GGT-2

γ-Glutamyltransferase ver.2 - Standardized against IFCC / Szasz

Materials provided

REF		CONTENT	Analyzer(s) on which cobas c pack(s) can be used
05168775190*	05168775500	γ-Glutamyltransferase ver.2 (1200 tests)	**cobas** c 701/702
05168775214*	05168775500	γ-Glutamyltransferase ver.2 (1200 tests)	**cobas** c 701/702

* Some kits shown may not be available in all countries.

For reagents, refer to the "Reagents" section.

Materials required (but not provided)

REF	Description	Code
10759350190	Calibrator f.a.s. (12 × 3 mL)	401
05117003190	PreciControl ClinChem Multi 1 (20 × 5 mL)	391
05947626190	PreciControl ClinChem Multi 1 (4 × 5 mL)	391
05117216190	PreciControl ClinChem Multi 2 (20 × 5 mL)	392
05947774190	PreciControl ClinChem Multi 2 (4 × 5 mL)	392
05172152190	Diluent NaCl 9 % (119 mL)	System-ID 08 6869 3
	General laboratory equipment	

System information

Short name	ACN (application code number)	Description
GGTI2	8220	assay standardized against IFCC
GGTS2	8480	assay standardized against Szasz

Intended use

In vitro test for the quantitative determination of γ-glutamyltransferase (GGT) in human serum and plasma on **cobas** c systems.

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

Reference[15]

Enzymatic colorimetric assay.

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

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.

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Reagents

R1	TRIS: 492 mmol/L, pH 8.25; glycylglycine: 492 mmol/L; preservative; additive
R3	L-γ-glutamyl-3-carboxy-4-nitroanilide: 22.5 mmol/L; acetate: 10 mmol/L, pH 4.5; stabilizer; preservative

R1 is in position B and R3 is in position C.

Warnings and precautions

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 safe disposal.

The Safety Data Sheet is available for professional users 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.

Hazardous components:

- 2-methyl-2H-isothiazol-3-one hydrochloride

Product safety labeling follows EU GHS guidance.

Contact phone for all countries: +49-621-7590

Storage and stability

Shelf life at 2-8 °C	See expiration date on **cobas** c pack label.
On-board in use and refrigerated on the analyzer	2 weeks
On-board on the Reagent Manager	1 hour

Calibration

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

The calibration interval may be extended based on acceptable calibration verification values determined by the laboratory.

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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 the control materials listed in the “Materials required (but not provided)” section or other suitable control material.

Adjust the limits and control intervals based on the laboratory’s individual requirements. If values fall outside the limits, each laboratory is advised to establish corrective measures.

Follow the applicable government regulations and local guidelines.

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 and K2 EDTA plasma.

Specimens derived from capillary blood were found acceptable.[16]

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing. 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.

Refer to the "Limitations and interferences" section for details on possible sample interferences.

Stability[17,18]	7 days at 15-25 °C
	7 days at 2-8 °C
	1 year at -20 °C (± 5 °C)

Freeze only once.

Test procedure

The product is ready for use.

For optimum performance of the assay, follow the instructions given in this document for the corresponding analyzer. For analyzer-specific assay instructions, refer to the corresponding User Guide.

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 701/702 test definition			
Assay type	Rate A		
Reaction time / Assay points	10 / 25-38		
Wavelength (sub/main)	700/415 nm		
Reaction direction	Increase		
Units	U/L (µkat/L)		
Reagent pipetting		Diluent (H_2O)	
R1	25 µL	75 µL	
R3	20 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	3 µL	–	–
Decreased	3 µL	15 µL	150 µL
Increased	6 µL	–	–

Calculation

The **cobas** c systems automatically calculate the analyte activity of each sample in the unit U/L (µkat/L).

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

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Limitations and interferences

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

Icterus:[19] no significant interference up to an I index of 50 for conjugated and 20 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 855 µmol/L or 50 mg/dL and approximate unconjugated bilirubin concentration: 342 µmol/L or 20 mg/dL).

Hemolysis:[19] no significant interference up to an H index of 200 (approximate hemoglobin concentration: 124 µmol/L or 200 mg/dL).

Lipemia (Intralipid):[19] no significant interference up to an L index of 700. 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.[20,21]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[22]

For diagnostic purposes, always assess the results 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 **cobas** c systems. All special wash programming necessary for avoiding carryover is available via **cobas** link. In certain cases, manual input is required. The latest version of the carryover evasion list can be found on the NaOHD - SMS - SmpCln1+2 - SCCS Method Sheet. For further instructions, refer to the User Guide.

