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SELECTED DIAGNOSTIC REAGENTS

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ACE

Angiotensin Converting Enzyme - Liquid Reagent

CE

In Vitro Diagnostic reagent for the quantitative determination of Angiotensin Converting Enzyme (ACE) in serum and plasma. Store at 2-8°C .

REF: ACE-101L

Summary:

Angiotensin converting enzyme is a glycoprotein peptidyldipeptide hydrolase that cleaves histidylleucine dipeptide from angiotensin I to angiotensin II, a potent vasoconstrictor. ACE also inactivates bradykinin. Elevated levels of ACE activity occur in serum of patients with active sarcoidosis, and occasionally in premature children with respiratory distress syndrome, in adults with tuberculosis, Gaucher's disease, leprosy, and in many other pathologic conditions involving lung and liver diseases.

Principle:

Furylacryloylphenylalanylglycylglycine (FAPGG) is hydrolysed to Furylacryloylphenylalanine (FAP) and Glycylglycine (GG). Hydrolysis of FAPGG results in a decrease in absorbance at 340nm. The rate of decrease in absorbance is directly proportional to ACE activity in the sample.

$$\text{FAPGG} \xrightarrow{\text{ACE}} \text{FAP} + \text{GG}$$

Composition:

Reagent: Boric Acid Buffer pH 8.3 - 80 mmol/l, FAPGG - 0.75 mmol/l
Calibrator: ACE - Lot specific

Precautions:

For In Vitro Diagnostics Use Only - For Professional Use Only
Carefully read instructions for use. Deviations from this procedure may alter performance of the assay.

Components Colour and Appearance:
Reagent 1: Colourless clear liquid.
Any significant changes could indicate that the assay might be compromised. Refer to Laboratory's QC program for actions to be taken. In case of serious damage to the bottle and/or cap, resulting in product leakage and/or contamination, do not use the reagent pack and contact your distributor.

Safety precautions:
This product is not hazardous under EU specifications. Material Safety Data Sheet is available upon request.

Handling precautions:
- Take the necessary precautions required for handling all laboratory reagents.
- Do not use components past the expiry date stated on the Bottles.
- Do not Freeze Reagents.

Do not use components for any purpose other than described in the "Intended Use" section.
- Do not interchange caps among components as contamination may occur and compromise test results.
- Refer to local legal requirements for safe waste disposal.

Instruments:

Instrument applications are available upon request.

Preparation:

Reagent is ready to use.
Before use, mix reagent by gently inverting each bottle.
If stored and handled properly, component is stable until expiry date stated on the label.

Samples:

Serum, is the preferred sample. Heparinised plasma can also be used.
It is recommended to follow NCCLS procedures (or similar standardised conditions) regarding sample handling. Sample should be collected in an appropriate sample container, with proper sample identification. Serum/Plasma should be separated from cells within 2 hours after collection.
Stability: up to 4 weeks at 4°C.

Equipment:

- ACE Control Level 1
- ACE Control Level 2
- Photometer
- General Laboratory Equipment

Procedure:

1. Assay conditions:
Wavelength: . . . . . 340 nm
Cuvette: . . . . . 1 cm. light path
Temperature . . . . . 30°C or 37°C

	Blank	Calibrator	Sample
R1 (µL)	1000	1000	1000
Sample (µL)	-	-	100
Calibrator (µL)	-	100	-

2.Gently mix and Incubate for 4 minutes, then measure the Optical Density (OD). Incubate for a further 5 minutes, mix and read OD
3. Calibration: Using recommended Calibrator, calibrate the assay:
- When using a new reagent kit or changing lot number.
- Following preventive maintenance or replacement of a critical part of the photometer used.
- When Quality Controls are out of range.

Calculations:

$$\frac{OD_{Sample} - OD_{Blank}}{OD_{Calibrator} - OD_{Blank}} \times \text{Concentration of Calibrator} = \text{ACE Activity}$$

(Conversion factor: Qty in µKat/l = Qty in U/l x 0.0167).

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

Over 14 years of age
U/l: 8 – 65
µkat/l: 0.13 – 1.10
Each laboratory should establish its own reference range. ACE results should always be reviewed with the patient's medical examination and history.

