cobas u pack

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REF		CONTENT	SYSTEM
06334601001	06334601500	400	**cobas u** 601 urine analyzer

English

Caution

Do not open the inner bag prior to use.

Immediately insert cassette into analyzer!

Intended use

The **cobas u** pack is a cassette with teststrips 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.

For professional use only.

Test principle

pH: The test paper contains the indicators methyl red, o-cresolphthalein and bromothymol blue and reacts specifically with H^+-ions.

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

Nitrite (NIT): The test is based on the principle of the Griess test and is specific for nitrite. The reaction reveals the presence of nitrite and hence indirectly nitrite-forming bacteria in the urine by a pink-to-red coloration of the test patch. Even a slight pink coloration is indicative of significant bacteriuria.

Protein (PRO): The test is based on the principle of the protein error of a pH indicator. It is particularly sensitive to albumin.

Glucose (GLU): The glucose determination is based on the specific glucose-oxidase/peroxidase reaction (GOD/POD method).

Ketones (KET): This test is based on the principle of Legal's test and is more sensitive to acetoacetic acid than to acetone.

Urobilinogen (UBG): A stable diazonium salt reacts almost immediately with urobilinogen to give a red azo dye.

Bilirubin (BIL): The test is based on the coupling of bilirubin with a diazonium salt. Even the slightest pink coloration constitutes a positive, i.e. pathologic, result. Other urinary constituents produce a more or less intense yellow coloration.

Blood (ERY/Hb): The peroxidase-like action of hemoglobin and myoglobin specifically catalyzes the oxidation of the indicator by means of the organic hydroperoxide contained in the test paper to give a blue-green coloration.

Compensation area (COMP): This white area, which is not impregnated with reagents, allows instrumental compensation for the intrinsic color of the urine while testing leukocytes, nitrite, glucose, ketones, urobilinogen, bilirubin, erythrocytes; and determination of the urine color (COL).

Reagents

Each test contains per 1 cm^2 test patch area the following:

pH: Bromothymol blue 13.9 µg; methyl red 1.1 µg; o-cresolphthalein 7.3 µg

Leukocytes: Indoxylcarbonic acid ester 15.5 µg; methoxymorpholinobenzene diazonium salt 5.5 µg

Nitrite: 3-hydroxy-1,2,3,4-tetrahydro-7,8-benzoquinoline 33.5 µg; sulfanilamide 29.1 µg

Protein: 3',3'',5',5''-tetrachlorophenol-3,4,5,6-tetrabromosulfophthalein 13.9 µg

Glucose: 3,3',5,5'-tetramethylbenzidine 103.5 µg; GOD 6 U, POD 35 U

Ketones: Sodium nitroprusside 96.5 µg

Urobilinogen: 4-methoxybenzene-diazonium-tetrafluoroborate 67.7 µg

Bilirubin: 2,6-dichlorobenzene-diazonium-tetrafluoroborate 16.7 µg

Blood: 3,3',5,5'-tetramethylbenzidine 52.8 µg; 2,5-dimethyl-2,5-dihydroperoxyhexane 297.2 µg

Precautions and warnings

For in vitro diagnostic use for laboratory professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

Note: If the cassette has been stored refrigerated, it must be left at room temperature for a minimum of one hour prior to use.

The cassette contains a non-toxic silicate-based desiccant which must not be removed. If ingested by accident, drink large quantities of water.

The stopper of the test strip vial contains a non-toxic silicate-based desiccant, which must not be removed. If ingested by accident, drink large quantities of water.

Reagent handling

Ready for use.

Storage and stability

Store the cassette at 2-30 °C.

After loading the cassette into the analyzer, the test strips are stable within the tightly closed cassette compartment for 14 days. After this period, the cassette has to be replaced by a new one.

Do not use the cassette after the specified expiry date.

Specimen collection and preparation

Use only clean, well-rinsed vessels to collect urine.

Do not add preservatives to the urine.

Use fresh urine that has not been centrifuged.[1] The urine specimen should not stand for more than 2 hours before testing.[1] For specimen collection and preparation only use suitable tubes or collection containers, as false positive readings, particularly for glucose and protein, can result from residues of detergent or strongly oxidizing disinfectants in the specimen collection vessel.[2]

Using midstream urine is recommended to avoid contamination by commensal urethral flora in both sexes.[2] Do not expose urine specimens to sunlight as this induces oxidation of bilirubin and urobilinogen and hence leads to artificially low results for these 2 parameters.[2] Vaginal secretion or menstrual blood may contaminate urine from females.[2]

Diagnosis or therapy should never be based on one test result alone but should be established in the context of all other medical findings. In doubtful cases, it is therefore advisable to repeat the test and consider potential interferences.

In case of a positive result it is advisable to use a follow-up investigation.

