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

A. 510(k) Number:

k183432

B. Purpose for Submission:

New device

C. Measurands:

Measurement of the following in urine: pH, leukocytes, nitrite, protein, glucose, ketones, urobilinogen, bilirubin, erythrocytes, color, and clarity

D. Types of Test:

Qualitative and semi-quantitative urinalysis

E. Applicant:

Roche Diagnostics

F. Proprietary and Established Names:

cobas u 601 urinalysis test system

G. Regulatory Information:

Regulation	Classification	Product Code	Panel
21 CFR §862.1340 Urinary glucose (nonquantitative) test system	II	JIL	Chemistry (75)
21 CFR §864.6550 Occult blood test	II	JIO	Hematology (81)
21 CFR §862.1785 Urinary urobilinogen (non-quantitative) test system	I	CDM	Chemistry (75)
21 CFR §862.1550 Urinary pH (nonquantitative) test system	I	CEN	Chemistry (75)

Regulation	Classification	Product Code	Panel
21 CFR §862.1435 Ketones (nonquantitative) test system	I	JIN	Chemistry (75)
21 CFR §862.1645 Urinary protein or albumin (nonquantitative) test system	I	JIR	Chemistry (75)
21 CFR §862.1115 Urinary bilirubin and its conjugates (nonquantitative) test system	I	JJB	Chemistry (75)
21 CFR §862.1510 Nitrite (nonquantitative) test system	I	JMT	Chemistry (75)
21 CFR §864.7675 Leukocyte peroxidase test	I	LJX	Hematology (81)
21 CFR §862.2900 Automated urinalysis system	I	KQO	Chemistry (75)

H. Intended Use:

1. Intended use:
   See indications for use.

2. Indications for use:
   The cobas u 601 urinalysis test system is comprised of the cobas u 601 urine analyzer and the cobas u pack.

   The cobas u 601 urine analyzer when used with the cobas u pack is a fully automated urinalysis system intended for the in vitro qualitative or semi- quantitative determination of urine analytes, including pH, leukocytes, nitrite, protein, glucose, ketones, urobilinogen, bilirubin, color, and erythrocytes, as well as clarity. These measurements are useful in the evaluation of renal, urinary, hepatic and metabolic disorders. This system is intended to be used by trained operators in clinical laboratories.

   The cobas u pack is a cassette loaded with cobas u 601 test strips for the in vitro qualitative or semi-quantitative determination of pH, leukocytes, nitrite, protein, glucose, ketones, urobilinogen, bilirubin, color, and erythrocytes in urine with the cobas u 601 urine analyzer. These measurements are useful in the evaluation of renal, urinary, hepatic and metabolic disorders.

3. Special conditions for use statement(s):
   Prescription use only
   The test strips are not for visual readings.

4. Special instrument requirements:
   cobas u 601 urine analyzer

I. Device Description:

The cobas u 601 urinalysis test system is comprised of the cobas u 601 urine analyzer and the cobas u pack.

The cobas u pack is a cassette which holds 400 test strips . Each cassette is identified by a unique radio frequency identification (RFID) tag. The RFID tag also contains information on expiration date and lot number.

The cobas u 601 urine analyzer is a fully automated urine analysis system. The cobas u 601 analyzer consists of several major components: computer, rack transport system, liquid handling system, test strip cassette compartment, automated test strip processing area, test strip reflectance measuring unit, and physical measurement cell (PMC) for clarity and specific gravity.

J. Substantial Equivalence Information:

1. Predicate device name:
   Cobas u 411 Test System

2. Predicate 510(k) number:
   k093555

3. Comparison with predicate:

Similarities and Differences		
Item	Candidate Device cobas u 601 urinalysis test system k183432	Predicate Device Cobas u 411 Test System k093555
Intended use	For qualitative and semi-quantitative determination of pH, leukocytes, nitrite, protein, glucose, ketones, urobilinogen, bilirubin, color and erythrocytes in urine	Same
Specimen type	Urine	Same
Test strips	Cassette which holds 400 cobas u 601 Test Strips	Chemstrip 10 UA test strip
Urine application	Automated dispense of urine onto each pad of test strip	Test strip manually dipped into urine sample

K. Standard/Guidance Document Referenced:

IEC 61010-1 Edition 3.0 2010-06 Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General requirements.

L. Test Principles:

cobas u pack

pH: Color indicator method using methyl red, phenolphthalein and bromothymol blue.

Leukocytes: The test reveals the presence of granulocyte esterases. The esterases cleave an indoxyl ester, and the indoxyl reacts with a diazonium salt to produce a violet dye.

Nitrite: The test is based on the principle of the Griess test and is specific for nitrite. Nitrite reacts with an aromatic amine to give a diazonium salt, which by coupling with a further compound yields a red-violet azo dye.

Protein: The detection of protein is based on the protein error of pH indicators method. When pH is held constant by a buffer, indicator dye (3',3",5',5"- tetrachlorophenol-3,4,5,6-tetrabromosulfophthalein) releases H^+ ions based on the amount of protein present and change color from yellow to light green.

Glucose: The glucose determination is based on the specific glucose-oxidase/peroxidase reaction. The reaction utilizes the glucose oxidase to catalyze the formation of gluconic acid and hydrogen peroxide from the oxidation of glucose. A second enzyme, peroxidase, catalyzes the reaction of hydrogen peroxide with the chromogen tetramethylbenzidine to form a green dye complex.

