BECKMAN COULTER

AU/DxC AU US

Instructions For Use

GGT
Gamma-Glutamyltransferase

REF OSR6119 4 x 15 mL R1, 4 x 15 mL R2
OSR6219 4 x 50 mL R1, 4 x 50 mL R2

For *in vitro* diagnostic use only.

For Rx use only

PRINCIPLE

INTENDED USE

System reagent for the quantitative determination of Gamma-Glutamyltransferase (EC 2.3.2.2) activity in human serum on Beckman Coulter AU/DxC AU analyzers.

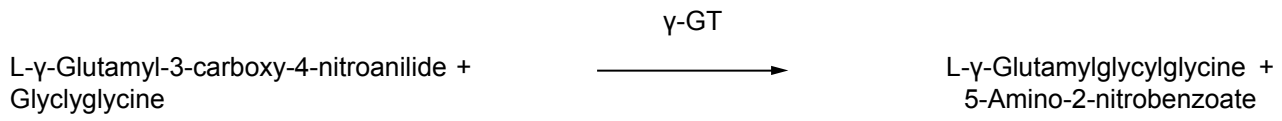
SUMMARY AND EXPLANATION

Gamma-glutamyltransferase measurements are used in the diagnosis and treatment of liver diseases such as alcoholic cirrhosis and primary and secondary liver tumors.

Elevated serum gamma-glutamyltransferase (GGT), sometimes called GGTP, is found in all forms of liver disease. It is more sensitive than alkaline phosphatase, the transaminases, and leucine aminopeptidase (LAP) in detecting obstructive jaundice, cholangitis, and cholecystitis. GGT levels rise earlier in liver disease and to higher values than LAP or 5'-nucleotidase levels.[1] Moderate elevations are seen in infectious hepatitis. However, elevated GGT levels have also been noted in chronic alcoholism, diabetes, and certain neurological disorders. Normal levels of GGT are seen in skeletal diseases; thus GGT in serum can be used to ascertain whether a disease is skeletal or hepatobiliary.

METHODOLOGY

This GGT procedure is a modification of the Szasz procedure.[2,3] GGT catalyzes the transfer of the gamma-glutamyl group from the substrate, gamma-glutamyl-3-carboxy-4-nitroanilide, to glycylglycine, yielding 5-amino-2-nitrobenzoate. The change in absorbance at 410/480 nm is due to the formation of 5-amino-2-nitrobenzoate and is directly proportional to the GGT activity in the sample.



SPECIMEN

SPECIMEN STORAGE AND STABILITY

The GGT determination should be performed as soon after specimen collection as possible. GGT is stable in serum and plasma for 7 days when stored at 4 - 25°C.[4]

Specimen storage and stability information provides guidance to the laboratory. Based on specific needs, each laboratory may establish alternative storage and stability information according to good laboratory practice or from alternative reference documentation.

Additional handling conditions as designated by this laboratory:

SPECIMEN COLLECTION AND PREPARATION

Serum samples, free from hemolysis, are the recommended specimens. If plasma must be used, the recommended anticoagulant is K2/K3 EDTA. Heparinized plasma becomes turbid in the reaction mixture; citrate, oxalate and fluoride depress activity by 10 to 15%.[1]

Additional instructions for patient sample preparation as designated by this laboratory:

Additional type conditions as designated by this laboratory:

REAGENTS

CONTENTS

GGT Reagent

Reagent storage location in this laboratory:

WARNING AND PRECAUTIONS

1. Exercise the normal precautions required for handling all laboratory reagents.
2. Dispose of all waste material in accordance with local guidelines.

REACTIVE INGREDIENTS

Final concentration of reactive ingredients:

Tris Buffer, pH 7.95 (37°C)	100 mmol/L
Glycylglycine	100 mmol/L
L-γ-Glutamyl-3-carboxy-4-nitroanilide	4.0 mmol/L
Also contains preservatives	

GHS HAZARD CLASSIFICATION

GGT R1	WARNING	
		
	H316	Causes mild skin irritation.
	H317	May cause an allergic skin reaction.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	P332+P313	If skin irritation occurs: Get medical advice/attention.
	P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
	P362+P364	Take off contaminated clothing and wash it before use.
		Tris(hydroxymethyl)– aminomethane 1 - 5%
		reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%
GGT R2	WARNING	
		
	H317	May cause an allergic skin reaction.
	P280	Wear protective gloves, protective clothing and eye/face protection.
	P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
	P362+P364	Take off contaminated clothing and wash it before use.
		reaction mass of: 5-chloro-2-methyl-4-isothiazolin -3-one [EC# 247-500-7] and 2-methyl-4-isothiazolin-3-one [EC# 220-239-6](3:1) < 0.05%

SDS	Safety Data Sheet is available at beckmancoulter.com/techdocs

EQUIPMENT AND MATERIALS

For use on the AU480, AU680, AU5800, DxC 500 AU, DxC 500i and DxC 700 AU Beckman Coulter Analyzers.