Materials provided

- REF 06334601001, Cassette with 400 test strips

Materials required (but not provided)

- REF 06390498001, **cobas u** 601 urine analyzer
- REF 06390579001, **cobas u** calibration strip
- Controls as indicated below
- General laboratory equipment

Assay

1. Unfold and cut open aluminum bag with scissors (illustration 1).
2. Remove test strip cassette from the packaging and remove the two protection pads (illustration 2).
3. Immediately place test strip cassette into the **cobas u** 601 urine analyzer (illustration 3).

   Follow the instructions in the Operators Manual of the instrument for correct insertion and positioning. These instructions also contain information on further handling precautions of the cassette.

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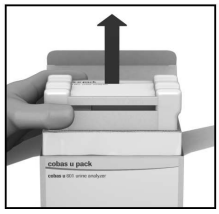
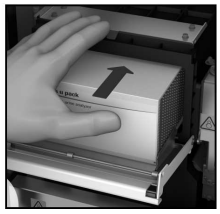

Note: If the cassette is stored in the opened bag or exposed to air (humidity, nitrogen oxides) for more than 3 minutes, environmental conditions may cause a color change of the test patches and damage of the reagents.

This has to be avoided. Do not use the cassette if the packaging shows severe damages, or the test strip layers in the cassette are not correctly aligned, or the test strips show unusual coloring.

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate Operators Manual for analyzer-specific assay instructions.

Calibration

cobas u calibration strips are used for the calibration of the photometer unit of the **cobas u** 601 urine analyzer. For details see the Operators Manual of the analyzer.

Quality control

For quality control, use commercially available urine controls, or other suitable control material.

Following quality controls from Bio-Rad are recommended to use:

- Bio-Rad qUAntify Plus Control
- Bio-Rad Liquichek Urinalysis Control

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

After the test strip has been accepted by the instrument, it is measured by means of reflectance photometry. The results are automatically calculated and printed on the report form in terms of "normal", "neg.", "pos." or as concentration values.

Limitations - interference

Therapeutic drugs and endogenous substances were tested for a potential interference to the test parameters of the **cobas u** pack.

All parameters were tested with negative urine samples and samples spiked to the first positive concentration range.

Therapeutic drugs were tested at concentrations in urine occurring under medication with the therapeutic dosage and above.

There are no significant therapeutic drug interferences up to the concentrations as presented below:

Parameter	Therapeutic drug	No interference up to	Effect above stated concentration
NIT	Ascorbic acid	1500 mg/L	false negative results
	Phenazopyridine	150 mg/L	false positive results
PRO	Salicyluric acid	4800 mg/L	false negative results
GLU	Ascorbic acid	250 mg/L	false normal results
KET	N-Acetylcysteine	30 mg/L	false positive results and elevated positive results
	Levodopa	125 mg/L	false positive results and elevated positive results
	Methyldopa	100 mg/L	false positive results and elevated positive results
UBG	Gabapentin	2400 mg/L	false normal results
	Phenazopyridine	150 mg/L	false positive results and elevated positive results
BIL	Amoxicillin	8000 mg/L	false negative results
	Ascorbic acid	600 mg/L	false negative results
ERY	Ascorbic acid	1000 mg/L	false negative results
	Gabapentin	7200 mg/L	false negative results
	Ibuprofen	750 mg/L	false negative results
	Levodopa	375 mg/L	false positive results and elevated positive results
	Methyldopa	800 mg/L	false positive results and elevated positive results
	Salicyluric acid	2400 mg/L	false negative results

There are no significant endogenous substance interferences up to the concentrations as presented below:

Parameter	Endogenous substance	No interference up to	Effect above stated concentration
LEU	Bilirubin	200 mg/L	false positive results and elevated positive results
	Glucose	10000 mg/L	false negative results
	Hemoglobin	200 mg/L	false positive results and elevated positive results
	Urobilinogen	150 mg/L	false negative results, false positive results and elevated positive results

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Parameter	Endogenous substance	No interference up to	Effect above stated concentration
NIT	Bilirubin	200 mg/L	false positive results
	Creatinine	9000 mg/L	false negative results
	Hemoglobin	400 mg/L	false positive results
	Urobilinogen	90 mg/L	false negative results and false positive results
PRO	Ammonium	5000 mg/L	false negative results
	Creatinine	6000 mg/L	elevated positive results
	Hemoglobin	70 mg/L	false positive results and elevated positive results
	Urea	75000 mg/L	false positive results and elevated positive results
	Urobilinogen	750 mg/L	false positive results
GLU	Ammonium	12500 mg/L	false normal results
	Bilirubin	400 mg/L	false normal results
	Urea	90000 mg/L	false normal results
	Urobilinogen	120 mg/L	false positive results
KET	Hemoglobin	600 mg/L	false positive results and elevated positive results
	Urobilinogen	1250 mg/L	false negative results
UBG	Bilirubin	400 mg/L	false normal results
	Nitrite	10 mg/L	false normal results
BIL	Urobilinogen	45 mg/L	false positive results and elevated positive results
	Nitrite	10 mg/L	false negative results
ERY	Nitrite	40 mg/L	false negative results
	Uric acid	800 mg/L	false negative results
	Urobilinogen	600 mg/L	false positive results and elevated positive results

