GLDH3

cobas®

GLDH Gen.3

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
11929992 216	GLDH Gen.3 (4 x 100 tests)	System-ID 07 6789 1	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	
04593138 190	**cobas c** pack MULTI		
On request	Open/Close tool		

English

System information

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

GLDH3: ACN 588

For **cobas c** 502 analyzer:

GLDH3: ACN 8588

Intended use

In vitro test for the quantitative determination of glutamate dehydrogenase (GLDH) in human serum and plasma on Roche/Hitachi **cobas c** systems.

Summary[1,2,3]

GLDH is a largely liver-specific enzyme found exclusively in the mitochondria and located predominantly within the liver cell acinus. GLDH activity in other organs such as the kidneys, pancreas, heart, brain and intestines is negligible. Determination of GLDH activity is performed to diagnose liver disorders, and in particular to assess the severity of damage to individual cells. Necrotizing liver damage such as acute hepatic dystrophy, necrotizing hepatitis, multiple liver metastases and obstructive jaundice are accompanied by elevated GLDH activities in serum.

In 1972, the German Society for Clinical Chemistry (DGKC) recommended the optimized standard method for determination of GLDH with optimized substrate concentration, NADH excess, and activation of GLDH by addition of ADP. The method described here is derived from the formulation recommended by the German Society for Clinical Chemistry (DGKC) and optimized for performance and stability.

Test principle

UV test according to a standardized method.

The GLDH enzyme catalyzes this NADH-dependent reaction; the equilibrium is on the side of glutamate and NAD.

$$\alpha\text{-ketoglutarate} + NADH + NH_4^+ \xrightarrow{GLDH} \text{glutamate} + NAD^+ + H_2O$$

The decrease in NADH is directly proportional to the GLDH activity.

Reagents - working solutions

R1	Triethanolamine buffer: 60 mmol/L, pH 8.0; EDTA: 3.1 mmol/L; ammonium acetate: 124 mmol/L; ADP: ≥ 1.36 mmol/L; NADH (yeast): 0.27 mmol/L; LDH (rabbit muscle): ≥ 45 µkat/L; stabilizers; preservative
R2	Triethanolamine buffer: 8.6 mmol/L, pH 7.9; α-ketoglutarate: 48 mmol/L; stabilizers; preservative

Reagent preparation and cobas c pack MULTI assembly

Reagent handling

R1	Connect one bottle 1 to one bottle 1a using the enclosed adapter and dissolve the lyophilizate completely in the buffer.
R2	Ready for use.

Labeling the **cobas c** *pack MULTI*

Turn the barcode labeled side of a new **cobas c** pack MULTI toward you. Affix the supplied GLDH3 barcode label directly over the existing barcode label.

Filling the **cobas c** *pack MULTI*

1. Turn the **cobas c** pack MULTI toward you as shown above.
2. Position A of the **cobas c** pack MULTI is now in the center, position B on the left side, position C on the right side of the **cobas c** pack.
3. Unscrew the screw cap of the bottle in position A in the center of the **cobas c** pack MULTI using the Open/Close tool.
4. Pour the content of bottle 1 (19 mL) into the opened bottle of the **cobas c** pack (position A).
5. Close the bottle tightly using the Open/Close tool.
6. Unscrew the screw cap of the bottle in position C on the right side of the **cobas c** pack MULTI using the Open/Close tool.
7. Pour the content of bottle 2 (5 mL) into the opened bottle of the **cobas c** pack (position C).
8. Close the bottle tightly using the Open/Close tool.
9. Leave position B empty.

The GLDH3 **cobas c** pack is now ready for use.

GLDH3

GLDH Gen.3

Note

Use only the **cobas c** *pack MULTI. Always use a new* **cobas c** *pack MULTI when preparing fresh reagent. Never reuse accessories designed for single use, as this may result in reagent contamination and could affect test results. If the* **cobas c** *pack MULTI bottles are not filled correctly, this may result in faulty reagent pipetting and could cause erroneous results.*

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.

Storage and stability

GLDH3

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	3 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 and K_2-EDTA plasma

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.

Centrifuge samples containing precipitates before performing the assay.

Stability:[4]	7 days at 15-25 °C 7 days at 2-8 °C 4 weeks at (-15)-(-25) °C

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 and plasma

cobas c 311 **test definition**

Assay type	Rate A		
Reaction time / Assay points	10 / 13-31		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Decrease		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H_2O)	
R1	90 µL	–	
R2	20 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	12.5 µL	–	–
Decreased	2.5 µL	–	–
Increased	12.5 µL	–	–

cobas c 501 **test definition**

Assay type	Rate A		
Reaction time / Assay points	10 / 19-46		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Decrease		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H_2O)	
R1	90 µL	–	
R2	20 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	12.5 µL	–	–
Decreased	2.5 µL	–	–
Increased	12.5 µL	–	–

cobas c 502 **test definition**

Assay type	Rate A		
Reaction time / Assay points	10 / 19-46		
Wavelength (sub/main)	700/340 nm		
Reaction direction	Decrease		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H_2O)	
R1	90 µL	–	
R2	20 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	12.5 µL	–	–
Decreased	2.5 µL	–	–
Increased	25 µL	–	–

Calibration

Calibrators	S1: H_2O S2: C.f.a.s.
Calibration mode	Linear
Calibration frequency	2-point calibration - after 7 days on board - after lot change - as required following quality control procedures

Traceability: This method has been standardized against the Roche system reagent using calibrated pipettes together with a manual photometer providing absolute values and the substrate-specific absorptivity, ε.