Ketones: The detection of ketones in urine is based on a method where sodium nitroprusside and glycine react with acetoacetate and acetone in an alkaline medium to form a violet dye complex.

Urobilinogen: Urobilinogen is coupled with 4-methoxybenzene-diazonium-tetrafluoroborate in an acid medium to form a red azo dye.

Bilirubin: The detection of bilirubin is based on the coupling reaction of a diazonium salt of 2,6-dichlorobenzene-diazonium-tetrafluoroborate with bilirubin in an acid medium. The reaction yields a pink to red‑violet color proportional to the total bilirubin concentration.

Erythrocytes: The chemical detection of blood is based on the pseudo-peroxidase action of erythrocytes and hemoglobin. Hemoglobin and myoglobin, if present, catalyze the oxidation of the indicator by the organic peroxide to give a blue-green coloration. Intact erythrocytes are hemolyze on the test paper and liberate hemoglobin which produces a green dot. Scattered or compacted green dots on the yellow test paper are indicative of intact

erythrocytes. A uniform green coloration of the test is indicative of free hemoglobin, myoglobin, or hemolyzed erythrocytes in the urine.

Color: Urine color is measured in a white area on the test strip which is not impregnated with reagents. Urine color is reported as Pale Yellow, Yellow, Amber, Orange, Brown, Red, Green, or other. The urine color measurement is also used in this urinalysis system for a color correction algorithm to compensate for intrinsically colored urine samples when testing for Leukocytes, Nitrite, Glucose, Ketone bodies, Urobilinogen, Bilirubin, and Erythrocytes. The measurements of protein and pH are not compensated for urine color.

cobas u 601 urine analyzer

The analyzer photometer conducts reflectance measurements on each pad of the test strip. The analyzer PMC measures urine clarity and specific gravity.

M. Performance Characteristics:

1. Analytical performance:

a. Precision/Reproducibility:

All test strip analytes

Repeatability

A repeatability study of the cobas u 601 urinalysis test system was conducted for the analytes measured from the test strip. Three controls and two human urine samples were used in the study. Control samples and human urine samples were measured in 2 runs with 21 replicates per run for a total of n=42 results per sample. A low positive control was measured in 1 run with 21 replicates.

Control Level 1

Analyte	Run 1			Run 2		
	Result	**Exact Agreement (%)**	**Agreement ± 1 block (%)**	**Result**	**Exact Agreement (%)**	**Agreement ± 1 block (%)**
Bilirubin	Negative	100	100	Negative	100	100
Erythrocytes	Negative	100	100	Negative	100	100
Ketones	Negative	100	100	Negative	100	100
Glucose	Normal	100	100	Normal	100	100
Leukocytes	Negative	100	100	Negative	100	100
Nitrite	Negative	100	100	Negative	100	100
Protein	Negative	100	100	Negative	100	100
Urobilinogen	Normal	100	100	Normal	100	100
Color	Yellow	100	100	Yellow	100	100
pH	6	100	100	6	100	100

Control Level 2

Analyte	Run 1			Run 2		
	Result	**Exact Agreement (%)**	**Agreement ± 1 block (%)**	**Result**	**Exact Agreement (%)**	**Agreement ± 1 block (%)**
Bilirubin	6 mg/dL	100	100	6 mg/dL	100	100
Erythrocytes	250 Ery/µL	100	100	250 Ery/µL	100	100
Ketones	150 mg/dL	100	100	150 mg/dL	100	100
Glucose	1000 mg/dL	100	100	1000 mg/dL	100	100
Leukocytes	500 Leu/µL	100	100	500 Leu/µL	100	100
Nitrite	Positive	100	100	Positive	100	100
Protein	100 mg/dL	100	100	100 mg/dL	100	100
Urobilinogen	8 mg/dL	100	100	8 mg/dL	100	100
Color	Brown	100	100	Brown	100	100
pH	7	100	100	7	100	100

Control Low positive

Analyte	Run 1		
	Result	**Exact Agreement (%)**	**Agreement ± 1 block (%)**
Bilirubin	1 mg/dL	100	100
Erythrocytes	10 Ery/µL	100	100
Ketones	5 mg/dL	100	100
Glucose	50 mg/dL	100	100
Leukocytes	25 Leu/µL	100	100
Protein	15 mg/dL	100	100
Urobilinogen	1 mg/dL	100	100
Color	Amber	100	100
pH	6	100	100

Human Urine, Negative / Normal

Analyte	Run 1			Run 2		
	Result	**Exact Agreement (%)**	**Agreement ± 1 block (%)**	**Result**	**Exact Agreement (%)**	**Agreement ± 1 block (%)**
Bilirubin	Negative	100	100	Negative	100	100
Erythrocytes	Negative	100	100	Negative	100	100
Ketones	Negative	100	100	Negative	100	100
Glucose	Normal	100	100	Normal	100	100
Leukocytes	Negative	100	100	Negative	100	100
Nitrite	Negative	100	100	Negative	100	100
Protein	Negative	100	100	Negative	100	100
Urobilinogen	Normal	100	100	Normal	100	100
Color	Yellow	100	100	Yellow	100	100
pH	6.5	90.5	100	6.5	100	100

