510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE

A. 510(k) Number:

k093555

B. Purpose for Submission:

New submission to add the Cobas u 411 Urine Analyzer for use with the Chemstrip 10 UA test strip k896454.

C. Measurand:

Urine pH, leukocytes, nitrite, protein, glucose, ketone, urobilinogen, bilirubin, blood, specific gravity and optional urine color

D. Type of Test:

Qualitative and semi-quantitative measurements based on reflectance photometry

E. Applicant:

Roche Diagnostics Corporation

F. Proprietary and Established Names:

Cobas u 411 Test System

G. Regulatory Information:

Classification Name	Product Code	Device Class	Regulation Number
Urinary glucose (non-quantitative) test system	JIL	II	21 CFR§862.1340
Occult blood test	JIO	II	21 CFR§864.6550
Urinary urobilinogen (non-quantitative) test system	CDM	I	21 CFR§862.1785
Urinary bilirubin and its conjugates (non-quantitative) test system	JJB	I	21 CFR§862.1115
Ketones (non-quantitative test system)	JIN	I	21 CFR§862.1435
Urinary protein or albumin (non-quantitative) test system	JIR	I	21 CFR§862.1645

Nitrite (non-quantitative) test system	JMT	I	21 CFR§862.1510
Leukocyte peroxidase test	LJX	I	21 CFR§864.7675
Urinary pH (non-quantitative) test system	CEN	I	21 CFR§862.1550
Specific Gravity	JRE	I	21 CFR§862.2800
Automated Urinalysis System	KQO	I	21 CFR§862.2900

Panel:

(75) Clinical Chemistry and (81) Hematology

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The cobas u 411 urinalysis analyzer is a semi-automated, bench top analyzer which is designed to read Chemstrip 10 UA (Combur^{10} Test M) test strips for urinalysis for the measurement of bilirubin, blood, glucose, ketones, leukocytes, nitrite, pH, protein, specific gravity, urobilinogen and color (if selected). These measurements are useful in the evaluation of renal, urinary and metabolic disorders. These measurements are useful in the evaluation of renal, urinary and metabolic disorders. Tests performed using the cobas u411 are intended for prescription, in vitro diagnostic use only.

3. Special conditions for use statement(s):

   Prescription use only

4. Special instrument requirements:

   Cobas u 411 urine analyzer

I. Device Description:

The cobas u 411 is a semiautomatic urinalysis system intended for in vitro qualitative or semi-quantitative determination of urine analytes, including specific gravity, (SG), pH, leukocytes, nitrite, protein, glucose, ketones, urobilinogen, bilirubin, erythrocytes, and color (if selected) using the Chemstrip 10 UA test strips (k896454).

The functions of the cobas u 411 analyzer include:

- Sample identification (with optional barcode scanner)
- Controlled incubation period

- Photometric measurements
- Result memory
- Optional formats for data output

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Roche Chemstrip Urine Analyzer

2. Predicate 510(k) number(s):
   k921087

3. Comparison with predicate:

Similarities		
Item	Cobas u411 urinalysis test system (candidate device)	Chemstrip Urine Analyzer (predicate device) k921087
Intended use/Indications for use	A semi-automated analyzer which is designed to read test strips for urinalysis for the measurement of bilirubin, blood, glucose, ketones, leukocytes, nitrite, pH, protein, specific gravity, and urobilinogen. These measurements are useful in the evaluation of renal, urinary and metabolic disorders. The device is for prescription in vitro diagnostic use only.	Same
Analyzer Technology	Reflectance Photometry	Same
Light Source	LEDs	Same
Reagent Strip	Chemstrip 10 UA test strip	Same
Urine application	Test strip dipped into urine sample	Same
Intrinsic color compensation	The test strip area not impregnated with reagents, allows instrumental compensation for the intrinsic color of the urine while testing.	Same
Calibration method	Calibration strips with specific reflectance values for calibration	Same