Common limitations:

NIT: Prolonged urinary retention in the bladder (4-8 hours) is essential in order to obtain an accurate result.[2]
More than 80 % of all bacteria responsible for urinary tract infections are Gram-negative rods (E.coli, Klebsiella, Enterobacter and Proteus species).[3] Gram-negative bacteria have the ability to reduce urinary nitrate to nitrite and can therefore be detected indirectly with the test strips.[2] Normal nutrition as a rule ensures a sufficiently high content of nitrate in the urine for the detection of bacteria.[4] Some common uropathogens, e.g. Enterococcus spp. and Staphylococcus spp. (5-15 % of bacteria responsible for urinary tract infections),[3] do not reduce urinary nitrate to nitrite and will therefore not be detected whatever their urinary concentration.[2] False-negative results may occur as a result of strong diuresis with frequent voiding of urine, insufficient intake or too short retention of urine in the bladder.[2]

Attention: Nitrogen oxides present in the atmosphere may have an influence on the stability of the nitrite test parameter.

PRO: False positive readings may be found after infusion of polyvinylpyrrolidone (blood substitute).[2]

UBG: Drugs that turn red in an acid environment (e.g. phenazopyridine) may produce false positive readings or reddish colorations on the test parameter for urobilinogen.[5]

BIL: Drugs that turn red in an acid environment (e.g. phenazopyridine) may produce false positive readings or reddish colorations on the test parameter for bilirubin.[5]

Blood/ERY: The result values refer to intact erythrocytes. At concentrations of about 5-50 Ery/µL, significant hemolysis (such as may occur on prolonged standing of the urine) leads to values which are higher than the corresponding concentrations given for intact erythrocytes. In women the test for blood may be falsified from 3 days before to 3 days after menstruation. It is therefore advisable not to perform the test during this time. After physical activity, e.g. strenuous jogging, raised values for erythrocytes and protein may occur without being signs of disease.[6]

Note: A selection of relevant commercially available drugs or their metabolites were tested. For questionable results, repeat the test after discontinuing a particular drug.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

Expected values

Based on literature. Current medical guidelines are leading.

Parameter	Expected value	Additional information
pH	5 - 9[7]	
LEU	< 10 Leu/µL[2]	10 - 100 Leu/µL borderline[2]
NIT	< 1 µmol/L (< 0.005 mg/dL)[8]	A positive result is indicative of urinary tract infection, but a negative result does not rule out UTI.[5]
PRO	≤ 30 mg/dL[9]	> 30 mg/dL proteinuria[9]
GLU	< 25 mg/dL < 1.4 mmol/L[10]	For daytime urine. Using semi-quantitative reagent strips, expected values in a healthy population are negative.[11]
KET	≤ 2 mg acetoacetic acid/dL[12]	Borderline > 2 mg up to 50 mg acetoacetic acid/dL[12]
UBG	< 1 mg/dL[a),4]	1 - 4 mg/dL borderline (4 mg/dL corresponding to 2+, indicating liver damage)[4]
BIL	neg.[12]	When this method is used, normal urine contains no detectable bilirubin.
ERY/Hb	< 18 Ery/µL (< 3 Ery/HPF)[12]	Hematuria ≥ 18 Ery/µL (≥ 3 Ery/HPF)[13,14]
	Conversion factor 5.8 to translate chamber counting HPF into µL[2]	

a) Values displayed by the instrument are rounded compared to conventional values.

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Result values

Parameter	Result values
pH	5, 6, 6.5, 7, 8, 9
LEU	NEG, 25, 100, 500 Leu/µL NEG, 1+, 2+, 3+
NIT	NEG, POS

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Parameter	Result values
PRO	NEG, 25, 75, 150, 500 mg/dL NEG, 0.25, 0.75, 1.5, 5.0 g/L NEG, 1+, 2+, 3+, 4+
GLU	NORM, 50, 100, 300, 1000 mg/dL NORM, 3, 6, 17, 56 mmol/L NORM, 1+, 2+, 3+, 4+
KET	NEG, 5, 15, 50, 150 mg/dL NEG, 0.5, 1.5, 5, 15 mmol/L NEG, 1+, 2+, 3+, 4+
UBG	NORM, 1, 4, 8, 12 mg/dL NORM, 17, 68, 135, 203 µmol/L NORM, 1+, 2+, 3+, 4+
BIL	NEG, 1, 3, 6 mg/dL NEG, 17, 50, 100 µmol/L NEG, 1+, 2+, 3+
ERY	NEG, 10, 25, 50, 150, 250 Ery/µL NEG, 1+, 2+, 3+, 4+, 5+
COL	pale yellow, yellow, amber, brown, orange, red, green, others

Specific performance data

Representative performance data are given below. Results obtained in individual laboratories may differ.

