BECKMAN COULTER

CE

AU

Instructions For Use

GGT
Gamma-Glutamyltransferase

REF OSR6020 4 x 18 mL R1, 4 x 18 mL R2
OSR6120 4 x 40 mL R1, 4 x 40 mL R2
OSR6620 4 x 173 mL R1, 4 x 173 mL R2

For *in vitro* diagnostic use only.

PRINCIPLE

INTENDED USE

Kinetic colour test for the quantitative determination of gamma-glutamyltransferase, EC 2.3.2.2 (GGT) in human serum and plasma on Beckman Coulter AU analysers.

OSR6620 for use on the AU5800, AU2700 and AU5400 systems only.

SUMMARY AND EXPLANATION

Reference[1,2,3]

Gamma glutamyltransferase (GGT) belongs to a group of peptidases which catalyse the transfer of amino acids from one peptide to another and thus act as amino acid transferases. The enzyme only reacts with peptides or peptide-like compounds containing a terminal glutamate residue joined to the remainder of the compound through the terminal carboxyl. GGT is present in all cells of the body except those in muscle however the enzyme present in serum appears to originate primarily from the hepatobiliary system. An increase in GGT is always a sign of liver damage if liver specific enzymes such as ALT, GLDH or CHE are also abnormal. GGT is however of little value in attempting to discriminate between different kinds of liver disease.

GGT is dramatically increased in cases of intrahepatic or posthepatic biliary obstruction. It is more sensitive than alkaline phosphatase in detecting obstructive jaundice, cholangitis and cholecystitis and its rise occurs earlier and persists longer. GGT is also increased in patients with infectious hepatitis, fatty livers, in acute and chronic pancreatitis and in patients receiving anticonvulsant drugs such as phenytoin and phenobarbital.

As elevated levels of GGT are observed in patients with alcoholic cirrhosis, and in the majority of sera from people who are heavy drinkers, GGT plays a role in the detection of alcoholism, alcoholic liver damage and in monitoring alcohol abstinence. The enzyme is also useful in ratio with HDL-cholesterol in cases of alcohol abuse, alkaline phosphatase in cases of alcoholic liver disease and aspartate aminotransferase for distinguishing neonatal hepatitis from biliary atresia.

METHODOLOGY

Reference[4]

Method based on the recommendations of the “International Federation for Clinical Chemistry” (IFCC).

GGT catalyses the transfer of the gamma-glutamyl group from the substrate, gamma-glutamyl-3-carboxy-4-nitroanlide, 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.

CHEMICAL REACTION SCHEME

L-γ-Glutamyl-3-carboxy-4-nitroanilide + Glycylglycine	γ-GT	L-γ-Glutamylglycylglycine + 5-Amino-2-nitrobenzoate

SPECIMEN

TYPE OF SPECIMEN

Serum and EDTA or heparinised plasma.

Stable in serum and plasma for 7 days when stored at 2…25°C.[5]

REAGENTS

WARNING AND PRECAUTIONS

Exercise the normal precautions required for handling all laboratory reagents.

Dispose of all waste material in accordance with local guidelines.

REACTIVE INGREDIENTS

Final concentration of reactive ingredients

Glycylglycine, pH 7.7 (37°C)	150 mmol/L
L-γ-glutamyl-3-carboxy-4-nitroanilide	6 mmol/L
Preservative	

The concentrations of the reactive components of the reagents shown on the kit label are the actual concentrations in the individual R1/R2 vials. The reagent composition which is shown in the Instructions For Use is the final concentration of these components in the reaction cuvette after addition of R1, Sample, and R2.

GHS HAZARD CLASSIFICATION

GGT R1	WARNING	
		
	H317	May cause an allergic skin reaction.
	H412	Harmful to aquatic life with long lasting effects.
	P273	Avoid release to the environment.
	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%
GGT R2	WARNING	
		
	H317	May cause an allergic skin reaction.
	H412	Harmful to aquatic life with long lasting effects.
	P273	Avoid release to the environment.
	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

REAGENT PREPARATION

The reagents are ready for use and can be placed directly on board the instrument.

STORAGE AND STABILITY

The reagents are stable, unopened, up to the stated expiry date when stored at 2…8°C. Once open, reagents stored on board the instrument are stable for 30 days.

CALIBRATION

CALIBRATION INFORMATION

The test is run in MB-mode. To provide a robust approach to generate the analyser specific MB factor, it is recommended that 5 separate calibration events should be used. A fresh vial of calibrator, utilising System Calibrator Cat No. 66300 in the AB calibration mode, should be used for each of these runs. When calculating the mean factor from the separate runs the data should be examined for obvious outliers which should be repeated and replaced. For the AU2700/AU5400 this procedure needs to be performed for each ring. Quality control procedures should be undertaken immediately following calibration in accordance with good laboratory practice.

The calibrator value is traceable to the IFCC reference method and IRMM/IFCC-452.

Re-establishment of the analyser specific MB factor is recommended when a critical part of the analyser is replaced.

