BECKMAN COULTER

AU/DxC AU US

Instructions For Use

LIP
Lipase

REF OSR6130 4 x 10 mL R1 Buffer, 4 x R1 Lyo, 4 x 3.3 mL R2, 2 x Calibrator
OSR6230 4 x 30 mL R1 Buffer, 4 x R1 Lyo, 4 x 10 mL R2, 2 x Calibrator

For *in vitro* diagnostic use only.

For Rx use only

PRINCIPLE

INTENDED USE

System reagent for the quantitative determination of Lipase activity in human serum on Beckman Coulter AU/DxC AU analyzers.

SUMMARY AND EXPLANATION

Measurements of serum lipase are used in the diagnosis and treatment of acute pancreatitis or pancreatic injury.

METHODOLOGY

The lipase procedure is based on the colorimetric method of Imamura, et al.[1] Pancreatic lipase hydrolyzes esters of long chain fatty acids from their triglycerides. The enzyme activity requires the presence of co-lipase. 1,2-Diglyceride is hydrolyzed to 2-monoglyceride and fatty acid. The 2-monoglyceride is then measured by coupled enzyme reactions catalyzed by monoglyceride lipase (MGLP), glycerol kinase (GK), glycerol phosphate oxidase (GPO) and peroxidase (POD).

1,2-Diglyceride $\xrightarrow{\text{Pancreatic Lipase}}$ 2-Monoglyceride + Fatty Acid

2-Monoglyceride $\xrightarrow{\text{MGLP}}$ Glycerol + Fatty Acid

Glycerol + ATP $\xrightarrow{\text{GK}}$ Glycerol-3-Phosphate + ADP

Glycerol-3-Phosphate + O_2 $\xrightarrow{\text{GPO}}$ DAP + H_2O_2

$$H_2O_2 + \text{4-AAP} + \text{TOOS} \xrightarrow{\text{POD}} \text{Quinone Diimine Dye} + 4\ H_2O$$

SPECIMEN

SPECIMEN STORAGE AND STABILITY

Lipase is stable in serum and plasma for 3 weeks when stored at 4-8°C, 7 days at 20-25°C and 1 year at -20°C. [2]

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.

Li/Na Heparinized plasma can also be used.

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

Additional type conditions as designated by this laboratory:

REAGENTS

CONTENTS

Lipase Reagent

Reagent storage location in this laboratory:

Lipase Calibrator

Storage location of the Calibrator 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.
3. WARNING: POTENTIAL BIOHAZARDOUS MATERIAL.

   The calibrator reagent is manufactured from human serum. Each human serum donor used in the preparation of this material was tested by an FDA approved method for the presence of the antibody to HIV-1/2 and HCV as well as for hepatitis B surface antigen and was not repeatedly reactive. Because no test method can offer complete assurance that HIV-1/2, HCV, hepatitis B virus or other infectious agents are absent from biological materials, all reagents should be handled at the Biosafety Level 2 as recommended for any infectious human serum or blood specimen in the Centers for Disease Control/National Institutes of Health manual, *Biosafety in Microbiological and Biomedical Laboratories,* 1993.
4. This product contains material of animal origin. The product should be considered as potentially capable of transmitting infectious diseases.

REACTIVE INGREDIENTS

Final concentration of reactive ingredients:

Buffers MES/BES (pH 6.8)	27 mmol/L
GPO (Streptococcus sp.)	> 15 KU/L
1,2-Diglyceride Substrate (Egg)	0.828 mmol/L
POD (Horseradish)	> 500 U/L
Monoglyceride Lipase (Bacillus sp.)	> 400 U/L
Colipase (Porcine)	> 15 KU/L
ATP	> 0.85 mmol/L
Glycerol Kinase (S. cannus)	> 100 U/L
TOOS	1.0 mol/L
4-aminophenazone	0.25 mmol/L

Deoxycholate	> 7.3 mmol/L
Cholic acid	> 2.0 mmol/L
TAPS (pH 8.7)	50 mmol/L

Also contains preservatives and surfactants.

⚠ CAUTION

Sodium azide preservative may form explosive compounds in metal drain lines. See NIOSH Bulletin: Explosive Azide Hazard (8/16/76).
To avoid the possible build-up of azide compounds, flush wastepipes with water after the disposal of undiluted reagent. Sodium azide disposal must be in accordance with appropriate local regulations.