Where required, special wash / carryover 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 that have higher activities via the rerun function. Dilution of samples via the rerun function is a 1:11 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 11.

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 0. The lower detection limit is calculated as the value lying 3 standard deviations above the value of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Values below the lower detection limit (< 3 U/L) will not be flagged by the instrument.

Expected values

Standardized against Szasz (Persijn, van der Slik)[23]		
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)[23,24]		
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)[25]		
Men	< 60 U/L	< 1.00 µkat/L
Women	< 40 U/L	< 0.67 µkat/L

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

Specific performance data

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

Precision

Precision was determined using human samples and controls based on an internal protocol, with repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 21 days). The following results were obtained on the **cobas** c 701 analyzer:

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Repeatability	Mean U/L (µkat/L)	SD U/L (µkat/L)	CV %
Precinorm U	39.2 (0.655)	0.5 (0.008)	1.4
Precipath U	181 (3.02)	1 (0.02)	0.5
Human serum A	18.0 (0.301)	0.6 (0.010)	3.3
Human serum B	472 (7.88)	2 (0.03)	0.3
Human serum C	867 (14.5)	4 (0.1)	0.5

Intermediate precision	Mean U/L (µkat/L)	SD U/L (µkat/L)	CV %
Precinorm U	44.1 (0.736)	0.8 (0.013)	1.8
Precipath U	221 (3.69)	4 (0.07)	1.7
Human serum 3	46.8 (0.782)	1.5 (0.025)	3.2
Human serum 4	256 (4.28)	9 (0.15)	3.7

Results for intermediate precision were obtained on the **cobas** c 501 analyzer.

The data obtained on the **cobas** c 501 analyzer are representative for the **cobas** c 701 analyzer.

Method comparison

γ-glutamyltransferase values for human serum and plasma samples obtained on a **cobas** c 701 analyzer (y) were compared with values determined using the corresponding reagent on a **cobas** c 501 analyzer (x).

Sample size (n) = 103

Passing/Bablok[26]	Linear regression
y = 1.014x – 0.39 U/L	y = 1.017x – 0.474 U/L
τ = 0.992	r = 1.000

The sample activities were between 14.0 and 1168 U/L (0.234 and 19.5 µkat/L).

Additional information

Additions, deletions, or changes are indicated by a change bar in the margin.

A point (period/stop) is always used in the English version of a Method Sheet as the decimal separator to mark the boundary between the integral and the fractional parts of a decimal numeral. The translated Method Sheets use decimal commas. Labels only use the decimal point as separator. Separators for thousands are not used.

Report any serious incident that has occurred in relation to the device to the manufacturer and the competent authority of the member state in which the user and/or patient is established.

Symbols

In addition to the ISO 15223-1 standard, Roche Diagnostics uses the following symbols and signs:

CONTENT	Contents of kit
→	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.

References

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Change log

For this document version only:

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Due to technical reasons, changes that have been made since the last version of this document are listed in the following table instead of indicated by change bars in the margin.

Section headers are indicated in bold letters.

In addition to the changes listed in the table below, this method sheet version contains several editorial and layout updates.

Section	Current version	Previous version
Materials provided	**Materials provided**	**Order information** **Materials provided**
Materials provided	**Materials provided** without System-ID	**Order information** with System-ID
Materials required (but not provided)	**Materials required (but not provided)**	**Order information** **Materials required (but not provided)**
Materials required (but not provided)	outphased: REF 12149435122 Precinorm U plus, REF 12149443122 Precipath U plus	with REF 12149435122 Precinorm U plus, REF 12149443122 Precipath U plus
Reagents	**Reagents**	**Reagents - working solutions**
Warnings and precautions	**Warnings and precautions**	**Precautions and warnings**
Warnings and precautions	laboratory	health care
Warnings and precautions	Hazardous components: • 2-methyl-2H-isothiazol-3-one hydrochloride	
Specimen collection and preparation	Specimens derived from capillary blood were found acceptable. [Maroto-García J et al.]	
Test procedure	**Test procedure**	**Reagent handling** **Assay**
Limitations and interferences	**Limitations and interferences**	**Limitations - interference**
Additional information	A point (period/stop) is always used in the English version of a Method Sheet as the decimal separator to mark the boundary between the integral and the fractional parts of a decimal numeral. The translated Method Sheets use decimal commas. Labels only use the decimal point as separator. Separators for thousands are not used.	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.
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