	5000
Creatinine	15000	3000
Calcium	3000	600
human IgG	5000	1000
Glucose	50000	10000
Nitrite	110	2
ß-3-Hydroxybutyrate	4500	150
Urea	200000	40000
Uric acid	1550	550
Urobilinogen	3000	120
pH: 4.5; 5.5; 6.5; 7.5; 8.5; 9.0		

The table below clarifies the prepared sample pools/solutions:

Sample pool/solution	**Description**
Analyte a1	Urine pool: all urine parameters are in the normal or negative range.
Analyte a2	Urine pool: all parameters are in the first positive range
Interferent c1	Solution with high drug concentration (X times of the maximum daily dosage, minimum 5 times) or high pathological concentration of endogenous substance
Interferent c2	Solution with a medical relevant drug concentration (single maximum daily dosage) or intermediate concentration of endogenous substance

Initially, each parameter was tested in a 10-fold determination in the combinations listed in the following table:

Test solutions:	**Description**
Analyte a1	Normal/negative urine
Analyte a2	First positive range urine
Analyte a1 + Interferent c1	Analyte in normal/negative range with high drug concentration or high pathological endogenous substance concentration
Analyte a1 + Interferent c2	Analyte in normal/negative range with low drug concentration or intermediate endogenous substance concentration
Analyte a2 + Interferent c1	Analyte in first positive range with high drug concentration or high pathological endogenous substance concentration
Analyte a2 + Interferent c2	Analyte in first positive range with low drug concentration or intermediate endogenous substance concentration

In the case of interference at c1 and/or c2, further interferent concentrations were tested to evaluate the maximum interferent concentration which still shows no influence on the measurement results. These additional sample concentrations are defined above their respective tables and are labeled as c3 through c8 depending on the number of concentrations tested. The results are calculated as % agreement rate to the interferent free samples (a1 or a2).

Acceptance Criteria:
There is no interference caused by the drug or endogenous interferent at the spiked concentration if 90% of the results (9 of 10 replicates) are found in the correct range of the range table for the tested analyte concentration.

Conclusion:
The tables below summarize the results of the Interference Studies performed on the **cobas u** 601 urine analyzer using the **cobas u** Pack.
The results obtained for the interference study are presented in the package insert.

Sections 1 through 3 below contain the results of the Interference studies performed on the **cobas u** 601 urine analyzer.

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Section 1. Interference Study cobas u Pack: Summary of Results

The following substances showed no interference when tested at interferent concentrations c1 and c2:

Acetaminophen	Amlodipin Besylat	Cetirizine
Cefoxitin	Hydrochlorothiazide	Lisinopril
Gentamycin Sulfate	Cyclosporine A	ß-3-Hydroxybutyrat
Ofloxacin	Human IgG	Uric acid
Tetracycline	Glucose	pH
Levothyroxine	Amoxicillin	

The following table, which is included in the cobas u pack method sheet, lists the therapeutic drugs which produced significant interference:

Parameter	**Therapeutic drug**	**No interference up to**	**Effect above stated conc.**
LEU	Cotrimoxazol	500 mg/L	elevated positive results
	Furosemide	1000 mg/L	elevated positive results
	Salicyl Uric Acid	3000 mg/L	false negative results
NIT	Ascorbic Acid	1500 mg/L	false negative results
PRO	Cotrimoxazol	1200 mg/L	false positive results
	Hydrochloroquine	600 mg/L	false positive results
	Phenazopyridine	200 mg/L	false positive results
GLU	Ascorbic Acid	400 mg/ L	false normal results
KET	N-Acetylcysteine	30 mg/L	false positive results and elevated positive results
	Levodopa	250 mg/L	elevated positive results
	Methyldopa	700 mg/L	elevated positive results
UBG	Phenazopyridine	200 mg/L	false positive results and elevated positive results
BIL	Cotrimoxazol	5000 mg/L	false negative results
	Phenazopyridine	100 mg/L	false positive results and elevated positive results
ERY	Ascorbic Acid	700 mg/L	false negative results
	Cotrimoxazol	3000 mg/L	false negative results
	Furosemide	1500 mg/L	false negative results
	Hydrochloroquine	200 mg/L	false negative results
	Ibuprofen	800 mg/L	false negative results