GHS HAZARD CLASSIFICATION

Lipase Substrate - R1L — WARNING

H316	Causes mild skin irritation.
H401	Toxic to aquatic life
H410	Very toxic to aquatic life with long lasting effects.
P273	Avoid release to the environment.
P332+P313	If skin irritation occurs: Get medical advice/attention.
P391	Collect spillage.
	Ethoxylated Nonylphenol 1 - 5%
	MES monohydrate 1 - 5%

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

1. R1 Working Reagent: Slowly add the contents of R1 buffer to the bottle containing R1 lyophilisate. Mix until lyophilisate is completely dissolved. Return the working solution to the R1 buffer bottle.
2. R2: Ready for use. No preparation is required.
3. Lipase Calibrator: Add 3.0 mL of deionized water to the lipase calibrator, mix until completely dissolved.

STORAGE AND STABILITY

1. The reagents are stable, if unopened, up to the stated expiration date when stored at 2 - 8°C.
2. Opened reagents are stable for 21 days when stored in the refrigerated compartment of the analyzer.
3. Reconstituted Lipase calibrator is stable for 60 days when stored at 2 - 8°C if uncontaminated.

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

The frequency of calibration is every 7 days. Calibration is accomplished by use of the Lipase calibrator.

Recalibration of this test is required when any of these conditions exist:

1. A reagent lot number has changed or there is an observed shift in control values.
2. Major preventative maintenance was performed on the analyzer.
3. A critical part was replaced.

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 multiplied by 0.0167.

REPORTING RESULTS

EXPECTED RESULTS

Adults [3] 3 - 73 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

Results of studies [4] show that the following substances interfere with Lipase determinations

Ascorbate:	Interference less than 10% or 5.7 U/L up to 20 mg/dL Ascorbate.
Bilirubin:	Interference less than 10% or 5.7 U/L up to 12 mg/dL Bilirubin.
Hemolysis:	Interference less than 10% or 5.7 U/L up to 500 mg/dL Hemolysate.
Lipemia:	Interference less than 10% or 5.7 U/L up to 500 mg/dL intralipid.

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

Patients treated with N-Acetyl Cysteine (NAC) for a acetaminophen overdose may generate a false low result for lipase.

Venipuncture immediately after or during the administration of Metamizole (Dipyrone) may lead to falsely low results for Lipase. Venipuncture should be performed prior to the administration of Metamizole.

N-acetyl-p-benzoquinone imine (metabolite of Acetominophen) will generate erroneously low results in samples for patients that have taken toxic doses of acetaminophen.

The release of Lipoprotein Lipase and Hepatic Lipase after the intravenous or subcutaneous administration of heparin may cause an elevation of the measured Lipase activity without any association with pancreatic disorders.[5]

Significant interference from exogenous lipases found in Triglyceride reagents has been identified, due to carryover in random access analyzers. Set up run to exclude running Triglyceride assays just prior to a lipase assay, or utilize manufacturer's recommended contamination parameters.
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. [6]

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

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 lipase procedure is linear from 3 – 600 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 utilizing the AUTO REPEAT RUN.

SENSITIVITY

Typical change in absorbance for 1 U/L of lipase is 0.17 mAbsorbance.

METHODS COMPARISON

Reference[7]

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	0.958
Intercept	-2.2
Correlation Coeff. (r)	0.9999
No. of Samples (n)	122
Range (U/L)	5 - 571

PRECISION

Reference[7]

Estimates of precision, based on CLSI recommendations[8], 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%**
33.5	0.6	1.9	1.7	5.1
79.8	0.9	1.2	3.7	4.6
282.8	2.0	0.7	12.7	4.5

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
LIP1U	Lipase (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

Lot or Lot + Bottle

† Beckman Coulter System Calibrator supplied with kit.

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

REVISION HISTORY

Updated Specimen Section

Updated REAGENTS section

Updated REPORTING RESULTS section

Updated Procedural Notes section

Updated References section

Preceding version revision history

Updated REAGENTS section

REFERENCES

1. Imamura, S., Hirayama, T., Arai, T., Takao, K., Misaki, H.: An enzymatic method using 1,2-diglyceride for pancreatic lipase test in serum: Clin. Chem. 35: 1126, 1989.
2. 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.2:36pp.
3. Jacobs, David S., DeMott Wayne R., Oxley, Dwight K. Laboratory Test Handbook Concise with Disease Index, 3rd Edition, Lexi-Comps, 2004: 852pp
4. CLSI. Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition. CLSI document EP07-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2005.
5. Two automated Fully Enzymatic Assays for Lipase Activity in Serum Compared: Positive Interference from Post-Heparin Lipase Activity. Demanet C, Goedhuys W, Haentjens M et al. Clin Chem 1992:38:288-92.
6. AACC Effects on Clinical Laboratory Tests: Drugs, Disease, Herbs and Natural Products 6ttps://clinfx.wiley.com/aaccweb/aacc/
7. Data is on file for specific AU/DxC AU analyzers.
8. CLSI. Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Third Edition. CLSI document EP05-A3. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

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