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.

GLDH3

GLDH Gen.3

cobas®

Calculation

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

Conversion factor: U/L x 0.0167 = µkat/L

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at a glutamate dehydrogenase activity of 6 U/L (0.1 µkat/L).

Icterus:[5] 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:[5] No significant interference up to an H index of 50 (approximate hemoglobin concentration: 31.0 µmol/L or 50 mg/dL). Contamination with erythrocytes will elevate results, because the analyte level in erythrocytes is higher than in normal sera. The level of interference may be variable depending on the content of analyte in the lysed erythrocytes.

Lipemia (Intralipid):[5] No significant interference up to an L index of 100. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Pyruvate: No significant interference up to a pyruvate concentration of 300 µmol/L (26 mg/dL).

Ammonia, which is produced in the cuvette when determining GLDH, interferes with the determination of urea/BUN. The GLDH reagent must therefore not be placed on the analyzer together with reagents for ammonia or the determination of urea/BUN.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[6,7].

Exceptions: Temozolomide at therapeutic concentrations may lead to erroneous results.

Physiological plasma concentrations of Sulfasalazine or Sulfapyridine may lead to false results.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[8]

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

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-SmpCln1+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

1-80 U/L (0.0167-1.34 µkat/L)

Determine samples having higher activities via the rerun function. For samples with higher activities, the rerun function decreases the sample volume by a factor of 5. The results are automatically multiplied by this factor.

Lower limits of measurement

Lower detection limit of the test:

1 U/L (0.0167 µkat/L)

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

Adults[2,9,a)]

Males	up to 6.4 U/L	(up to 0.11 µkat/L)
Females	up to 4.8 U/L	(up to 0.08 µkat/L)

Consensus values for adults[10]

Males	up to 7.0 U/L	(up to 0.12 µkat/L)
Females	up to 5.0 U/L	(up to 0.08 µkat/L)

Reference ranges for children are given in the brochure "Reference Ranges for Adults and Children. Pre-Analytical Considerations". Heil W, Koberstein R, Zawta B (published by Roche Diagnostics GmbH, 2004).

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

a) Calculated with a temperature conversion factor of 1.61 (25 -> 37 °C).[11]

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 with repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 3 days). The following results were obtained:

Repeatability	*Mean U/L (µkat/L)*	*SD U/L (µkat/L)*	*CV %*
Precinorm U	20.8 (0.347)	0.2 (0.003)	0.8
Precipath U	30.4 (0.508)	0.1 (0.002)	0.5
Human serum 1	4.78 (0.017)	0.14 (0.002)	2.9
Human serum 2	10.1 (0.169)	0.2 (0.003)	2.0
Intermediate precision	*Mean U/L (µkat/L)*	*SD U/L (µkat/L)*	*CV %*
Precinorm U	23.8 (0.397)	0.2 (0.004)	1.0
Precipath U	32.7 (0.546)	0.3 (0.004)	0.8
Human serum 3	1.04 (0.017)	0.21 (0.003)	20.0
Human serum 4	21.3 (0.356)	0.3 (0.005)	1.5

Method comparison

Glutamate dehydrogenase values for human serum and plasma samples obtained on a Roche/Hitachi **cobas c** 501 analyzer (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x).

Sample size (n) = 59

Passing/Bablok[12]	Linear regression
y = 0.982x + 0.296 U/L	y = 0.995x + 0.254 U/L
τ = 0.902	r = 0.998

The sample activities were between 1.00 and 70.0 U/L (0.017 and 1.17 µkat/L).

References

1 Greiling H, Gressner AM, eds. Lehrbuch der Klinischen Chemie und Pathobiochemie, 3rd ed. Stuttgart/New York: Schattauer Verlag 1995.

2 Chemnitz G, Schmidt E, Schmidt FW, et al. Diagnostische und prognostische Bedeutung massiv erhöhter Glutamat-Dehydrogenase-Aktivität im Serum. Dtsch Med Wschr 1984;109:1789-1793.

3 Deutsche Gesellschaft für Klinische Chemie: Empfehlungen der Deutschen Gesellschaft für Klinische Chemie (DGKC). J Clin Chem Clin Biochem 1972;10:182-193.

4 Guder WG, Narayanan S, Wisser H, et al. List of Analytes; Preanalytical Variables. Brochure in: Samples: From the Patient to the Laboratory. Darmstadt: GIT-Verlag 1996.

5 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

6 Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.

7 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.

8 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

9 Wallnöfer H, Schmidt E, Schmidt FW, eds. Synopsis der Leberkrankheiten. Stuttgart: Georg Thieme Verlag 1974.

10 Thomas L, Müller M, Schumann G, et al Consensus of DGKL and VDGH for interim reference intervals on enzymes in serum. J Lab Med 2005; 29(5):301-308.

11 Zawta B, Klein G, Bablok W. Temperature Conversion in Clinical Enzymology? Klin Lab 1994;40:33-42.

12 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

CE

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com