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

QUALITY CONTROL

Controls Cat. No. ODC0003 and ODC0004 or other control materials with values determined by this Beckman Coulter system may be used.

Each laboratory should establish its own control frequency.

Good laboratory practice suggests that controls be tested each day patient samples are tested and each time calibration is performed. Values obtained for the controls should fall within specified limits as defined by the user. If any trends or sudden shifts in values are detected, review all operating parameters.

Each laboratory should establish guidelines for corrective action to be taken if controls do not recover within the specified limits.

TESTING PROCEDURE(S)

Refer to the appropriate Beckman Coulter AU analyser User Guide/Instructions For Use (IFU) for analyser-specific assay instructions for the sample type as listed in the Intended Use statement. The paediatric application is suitable for use with small volume serum/plasma samples.

CALCULATIONS

The Beckman Coulter analysers automatically compute the GGT activity of each sample.

REPORTING RESULTS

REFERENCE INTERVALS

Male (Adult)[6]	< 55 U/L (0.92 µkat/L)
Female (Adult)	< 38 U/L (0.63 µkat/L)

Children[1]	Male	Female
1-182 days	12-122 U/L (0.2-2.03 µkat/L)	15-132 U/L (0.25-2.2 µkat/L)
183-365 days	1-39 U/L (0.02-0.65 µkat/L)	1-39 U/L (0.02-0.65 µkat/L)
1-12 years	3-22 U/L (0.05-0.37 µkat/L)	4-22 U/L (0.07-0.37 µkat/L)
13-18 years	2-42 U/L (0.03-0.7 µkat/L)	4-24 U/L (0.07-0.4 µkat/L)

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.

PROCEDURAL NOTES

INTERFERENCES

Results of studies conducted to evaluate the susceptibility of the method to interference were as follows:

Icterus:	Interference less than 3% up to 40 mg/dL or 684 µmol/L bilirubin
Haemolysis:	Interference less than 5% up to 2.5 g/L haemoglobin
Lipemia:	Interference less than 5% up to 1,000 mg/dL Intralipid

In very rare cases, gammopathy, especially monoclonal IgM (Waldenström's macroglobulinemia) can cause unreliable results.

Refer to Young[7] for further information on interfering substances.

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.

LINEARITY

The test is linear within an enzyme activity range of 5 - 1,200 U/L (0.08 – 20.00 µkat/L).

SENSITIVITY

The lowest detectable level in serum on an AU5800 analyzer was estimated at 2 U/L.

The lowest detectable level represents the lowest measurable level of GGT that can be distinguished from zero. It is calculated as the absolute mean plus three standard deviations of 20 replicates of an analyte free sample.

METHODS COMPARISON

Patient serum samples were used to compare this GGT OSR6120 assay on the AU640 against the IFCC Reference method. Results of linear regression analysis were as follows:

y = 1.026x - 3	r = 1.000	n = 94	Sample range = 11 - 269 U/L

PRECISION

The following data was obtained on an AU680 using 3 serum pools analysed over 20 days

n = 80	Within-run		Total	
Mean U/L	**SD**	**CV %**	**SD**	**CV %**
21	0.35	1.63	0.51	2.40
49	0.79	1.62	0.93	1.90
313	1.36	0.44	4.48	1.43

ADDITIONAL INFORMATION

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

Test Name	Description
GGT2N	GGT (Serum)
GGT2NP	GGT (Serum Paediatric)

Setting Sheet Footnotes
User defined
* Values set for working in U/L. To work in SI units (µkat/L) divide by 60.
§ For use in AB mode only, refer to IFU for further instruction.

REVISION HISTORY

Added new languages

Preceding version revision history

Revised GHS section

REFERENCES

1. Thomas L. Gamma glutamyltransferase (GGT). In:Thomas L, ed. Clinical laboratory diagnostics. Use and assessment of clinical laboratory results. Frankfurt/Main: TH-Books Verlagsgesellschaft, 1998:80-86.

2. Tietz NW, ed. Clinical guide to laboratory tests, 3rd ed. Philadelphia: WB Saunders Company,1995:286-87.

3. Moss DW, Henderson RA. Clinical enzymology. In: Burtis CA, Ashwood ER, eds. Tietz textbook of clinical chemistry. Philadelphia:WB Saunders Company, 1999; 686-89.

4. Shaw M, Stromme H. London L, Theodorsen L. Part 4 IFCC method for y-glutamyltransferase. Clin Chem Clin Biochem 1983;21(10):633-646.

5. Ehret W, Heil W, Schmitt Y, Töpfer G, Wisser H, Zawta B, et al. Use of Anticoagulants in Diagnostic Laboratory Investigations and Stability of Blood, Plasma and Serum Samples. WHO/DIL/LAB/99.1 Rev.2:32pp.

6. Schumann G, Klauke R. New IFCC reference procedures for the determination of catalytic activity concentrations of five enzymes in serum: preliminary upper reference limits obtained in hospitalised subjects. Clin Chim Acta 2003;327:69-79.

7. Young DS. Effects of Drugs on Clinical Laboratory Tests, AACC, 5th ed. AACC Press, 2000.

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