BECKMAN COULTER CE 2797

AU/DxC AU
Instructions For Use

GLUC
GLUCOSE

REF OSR6121 4 x 25 mL R1, 4 x 12.5 mL R2
OSR6221 4 x 53 mL R1, 4 x 27 mL R2
OSR6621 4 x 173 mL R1, 4 x 91 mL R2

For *in vitro* diagnostic use only.

PRINCIPLE

INTENDED PURPOSE

Glucose reagent is an in vitro diagnostic medical device intended to be used by healthcare professionals for the quantitative enzymatic UV measurement of glucose in human serum, plasma, urine and cerebrospinal fluid (CSF) using the automated Beckman Coulter AU/DxC AU analyzers.

Measurement of glucose is intended to be used as an aid in the diagnosis and treatment of disorders of carbohydrate metabolism including diabetes mellitus, neonatal hypoglycemia, and insulinoma.

Measurement of glucose in CSF is intended to be used as an aid in diagnosis of CNS infection.

SUMMARY AND EXPLANATION

Reference[1,2,3,4,5]

In the fasting state, blood sugar levels are regulated by the liver, which ensures that levels are maintained within precise limits. The rapid and precise manner in which fasting blood sugar levels are regulated is in marked contrast to the rapid increase in blood sugar, which occurs during ingestion of carbohydrates. A fall in blood glucose to a critical level (approximately 2.5 mM) leads to dysfunction of the central nervous system. This manifests as hypoglycaemia, and is characterised by muscle weakness, lack of coordination and mental confusion. Further decrease in blood glucose levels leads to hypoglycaemic coma. Blood glucose concentrations show intra-individual fluctuations, which are dependent on muscular activity and the time interval since food intake. These fluctuations are increased further where there is dysregulation, such as occurs in a number of pathological conditions in which blood glucose may be elevated (hyperglycaemia) or depressed (hypoglycaemia).

Hyperglycaemia most commonly occurs as a result of a deficiency in either the amount or efficiency of insulin, a condition known as diabetes mellitus. This disease is characterised by the elevation of blood glucose to such an extent that the renal threshold is exceeded and sugar appears in the urine (glycosuria). Blood glucose measurement is used as a screening test for diabetes mellitus, where there is suspected hyperglycaemia, monitoring of therapy in diabetes mellitus, evaluation of carbohydrate metabolism, for example in gestational diabetes acute hepatitis, acute pancreatitis and Addison's disease. Hypoglycaemia is associated with a range of pathological conditions including neonatal respiratory distress syndrome, toxaemia of pregnancy, congenital enzyme defects, Reye's syndrome, alcohol ingestion, hepatic dysfunction, insulin-producing pancreatic tumours (insulinomas), insulin antibodies, nonpancreatic neoplasms, septicaemia and chronic renal failure.

Using a ratio of CSF to serum glucose of less than 0.4, an 80% sensitivity and 98% specificity was found for distinguishing bacterial (n=119) versus aseptic cases (n=98) of meningitis.[4] CSF glucose concentrations less than 18 mg/dL (1.0 mmol/L) are strongly predictive of bacterial meningitis.[5]

METHODOLOGY

Reference[6]

Glucose is phosphorylated by hexokinase (HK) in the presence of adenosine triphosphate (ATP) and magnesium ions to produce glucose-6-phosphate and adenosine diphosphate (ADP). Glucose-6-phosphate dehydrogenase (G6P-DH) specifically oxidises glucose-6-phosphate to gluconate-6-phosphate with the concurrent reduction of NAD^+ to NADH. The increase in absorbance at 340nm is proportional to the glucose concentration in the sample.

CHEMICAL REACTION SCHEME

$$\text{Glucose + ATP} \xrightarrow{\text{HK, } Mg^{2+}} \text{Glucose-6-phosphate + ADP}$$

$$\text{Glucose-6-Phosphate + } NAD^+ \xrightarrow{\text{G6P-DH}} \text{Gluconate-6-P + NADH + } H^+$$

SPECIMEN

TYPE OF SPECIMEN

Serum and K2/K3-EDTA or Li/Na- heparinized plasma, urine or CSF.[7,8]

SPECIMEN STORAGE AND STABILITY

Unstabilised glucose in blood will decrease after 10 minutes. To minimise loss of glucose through glycolysis serum should be removed from red cells as soon as possible. Specimens that cannot be rapidly separated should be collected into tubes containing stabilisers such as fluoride, monoiodoacetate or mannose. Glucose in stabilised serum/plasma is stable for up to 7 days when stored at 4…8°C and 2 days when stored at 20…25°C. Icteric and strongly lipemic samples should be avoided. [7, 8]

Urine: Fresh, random collections are recommended for urine specimens.[9] Stable in urine for 2 hours when stored at 4…25°C. Analyse as soon as possible. [7]

Cerebrospinal fluid:[9] Glucose in CSF is stable up to 5 hours when stored at 20…25°C [7]. Process immediately to avoid falsely low results.