The following table, which is included in the cobas u pack method sheet, lists the endogenous substances which produced significant interference:

Parameter	**Endogenous substance**	**No interference up to**	**Effect above stated conc.**
LEU	Calcium	2200 mg/L	elevated positive results
	Urobilinogen	150mg/L	false positive results and elevated positive results
NIT	Hemoglobin	259 mg/L	false positive results
	Urobilinogen	120 mg/L	false positive results
PRO	Hemoglobin	false positive and false elevated results due to unspecific protein detection may occur	
	Ammonium	5000 mg/L	false negative results
	Creatinine	7500 mg/L	false positive results and elevated positive results
	Urea	120000 mg/L	false positive results and elevated positive results
	Urobilinogen	1000 mg/L	false positive results
GLU	Ammonium	15000 mg/L	false normal results
	Urea	120000 mg/L	false normal results
	Urobilinogen	2500 mg/L	false normal results
KET	Creatinine	3000 mg/L	elevated positive results
	Hemoglobin	259 mg/L	elevated positive results
	Urobilinogen	1500 mg/L	false negative results
UBG	Nitrite	10 mg/L	false normal results
BIL	Nitrite	20 mg/L	false negative results
ERY	Nitrite	10 mg/L	false negative results
	Urobilinogen	120 mg/L	false positive results

Section 2. Interference Study cobas u Pack: Detailed Results Drug Testing

Table 2.1 Results Acetaminophen (c1 = 3000 mg/L; c2 = 500 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

No interference for all analytes up to 3000 mg/L Acetaminophen

Table 2.2 Results N-Acetyl cysteine (c1 = 200 mg/L; c2 = 100 mg/L; c3 = 30 mg/L; c4= 20 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
KET neg	KET 5 mg/dL	100	100	100	100

KET: no interference up to 30 mg/L N-Acetyl cysteine; all other analytes: no interference up to 200 mg/L N-Acetyl cysteine

Interference Study, continued

Table 2.3 Results Ascorbic Acid (c1 = 4000 mg/L ; c2 =400mg/L; c3 = 700 mg/L; c4 = 600 mg/L; c5 = 1500 mg/L; c6 = 1000 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
LEU neg	25 Leu/µL	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	0	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
ERY neg	10 Ery/µL	100	100	100	100
		Analyte a1+ Interferent c5	Analyte a2+ Interferent c5	Analyte a1+ Interferent c6	Analyte a2+ Interferent c6
NIT neg	NIT positive	100	100	100	100

GLU: no interference up to 400 mg/L Ascorbic Acid; ERY: no interference up to 700 mg/L Ascorbic Acid; NIT: no interference up to 1500 mg/L Ascorbic Acid, all other analytes: no interference up to 4000 mg/L Ascorbic Acid

Interference Study, continued

Table 2.4 Results Cefoxitin (c1 = 12000 mg/L; c2 =2000mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	90	100	90
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

No interference for all analytes up to 12000 mg/L Cefoxitin

Table 2.5 Results Gentamycin Sulfate (c1 = 400 mg/L; c2 =80 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	90	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

No interference for all analytes up to 400 mg/L Gentamycin Sulfate

Interference Study, continued

Table 2.6 Results Ibuprofen (c1 =2500 mg/L; c2 =500 mg/L; c4 = 1000 mg/L; c5 = 800 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c4	Analyte a2+ Interferent c4	Analyte a1+ Interferent c5	Analyte a2+ Interferent c5
ERY neg	10 Ery/µL	100	70	100	100

ERY: no interference up to 800 mg/L Ibuprofen; all other analytes: no interference up to 2500 mg/L Ibuprofen

Interference Study, continued

Table 2.7 Results Levodopa (c1 =1250 mg/L; c2 =250 mg/L; c3 =200 mg/L; c4= 150 mg/dL)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	90
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
KET neg	KET 5 mg/dL	100	100	100	100

KET: no interference up to 250 mg/L Levodopa; all other analytes: no interference up to 1250 mg/L Levodopa

Table 2.8 Results Methyldopa (c1 =2000 mg/L; c2 = 200mg/L; c4 = 1000 mg/L; c5 = 700 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	90	100	90
NIT neg	NIT positive	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c4	Analyte a2+ Interferent c4	Analyte a1+ Interferent c5	Analyte a2+ Interferent c5
KET neg	KET 5 mg/dL	80	80	100	90