Differences		
Item	Cobas u 411 urinalysis test system (candidate device)	Chemstrip Urine Analyzer (predicate device) k921087
Measuring Unit	Light Emitting Diodes (LEDs) Wavelength: Orange: 620 nm Green: 555 nm Blue: 470 nm Sensor: 11 wide range photo sensors	Light Emitting Diodes (LEDs) Wavelength: Orange: 620 nm Green: 555 nm Red: 660 nm Reader Head: 2 heads with 3 LEDs each
Storage Medium	USB Stick	Floppy Disks
Strip Detector	Two strip detectors	One strip detector
Urine color parameter	Optional Urine color parameter	None

K. Standard/Guidance Document Referenced (if applicable):

EN ISO 14971 Medical devices-Application of risk management to medical devices (ISO14971:2007)

L. Test Principle:

Several light emitting diodes (LEDs) use a light pipe to transmit light of a defined wavelength onto the surface of all test pads. The light that hits the test pad is reflected with an intensity that is dependent upon the color of the test pads. A photodiode detector positioned directly above the test pad receives the reflected light. The photodiode detector transmits an analog electrical signal to the analog-to digital convertor, which changes the analog signal to a digital value. The computer then converts the digital value into the semiquantitative result.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Repeatability (within run) precision of the cobas u 411 analyzer was evaluated at 3 clinical sites using two commercially available urine controls over various days. The controls, which were comprised of a normal and an elevated analyte sample, were tested in three individual runs. Each run was comprised of 21 replicates. The samples were split into seven aliquots with 3 measurements. In total, there were 48 runs performed and three analyzers were used in the testing.

Example: 3 runs x 21 replicates (7 aliquots/3 measurements per aliquot) x 3 analyzers= 189 replicates.

Commercial Urinalysis Control, Level 1 values confirmed with Cobas u 411

Analyte	Mean	Unit	Results = Mean (%)	Results of ± 1 block of Mean (%)	n
Specific Gravity	1.015	-	98	99	189
pH	6.0	-	94	100	189
Leukocyte Esterase	Negative	Leu/µL	100	100	189
Nitrite	Negative	-	100	100	189
Protein	Negative	mg/dL	100	100	189
Glucose	Normal	mg/dL	100	100	189
Ketone	Negative	mg/dL	100	100	189
Urobilinogen	Normal	mg/dL	100	100	189
Bilirubin	Negative	mg/dL	100	100	189
Blood	Negative	Ery/µL	100	100	189
Color	Pale Yellow	-	97	100	189

Commercial Urinalysis Control, Level 2 values confirmed with Cobas u 411

Analyte	Mean	Unit	Results = Mean (%)	Results of ± 1 block of Mean (%)	n
Specific Gravity	1.010	-	67	99	189
pH	7.0	-	100	100	189
Leukocyte Esterase	500	Leu/µl	100	100	189
Nitrite	Positive	-	100	100	189
Protein	150	mg/dl	97	100	189
Glucose	1000	mg/dl	99	100	189
Ketone	150	mg/dl	100	100	189
Urobilinogen	12	mg/dl	100	100	189
Bilirubin	6	mg/dl	100	100	189
Blood	250	Ery/µl	100	100	189
Color	Brown	-	100	100	189

Precision was determined using two levels of commercially available control material. Day to day precision was evaluated by testing several replicates of each control level per three instruments over multiple days.

Level 1 Normal

Analyte	Mean	Unit	Results = Mean (%)	Results of ± 1 block of Mean (%)	n
Specific Gravity	1.015	-	100	100	99
pH	6.0	-	99	100	99
Leukocyte Esterase	Negative	Leu/µl	100	100	99
Nitrite	Negative	-	100	100	99
Protein	Negative	mg/dl	100	100	99
Glucose	Normal	mg/dl	100	100	99
Ketone	Negative	mg/dl	100	100	99
Urobilinogen	Normal	mg/dl	100	100	99
Bilirubin	Negative	mg/dl	100	100	99
Blood	Negative	Ery/µl	100	100	99
Color	Pale Yellow	-	89	100	99

Level 2 Abnormal

Analyte	Mean	Unit	Results = Mean (%)	Results of ± 1 block of Mean (%)	n
Specific Gravity	1.005	-	55	100	99
pH	7.0	-	100	100	99
Leukocyte Esterase	500	Leu/µl	100	100	99
Nitrite	Positive	-	100	100	99
Protein	150	mg/dl	94	100	99

Glucose	1000	mg/dl	100	100	99
Ketone	150	mg/dl	100	100	99
Urobilinogen	12	mg/dl	100	100	99
Bilirubin	6	mg/dl	100	100	99
Blood	250	Ery/µl	100	100	99
Color	Brown	-	100	100	99

b. Linearity/assay reportable range:

Please see the method comparison section 2.a below and detection limit section 1.d. below.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The sponsor recommends using commercially available control materials for use on the cobas u 411 urine analyzer.