Human Urine, Positive

Analyte	Run 1			Run 2		
	Result	**Exact Agreement (%)**	**Agreement ± 1 block (%)**	**Result**	**Exact Agreement (%)**	**Agreement ± 1 block (%)**
Bilirubin	3 mg/dL	100	100	3 mg/dL	100	100
Erythrocytes	250 Ery/µL	100	100	250 Ery/µL	100	100
Ketones	50 mg/dL	100	100	50 mg/dL	100	100
Glucose	1000 mg/dL	100	100	1000 mg/dL	100	100
Leukocytes	500 Leu/µL	100	100	500 Leu/µL	100	100
Nitrite	Positive	100	100	Positive	100	100
Protein	100 mg/dL	100	100	100 mg/dL	100	100
Urobilinogen	4 mg/dL	95.2	100	4 mg/dL	95.2	100
Color	Amber	100	100	Orange	100	100
pH	9	100	100	8	100	100

Within-laboratory precision

A within-laboratory precision study of the cobas u 601 urinalysis test system was conducted for the analytes measured from the test strip. Three controls and two human urine samples were used in the study. For each analyte three controls with different concentrations were measured over 21 days with 2 runs per day, and 2 replicates per run for a total of n=84 results per sample. The result are given below.

Control level 1

Analyte	Result	Exact Agreement (%)	Agreement ± 1 block (%)
Bilirubin	Negative	100	100
Erythrocytes	Negative	100	100
Ketones	Negative	100	100
Glucose	Normal	100	100
Leukocytes	Negative	100	100
Nitrite	Negative	100	100
Protein	Negative	100	100
Urobilinogen	Normal	100	100
Color	yellow	100	100
pH	6	100	100

Control level 2

Analyte	Result	Exact Agreement (%)	Agreement ± 1 block (%)
Bilirubin	6 mg/dL	100	100
Erythrocytes	250 Ery/µL	100	100
Ketones	150 mg/dL	100	100
Glucose	1000 mg/dL	100	100
Leukocytes	500 Leu/µL	95.2	100
Nitrite	Positive	100	100
Protein	100 mg/dL	100	100
Urobilinogen	8 mg/dL	100	100
Color	Brown	100	100
pH	7	100	100

Control low positive

Analyte	Result	Exact Agreement (%)	Agreement ± 1 block (%)
Bilirubin	1 mg/dL	100	100
Erythrocytes	10 Ery/µL	97.6	100
Ketones	5 mg/dL	100	100
Glucose	50 mg/dL	100	100
Leukocytes	25 Leu/µL	98.8	100
Protein	15 mg/dL	100	100
Urobilinogen	1 mg/dL	100	100
Color	Amber	100	100

Urine Clarity

Repeatability

A repeatability study of the cobas u 601 urinalysis test system was conducted for the analyzer measured parameter of clarity. For the study, there were two controls and three human urine samples measured in 2 runs with 21 replicates per run for a total of n=42 results per control. Human urine samples were measured in 1 run with 21 replicates. The results are given as follows.

Sample	Result	Exact agreement (%)	Agreement ± 1 block (%)
Control 1	Clear	100	100
Control 2	Clear	100	100
Human urine sample	Light turbid	100	100
Human urine sample	Turbid	100	100
Human urine sample	Clear	100	100

Within-laboratory precision

A within-laboratory precision study was conducted for the analyzer measured parameter of clarity. Two control samples were measured over 21 days with 2 runs per day and 2 replicates per run for a total of n = 84 results per control sample.

Sample	Result	Exact agreement (%)	Agreement ± 1 block (%)
Control level 1	Clear	100	100
Control level 2	Clear	100	100

b. Linearity/assay reportable range:

A study was conducted to evaluate the assay reportable range for each analyte of the cobas u pack and clarity. The reportable range was evaluated by measuring samples with known concentrations, and known clarity covering all measurement blocks. Samples were measured using 3 lots of cobas u pack cassettes and 3 analyzers in replicates of 21 per lot/analyzers for a total of 63 measurements per sample. The results are summarized below:

pH			
Test pH	**Output**	**Exact match**	**±1 color block match**
5.0	5.0	100%	100%
6.0	6.0	100%	100%
6.5	6.5	100%	100%
7.0	7.0	100%	100%
8.0	8.0	100%	100%
9.0	9.0	100%	100%

Glucose			
Test concentration (mg/dL)	**Output (mg/dL)**	**Exact match**	**±1 color block match**
0	norm (norm)	100%	100%
45	50 (1+)	100%	100%
120	100 (2+)	100%	100%
250	250 (3+)	100%	100%
650	1000 (4+)	100%	100%

Protein			
Test concentration (mg/dL)	**Output (mg/dL)**	**Exact match**	**±1 color block match**
0	neg (neg)	100%	100%
10	15 (1+)	95%	100%
25	30 (2+)	100%	100%
100	100 (3+)	100%	100%
400	500 (4+)	100%	100%

Bilirubin			
Test concentration (mg/dL)	**Output (mg/dL)**	**Exact match**	**±1 color block match**
0	neg (neg)	100%	100%
1	1 (1+)	100%	100%
2	3 (2+)	100%	100%
6	6 (3+)	100%	100%