Performance characteristics:

Performance results can vary with the instrument used. Data obtained in each individual laboratory may differ from these values.
Linearity:
This assay is linear up to 166 U/l (2.8 µkat/l)
For samples with a higher concentration, dilute 1:1 with 0.9% NaCl (9g/l) and re-assay. Multiply result by 2.
Interfering substances:
Results of study are as follows:
Bilirubin (mixed isomers): Less than 10% interference up to 600 µmol/l Bilirubin
Haemolysis: Less than 10% interference up to 1.25 g/l Haemoglobin.
Lipemia: Less than 10% interference up to 1.25 g/l Intralipid.
Sensitivity:
The Lowest Detectable Level of ACE was estimated at 5.4 U/l (0.09 µkat/l).
Precision:

	Intra-assay			Inter-assay		
N=20	Mean (µmol/L)	SD	%CV	Mean (µmol/L)	SD	%CV
level 1	26.3	0.90	3.42	27	1.01	3.80
level 2	88.9	1.79	2.01	94	3.71	3.97

Method comparison:
Using 50 samples, a comparison, between this ACE test (y) and another commercially available test (x), gave the following results:
y = 1.015x + 7.690
r = 0.991
Sample range: 12 to 124 U/l

References:

1. Burtis CA, Ashwood ER. Tietz Fund. Of Clin. Chem. 5th ed. 30-54, 352, 384-385 and 965.
2. Maguire GA, Price CP. Ann. Clin. Biochem. 1985; 22:204-210.

CK-NAC

Creatine Kinase Liquid Reagent

CE

In Vitro Diagnostic reagent for the quantitative determination of Creatine Kinase (CK-NAC) in serum and plasma. Store at 2-8ºC .

REF: NAC-017B1 / NAC-017B2

Summary:

CK is a dimeric enzyme occurring in 4 different forms, a Mitochondrial Iso-enzyme and 3 Cytoplasmic Iso- enzymes. CK MM is a muscle enzyme, CK BB is a brain enzyme and CK MB is the heart enzyme. CK activity is elevated in many diseases including those involving skeletal muscle, heart, central nervous system and the thyroid. Most determinations of CK in the clinical laboratory are used for the early detection of Myocardial Infarction in which the enzyme is elevated within 3 to 8 hours after the attack.

Principle:

Creatine Phosphate+ ADP $\xrightarrow{CK}$ Creatine + ATP

ATP + Glucose $\xrightarrow{Hexokinase}$ Glucose-6-Phosphate + ADP

Glucose-6-Phosphate + $NADP^+$ $\xrightarrow{G6P\text{-}DH}$ 6-phosphogluconate + NADPH + H^+

Composition:

R1: Imidazole Buffer pH 6.7 - 100 mmol/l, Glucose - 20 mmol/l, Magnesium Acetate - 10 mmol/l, EDTA - 2.0 mmol/l, ADP - 2.0 mmol/l, AMP - 5.0 mmol/l, NADP - 2.0 mmol/l,
HK - >2.5 U/ml, N-acetylcysteine - 20 mmol/l
R2: Creatine Phosphate - 30 mmol/l, G6P-DH - >1.5 U/ml,
Diadenosine pentaphosphate - 10 µmol/l

Precautions:

For In Vitro Diagnostics Use Only - For Professional Use Only
Carefully read instructions for use. Deviations from this procedure may alter performance of the assay.
Components Colour and Appearance:
Both Reagent: Clear colourless liquid.
Any significant changes could indicate that the assay might be compromised. Refer to Laboratory's QC program for actions to be taken. In case of serious damaged to the bottle and/or cap, resulting in product leakage and/or contamination: do not use the reagent pack and contact your distributor .
Safety precautions:
Contains small quantities of Sodium Azide. Material Safety Data Sheet is available upon request.
Handling precautions:
- Take the necessary precautions required for handling all laboratory reagents.
- Do not use components past the expiry date stated on the Bottles.
- Do not Freeze Reagents.
- Do not use components for any purpose other than described in the "Intended Use" section.
- Do not interchange caps among components as contamination may occur and compromise test results.
- Refer to local legal requirements for safe waste disposal.

Instruments:

Instrument applications are available upon request.

Preparation:

Before use, mix reagent by gently inverting each bottle.
If stored and handled properly, unopened components are stable until the expiry date stated on the label.
Monoreagent procedure: Mix 4 volumes of R1 with 1 volume of R2. Working reagent is stable 20 days at 2-8°C.
Bireagent procedure: Liquid reagent 1 and 2 are ready for use.

Samples:

Serum free of haemolysis is the preferred sample as plasma may produce unpredictable reaction rates.
It is recommended to follow NCCLS procedures (or similar standardised conditions) regarding sample handling. Serum should be separated from cells as rapidly as possible after collection.
Stability: up to 7 days if stored in a lightproof, tightly closed tube and maintained at 4°C

Equipment:

- General Chemistry Calibrator
- General Chemistry Control Level 1
- General Chemistry Control Level 2
- Photometer
- General Laboratory Equipment

Procedure:

1. Assay conditions:
Wavelength: . . . . λ: 340 (334/365) nm
Cuvette: . . . . .1 cm. light path
Temperature . . . . . .30°C (25°C or 37°C)

2.Monoreagent Procedure:

	Blank	Calibrator	Sample
Working Reagent (µL)	1000	1000	1000
Sample (µL)	-	-	-
Calibrator (µL)	-	40	-

Gently mix and Incubate at 25°C, 30°C or 37°C for 2 minutes.
Measure the change of Optical Density per minute (ΔOD/min) over the next 3 minutes.

