05402425001V8.0

GGT-2

cobas®

γ-Glutamyltransferase ver.2

Order information

REF	CONTENT	Analyzer(s) on which kit(s) can be used
05401461190	γ-Glutamyltransferase ver.2 (2 × 100 tests)	**cobas c** 111

Materials required (but not provided):

10759350190	Calibrator f.a.s. (12 × 3 mL)	Code 401	
12149435122	Precinorm U plus (10 × 3 mL)	Code 300	
12149443122	Precipath U plus (10 × 3 mL)	Code 301	
05117003190	PreciControl ClinChem Multi 1 (20 × 5 mL)	Code 391	
05947626190	PreciControl ClinChem Multi 1 (4 × 5 mL)	Code 391	
05117216190	PreciControl ClinChem Multi 2 (20 × 5 mL)	Code 392	
05947774190	PreciControl ClinChem Multi 2 (4 × 5 mL)	Code 392	

English

System information

GGTS2: ACN 480: Szasz standardization

GGTI2: ACN 220: IFCC standardization

Intended use

In vitro test for the quantitative determination of γ-glutamyltransferase in human serum and plasma on the **cobas c** 111 system.

Summary

Measurements of γ-glutamyltransferase (GGT) performed with this assay in human serum and plasma are used in the diagnosis and monitoring of hepatobiliary diseases, as well as a screening test for occult alcoholism.

Mature GGT is a dimeric glycoprotein weighing 68 kDa. It is found in the kidneys, liver, pancreas, and intestine, with the highest abundance in renal tissue. However, the primary source of GGT activity in the serum is the liver.[1]

In clinical practice, GGT serum levels are typically measured alongside a full blood count, bilirubin, albumin, transaminases (ALT and AST), and alkaline phosphatases (ALP) as an initial investigation for potential liver disease.[2] GGT is considered one of the most reliable indicators for the development of liver disease.[3] Multiple guidelines recommend GGT testing as part of the diagnostic workup and monitoring for various liver diseases. Additionally, GGT serves as a well-established marker for alcohol-related liver disease and excessive alcohol consumption.[4,5,6,7,8,9,10] Increased GGT is observed as a result of obesity, excess alcohol consumption or may be induced by drugs, including phenobarbital and phenytoin.[1]

In 1969, Szasz published the first kinetic procedure for GGT in serum using γ-glutamyl-p-nitroanilide as substrate and glycylglycine as acceptor.[11] In order to circumvent the poor solubility of γ-glutamyl-p-nitroanilide, Persijn and van der Slik investigated various derivatives and found the water-soluble substrate L-γ-glutamyl-3-carboxy-4-nitroanilide to be superior in terms of stability and solubility.[12] The results correlate with those derived using the original substrate.

In 2002, the International Federation of Clinical Chemistry (IFCC) recommended the standardized method for determining GGT including optimization of substrate concentrations, employment of NaOH, glycylglycine buffer and sample start.[13,14] The GGT liquid reagent follows the formulation recommendation according to Szasz, but was optimized for performance and stability. The assay is optionally standardized against the original IFCC and Szasz methods. The performance claims and data presented here are independent from the standardization.

Test principle[15]

Enzymatic colorimetric assay

γ-glutamyltransferase transfers the γ-glutamyl group of L-γ-glutamyl-3-carboxy-4-nitroanilide to glycylglycine.

$$\text{L-γ-glutamyl-3-carboxy-4-nitroanilide + glycylglycine} \xrightarrow{\text{GGT}} \text{L-γ-glutamyl-glycylglycine + 5-amino-2-nitrobenzoate}$$

The amount of 5-amino-2-nitrobenzoate liberated is proportional to the GGT activity in the sample. It is determined by measuring the increase in absorbance photometrically.

Reagents - working solutions

R1 TRIS: 492 mmol/L, pH 8.25; glycylglycine: 492 mmol/L; preservative; additive

SR L-γ-glutamyl-3-carboxy-4-nitroanilide: 22.5 mmol/L; acetate: 10 mmol/L, pH 4.5; stabilizer; preservative

Precautions and warnings

For in vitro diagnostic use for health care 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.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317	May cause an allergic skin reaction.

Prevention:

P261	Avoid breathing mist or vapours.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves.

Response:

P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

Disposal:

P501	Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.
Contact phone: all countries: +49-621-7590

Reagent handling

Ready for use

GGT-2

γ-Glutamyltransferase ver.2

cobas®

Storage and stability

Shelf life at 2-8 °C:	See expiration date on reagent
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: Collect serum using standard sampling tubes.
Plasma: Li-heparin, K_3-EDTA plasma.
Note: K_3-EDTA plasma values are approximately 6 % lower than serum values.

