

Glucose HK**Order information**

REF	CONTENT		Analyzer(s) on which cobas c pack(s) can be used
04404483 190	Glucose HK 800 tests	System-ID 07 6831 6	Roche/Hitachi cobas c 311, cobas c 501/502
10759350 190	Calibrator f.a.s. (12 x 3 mL)	Code 401	
12149435 122	Precinorm U plus (10 x 3 mL)	Code 300	
12149443 122	Precipath U plus (10 x 3 mL)	Code 301	
10171743 122	Precinorm U (20 x 5 mL)	Code 300	
10171735 122	Precinorm U (4 x 5 mL)	Code 300	
10171778 122	Precipath U (20 x 5 mL)	Code 301	
10171760 122	Precipath U (4 x 5 mL)	Code 301	
05117003 190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626 190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05117216 190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774 190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
04489357 190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English**System information**

For **cobas c** 311/501 analyzers:

GLUC3: ACN 717

SGLU3: ACN 668 (STAT, reaction time: 7)

For **cobas c** 502 analyzer:

GLUC3: ACN 8717

SGLU3: ACN 8668 (STAT, reaction time: 7)

Intended use

In vitro test for the quantitative determination of glucose in human serum, plasma, urine and CSF on Roche/Hitachi **cobas c** systems.

Summary^{1,2,3}

Glucose is the major carbohydrate present in the peripheral blood. Oxidation of glucose is the major source of cellular energy in the body. Glucose derived from dietary sources is converted to glycogen for storage in the liver or to fatty acids for storage in adipose tissue. The concentration of glucose in blood is controlled within narrow limits by many hormones, the most important of which are produced by the pancreas.

The most frequent cause of hyperglycemia is diabetes mellitus resulting from a deficiency in insulin secretion or action. A number of secondary factors also contribute to elevated blood glucose levels. These include pancreatitis, thyroid dysfunction, renal failure and liver disease.

Hypoglycemia is less frequently observed. A variety of conditions may cause low blood glucose levels such as insulinoma, hypopituitarism or insulin induced hypoglycemia. Glucose measurement in urine is used as a diabetes screening procedure and to aid in the evaluation of glycosuria, to detect renal tubular defects, and in the management of diabetes mellitus. Glucose measurement in cerebrospinal fluid is used for evaluation of meningitis, neoplastic involvement of meninges and other neurological disorders.

Test principle

UV test

Enzymatic reference method with hexokinase.^{4,5}

Hexokinase catalyzes the phosphorylation of glucose to glucose-6-phosphate by ATP.



Glucose-6-phosphate dehydrogenase oxidizes glucose-6-phosphate in the presence of NADP to gluconate-6-phosphate. No other carbohydrate is oxidized. The rate of NADPH formation during the reaction is directly proportional to the glucose concentration and is measured photometrically.

**Reagents - working solutions**

R1 MES buffer: 5.0 mmol/L, pH 6.0; Mg²⁺: 24 mmol/L; ATP: ≥ 4.5 mmol/L; NADP: ≥ 7.0 mmol/L; preservative

R2 HEPES buffer: 200 mmol/L, pH 8.0; Mg²⁺: 4 mmol/L; HK (yeast): ≥ 300 µkat/L; G-6-PDH (E. coli): ≥ 300 µkat/L; preservative

R1 is in position B and R2 is in position C.

Precautions and warnings

For in vitro diagnostic use.

Exercise the normal precautions required for handling all laboratory reagents.

Disposal of all waste material should be in accordance with local guidelines. Safety data sheet available for professional user on request.

Reagent handling

Ready for use

Storage and stability**GLUC3**

Shelf life at 2-8 °C: See expiration date on **cobas c** pack label.

On-board in use and refrigerated on the analyzer: 8 weeks

Diluent NaCl 9 %

Shelf life at 2-8 °C: See expiration date on **cobas c** pack label.

On-board in use and refrigerated on the analyzer: 12 weeks

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable. Serum.

Plasma: Li-heparin, K₂-EDTA, NaF/Na₂EDTA, KF/Na₂EDTA, NaF/K-Oxalate and NaF/citrate/Na₂-EDTA.