Calibration verification is performed using a Calibration Strip which is included with the analyzer. This is a gray strip which checks the reflectance values for each test. The reflectance values are compared with the previous user calibration values and the values of the internal Calibration Strip. Recommendations for calibration verification are included in the operator's manual.

d. Detection limit:

The sensitivity of the Chemstrip 10UA Urine Test Strip on the cobas u411 was evaluated by spiking negative pooled human urine with the appropriate substance to obtain the desired concentrations. Multiple samples were tested for each concentration. The prepared samples were then assayed on the cobas u 411 analyzer. Sensitivity was defined as the cutoff in which 90% of the contrived pooled measurements were positive.

Parameter	Claim (Package Insert Chemstrip UA)	Point at which sensitivity meets criteria of >90% detection
Erythrocytes	5 - 10 Ery/µl	7 E/µl
Leukocytes	20- 25 Leu/µl	23 L/µl
Protein	8 – 12 mg/dL	8 mg/dl
Glucose	30 – 40 mg/dl	40 mg/dl
Ketones	3 – 6 mg/ dl	4 mg/dl
Nitrite	0.05 – 0.07 mg/dl	0.06 mg/dl
Bilirubin	0.4 – 0.6 mg/dl	0.6 mg/dl
Urobilinogen	1.0 – 1.6 mg/dl	1.2 mg/dl

e. Analytical specificity

A urine pool was prepared using fresh normal/negative urine and urine samples with parameters in the first positive range. Solutions were also prepared using high drug concentrations and prepared with the maximum daily dosage of the medical relevant

drug concentration. Multiple replicates of the urine pool and the drug solutions were measured.

Interfering substances and their effects on the various analytes:

Test	Interfering substances	Impact on Test
Leukocytes	n-Acetyl Cysteine ≥ 1 mg/l, Cefoxitin ≥ 1000 mg/l, Curcumin ≥ 3500 mg/l, Levodopa ≥ 250 mg/l, p-Aminosalicylic Acid ≥ 12740 and Tetracycline ≥ 100 mg/l	False positive
	Gentamicin Sulfate ≥ 80 mg/l, Imipenem ≥ 3000 mg/l, Meropenem ≥ 4000 mg/l, Formaldehyde ≥ 2000 mg/l	False positive
	Captopril ≥ 100 mg/l	False negative
	Elevated glucose >5 g/dL	False negative
	High pH values caused by urinary tract infections and a low specific gravity	False positive
Nitrite	2-mercaptoethanesulphonate sodium (MESNA) ≥ 11400 mg/l	False negative
Protein	Acetaminophen ≥ 500 mg/l, Chloroquine ≥ 380 mg/l, Levodopa ≥ 250 mg/l, Nitrofurantoin ≥ 200 mg/l	False positive
Glucose	Ascorbic Acid ≥75mg/dL	False negative
	Nitrofurantoin ≥ 200 mg/l	False negative
	MESNA ≥ 11400 mg/l	False positive
	Oxidizing cleaning agents ≥ 110 mg/l, Mecetronium Etilsulfate ≥ 40 mg/l	False positive
Ketones	Captropril ≥ 100 mg/l, Curcumin ≥ 3500 mg/l, Imipenem ≥ 3000 mg/l, MESNA ≥ 11400 mg/l or other sulfhydryl containing compounds.	False positive
	Formaldehyde ≥ 2000 mg/l	False positive
Bilirubin	Ascorbic Acid >40 mg/dL	False negative
	Imipenem ≥ 3000 mg/l, Penicillin ≥ 8150 mg/l, p-Aminosalicylic Acid ≥ 12740 mg/l, Hydrochloric Acid ≥ 6660 mg/l	False positive
	MESNA ≥ 11400 mg/l	False negative
	Urobilinogen ≥ 120 mg/l	False positive
	pH >9.0	False positive
Urobilinogen	p-Aminosalicylic Acid ≥ 12740 mg/l, Sulfamethoxazol ≥ 1070 mg/l	False positive
	Formalin concentrations >200 mg/dL	False negative
	Nitrite concentrations >0.6 mg/dL	False negative
	pH >9.0	False positive
Blood	Ascorbic Acid >75 mg/dL	False negative
	Phenazopyridine ≥ 50 mg/l	False positive
	Nitrofurantoin ≥ 200 mg/l, Quinidine ≥ 320 mg/l	False negative
	MESNA ≥ 11400 mg/l	False positive and false negative
	Leukocytes ≥ 500 LEU/µl	False positive
	pH >9.0	False positive