Storage location of test tubes or sample cups in this laboratory:

REAGENT PREPARATION

The GGT Reagent is ready for use. No preparation is required.

STORAGE AND STABILITY

1. The unopened reagents are stable until the expiration date printed on the label when stored at 2 – 8°C.
2. Opened reagents are stable for 30 days when stored in the refrigerated compartment of the analyzer.

INDICATIONS OF DETERIORATION

Visible signs of microbial growth, turbidity or precipitate, or any change in reagent color may indicate degradation and warrant discontinuance of use.

Additional storage requirements as designated by this laboratory:

STABILITY OF FINAL REACTION MIXTURE

The Beckman Coulter AU/DxC AU analyzer automatically computes every determination at the same time interval.

CALIBRATION

CALIBRATION INFORMATION

Calibration of this GGT procedure is based upon the measured extinction coefficient for 5-amino-2-nitrobenzoate, which has a molar absorptivity of 7453 at 410/480nm.

The theoretical extinction coefficient for GGT on the AU5800 is 4376. The theoretical extinction coefficient for GGT on all other AU/DxC AU analyzers is 4361.

DxC 500 AU and DxC 500i CALIBRATION INFORMATION ONLY

Ensure that Manufacturer Factor A is 1.0.

Prepare 3 fresh vials of System Calibrator Cat No. 66300X and run as samples in duplicate. Examine the data for outliers which should be repeated and replaced and calculate the **Overall Mean** Value. Calculate the analyzer specific Manufacturer Factor A:

$$\text{Calculated Factor} = \frac{\text{System Calibrator REF 66300X Set Point per product Insert}}{\text{Overall Mean Value}}$$

Enter the **Calculated Factor** in the Manufacturer Factor A field in the General Parameters section of the Chemistry Details Screen. Quality control procedures should be undertaken immediately following calibration in accordance with good laboratory practice.

Re-establishment of the analyzer specific Manufacturer Factor A is recommended when QC results are not within the laboratories' established ranges following replacement of a critical part of the analyzer.

Reagent blank measurement is recommended when changing to a new lot of reagent.

AU480 / AU680 / DxC 700 AU / AU5800 CALIBRATION INFORMATION ONLY

Ensure that the MB Factor in the MB Type Factor field is set to the assay specific **Theoretical Extinction Coefficient.** Prepare 3 fresh vials of System Calibrator Cat No. 66300X and run as samples in duplicate. Examine the data for outliers which should be repeated and replaced and calculate the **Overall Mean** Value. Calculate the **Derived Multiplier:**

$$\text{Derived Multiplier} = \frac{\text{System Calibrator REF 66300X Set Point per product Insert}}{\text{Overall Mean Value}}$$

Multiply the **Theoretical Extinction Coefficient** for the assay by the **Derived Multiplier** to get the **analyzer specific MB type factor.** Enter the **analyzer specific MB type Factor** in the MB Type Factor section of the calibration specific menu.

For the AU5800, ensure the correct unit and cuvette wheel is selected. Quality control procedures should be undertaken immediately following calibration in accordance with good laboratory practice.

Re-establishment of the analyzer specific MB factor is recommended when QC results are not within the laboratories' established ranges following replacement of a critical part of the analyzer.

Reagent blank measurement is recommended when changing to a new lot of reagent.

Note for the AU5800 analyzer: the analyzer specific MB Factor is generated for each analyzer unit and cuvette wheel that the enzyme assay is used.

QUALITY CONTROL

During operation of the Beckman Coulter AU/DxC AU analyzer, at least two levels of an appropriate quality control material should be tested a minimum of once a day. In addition, controls should be performed after calibration, with each new lot of reagent, and after specific maintenance or troubleshooting steps described in the appropriate Beckman Coulter AU/DxC AU analyzer Instructions For Use (IFU) and Reference Manual. Quality control testing should be performed in accordance with regulatory requirements and each laboratory's standard procedure.

Location of controls used at this laboratory.

CONTROL NAME	SAMPLE TYPE	STORAGE

TESTING PROCEDURE(S)

A complete list of test parameters and operational procedures are provided in the relevant AU/DxC AU analyzer IFU and Reference Manual.