KET: no interference up to 700 mg/L Methyldopa; all other analytes: no interference up to 2000 mg/L Methyldopa

Table 2.9 Results Ofloxacin (c1 = 900 mg/L; c2 = 100 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

No interference up to 900 mg/L Ofloxacin for all analytes

Interference Study, continued

Table 2.10 Results Phenazopyridin (c1 = 300mg/L; c2 =50 mg/L; c3= 200 mg/L; c4 = 150 mg/L, c5 = 100 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	90
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c4	Analyte a2+ Interferent c4	Analyte a1+ Interferent c5	Analyte a2+ Interferent c5
BIL neg	BIL 1.6 mg/dL	40	70	100	100

BIL: no interference up to 100 mg/L Phenazopyridine; PRO, UBG: no interference up to 200 mg/L Phenazopyridine; all other analytes: no interference up to 300 mg/L Phenazopyridine

Table 2.11 Results Salicyl uric acid (c1 =6000 mg/L; c2 =100 mg/L; c3 = 3000 mg/L; c4 = 2000 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	90	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
LEU neg	25 Leu/µL	100	100	100	100

LEU: no interference up to 3000 mg/L Salicyl uric acid; all other analytes: no interference up to 6000 mg/L Salicyl uric acid

Table 2.12 Results Tetracycline (c1 = 500 mg/L; c2 =100 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

No interference up to 500mg/L Tetracycline for all analytes

Table 2.13 Results Amoxicillin (c1 =10000 mg/L; c2 =2000 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	90	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

No interference up to 10000 mg/L Amoxicillin for all analytes

Table 2.14 Results Cetirizine (c1 = 66.6 mg/L; c2 = 13.3 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

No interference up to 66.6 mg/L Cetirizine for all analytes

Interference Study, continued

Table 2.15 Results Cotrimoxazol

(c1 = 6000 mg/L ; c2 = 1200mg/L; c3 = 3000 mg/L; c4 = 2500 mg/L; c5 = 1000 mg/L; c6= 500 mg/L; c7 = 5000mg/L; c8 = 4000 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	20	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
ERY neg	10 Ery/µL	100	100	100	100
Further testing:		Analyte a1+ Interferent c5	Analyte a2+ Interferent c5	Analyte a1+ Interferent c6	Analyte a2+ Interferent c6
LEU neg	25 Leu/µL	100	40	100	100
Further testing:		Analyte a1+ Interferent c7	Analyte a2+ Interferent c7	Analyte a1+ Interferent c8	Analyte a2+ Interferent c8
BIL neg	BIL 1.6 mg/dL	100	100	100	100

PRO: no interference up to 1200 mg/L Cotrimoxazol; ERY: no interference up to 3000 mg/dL Cotrimoxazol; LEU: no interference up to 500 mg/L Cotrimoxazol; BIL: no interference up to 5000 mg/L Cotrimoxazol; all other analytes: no interference up to 6000 mg/L Cotrimoxazol

Interference Study, continued

Table 2.16 Results Lisinopril (c1 = 133.3 mg/L; c2 =26.6 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

No interference for all analytes up to 133.3 mg/L Lisinopril

Table 2.17 Results Levothyroxine (c1 =1.0 mg/L; c2 = 0.2 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

No interference for all analytes up to 1.0 mg/L Levothyroxine

Table 2.18 Results Amlodipine Besylat (c1 = 33.3 mg/L; c2 =6.6 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

No interference for all analytes up to 33.3 mg/L Amlodipine Besylat

Table 2.19 Results Hydrochlorothiazide (c1 =333 mg/L; c2 = 66.6 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

No interference for all analytes up to 333 mg/L Hydrochlorothiazide

Interference Study, continued

Table 2.20 Results Furosemide (c1 = 3333 mg/L; c2 =666 mg/L; c3 = 1500 mg/L; c4 = 1000 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	80	100	100

ERY: no interference up to 1500 mg/L Furosemide; LEU: no interference up to 1000 mg/L Furosemide; all other analytes: no interference up to 3333 mg/l Furosemide