Urobilinogen			
Test concentration (mg/dL)	**Output (mg/dL)**	**Exact match**	**±1 color block match**
0	norm (norm)	100%	100%
1.3	1 (1+)	100%	100%
3	4 (2+)	100%	100%
7	8 (3+)	100%	100%
12	12 (4+)	99%	100%

Erythrocytes			
Test concentration (ERY/µL)	**Output (ERY/µL)**	**Exact match**	**±1 color block match**
0	neg (neg)	100%	100%
10	10 (1+)	100%	100%
20	25 (2+)	100%	100%
40	50 (3+)	100%	100%
100	150 (4+)	100%	100%
400	250 (5+)	100%	100%

Ketone			
Test concentration (mg/dL)	**Output (mg/dL)**	**Exact match**	**±1 color block match**
0	neg (neg)	100%	100%
5.5	5 (1+)	100%	100%
14	15 (2+)	100%	100%
45	50 (3+)	100%	100%
100	150 (4+)	100%	100%

Nitrite			
Test concentration (mg/dL)	**Output**	**Exact match**	**±1 color block match**
0	neg	100%	100%
0.06	pos	100%	100%

Leukocytes			
Test concentration (Leu/µL)	**Output (Leu/µL)**	**Exact match**	**±1 color block match**
neg	neg (neg)	100%	100%
23	25 (1+)	95%	100%
112	100 (2+)	99%	100%
450	500 (3+)	95%	100%

Clarity			
Test condition	**Output**	**Exact match**	**±1 color block match**
clear	clear	100%	100%
light turbid	light turbid	100%	100%
turbid	turbid	100%	100%

The results of the assay reportable range studies support the following measurement ranges on the cobas u 601 urinalysis test system:

Analyte	Measurement range
pH	semi-quantitative: 5, 6, 6.5, 7, 8, 9
Erythrocytes	semi-quantitative: NEG, 10, 25, 50, 150, 250 Ery/µL qualitative: NEG, 1+, 2+, 3+, 4+ 5+
Leukocytes	semi-quantitative: NEG, 25, 100, 500 Leu/µL qualitative: NEG, 1+, 2+, 3+
Nitrite	qualitative: NEG, POS
Protein	semi-quantitative: NEG, 15, 30, 100, 500 mg/dL qualitative: NEG, 1+, 2+, 3+, 4+
Glucose	semi-quantitative: NORM, 50, 100, 250, 1000 mg/dL qualitative: NEG, 1+, 2+, 3+, 4+
Ketones	semi-quantitative: NEG, 5, 15, 50, 150 mg/dL qualitative: NEG, 1+, 2+, 3+, 4+
Urobilinogen	semi-quantitative: NORM, 1, 4, 8, 12 mg/dL qualitative: NEG, 1+, 2+, 3+, 4+
Bilirubin	semi-quantitative: NEG, 1, 3, 6 mg/dL qualitative: NEG, 1+, 2+, 3+
Color	pale yellow, yellow, amber, brown, orange, red, green, other
Clarity	clear, light turbid, turbid

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

Traceability
The sponsor did not describe any traceability for the test system.

d. Detection limit:

Study 1 - Analytical sensitivity:
The detection limit for each analyte on the test strip was established in an analytical sensitivity study which measured for each analyte the concentration which transitioned the lowest measurement block (negative or normal) to the next level measurement block (positive). The sponsor defined analytical sensitivity as the lowest analyte concentration where ≥90% of the measurement results were positive.

In the study, a negative native urine pool was spiked with the analyte to 5 to 7 concentration levels. Each concentration level was measured in replicates of 20 on each of the three analyzers using three lots of cobas u pack for a total of n=2820 measurements across all analytes. The results are summarized in the following table:

Analyte	Analytical Sensitivity
Leukocytes (Subtilisin)	10 Leu/µL
Nitrite	0.045 mg/dL
Protein (albumin)	9 mg/dL
Glucose	25 mg/dL
Ketones (acetoacetate)	4 mg/dL
Bilirubin	0.6 mg/dL
Urobilinogen	1.15 mg/dL
Erythrocytes	7 Ery/µL

Study 2 – Measurement block cut-off:

Transition points studies were performed with the cobas u 601 urinalysis test system to determine the cut-off concentration between each semi-quantitative block. The cut-off concentration was defined as the lowest sample concentration at which ≥ 55% of the test results are positive with respect to the transited from block. Samples were prepared from native negative urine spiked with the analyte to 5 concentrations spanning the expected cut-off concentration. Each concentration level was measured in replicates of 20 on each of the three analyzers using three lots of cobas u pack. The cut-off concentration between each measurement block is summarized in the table below where the block output is the transitioned to block.

pH		
Block output	**Cut-off**	**% Positive**
6.0	5.7	100%
6.5	6.2	100%
7.0	6.5	98%
8.0	7.2	68%
9.0	8.5	88%

Glucose		
Block output	**Cut-off, mg/dL**	**% Positive**
100 (2+)	60	100%
250 (3+)	200	100%
1000 (4+)	550	100%

Protein		
Block output	**Cut-off, mg/dL**	**% Positive**
30 (2+)	14.5	88%
100 (3+)	45	95%
500 (4+)	280	83%