	Specific Gravity <1.005	False positive
	Nitrite >0.6 mg/dL	False negative
	Hydrochloric Acid ≥ 6660 mg/l	False positive
	Formaldehyde ≥ 2000 mg/l	False negative

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Both fresh and spiked samples were used to cover the entire analytical range. Each sample was split into two aliquots.

The clinical study was performed at three different clinical sites. At least two intended users operated the device at each site.

Cobas u411 urinalysis test system with Chemstrip 10 UA Test strip vs. Chemstrip Urine analyzer with Chemstrip 10 UA Test strip:

	Predicate Device					
Erythrocytes (Blood)	**0 Neg**	**10**	**25**	**50**	**150**	**250**
Candidate Device						
0 Neg	207	6				
10	13	99	2			
25		5	93	4		
50			8	71	6	
150				3	83	11
250					1	101
Total	220	110	103	78	90	112
%Agreement (Exactly match)	94	90	90	91	92	90
%Agreement (+/- 1 Color Block)	100	100	100	100	100	100

	Predicate Device			
Leukocytes	**Neg**	**25**	**100**	**500**
Candidate Device				
Neg	187	4		
25	5	101	3	
100		2	69	3
500			2	93
Total	192	107	74	96
%Agreement (Exactly match)	97	94	93	97
%Agreement (+/- 1 Color Block)	100	100	100	100

	Predicate Device	
Nitrite	**Negative**	**Positive**
Candidate Device		
Negative	104	2
Positive	4	80
Total	108	82
%Agreement (Exactly match)	96	98
%Agreement (+/- 1 Color Block)	100	100

	Predicate Device				
Ketone	**0 Neg**	**5**	**15**	**50**	**150**
Candidate Device					
0 Neg	360	2			
5	36	69	2		
15	1	3	80	6	
50			1	81	1
150				3	65
Total	397	74	83	90	66
%Agreement (Exactly match)	91	93	96	90	99
%Agreement (+/- 1 Color Block)	100	100	100	100	100

	Predicate Device				
Glucose	**Norm**	**50**	**100**	**250**	**1000**
Candidate Device					
Norm	121	2			
50	3	68	8		
100		2	89	4	
250			2	73	4
1000			1		102
Total	124	72	100	77	106
%Agreement (Exactly match)	98	94	89	95	96
%Agreement (+/- 1 Color Block)	100	100	99	100	100

	Predicate Device				
Protein	**Neg**	**15**	**30**	**100**	**500**
Candidate Device					
Neg	310	5	1		
15	26	73	13		
30	1	5	146	16	
100			3	123	1
500				3	63
Total	337	83	163	142	64
%Agreement (Exactly match)	92	88	90	87	98
%Agreement (+/- 1 Color Block)	100	100	99	100	100

	Predicate Device			
Bilirubin	**Neg**	**1**	**3**	**6**
Candidate Device				
Neg	301	4		
1	26	142		
3		18	87	3
6			10	68
Total	327	164	97	71
%Agreement (Exactly match)	92	87	90	96
%Agreement (+/- 1 Color Block)	100	100	100	100

	Predicate Device				
Urobilinogen	**Norm**	**1**	**4**	**8**	**12**
Candidate Device					
Norm	419				
1	36	61	1		
4		2	62	4	
8			2	68	5
12				2	67
Total	455	63	65	74	72
%Agreement (Exactly match)	92	97	95	92	93
%Agreement (+/- 1 Color Block)	100	100	100	100	100