The values specified for the analytical sensitivity are defined as the concentration of the analyte which leads to a positive result in ≥ 90 % of the examined urines. For pH, analytical sensitivity is not applicable (N.A.). The method comparison data of **cobas u** 601 urine analyzer with **cobas u** 411 urine analyzer and **cobas u** 601 urine analyzer with URISYS 2400 Analyzer (for COL) using at least 1348 clinical samples are presented below. Method comparison results for specific gravity and clarity are presented in the Performance Data Document of the **cobas u** 601 urine analyzer, addendum to the Operators Manual.

Parameter	Analytical sensitivity	Method comparison[b)]
pH	N. A.	Ident.: 77 % pH 5+6: 98 % pH 8+9: 88 %
LEU	10 - 30 Leu/µL	NEG: 91 % POS: 97 %
NIT	0.03 - 0.07 mg/dL	NEG: 95 % POS: 94 %
PRO	10 - 18 mg/dL albumin	NEG: 96 % POS: 93 %
GLU	20 - 40 mg/dL	NEG: 98 % POS: 100 %
KET	3 - 7 mg/dL	NEG: 94 % POS: 96 %
UBG	1.0 - 1.6 mg/dL	NEG: 96 % POS: 98 %
BIL	0.4 - 0.6 mg/dL	NEG: 93 % POS: 95 %
ERY	3 - 15 Ery/µL	NEG: 95 % POS: 96 %
COL	N. A.	Pale yellow+yellow: 94 % Amber: 73 % Brown: 92 % Red: 100 %

b) The values for neg and pos indicate the proportion of concordant negative or positive results.

Precision

Precision experiments comprised an assessment of repeatability (within-run precision) and intermediate precision.

Repeatability was checked in 2 separate runs with 21 measurements each for the tested controls. In total there were 42 measurements performed per used control.

Intermediate precision was assessed over 21 days with 2 runs per day and duplicate measurements per used control. In total there were 84 measurements performed per used control.

The following results were obtained:

Repeatability			
Parameter	**Control[c)]**	**Result**	**Exact agreement**
pH	Level 1	6.5	100 %
	Level 2	7	100 %
LEU	Level 1	NEG	100 %
	Level 2	500 Leu/µL	100 %
NIT	Level 1	NEG	100 %
	Level 2	POS	100 %
PRO	Level 1	NEG	100 %
	Level 2	150 mg/dL	100 %
GLU	Level 1	NORM	100 %
	Level 2	1000 mg/dL	100 %
KET	Level 1	NEG	100 %
	Level 2	150 mg/dL	100 %
UBG	Level 1	NORM	100 %
	Level 2	12 mg/dL	100 %
BIL	Level 1	NEG	100 %
	Level 2	6 mg/dL	100 %
ERY	Level 1	NEG	100 %
	Level 2	250 Ery/µL	100 %
COL	Level 1	Yellow	100 %
	Level 2	Brown	100 %

c) BIO-RAD Liquichek

Intermediate precision			
Parameter	**Control[c)]**	**Result**	**Exact agreement**
pH	Level 1	6.5	100 %
	Level 2	7	100 %
LEU	Level 1	NEG	100 %
	Level 2	500 Leu/µL	100 %
NIT	Level 1	NEG	100 %
	Level 2	POS	100 %
PRO	Level 1	NEG	100 %
	Level 2	150 mg/dL	100 %
GLU	Level 1	NORM	100 %
	Level 2	1000 mg/dL	100 %
KET	Level 1	NEG	100 %
	Level 2	150 mg/dL	100 %
UBG	Level 1	NORM	100 %
	Level 2	12 mg/dL	100 %
BIL	Level 1	NEG	100 %
	Level 2	6 mg/dL	100 %

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Intermediate precision			
Parameter	**Control[c)]**	**Result**	**Exact agreement**
ERY	Level 1	NEG	100 %
	Level 2	250 Ery/µL	100 %
COL	Level 1	Yellow	100 %
	Level 2	Brown	100 %

References

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For further information, please refer to the appropriate Operators Manual for the analyzer concerned, and the Method Sheets of all necessary components.

A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

CONTENT	Contents of kit
SYSTEM	Analyzers/Instruments on which reagents can be used
REAGENT	Reagent
CALIBRATOR	Calibrator
→	Volume for reconstitution
GTIN	Global Trade Item Number
UDI	Unique Device Identifier

Rx only

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

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