3.Bireagent Procedure:

	Blank	Calibrator	Sample
R1(µL)	800	800	800
Sample (µL)	-	-	40
Calibrator (µL)	-	40	-

Gently mix and Incubate at 37°C for 5 minutes

R2(µL)	200	200	200

Gently mix and Incubate at 37°C for 2 minutes
Measure the change of Optical Density per minute (ΔOD/min) over the next 4 minutes

Enzyme Calibration:
Using recommended Calibrator, calibrate the assay:
- When using a new reagent kit or changing lot number.
- Following preventive maintenance or replacement of a critical part of the photometer used.
- When Quality Controls are out of range.

Calculations:

$$\frac{\Delta OD\ Sample - \Delta OD\ Blank}{\Delta OD\ Calibrator - \Delta OD\ Blank} \times Concentration\ of\ Calibrator. = CK\ NAC\ Activity$$

(Conversion factor: Qty in µKat/l = Qty in U/l x 0.0167).

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

The probability of myocardial injury is high when the following 3 conditions are met:

			U/L at 25°C	µkat/l at 25°C	U/L at 30°C	µkat/l at 30°C	U/L at 37°C	µkat/l at 37°C
1.	CK	Men	> 80	> 1.33	> 130	> 2.17	>190	> 3.17
		Women	> 70	> 1.17	> 110	> 1.83	> 167	> 2.87
2.	CK- MB		> 10	> 0.17	> 15	> 0.25	> 24	> 0.40
3.	CK-MB activity accounts for 6 – 25% of the total CK activity							

* Calculated values. Temperature conversion factors: 25°C to 30°C: 1.53. 25°C to 37°C: 2.38
Each laboratory should establish its own reference range. CK-MB results should always be reviewed with the patient's medical examination and history.

Performance characteristics:

Performance results can vary with the instrument used. Data obtained in each individual laboratory may differ from these values.
Linearity:
Linear up to 1806 U/L (30 µkat/l).
For samples with a higher concentration, dilute 1:1 with 0.9% NaCl (9g/l) and re-assay. Multiply result by 2.
Interfering substances:
Bilirubin (mixed isomers): Less than 10% interference up to 400µmol/l Bilirubin
Haemolysis: Less than 10% interference up to 1.25 g/l Haemoglobin.
Lipemia: Less than 10% interference up to 5 g/l Intralipid.
Sensitivity:
The Lowest Detectable Level is estimated at 5 U/L (0.42 µkat/l).
Precision:

	Intra-assay			Inter-assay		
N=20	Mean (µmol/L)	SD	%CV	Mean (µmol/L)	SD	%CV
level 1	177	2.5	1.41	169	1.50	0.89
level 2	408	3.43	0.84	383	1.29	0.34

Method comparison:
Using 50 samples, a comparison, between this CK-NAC test (y) and another commercially available test (x), gave the following results:
y =0.997x + 5.765
r = 0.986
Sample range: 9 to 395 U/l

References:

1. Ann. Biol. Clin.40 (1982) 99. & Stein W. Med Weit. 1985, 36:572.
2. Stein W. Med Weit. 1985, 36:572 & Burtis CA, Ashwood ER. Tietz Fund. Of Clin. Chem. 5th ed. 30-54, 352-390 and 974-97
3. Szasz G, Busch EW. Third European Congress of Clinical Chemistry, Brighton, England, 3-8 June 1979 (abstract)

CK-MB

Creatine Kinase MB liquid reagent

CE

In Vitro Diagnostic reagent for the quantitative determination of Creatine Kinase (CK-MB) in serum and plasma. Store at 2-8°C .

REF: LCKMB-001 / LCKMB-002

Summary:

CK-MB is an enzyme formed by the association of two subunits from muscle (M) and nerve cells (B). CK-MB is usually present in serum at low concentration; it is increased after an acute infarct of myocardium and later descends at normal levels. Also is increased, rarely, in skeletal muscle damage.