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.

See the limitations and interferences section for details about possible sample interferences.

Stability:[16,17]	7 days at 15-25 °C
	7 days at 2-8 °C
	1 year at -20 °C (± 5 °C)

Freeze only once.

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 111 **test definition**

Measuring mode	Absorbance
Abs. calculation mode	Kinetic
Reaction direction	Increase
Wavelength A/B	409/659 nm
Calc. first/last	26/38
Unit	U/L
Reaction mode	R1-S-SR

Pipetting parameters

		Diluent (H_2O)
R1	25 µL	35 µL
Sample	3 µL	20 µL
SR	20 µL	20 µL
Total volume	123 µL	

Calibration

Calibrators	Calibrator f.a.s. Standard 2 is defined by a fixed value.
Calibration mode	Linear regression
Calibration interval	Each lot and as required following quality control procedures.

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against the original IFCC formulation (2002)[13] and against the GGT method published by Persijn and van der Slik (1976),[12] respectively.

Use the appropriate calibrator value for the corresponding application.

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

The **cobas c** 111 analyzer automatically calculates the analyte activity of each sample.

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

Limitations - interference

Criterion: Recovery within ± 4 U/L of initial values of samples ≤ 40 U/L and within ± 10 % for samples > 40 U/L

Icterus:[18] No significant interference up to an I index of 20 for conjugated bilirubin and 48 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 342 µmol/L or 20 mg/dL; approximate unconjugated bilirubin concentration: 821 µmol/L or 48 mg/dL).

Hemolysis:[18] No significant interference up to an H index of 250 (approximate hemoglobin concentration: 402 µmol/L or 250 mg/dL).

Lipemia (Intralipid):[18] No significant interference up to an L index of 800. 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.[19,20]

In very rare cases, gammopathy, in particular type IgM (Waldenström’s macroglobulinemia), may cause unreliable results.[21]

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 the **cobas c** 111 analyzer. For information about test combinations requiring special wash steps, please refer to the latest version of the carry-over evasion list found with the CLEAN Method Sheet and the operator’s manual for further instructions.
Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

3-1200 U/L (0.05-20.0 µkat/L)

Determine samples having higher activities via the rerun function. Dilution of samples via the rerun function is a 1:10 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 10.

GGT-2

γ-Glutamyltransferase ver.2

cobas®

Lower limits of measurement

Lower detection limit of the test:
3 U/L (0.05 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

Standardized against Szasz (Persijn, van der Slik)[22]

Men	8-61 U/L	(0.13-1.02 µkat/L)
Women	5-36 U/L	(0.08-0.60 µkat/L)

Standardized against IFCC

Reference Interval Study at 37 °C (corrected in 2005)[22,23]

Men (n = 216)	10-71 U/L	(0.17-1.19 µkat/L)
Women (n = 228)	6-42 U/L	(0.10-0.70 µkat/L)

Consensus values (IFCC)[24]

Men	< 60 U/L	(< 1.00 µkat/L)
Women	< 40 U/L	(< 0.67 µkat/L)

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 **cobas c** 111 analyzer 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, 10 days). The following results were obtained on the **cobas c** 111 analyzer:

Repeatability	*Mean U/L (µkat/L)*	*SD U/L (µkat/L)*	*CV %*
Precinorm U	44.2 (0.74)	0.6 (0.01)	1.4
Precipath U	221 (3.69)	1 (0.02)	0.4
Human serum 1	29.1 (0.49)	0.6 (0.01)	1.9
Human serum 2	481 (8.03)	2 (0.03)	0.4

Intermediate precision	*Mean U/L (µkat/L)*	*SD U/L (µkat/L)*	*CV %*
Precinorm U	38.3 (0.64)	0.7 (0.01)	1.9
Precipath U	194 (3.24)	1 (0.02)	0.7
Human serum 3	18.1 (0.30)	0.6 (0.01)	3.5
Human serum 4	322 (5.38)	2 (0.03)	0.6

Method comparison

γ-glutamyltransferase values for human serum and plasma samples obtained on a **cobas c** 111 analyzer (y) using the γ-Glutamyltransferase ver.2 reagent (GGT-2) and the application GGTS2 were compared with those determined using the corresponding reagent on a COBAS INTEGRA 400 analyzer (x).
Sample size (n) = 79

Passing/Bablok[25]	Linear regression
y = 1.017x - 0.829 U/L	y = 1.022x - 1.03 U/L
τ = 0.982	r = 1.00

The sample activities were between 8.00 and 1142 U/L (0.134 and 19.1 µkat/L).