Collect blood by venipuncture from fasting individuals using an evacuated tube system. The stability of glucose in specimens is affected by storage temperature, bacterial contamination, and glycolysis. Plasma or serum samples without preservative (NaF) should be separated from the cells or clot within half an hour of being drawn. When blood is drawn and permitted to clot and to stand uncentrifuged at room temperature, the average decrease in serum glucose is ~ 7 % in 1 hour (0.28 to 0.56 mmol/L or 5 to 10 mg/dL). This decrease is the result of glycolysis. Glycolysis can be inhibited by collecting the specimen in fluoride tubes.¹

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all

available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Stability (no hemolysis): ⁵	8 hours at 15-25 °C
	72 hours at 2-8 °C
Stability in fluoride plasma: ⁶	3 days at 15-25 °C

Urine.

Collect urine in a dark bottle. For 24-hour urine collections, glucose may be preserved by adding 5 mL of glacial acetic acid to the container before collection. Unpreserved urine samples may lose up to 40 % of their glucose after 24-hour storage at room temperature.³ Therefore, keep samples on ice during collection.⁵

CSF.

Cerebrospinal fluid may be contaminated with bacteria and often contains other cellular constituents. CSF samples should therefore be analyzed for glucose immediately or stored at 4 °C or -20 °C.^{3,5}

Centrifuge samples containing precipitates before performing the assay.

Materials provided

See "Reagents – working solutions" section for reagents.

Materials required (but not provided)

- See "Order information" section
- General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator's manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum, plasma, urine and CSF

cobas c 311 test definition

Assay type	2-Point End		
Reaction time / Assay points	10 / 6-32 (STAT 7 / 6-32)		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Increase		
Units	mmol/L (mg/dL, g/L)		
Reagent pipetting	Diluent (H ₂ O)		
R1	28 µL	141 µL	
R2	10 µL	20 µL	

Sample volumes	Sample	Sample dilution	
		Sample	Diluent (NaCl)
Normal	2 µL	–	–
Decreased	10 µL	15 µL	135 µL
Increased	2 µL	–	–

cobas c 501 test definition

Assay type	2-Point End		
Reaction time / Assay points	10 / 10-47 (STAT 7 / 10-47)		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Increase		
Units	mmol/L (mg/dL, g/L)		
Reagent pipetting	Diluent (H ₂ O)		
R1	28 µL	141 µL	

R2	10 µL	20 µL	
Sample volumes	Sample	Sample dilution	
		Sample	Diluent (NaCl)
Normal	2 µL	–	–
Decreased	10 µL	15 µL	135 µL
Increased	2 µL	–	–

cobas c 502 test definition

Assay type	2-Point End		
Reaction time / Assay points	10 / 10-47 (STAT 7 / 10-47)		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Increase		
Units	mmol/L (mg/dL, g/L)		
Reagent pipetting	Diluent (H ₂ O)		
R1	28 µL	141 µL	
R2	10 µL	20 µL	

Sample volumes	Sample	Sample dilution	
		Sample	Diluent (NaCl)
Normal	2 µL	–	–
Decreased	10 µL	15 µL	135 µL
Increased	4 µL	–	–

Calibration

Calibrators	S1: H ₂ O S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	2-point calibration - after reagent lot change - as required following quality control procedures

Traceability: This method has been standardized against ID/MS.

Quality control

For quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

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

Roche/Hitachi **cobas c** systems automatically calculate the analyte concentration of each sample.

Conversion factors:	mmol/L x 18.02 = mg/dL
	mmol/L x 0.1802 = g/L
	mg/dL x 0.0555 = mmol/L

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at a glucose concentration of 3.9 mmol/L (70.3 mg/dL).