Bilirubin		
Block output	**Cut-off, mg/dL**	**% Positive**
3 (2+)	1.35	97%
6 (3+)	2.75	82%

Urobilinogen		
Block output	**Cut-off, mg/dL**	**% Positive**
4 (2+)	1.85	85%
8 (3+)	4.5	92%
12 (4+)	9.5	100%

Erythrocytes		
Block output	**Cut-off, mg/dL**	**% Positive**
25 (2+)	12	75%
50 (3+)	30	67%
150 (4+)	110	70%
250 (5+)	290	72%

Ketones		
Block output	**Cut-off, mg/dL**	**% Positive**
15 (2+)	8	93%
50 (3+)	20	95%
150 (4+)	62.5	82%

Leukocytes		
Block output	**Cut-off, mg/dL**	**% Positive**
100 (2+)	88	98%
500 (3+)	400	83%

e. Analytical specificity:

Analytical specificity studies were conducted to assess for interfering effects of endogenous substances and therapeutic drugs on the cobas u 601 urinalysis test system (except color and clarity). In the study, samples were prepared from pooled analyte negative urine at two levels for each analyte (except pH which was tested at one normal level): (1) negative/normal range and (2) first positive range. Each of these samples was further aliquoted into three. Two of these were spiked at two different concentrations of interfering substance. A third aliquot was used as a reference without interfering substance. For therapeutic drug substances, the highest concentration tested was approximately 5 times the maximal daily dosage. For endogenous substances the highest concentration tested was approximately 5 times the highest pathological level. Each sample aliquot was tested in replicates of 10 across 2 analyzers and 2 cobas u pack lots. The sponsor defined no significant

interference if ≥90% (≥9 of 10 replicates) of the results were found in the correct block and 100% of results are within +/- 1 block of the correct block. No significant interference was observed for the following substances at that concentration, with certain exceptions as noted below:

Substance	Highest concentration at which no interference was observed unless noted below***
Therapeutic drugs	
Acetaminophen	300 mg/dL
Amoxicillin	1333 mg/dL
Ascorbic acid	400 mg/dL
Biotin	100 mg/dL
Cefoxitin	1200 mg/dL
Furosemide	200 mg/dL
Gabapentin	1200 mg/dL
Gentamycin Sulfate	40 mg/dL
Ibuprofen	250 mg/dL
Levodopa	125 mg/dL
Lisinopril	27 mg/dL
Metformin	850 mg/dL
Methyldopa	200 mg/dL
Methenamine + Methylene blue	400 + 66.5 mg/dL
N-Acetylcysteine	20 mg/dL
Ofloxacin	90 mg/dL
Phenazopyridine	30 mg/dL
Salicyluric acid	600 mg/dL
Tetracycline	50 mg/dL
Endogenous substances	
3-Hydroxybutyrate	450 mg/dL
Ammonium chloride	2500 mg/dL
Bilirubin conjugate	80 mg/dL
Calcium chloride	300 mg/dL
Creatinine	1500 mg/dL
Glucose	10,000 mg/dL
Lysed erythrocytes as hemoglobin	83 mg/dL
human IgG	500 mg/dL
Nitrite	11 mg/dL
Urea	20,000 mg/dL
Uric acid	155mg/dL
Urobilinogen	300 mg/dL

*** Not all of the substances tested for interference demonstrated no significant interference for all analytes. For those substances that on initial screening where found to interfere with certain analytes, dose response testing was conducted to

establish the concentration limit below which no significant interference is expected. The results are given in the table below:

Analyte	Substance	Concentration limit with no significant interference	Effect when above the concentration limit
Urobilinogen	Acetaminophen	24 mg/dL	At 42 mg/dL elevated from 1+ to 2+
	Bilirubin	40 mg/dL	At 60 mg/dL decreased from 1+ to normal
	Gabapentin	1080 mg/dL	At 1200 mg/dL decreased from 1+ to normal
	Methenamine + Methylene blue	2.4 + 0.4 mg/dL	At 6.7 + 40 mg/dL elevated from 1+ to 2+
	Phenazopyridine	12 mg/dL	At 30 mg/dL elevated from normal to 1+ and at 24 mg/dL elevated from 1+ to 2
	Nitrite	0.7 mg/dL	At 1.4 mg/dL decreased from 1+ to normal
Leukocytes	Amoxicillin	1067 mg/dL	At 1200 mg/dL decrease from 1+ to negative
	Bilirubin	40 mg/dL	At 80 mg/dL increase from negative to 1+
	Ibuprofen	20 mg/dL	At 125 mg/dL decreased from 1+ to negative
	Methenamine + Methylene blue	4 + 0.67 mg/dL	At 6.7 + 40 mg/dL elevated from negative to 1+ and at 6.7 + 40 mg/dL elevated from 1+ to 2+
	Calcium chloride	243 mg/dL	At 300 mg/dL decreased from 1+ to negative
	Glucose	1000 mg/dL	At 2000 mg/dL decreased from 1+ to negative
	Lysed erythrocytes as hemoglobin	75 mg/dL	At 83 mg/dL increase from negative to 1+