RESULTS INTERPRETATION

The default unit of measure is U/L, for conversion to SI units (µkat/L) the result is divided by 60.

REPORTING RESULTS

EXPECTED RESULTS

Adults:[5] 9 – 64 U/L

Reference Intervals shown above were taken from the literature. Expected values may vary with age, sex, sample type, diet and geographical location. Each laboratory should verify the transferability of the expected values to its own population, and if necessary determine its own reference interval according to good laboratory practice. For diagnostic purposes, results should always be assessed in conjunction with the patient's medical history, clinical examinations and other findings.

Expected reference ranges in this laboratory:

INTERVALS	SAMPLE TYPE	UNITS

Additional reporting information as designated by this laboratory:

PROCEDURAL NOTES

INTERFERENCES

It has been found that some antiepileptic drugs (phenytoin, barbiturates) may result in falsely elevated GGT values.[6] Heavy alcohol consumption just prior to specimen collection may falsely elevate serum GGT.[7]

Results of studies[8] show that the following substances interfere with this GGT procedure.

The criteria for no significant interference is recovery within 10% of the initial value.

Bilirubin:	No significant interference up to 40 mg/dL Bilirubin
Hemolysis:	No significant interference up to 350 mg/dL Hemolysate
Lipemia:	No significant interference up to 1,000 mg/dL Intralipid*

*Intralipid, manufactured by KabiVitrium Inc., is a 20% IV fat emulsion used to emulate extremely turbid samples.

The information presented is based on results from Beckman Coulter studies and is current at the date of publication. Beckman Coulter Inc., makes no representation about the completeness or accuracy of results generated by future studies. Further information on interfering substances is available.[9]

Laboratory specific procedure notes:

PERFORMANCE CHARACTERISTICS

PERFORMANCE CHARACTERISTICS

Data contained within this section is representative of performance on Beckman Coulter systems. Data obtained in your laboratory may differ from these values.

DYNAMIC RANGE / ANALYTICAL MEASURING RANGE

The GGT procedure is linear from 3 to 1,200 U/L. Samples exceeding the upper limit of linearity should be diluted and repeated. The sample may be diluted, repeated and multiplied by the dilution factor automatically by utilizing the AUTO REPEAT RUN.

SENSITIVITY

Typical change in absorbance per minute for 1 U/L of Gamma-Glutamyltransferase is 0.23 mAbsorbance.

METHODS COMPARISON

Reference[10]

Patient serum samples were evaluated in method comparison studies.

Results of Deming regression analysis were as follows:

Y Method	DxC 700 AU
X Method	AU5800

Slope	1.036
Intercept	-0.165
Correlation Coeff. (r)	1.000
No. of Samples (n)	123
Range (U/L)	4 - 1080

PRECISION

Reference[10]

Estimates of precision, based on CLSI recommendations,[11] are consistent with typical performance. The within run precision is less than 5% CV and total precision is less than 10% CV. Assays of control sera were carried out and data reduced following CLSI guidelines above.

N=80	Within-run		Total	
Mean, U/L	**SD**	**CV%**	**SD**	**CV%**
21.6	0.18	0.8	0.32	1.5
47.3	0.31	0.7	0.39	0.8
246.2	1.38	0.6	2.01	0.8
993.0	5.76	0.6	6.66	0.7

ADDITIONAL INFORMATION

DxC 700 AU analyzers require that each reagent application has a standard format of abbreviated Test Name. This Test Name is required to allow automated loading of the calibrator information for each application. Refer to the table below for the Test Name assigned to each application for this assay.

Test Name	Description
GGT1U	GGT (Serum)

Refer to the Beckman Coulter Chemistry Systems Reagent Guide (BAGUIDE) for specific chemistry information for the AU/DxC AU clinical chemistry systems and guidance on symbols used on all AU/DxC AU product labelling.

Setting Sheet Footnotes

User defined

* Values set for working in U/L. To work in SI units (µkat/L) divide by 60.

The theoretical extinction coefficient is 4361

Ψ Analyzer Specific MB Factor = Theoretical Extinction Coefficient*Derived Multiplier.

AU5800 only:

The theoretical extinction coefficient is 4376

MB Factor adjustment must be completed separately for each ring.

REVISION HISTORY

Add DxC 500i instrument to IFU

Preceding version revision history

Updated Specimen Section

Updated REPORTING RESULTS section

Updated PROCEDURAL NOTES section

Updated Performance Characteristics section

Updated References section

REFERENCES

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