Serum/plasma

Icterus:⁷ No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:⁷ No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):⁷ No significant interference up to an L index of 1000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.^{8,9}

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.¹⁰

Urine

Drugs: No interference was found at therapeutic concentrations using common drug panels.⁹

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

NOTE: Glucose values achieved on some proficiency testing materials, when evaluated against a glucose oxidase-oxygen electrode comparison method, demonstrate an approximate 3 % positive bias on average.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on Roche/Hitachi **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/Multiclean/SCCS or the NaOHD/SMS/SmpCin1+2/SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is not required.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

Serum, plasma, urine and CSF

0.11-41.6 mmol/L (2-750 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:2 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 2.

Lower limits of measurement

Lower detection limit of the test

0.11 mmol/L (2 mg/dL)

Limit of Blank = 0.11 mmol/L (2 mg/dL)

Limit of Detection = 0.11 mmol/L (2 mg/dL)

Limit of Quantitation = 0.11 mmol/L (2 mg/dL)

The Limit of Blank and Limit of Detection were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A requirements.

The Limit of Blank is the 95th percentile value from $n \geq 60$ measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a total error of 20 %. It has been determined using low concentration glucose samples.

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 3 standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, $n = 21$).

Expected values

Plasma¹¹

Fasting 4.11-6.05 mmol/L (74-109 mg/dL)

Urine¹²

1st morning urine 0.3-1.1 mmol/L (6-20 mg/dL)

24-hour urine 0.3-0.96 mmol/L (6-17 mg/dL)

(average of 1350 mL urine/24 h)

acc. to Tietz:⁵

Serum, plasma

Adults 4.11-5.89 mmol/L (74-106 mg/dL)

60-90 years 4.56-6.38 mmol/L (82-115 mg/dL)

> 90 years 4.16-6.72 mmol/L (75-121 mg/dL)

Children 3.33-5.55 mmol/L (60-100 mg/dL)

Neonates (1 day) 2.22-3.33 mmol/L (40-60 mg/dL)

Neonates (> 1 day) 2.78-4.44 mmol/L (50-80 mg/dL)

Urine

24-hour urine < 2.78 mmol/24 h (< 0.5 g/24 h)

Random urine 0.06-0.83 mmol/L (1-15 mg/dL)

CSF

Children 3.33-4.44 mmol/L (60-80 mg/dL)

Adults 2.22-3.89 mmol/L (40-70 mg/dL)

CSF glucose values should be approximately 60 % of the plasma values and must always be compared with concurrently measured plasma values for adequate clinical interpretation.

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

Specific performance data

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

Precision

Precision was determined using human samples and controls in an internal protocol serum/plasma: with repeatability ($n = 21$) and intermediate precision (3 aliquots per run, 1 run per day, 21 days); urine/CSF: with repeatability ($n = 21$) and intermediate precision (3 aliquots per run, 1 run per day, 10 days). The following results were obtained:

Serum/plasma

Repeatability	Mean	SD	CV
	mmol/L (mg/dL)	mmol/L (mg/dL)	%
Precinorm U	5.49 (98.9)	0.05 (0.9)	1.0
Precipath U	13.6 (245)	0.1 (2)	0.9
Human serum 1	7.74 (139)	0.05 (1)	0.7
Human serum 2	5.41 (97.5)	0.04 (0.7)	0.7

Intermediate precision

Intermediate precision	Mean	SD	CV
	mmol/L (mg/dL)	mmol/L (mg/dL)	%
Precinorm U	5.38 (96.9)	0.07 (1.3)	1.3
Precipath U	13.4 (241)	0.2 (2)	1.1
Human serum 3	7.61 (137)	0.09 (2)	1.2
Human serum 4	5.28 (95.1)	0.06 (1.1)	1.1

Urine

Repeatability	Mean	SD	CV
	mmol/L (mg/dL)	mmol/L (mg/dL)	%
Control Level 1	1.54 (27.8)	0.02 (0.4)	1.1
Control Level 2	15.7 (283)	0.1 (2)	0.9
Human urine 1	5.00 (90.1)	0.05 (0.9)	1.0
Human urine 2	10.5 (189)	0.1 (2)	1.1