	Urobilinogen	12 mg/dL	At 300 mg/dL elevated from 1+ to 2+
Erythrocytes	Ascorbic Acid	75 mg/dL	At 112 mg/dL decrease from 1+ to negative
	Furosemide	180 mg/dL	At 200 mg/dL decrease from 1+ to negative
	Ibuprofen	75 mg/dL	At 125 mg/dL decreased from 1+ to negative
	Levodopa	62 mg/dL	At 94 mg/dL elevated from negative to 1+ and elevated from 1+ to 2+
	Methyldopa	80 mg/dL	At 200 mg/dL elevated from negative to 1+ and at 120 mg/dL elevated from 1+ to 2+
	Methenamine + Methylene blue	0.8 + 0.13 mg/dL	At 2.7 + 16 mg/dL elevated from 1+ to 2+
	Calcium chloride	243 mg/dL	At 300 mg/dL elevated from negative to 1+
	Nitrite	4 mg/dL	At 8 mg/dL decreased from 1+ to negative
	Urobilinogen	48 mg/dL	At 120 mg/dL elevated from negative to positive and at 300 mg/dL elevated from 1+ to 2+
Nitrite	Ascorbic Acid	150 mg/dL	At 200 mg/dL decreased from positive to negative
	Bilirubin	40 mg/dL	At 80 mg/dL decreased from positive to negative
	Methenamine + Methylene blue	2.8 + 0.47 mg/dL	At 6.7 + 40 mg/dL elevated from negative to positive
	Phenazopyridine	12 mg/dL	At 30 mg/dL elevated from negative to positive
	Urobilinogen	9 mg/dL	At 10 mg/dL elevated from negative to positive
Glucose	Ascorbic Acid	20 mg/dL	At 40 mg/dL decreased from 1+ to normal

	Bilirubin	40 mg/dL	At 80 mg/dL decreased from 1+ to normal
	Methenamine + Methylene blue	12 + 2 mg/dL	At 6.7 + 40 mg/dL decreased from 1+ to normal
	Ammonium chloride	1030 mg/dL	At 1520 mg/dL decreased from 1+ to normal
	Urea	8900 mg/dL	At 1260 mg/dL decreased from 1+ to normal
	Urobilinogen	125 mg/dL	At 300 mg/dL mg/dL decreased from 1+ to normal
Bilirubin	Ascorbic Acid	200 mg/dL	At 40 mg/dL decreased from 1+ to negative
	Biotin	80 mg/dL	At 100 mg/dL elevated from 1+ to 2+
	Methenamine + Methylene blue	14 + 2.33 mg/dL	At 6.7 + 40 mg/dL decreased from 1+ to negative
	Phenazopyridine	12 mg/dL	At 30 mg/dL elevated from negative to 1+ and at 24 mg/dL elevated from 1+ to 2
	Nitrite	0.7 mg/dL	At 1.4 mg/dL decreased from 1+ to negative
	Urobilinogen	6 mg/dL	At 12 mg/dL increased from negative to 2+ and 7 mg/dL increased from 1+ to 2+
Protein	Bilirubin	40 mg/dL	At 60 mg/dL increase from negative to 1+
	Gabapentin	240 mg/dL	At 360 mg/dL elevated from 1+ to 2+
	Ibuprofen	225	At 125 mg/dL decreased from 1+ to negative
	Methenamine + Methylene blue	0.4 + 0.067 mg/dL	At 6.7 + 40 mg/dL elevated from 1+ to 2+
	Phenazopyridine	12 mg/dL	At 30 mg/dL elevated from negative to 1+ and at 24 mg/dL elevated from 1+ to 2+

	Ammonium chloride	172 mg/dL	At 500 mg/dL decreased from1+ to negative
	Calcium chloride	243 mg/dL	At 300 mg/dL decreased from 1+ to negative
	Creatinine	285 mg/dL	At 1500 mg/dL elevated from negative to 1+ and at 420 mg/dL elevated from 1+ to 2+
	Lysed erythrocytes as hemoglobin	6.6 mg/dL	At 30 mg/dL elevated from negative to 1+ and at 13 mg/dL elevated from 1+ to 2+
	Urea	5200 mg/dL	At 8900 mg/dL elevated from negative to 1+ and at 8900 mg/dL elevated from 1+ to 2+
	Urobilinogen	12 mg/dL	At 300 mg/dL elevated from negative to 1+ and at 300 mg/dL elevated from 1+ to 2+
Ketones	Bilirubin	40 mg/dL	At 80 mg/dL decrease from 1+ to negative
	Levodopa	62 mg/dL	At 94 mg/dL elevated from 1+ to 2+
	Methyldopa	120 mg/dL	At 200 mg/dL elevated from negative to 1+ and 160 mg/dL elevated from 1+ to 2+
	Methenamine + Methylene blue	16 + 2.7 mg/dL	At 6.7 + 40 mg/dL decreased from 1+ to negative
	N-Acetylcysteine	3 mg/dL	At 10 mg/dL elevated from negative to 1+ and at 5 mg/dL elevated from 1+ to 2+ positive
	Urobilinogen	90 mg/dL	At 300 mg/dL decreased from 1+ to negative

Interference effect of urine pH

Studies were conducted to assess the effect of urine pH on the test results. For all test strip analytes, except leukocytes there was no interference from pH across a range of 4.5 to 9.0. For leukocytes, urine pH values lower than 5.5 may yield a false negative result.