	Predicate Device					
pH	**5.0**	**6.0**	**6.5**	**7.0**	**8.0**	**9.0**
Candidate Device						
5.0	228	2				
6.0	29	110	22	1		
6.5		7	93	11		
7.0			5	118	12	
8.0				2	101	13
9.0					4	75
Total	257	119	120	132	117	88
%Agreement (Exactly match)	89	92	78	89	86	85
%Agreement (+/- 1 Color Block)	100	100	100	99	100	100

	Predicate Device						
Specific Gravity	**1.000**	**1.005**	**1.010**	**1.015**	**1.020**	**1.025**	**1.030**
Candidate Device							
1.000	9	5	1				
1.005	4	67	14	1			
1.010		13	177	36	4		
1.015			11	141	18		
1.020			1	8	131	14	
1.025				0	10	92	5
1.030		1		1		2	70
Total	13	86	204	187	163	108	75
%Agreement (Exactly match)	69	78	87	75	80	85	93
%Agreement (+/- 1 Color Block)	100	99	99	99	98	100	100

Summary of Data

Analyte	% Agreement (within ± 1 color block)	% Agreement (exact match)	Analyte	% Agreement (within ± 1 color block)	% Agreement (exact match)
Blood (Erythrocytes)	100 (713/713)	91.7 (654/713)	Protein	99.8 (788/789)	90.6 (715/789)
Leukocytes	100 (469/469)	95.9 (450/469)	Bilirubin	100 (659/659)	90.7 (598/659)
Nitrite	100 (190/190)	96.8 (184/190)	Urobilinogen	100 (729/729)	92.8 (677/729)
Ketone	99.7 (708/710)	90.7 (655/710)	pH	99.9 (832/833)	87.0 (725/833)
Glucose	100 (479/479)	94.6 (453/479)	Specific Gravity	99.2 (830/836)	82 (687/836)

Cobas u411 optional Urine Color parameter vs. Visual Read

	Visual Reading				
Urine Color	**pale yellow/ yellow**	**orange**	**amber**	**brown**	**red**
Candidate Device					
pale yellow/ yellow	176		6		
orange					2
amber	12		37		
brown	8		36	53	
red					8

b. Matrix comparison:

Not applicable, this device is only used with urine samples.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off**:**

   Not applicable

   Expected values/Reference range:

   Complete details of the expected analyte values are provided in the labeling.

   The labeling states that each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference range.

N. Instrument Name:

Cobas u411 Urinalysis Test System

O. System Descriptions:

1. Modes of Operation:

   The Cobas Urinalysis Test system is an automated urine analyzer using reflectance photometry for the semi quantitative determination of Specific Gravity, pH, Leukocyte esterase, Nitrite, Protein, Glucose, Ketones, Urobilinogen, Bilirubin and Erythrocytes.

2. Software:

   FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

   Yes _____X___ or No _____

3. Specimen Identification:

   Numerical specimen identification information can be entered manually via the touch screen keyboard on the analyzer. The analyzer is also available for use with a bar code scanner using the BC scanner interface located in the back of the instrument.

4. Specimen Sampling and Handling:

   Cobas u 411 Urinalysis Test system can analyze multiple strips. The user dips the test strip into the urine sample and places it on a sample tray. The test strip is then drawn inside the analyzer to begin timing and analysis.

5. Calibration:

   Calibration is based on the analysis of a calibration strip with known reflectance values. The calibration strip is initially provided with the device and may also be purchased separately. This internal calibration strip must be replaced at least once a year or in the event that the cobas u 411 analyzer cannot be calibrated. This must only be performed using the Control-Test M calibration strip manufactured by Roche Diagnostics. The calibration strip is made of gray plastic material of constant reflectance characteristics. Labeling recommends that the cobas u411 analyzer be calibrated once every four weeks.

6. Quality Control:

   Quality Control is analyzed like the patient samples. The labeling recommends that a positive and a negative external control be assayed daily according to state, federal and local guidelines and 1) when starting a new lot of test strips 2) when starting a new container of test strips 3) when there are questionable results 4) every 30 days to check the storage conditions of the test strips 5) after using the calibration strip 6) after maintenance or service and 7) when changing operators.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.