Intermediate precision	Mean	SD	CV
	mmol/L (mg/dL)	mmol/L (mg/dL)	%
Control Level 1	1.51 (27.2)	0.01 (0.2)	1.0
Control Level 2	15.4 (278)	0.1 (2)	0.8
Human urine 3	4.86 (87.6)	0.05 (0.9)	1.0
Human urine 4	10.3 (186)	0.1 (2)	0.8

CSF

Repeatability	Mean	SD	CV
	mmol/L (mg/dL)	mmol/L (mg/dL)	%
Precinorm U	5.43 (97.8)	0.04 (0.7)	0.8
Precipath U	13.6 (245)	0.1 (2)	0.8
Human CSF 1	3.04 (54.8)	0.03 (0.5)	0.9
Human CSF 2	8.43 (152)	0.08 (1)	1.0

Intermediate precision	Mean	SD	CV
	mmol/L (mg/dL)	mmol/L (mg/dL)	%
Precinorm U	5.37 (96.8)	0.07 (1.3)	1.3
Precipath U	13.4 (241)	0.2 (4)	1.1
Human CSF 3	3.00 (54.1)	0.04 (0.7)	1.5
Human CSF 4	8.30 (150)	0.10 (2)	1.2

Method comparison

Glucose values for human serum, plasma, urine and CSF samples obtained on a Roche/Hitachi **cobas c** 501 analyzer (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi MODULAR P analyzer (x).

Serum/plasma

Sample size (n) = 75

Passing/Bablok ¹³	Linear regression
$y = 1.000x + 0.118 \text{ mmol/L}$	$y = 0.996x + 0.179 \text{ mmol/L}$
$\tau = 0.983$	$r = 1.000$

The sample concentrations were between 1.64 and 34.1 mmol/L (28.8 and 614 mg/dL).

Urine

Sample size (n) = 75

Passing/Bablok ¹³	Linear regression
$y = 1.000x + 0.060 \text{ mmol/L}$	$y = 1.001x + 0.045 \text{ mmol/L}$
$\tau = 0.972$	$r = 1.000$

The sample concentrations were between 0.16 and 39.5 mmol/L (2.88 and 712 mg/dL).

CSF

Sample size (n) = 75

Passing/Bablok ¹³	Linear regression
$y = 1.000x - 0.020 \text{ mmol/L}$	$y = 1.001x - 0.038 \text{ mmol/L}$

$\tau = 0.980$

$r = 1.000$

The sample concentrations were between 0.92 and 38.0 mmol/L (16.6 and 685 mg/dL).

References

- Sacks DB. Carbohydrates. In: Tietz NW, ed. Fundamentals of Clinical Chemistry. 4th ed. Philadelphia: WB Saunders 1996;351-374.
- Knudson PE, Weinstock RS. Carbohydrates. In: Henry JB, ed. Clinical Diagnosis and Management by Laboratory Methods. 20th ed. Philadelphia: WB Saunders 2001;211-223.
- Sacks DB. Carbohydrates. In: Burtis CA, Ashwood ER, eds. Tietz Textbook of Clinical Chemistry. 3rd ed. Philadelphia: WB Saunders 1999;750-785.
- Kunst A, Draeger B, Ziegenhorn J. In: Bergmeyer. Methods of Enzymatic Analysis, 3rd ed. Volume VI, Metabolites 1: Carbohydrates 1984;163-172.
- Tietz NW, ed. Clinical Guide to Laboratory Tests, 4th ed. Philadelphia: WB Saunders Co 2006;444-451.
- Tietz NW. Fundamentals of Clinical Chemistry, 6th ed. Saunders Elsevier 2008;389.
- Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.
- Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.
- Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001;38:376-385.
- Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.
- Thomas L, ed. Blutglucose. In: Thomas L, ed. Labor und Diagnose, 6th ed. Frankfurt/Main: TH-Books 2005;193-199.
- Krieg M, Gunsser KJ, Steinhagen-Thiessen E, et al. Comparative quantitative clinico-chemical analysis of the characteristics of 24-hour urine and morning urine. J Clin Chem Clin Biochem 1986 Nov;24(11):863-869.
- Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

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.

Symbols

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

 CONTENT

Contents of kit



Volume after reconstitution or mixing

 GTIN

Global Trade Item Number

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