Interference effect of intrinsic urine color

The candidate device includes a feature that corrects for intrinsic urine color. Studies were conducted to verify that the test strip analytes of erythrocytes, leukocytes, nitrite, ketones, glucose, urobilinogen and bilirubin were insensitive to interference from red, orange, and brown colored urine samples. Other urine colors were not tested. The results demonstrated that red, orange, and brown urine do not significantly impact the results for those analytes tested since all results were within +/- 1 color block when testing red, orange and brown colored urine for these parameters.

Interference effect of urine specific gravity

Studies were conducted to assess the effect of urine specific gravity on the test results. For all test strip analytes, except leukocytes there was no interference from changes in specific gravity across a range of 1.015 (normal) to 1.050 (high) g/cm^3. For leukocytes, false negative results were found at urine specific gravity values higher than 1.030 g/cm^3.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

The accuracy performance of the test system was assessed by method comparison for agreement to comparator devices for each analyte/parameter on the cobas u 601 urinalysis test system.

Study #1 – All analytes except urine clarity

A method comparison study for the test strip analytes was conducted at one clinical laboratory using left-over urine specimens from routine use and were measured within two hours from collection. All measurements were performed using native samples only - there were no contrived samples. Each sample was split in two aliquots and measured in one-fold determination on the candidate device and the predicate device (the cobas u 411 urinalysis test system.) The data are presented in concordance charts, as shown in the tables below.

Erythrocytes	Comparator					
cobas u 601	neg	10 Ery/µL	25 Ery/µL	50 Ery/µL	150 Ery/µL	250 Ery/µL
Neg	187	1	0	0	0	0
10 Ery/µL	2	25	1	0	0	0
25 Ery/µL	0	2	40	2	0	0
50 Ery/µL	0	0	6	30	0	0
150 Ery/µL	0	0	0	3	21	1
250 Ery/µL	0	0	0	0	0	21
Total	189	28	47	35	21	22
Exact agreement %	99%	89%	85%	86%	100%	95%
Agreement ± 1 block	100%	100%	100%	100%	100%	100%

Leukocytes	Comparator			
cobas u 601	neg	25 Leu/µL	100 Leu/µL	500 Leu/µL
Neg	185	3	0	0
25 Leu/µL	1	30	2	0
100 Leu/µL	0	1	30	2
500 Leu/µL	0	0	1	42
Total	186	34	33	44
Exact agreement %	99%	88%	91%	95%
Agreement ± 1 block	100%	100%	100%	100%

Nitrite	Comparator	
cobas u 601	Neg	Pos
Neg	188	0
Pos	2	40
Total	190	40
Exact agreement %	99%	100%

Ketones	Comparator				
cobas u 601	Neg	5 mg/dL	15 mg/dL	50 mg/dL	150 mg/dL
Neg	189	3	0	0	0
5 mg/dL	1	21	2	0	0
15 mg/dL	0	0	21	1	0
50 mg/dL	0	0	0	20	2
150 mg/dL	0	0	0	0	20
Total	190	24	23	21	22
Exact agreement %	99%	88%	91%	95%	91%
Agreement ± 1 block	100%	100%	100%	100%	100%

Glucose	Comparator				
cobas u 601	Norm	50 mg/dL	100 mg/dL	250 mg/dL	1000 mg/dL
Norm	190	0	0	0	0
50 mg/dL	2	23	0	0	0
100 mg/dL	0	1	20	3	0
250 mg/dL	0	0	0	21	4
1000 mg/dL	0	0	0	0	25
Total	192	24	20	24	29
Exact agreement %	99%	96%	100%	88%	86%
Agreement ± 1 block	100%	100%	100%	100%	100%

Protein	Comparator				
cobas u 601	Norm	15 mg/dL	30 mg/dL	100 mg/dL	500 mg/dL
Norm	187	0	0	0	0
15 mg/dL	3	21	4	0	0
30 mg/dL	0	1	33	1	0
100 mg/dL	0	0	0	20	4
500 mg/dL	0	0	0	1	26
Total	190	22	37	22	30
Exact agreement %	98%	95%	89%	91%	87%
Agreement ± 1 block	100%	100%	100%	100%	100%

Bilirubin	Comparator			
cobas u 601	neg	1 mg/dL	3 mg/dL	6 mg/dL
Neg	188	2	0	0
1 mg/dL	0	21	1	0
3 mg/dL	0	0	33	2
6 mg/dL	0	0	0	20
Total	188	23	34	22
Exact agreement %	100%	91%	97%	91%
Agreement ± 1 block	100%	100%	100%	100%

Urobilinogen	Comparator				
cobas u 601	Norm	1 mg/dL	4 mg/dL	8 mg/dL	12 mg/dL
Norm	189	3	0	0	0
1 mg/dL	1	26	5	0	0
4 mg/dL	0	1	44	2	0
8 mg/dL	0	0	1	21	1
12 mg/dL	0	0	0	0	30
Total	190	30	50	23	31
Exact agreement %	99%	87%	88%	91%	97%
Agreement ± 1 block	100%	100%	100%	100%	100%

pH	Comparator					
cobas u 601	pH 5	pH 6	pH 6.5	pH 7	pH 8	pH 9
pH 5	44	6	0	0	0	0
pH 6	5	62	2	0	0	0
pH 6.5	0	3	14	1	0	0
pH 7	0	0	4	35	1	0
pH 8	0	0	0	1	28	4
pH 9	0	0	0	0	0	24
Total	49	71	20	38	29	29
Exact agreement %	90%	87%	70%	95%	97%	86%
Agreement ± 1 block	100%	100%	100%	100%	100%	100%