Interference Study, continued

Table 2.21 Results Hydroxychloroquine (c1 =1333 mg/L; c2 = 266 mg/L; c3 = 800 mg/L; c4 = 600 mg/L; c5= 200 mg/L; c6=150 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c5	Analyte a2+ Interferent c5	Analyte a1+ Interferent c6	Analyte a2+ Interferent c6
ERY neg	10 Ery/µL	100	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
PRO neg	PRO 25 mg/dL	60	100	100	100

ERY: no interference up to 200 mg/L Hydroxychloroquine; PRO: no interference up to 600 mg/L Hydroxychloroquine;

all other analytes: no interference up 1333 mg/L Hydroxychloroquine

Interference Study, continued

Table 2.22 Results Cyclosporine A (c1 = 80 mg/L; c2 = 16 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

No interference for all analytes up to 80 mg/L Cyclosporine A

Section 3. Interference Study cobas u Pack: Detailed Results Endogenous Substance Testing

Table 3.1 Results Hemoglobin

(c1 = 750 mg/L =25000 Ery/µL; c2 =300 mg/L =10000 Ery/µL; c3 = 259 mg/L = 8360 Ery/µL; c4 = 104 mg/L =3350 Ery/µL)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
LEU neg	25 Leu/µL	0	80	30	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	0	0	0	0
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	90	100	100

LEU: false positive results due to Leukocytes in the blood standard used for spiking:

c1 = 25000 ERY/µL standard includes app. 61 Leu/µL; c2= 10000 Ery/µL standard includes app. 25 Leu/µL

GLU, UBG, BIL: no interference up to 750 mg/L Hemoglobin; PRO: false positive and false elevated results due to unspecific protein detection (hemoglobin); NIT, KET: no interference up to 259 mg/L Hemoglobin

Interference Study, continued

Table 3.2 Results Ammonium (c1 =25000mg/L ; c2 = 5000mg/L; c3 = 20000 mg/L; c4 = 15000 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	0	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
GLU norm	GLU 50 mg/dL	100	0	100	100

PRO: no interference up to 5000 mg/L Ammonium; GLU: no interference up to 15000 mg/L Ammonium; all other analytes: no interference up to 25000 mg/L Ammonium

Interference Study, continued

Table 3.3 Results Creatinine (c1 =15000 mg/L; c2 = 3000 mg/L; c3 =7500 mg/L; c4 = 5000 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	0	100	90
GLU norm	GLU 50 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
PRO neg	PRO 25 mg/dL	100	100	100	100

KET: no interference up to 3000 mg/L Creatinine; PRO: no interference up to 7500 mg/L Creatinine; all other analytes: no interference up to 15000 mg/L Creatinine

Interference Study, continued

Table 3.4 Results Calcium (c1 = 3000 mg/L; c2 = 600 mg/L, c3 = 2200 mg/L; c4= 1400 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
LEU neg	25 Leu/µL	100	100	100	100

LEU: no interference up to 2200 mg/L Calcium; all other analytes: no interference up to 3000 mg/L Calcium

Table 3.5 Results human IgG (c1 = 5000 mg/L; c2 = 1000 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

All analytes: no interference up to 5000 mg/L human IgG

Interference Study, continued

Table 3.6 Results Glucose (c1 =50000 mg/L; c2 = 10000 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	90	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

All analytes: no interference up to 50000 mg/L Glucose

Interference Study, continued

Table 3.7 Results Nitrite (c1 =110 mg/L; c2 = 2 mg/L; c3 = 10 mg/L; c4 =6 mg/L; c5 = 20 mg/L; c6 = 5 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
LEU neg	25 Leu/µL	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
ERY neg	10 Ery/µL	100	100	100	100
Further testing:		Analyte a1+ Interferent c5	Analyte a2+ Interferent c5	Analyte a1+ Interferent c3	Analyte a2+ Interferent c3
UBG norm	UBG 1 mg/dL	100	0	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

ERY, UBG: no interference up to 10 mg/L Nitrite; BIL: no interference up to 20 mg/L Nitrite; all other analytes: no interference up to 110 mg/L Nitrite

Table 3.8 Results ß-Hydroxybutyrate (c1 = 4500 mg/L; c2 = 150 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	90
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	90
BIL neg	BIL 1.6 mg/dL	100	100	100	100