References

1 Panteghini M. Serum Enzymes. In: Rifai N, Chiu RWK, Young I, Burnham CAD, Wittwer CT, editors. Tietz Textbook of Laboratory Medicine, Saunders Elsevier, Philadelphia, 7th edition, 2023, chapter 32, p. 350-350.e36.

2 Rosenberg WMC, Badrick T, Lo SF, et al. Liver Disease. In: Rifai N, Chiu RWK, Young I, Burnham CAD, Wittwer CT, editors. Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 7th ed. 2023; p. 701-763.e21.

3 Dillon JF, Miller MH. Gamma glutamyl transferase 'To be or not to be' a liver function test? Ann Clin Biochem 2016 Nov;53(6):629-631.

4 Kwo PY, Cohen SM, Lim JK. ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries. Am J Gastroenterol 2017 Jan;112(1):18-35. doi: 10.1038/ajg.2016.517.

5 Newsome PN, Cramb R, Davison SM, et al. Guidelines on the management of abnormal liver blood tests. Gut 2018 Jan;67(1):6-19. doi: 10.1136/gutjnl-2017-314924.

6 O'Shea RS, Dasarathy S, McCullough AJ; Practice Guideline Committee of the American College of Gastroenterology. Alcoholic liver disease. Hepatology 2010 Jan;51(1):307-328.

7 European Association for the Study of the Liver. Electronic address: easloffice@easloffice.eu; Clinical practice guidelines panel; Wendon, J; Panel members; Cordoba J, Dhawan A, Larsen FS, et al.; EASL Governing Board representative; Bernardi M. EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure. J Hepatol 2017 May;66(5):1047-1081.

8 WHO. Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection [Internet]. 2015 March. [cited 2024 Apr 15]. Available from: https://www.who.int/publications/i/item/9789241549059

9 National Institute for Health and Care Excellence (NICE) (2013). Hepatitis B (chronic): diagnosis and management. (Clinical guideline [CG165]) [updated 2017 October; cited 2024 Apr 15]. Available from: https://www.nice.org.uk/guidance/cg165

10 National Institute for Health and Care Excellence (NICE) (2011). Alcohol-use disorders: diagnosis, assessment and management of harmful drinking (high-risk drinking) and alcohol dependence (Clinical guideline [CG115]) [updated 2022 October; cited 2024 Apr 15]. Available from: https://www.nice.org.uk/guidance/cg115

11 Szasz G. A kinetic photometric method for serum γ-glutamyl-transferase. J Clin Chem 1969;15:124-136.

12 Persijn JP, van der Slik W. A new Method for the Determination of γ-Glutamyltransferase. J Clin Chem Clin Biochem 1976;4:421.

13 Schumann G, Bonora R, Ceriottiet F et al. IFCC Primary Reference Procedures for the Measurement of Catalytic Activity Concentrations of Enzymes at 37 °C – Part 6. Reference Procedure for the Measurement of Catalytic Activity Concentrations of gamma-glutamyltransferase. Clin Chem Lab Med 2002;40(7):734-738.

14 Klauke R, Schmidt E, Lorentz K. Recommendations for carrying out standard ECCLS procedures (1988) for the catalytic concentrations of creatine kinase, aspartate aminotransferase, alanine aminotransferase and gamma-glutamyltransferase at 37 degrees. Eur J Clin Chem Clin Biochem 1993;31(12):901-909.

15 Szasz G, Weimann G, Stähler F, et al. New Substrates for measuring gamma-glutamyl-transpeptidase activity. Z Klin Chem Klin Biochem 1974;12:228-233.

16 Szasz G. Methods of Enzymatic Analysis. 2nd English ed. New York. Academic Press, Inc 1974;717.

17 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia PA: WB Saunders Company 1995;286.

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

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

20 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.

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

22 Abicht K, El-Samalouti V, Junge W, et al. Multicenter evaluation of new GGT and ALP reagents with new reference standardization and determination of 37 °C reference intervals. Clin Chem Lab Med 2001;39:Special Supplement pp S 346.

23 Kytzia H-J. Reference intervals for GGT according to the new IFCC 37°C reference procedure. Clin Chem Lab Med 2005;43:A69 [abstract].

24 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.

25 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.

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
REAGENT	Reagent
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com
+800 5505 6606