Color	Comparator					
cobas u 601	Pale yellow	Yellow	Amber	Brown	Orange	Red
Pale yellow	126	7	0	0	0	0
Yellow	23	85	2	0	0	0
Amber	1	29	58	0	0	0
Brown	0	0	24	50	0	0
Orange	5	0	5	7	15	3
Red	0	0	0	0	7	31
Total	155	121	89	57	22	34
Exact agreement %	81%	70%	65%	88%	68%	91%

Study #2 – Urine clarity

A method comparison study for the analyzer measured parameter of clarity was conducted at three clinical laboratories using left-over urine specimens from routine use and were measured within two hours from collection. All measurements were performed using native samples only - there were no contrived samples. Urine samples were measured to cover the analytical measurement range of clarity. Each sample was split in two aliquots and measured in one-fold determination on the candidate device and on a comparator method. The data from each site was combined and analyzed in a concordance chart:

Clarity	Comparator		
cobas u 601	Clear	Light turbid	Turbid
Clear	921	23	0
Light turbid	114	173	18
Turbid	2	21	92
total	1037	217	110
Exact agreement %	89%	80%	84%
Agreement ± 1 block	99.8%	100%	100%

b. Matrix comparison:

Not applicable, the assays on the platform are only for testing human urine.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

c. Other clinical supportive data:

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The following expected values are listed in the u pack cassette product labeling:

Analyte	Expected values
pH	4.8 – 7.4
Erythrocytes	0 – 5 Ery/µL
Leukocytes	< 10 Leu/µL
Nitrite	–
Protein	< 10 mg/dL
Glucose	< 30 mg/dL
Ketones	< 5 mg/dL
Urobilinogen	< 1 mg/dL
Bilirubin	< 0.2 mg/dL

N. Instrument Name:

cobas u 601 urine analyzer

O. System Descriptions:

1. Modes of Operation:
Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

Yes ____X___ or No _____

Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

Yes _____ or No ___X____

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 (ID):
   A patient ID is entered either manually using the touch screen or scanned using the barcode reader.

4. Specimen Sampling and Handling:
   Samples tubes are manually placed into a rack, which is loaded into the analyzer. The rack is automatically moved within the analyzer fluid handling station using a rack conveyor. During a run, the urine sample is aspirated into the fluid system and pipetted onto test pads of a test strip.

5. Calibration:
   A calibration of the analyzer's PMC is performed every 4 weeks by measuring the clarity and specific gravity of water.

   A calibration of the analyzer's photometer unit is performed every 4 weeks by measuring the reflectance of a dedicated calibration strip; i.e. cobas u calibration strip. The results are compared against a reference plate built into the analyzer.

   There are no external calibrators for the test system. The analyzer reference plate is measured along with each test strip measurement, and the assay reflectance measurements are normalized to the reference plate when calculating the results.

6. Quality Control:
   The following quality controls are recommended:

   ▪ qUAntify Plus Control
   ▪ Liquichek Urinalysis Control

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

1. Instrument / sample carryover

   Study #1 – all analytes, except urine clarity:
   The carryover on the cobas u 601 urine analyzer for all analytes measured by reflectance from the test strip was evaluated. Sample carry-over was assessed by alternatively measuring 5 high samples followed by 5 low samples, and repeating the cycle 4 times. The magnitude of the elevation of the low sample caused by carryover from the high

sample was determined by comparison of low sample result to a reference run of negative samples with n=25 replicates. The carryover study was performed on one instrument. For all analytes, all negative/normal samples read as negative/normal, and therefore no significant carryover found in the study. For urine color, all pale yellow samples were measured in the same color range after pipetting of brown urine samples.

Analyte	Reference run	% Match	Carryover run	% Match
BIL	Neg	100	Neg	100
ERY	Neg	100	Neg	100
GLU	Norm	100	Norm	100
KET	Neg	100	Neg	100
LEU	Neg	100	Neg	100
NIT	Neg	100	Neg	100
pH	6	100	6	100
PRO	neg	100	neg	100
UBG	norm	100	norm	100
Color	Pale yellow	100	Pale yellow	100

Study #2 – Clarity:
The PMC carryover on the cobas u 601 urine analyzer was evaluated in terms of urine clarity. Sample carry-over was assessed by alternatively measuring 5 high samples followed by 5 low samples, and repeating the cycle 4 times. The magnitude of the elevation of the low sample caused by carryover from the high sample was determined by comparison of low sample result to a reference run of negative samples with n=25 replicates. The carryover study was performed on one instrument. For urine clarity, the carryover was within the same color block, and therefore not significant.

2. Electromagnetic Compatibility (EMC)
   The sponsor provided documentation certifying that EMC testing was performed on the cobas u 601 urine analyzer and was found to be compliant of the requirements of the EMC specifications.

3. Electrical Safety
   The sponsor provided documentation certifying that electrical safety testing was performed on the cobas u 601 urine analyzer and that all requirements for electrical safety were met.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

R. Conclusion:

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