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.

REAGENTS

WARNING AND PRECAUTIONS

Exercise the normal precautions required for handling all laboratory reagents.

Dispose of all waste material in accordance with local guidelines.

This product contains material of animal origin. The product should be considered as potentially capable of transmitting infectious diseases.

ACTIVE INGREDIENTS

Final concentration of active ingredients:

PIPES buffer (pH 7.6)	24.0 mmol/L
ATP	≥ 2.0 mmol/L

NAD^+	≥ 1.32 mmol/L
Mg^{2+}	2.37 mmol/L
Hexokinase	≥ 0.59 kU/L
G6P-DH	≥ 1.58 kU/L
Preservative	

The concentrations of the 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.

⚠ 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

Not classified as hazardous

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.

REAGENT STORAGE AND STABILITY

Closed vial shelf life per stability study: 24 months.

The reagents are stable, unopened, up to the stated expiry date when stored at 2…8°C.

Opened bottles of reagent are stable for 30 days when stored in the refrigerated compartment of the analyzer.

INDICATIONS OF DETERIORATION

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

CALIBRATION

CALIBRATOR REQUIRED

Serum/plasma/CSF application: Use System Calibrator Cat. No. 66300.

Urine application: Urine Calibrator Cat. No. B64606

The reagent blank and calibration curves should be visually reviewed for acceptability. Instructions on how to perform the review are provided in the relevant AU/DxC AU analyzer IFU and Reference Manual. Quality control (QC) procedures should be undertaken immediately following calibration in accordance with good laboratory practice.

Recalibrate the assay every 30 days, or when the following occur:

Change in reagent lot or significant shift in control values;

Major preventative maintenance was performed on the analyzer or a critical part was replaced.

TRACEABILITY

The glucose value of System Calibrator Cat. No. 66300 is traceable to the National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 965. The urine calibrator Cat. No. B64606 is traceable to the National Institute of Standards and Technology (NIST) Standard Reference Material (SRM) 965b L4.

QUALITY CONTROL

Serum/plasma: controls Cat. No. ODC0003 and ODC0004 or other control materials with values determined by this Beckman Coulter system may be used.

Urine/CSF: Control materials with values determined by this Beckman Coulter system may be used.

Each laboratory should establish its own control frequency however good laboratory practice suggests that controls be tested each day patient samples are tested and each time calibration/blanking is performed.

The results obtained by any individual laboratory may vary from the given mean value. It is therefore recommended that each laboratory generates analyte specific control target values and intervals based on multiple runs according to their requirements. These target values should fall within the corresponding acceptable ranges given in the relevant product literature.

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/DxC AU analyzer Instructions For Use (IFU) for analyzer-specific assay instructions for the sample type as listed in the Intended Purpose statement.

The low sample volume application is available for use with serum/plasma samples on AU/DxC AU analyzers.

CALCULATIONS

The Beckman Coulter analyzers automatically compute the glucose concentration of each sample.

REPORTING RESULTS

REFERENCE INTERVALS

Reference [1,10,11]

Reference Range		mmol/L	mg/dL
Serum/Plasma (fasting)	Adult	4.1 - 5.6	74 - 100
	Child	3.3 - 5.6	60 - 100
	Premature	1.1 - 3.3	20 - 60
	Neonate	1.7 - 3.3	30 - 60

Reference Range		mmol/L	mg/dL
CSF	Adult	2.2 - 3.9	40 - 70 ≈ 60% of plasma value
	Infant, child	3.3 - 4.5	60 - 80
Urine		0.1 - 0.8	1 - 15

The generally accepted criteria for the diagnosis of diabetes are:[12]

(a) random plasma glucose of ≥ 11.1 mmol/L

(b) fasting plasma glucose (FPG) ≥ 7.0 mmol/L or

(c) 2-h postload glucose ≥ 11.1 mmol/L during an oral glucose tolerance test (OGTT).

If any one of these criteria is met, results must be confirmed by repeat testing on a subsequent day, unless there is unequivocal hyperglycaemia with acute metabolic decompensation.

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

Ascorbate :	Interference less than 3% or 0.30 mmol/L up to 20 mg/dL ascorbate
Icterus:	Interference less than 10% or 0.30 mmol/L up to 40 mg/dL or 684 µmol/L bilirubin
Haemolysis:	Interference less than 3% or 0.30 mmol/L up to 5 g/L haemoglobin
Lipemia:	Interference less than 10% or 0.30 mmol/L up to 700 mg/dL Intralipid

Eltrombopag and its metabolites may interfere with this assay causing erroneously high patient results.