All analytes: no interference up to 4500 mg/L Hydroxybutyrate

Table 3.9 Results Urea (c1 =200000 mg/L; c2 =40000mg/L; c4 =120000 mg/L; c5 = 80000 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	100	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c4	Analyte a2+ Interferent c4	Analyte a1+ Interferent c5	Analyte a2+ Interferent c5
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100

GLU, PRO: no interference up to 120000 mg/L Urea; all other analytes: no interference up to 200000 mg/L Urea

Interference Study, continued

Table 3.10 Results Uric Acid (c1 =1550 mg/L; c2 = 550 mg/L)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	100	100	100	100
LEU neg	25 Leu/µL	100	90	100	100
NIT neg	NIT positive	100	100	100	100
KET neg	KET 5 mg/dL	100	100	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
PRO neg	PRO 25 mg/dL	100	100	100	100
UBG norm	UBG 1 mg/dL	100	100	100	100
BIL neg	BIL 1.6 mg/dL	100	100	100	100

All analytes: no interference up to 1550 mg/L Uric Acid

Interference Study, continued

Table 3.11 Results Urobilinogen

(c1 =3000 mg/L; c2 =120 mg/L; c3 = 200mg/L; c4 = 150mg/L ; c5 =1000 mg/L ; c6 = 500 mg/L; c7=2500 mg/L; c8 = 1500 mg/L;)

Reference		Agreement to Reference[%]			
Analyte concentration a1	Analyte concentration a2	Analyte a1+ Interferent c1	Analyte a2+ Interferent c1	Analyte a1+ Interferent c2	Analyte a2+ Interferent c2
ERY neg	10 Ery/µL	0	100	100	90
NIT neg	NIT positive	0	100	100	100
Further testing:		Analyte a1+ Interferent c3	Analyte a2+ Interferent c3	Analyte a1+ Interferent c4	Analyte a2+ Interferent c4
LEU neg	25 Leu/µL	100	80	100	100
Further testing:		Analyte a1+ Interferent c7	Analyte a2+ Interferent c7	Analyte a1+ Interferent c8	Analyte a2+ Interferent c8
KET neg	KET 5 mg/dL	100	60	100	100
GLU norm	GLU 50 mg/dL	100	100	100	100
Further testing:		Analyte a1+ Interferent c5	Analyte a2+ Interferent c5	Analyte a1+ Interferent c6	Analyte a2+ Interferent c6
PRO neg	PRO 25 mg/dL	100	100	100	100

ERY, NIT: no interference up to 120 mg/L Urobilinogen; LEU: no interference up to 150mg/L Urobilinogen; KET: no interference up to 1500 mg/L Urobilinogen; GLU: no interference up to 2500 mg/L Urobilinogen; PRO: no interference up to 1000 mg/L Urobilinogen;

Interference Study, continued

Table 3.12 Results pH (4.5, 5.5, 6.5, 7.5, 8.5, 9.0)

Reference	Agreement to Reference[%]					
Analyte concentration a1	Analyte a1+ pH 4.5	Analyte a1+ pH 5.5	Analyte a1+ pH 6.5	Analyte a1+ pH 7.5	Analyte a1+ pH 8.5	Analyte a1+ pH 9.0
ERY neg	100	100	100	100	100	100
LEU neg	100	100	100	100	100	100
NIT neg	100	100	100	100	100	100
KET neg	100	100	100	100	100	100
GLU norm	100	100	100	100	100	100
PRO neg	100	100	100	100	100	100
UBG norm	100	100	100	100	100	100
BIL neg	100	100	100	100	100	100
Reference	Agreement to Reference[%]					
Analyte concentration a2	Analyte a2+ pH 4.5	Analyte a2+ pH 5.5	Analyte a2+ pH 6.5	Analyte a2+ pH 7.5	Analyte a2+ pH 8.5	Analyte a2+ pH 9.0
10 Ery/µL	100	100	100	100	100	100
25 Leu/µL	100	100	100	100	100	100
NIT positive	100	100	100	100	100	100
KET 5 mg/dL	100	100	100	100	100	100
GLU 50 mg/dL	100	100	100	100	100	100
PRO 25 mg/dL	100	100	100	100	100	100
UBG 1 mg/dL	100	100	100	100	100	100
BIL 1.6 mg/dL	100	100	100	100	100	100

All analytes: no pH interference from pH 4.5 up to pH 9.0