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

Ascorbate :	Interference less than 3% or 0.24 mmol/L up to 50 mg/dL ascorbate
Icterus:	Interference less than 3% or 0.24 mmol/L up to 40 mg/dL or 684 µmol/L bilirubin

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

Haemolysis:	Interference less than 3% or 0.4 mmol/L up to 5 g/L haemoglobin
Icterus:	Interference less than 3% or 0.4 mmol/L up to 40 mg/dL or 684 µmol/L bilirubin

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

Further information on interfering substances is available.[13]

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.

ANALYTICAL MEASURING RANGE/LINEARITY

ANALYTICAL MEASURING RANGE	mmol/L	mg/dL
Serum/Plasma/CSF	0.6 - 45	10 - 810
Urine	0.2 - 45	3.6 - 810

SENSITIVITY

The Limit of Detection (LoD) and Limit of Quantitation (LoQ) were determined in accordance with the CLSI EP17-A2 guideline[14].

Correctly operating AU/DxC AU systems should exhibit the following LoD/LoQ:

LoD/LoQ	mmol/L	mg/dL
Serum	≤0.6	≤10.8
Urine	≤0.2	≤3.6
CSF	≤0.6	≤10.8

LoD is defined as the lowest concentration that can be detected with a probability of 95%.

LoQ is the lowest level of measurand which can be quantitatively determined with a within-laboratory CV of ≤ 20%, established as per EP17-A2.

METHODS COMPARISON

Patient serum samples were evaluated in method comparison studies.

Results of Deming regression analysis were as follows:

AU5800 versus AU2700

Regression Equation	r	n	Range
Y=0.965x+0.003	0.9994	176	0.67 - 43.31 mmol/L

Patient Urine samples were evaluated in method comparison studies.

Results of Deming regression analysis were as follows:

DxC 700 AU versus AU680

Regression Equation	r	n	Range
Y=1.022x-0.180	1.000	123	0.22 - 41.98 mmol/L

Patient CSF samples were evaluated in method comparison studies.

Results of Deming regression analysis were as follows:

DxC 700 AU versus AU5800

Regression Equation	r	n	Range
Y=1.017x-0.0696	1.000	120	0.614 - 43.572 mmol/L

PRECISION

Correctly operating AU/DxC AU systems should exhibit the following precision values:

	Serum/Plasma/Urine/CSF
TYPE OF IMPRECISION	**% CV**
Repeatability (Within-run)	≤ 3
Within Laboratory (Total)	≤ 3

Estimates of precision, based on CLSI recommendations[15] are consistent with typical performance.

The following data was obtained on a representative analyzer using 3 serum pools analyzed over 20 days:

AU5800

n = 80	Repeatability (Within Run)		Within Laboratory (Total)	
Mean mmol/L	**SD**	**CV%**	**SD**	**CV%**
2.99	0.02	0.7	0.03	0.9
6.43	0.03	0.5	0.04	0.6
16.31	0.05	0.3	0.11	0.7

The following data was obtained on a representative analyzer using 3 urine pools analyzed over 20 days.

AU5800

n = 80	Repeatability (Within-run)		Within Laboratory (Total)	
Mean mmol/L	**SD**	**CV%**	**SD**	**CV%**
0.95	0.014	1.5	0.023	2.4
12.4	0.081	0.7	0.121	1.0
42.2	0.204	0.5	0.403	1.0

The following data was obtained on a representative analyzer using 3 CSF pools analyzed over 20 days:

DxC 700 AU

n = 80	Repeatability (Within-run)		Within Laboratory (Total)	
Mean mmol/L	**SD**	**CV%**	**SD**	**CV%**
1.67	0.01	0.6	0.04	2.5
4.39	0.02	0.5	0.11	2.4
10.41	0.04	0.4	0.25	2.4

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
GLU1N	Glucose (Serum)
GLU1N	Glucose (CSF)
GLU1N, GLU1NP	Glucose (Urine)
GLU1NP	Glucose (Serum Low sample volume)

Setting Sheet Footnotes

User defined

Serum: † System Calibrator Cat. No.: 66300.

Urine: † Urine Calibrator Cat. No: B64606. Ensure relevant value sheet is used.

* Values set for working in SI units (mmol/L). To work in mg/dL multiply by 18.

** GLU1N to link with Serum Application, GLU1NP to link with Low sample volume Serum Application

** Test Name 'GLUC' to link with Low sample volume Serum Application 'GLUCP'

ʊ BLOSR6x21EU (IVDR): Enter Dynamic Range Low value of 0.2

ʊ BLOSR6x21EU (IVDR): Enter Analytical Measuring Range Low value of 0.2

Notice to User

Any serious incident that has occurred in relation to this device should be reported to Beckman Coulter and the competent authority of the Member State in which the user and/or patient is established.

The Summary of Safety and Performance is available from the EUDAMED database: ec.europa.eu/tools/eudamed

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

OSR6621 for use on the AU5800 system only.

REVISION HISTORY

Updated based on IVDR 2017/746 requirements.

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