Principle:

Creatine Phosphate + ADP $\xrightarrow{CK}$ Creatine + ATP

ATP + Glucose $\xrightarrow{HK}$ ADP + Glucose-6-phosphate (G-6-P)

G-6-P + NADP+ $\xrightarrow{G6P\text{-}DH}$ 6-phosphogluconate + NADPH + H+

Composition:

R1: Imidazole Buffer pH 6.7 - 100 mmol/l, Glucose - 20 mmol/l, Magnesium Acetate - 10 mmol/l, EDTA - 2.0 mmol/l, ADP - 2.0 mmol/l, AMP - 5.0 mmol/l, NADP - 2.0 mmol/l, CK-M Inhibiting Antibody - 8000 U/l, HK - >2.5 U/ml, N-acetylcysteine - 20 mmol/l
R2: Creatine Phosphate - 30 mmol/l, G6P-DH - >1.5 U/ml, Diadenosine pentaphosphate - 10 umol/l, Preservatives
Calibrator: CKMB - Cal - lot specific

Precautions:

For In Vitro Diagnostics Use Only - For Professional Use Only
Carefully read instructions for use. Deviations from this procedure may alter performance of the assay.
Components Colour and Appearance:
Both Reagent: Clear colourless liquid.
Any significant changes could indicate that the assay might be compromised. Refer to Laboratory's QC program for actions to be taken. In case of serious damaged to the bottle and/or cap, resulting in product leakage and/or contamination: do not use the reagent pack and contact your distributor .
Safety precautions:
Contain small quantities of Sodium Azide. Material Safety Data Sheet is available upon request.

Instruments:

Instrument applications are available upon request.

Preparation:

Before use, mix reagent by gently inverting each bottle.
If stored and handled properly, unopened components are stable until the expiry date stated on the label
Monoreagent procedure: Mix 4 volumes of R1 with 1 volume of R2. Working reagent is stable 20 days at 2-8°C.
Bireagent procedure: Liquid reagent 1 and 2 are ready for use.

Samples:

Use serum free from haemolysis, heparin or EDTA plasma.
It is recommended to follow NCCLS procedures (or similar standardised conditions) regarding sample handling.
Serum/plasma should be separated from cells immediately after collection and stored in the dark. Stability: up to 7 days at 2-8°C.

Equipment:

- CK-MB Control: Photometer
- CK-MB Calibrator: General Laboratory Equipment

Procedure:

1. Assay conditions:
Wavelength: . . . . λ: 340 (334/365) nm
Cuvette: . . . . .1 cm. light path
Temperature . . . . . .30°C (25°C or 37°C)

2. Monoreagent procedure:

	Blank	Sample
R1 (µL)	1000	1000
Sample (µL)	-	40

Gently mix and Incubate at 30°C (25°C or 37°C) for 2 minutes, then measure the change of Optical Density per minute (ΔOD/min) for the next 3 minutes.

3. Bireagent procedure:

	Blank	Calibrator	Sample
R1 (µL)	800	800	800
Sample (µL)	-		40
Calibrator (µL)	-	40	-

4. Gently mix and Incubate at 37°C for 5 minutes

5. Add:

R2(µL)	200	200	200

6. Gently mix and Incubate at 37°C for 2 minutes, then measure the change of Optical Density per minute ΔOD/min) for the next 4 minutes.

7. Enzyme Calibration:
Using calibrator provided, calibrate the assay:
- When using a new reagent kit or changing lot number.
- Following preventive maintenance or replacement of a critical part of the photometer used.
- When Quality Controls are out of range.

Calculations:

$$\frac{\Delta OD\ Sample - \Delta OD\ Blank}{\Delta OD\ Calibrator - \Delta OD\ Blank} \times \text{Concentration of Calibrator.} = \text{CK MB Activity}$$

(Conversion factor: Qty in µKat/l = Qty in U/l x 0.0167).

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

The probability of myocardial injury is high when the following 3 conditions are met:

			U/L at 25°C	µkat/l at 25°C	U/L at 30°C	µkat/l at 30°C	U/L at 37°C	µkat/l at 37°C
1.	CK	Men	> 80	> 1.33	> 130	> 2.17	>190	> 3.17
		Women	> 70	> 1.17	> 110	> 1.83	> 167	> 2.87
2.	CK- MB		> 10	> 0.17	> 15	> 0.25	> 24	> 0.40
3.	CK-MB activity accounts for 6 – 25% of the total CK activity							

* Calculated values. Temperature conversion factors: 25°C to 30°C: 1.53. 25°C to 37°C: 2.38

Performance characteristics:

Performance results can vary with the instrument used. Data obtained in each individual laboratory may differ from these values.
Linearity:
Linear up to 1000 U/L.
For samples with a higher concentration, dilute 1:1 with 0.9% NaCl (9g/l) and re-assay. Multiply result by 2.
Interfering substances:
Bilirubin (mixed isomers): Less than 10% interference up to 600µmol/l Bilirubin.
Haemolysis: Less than 10% interference up to 1.25 g/l Haemoglobin.
Lipemia: Less than 10% interference up to 2.5 g/l Intralipid.
Sensitivity:
The Lowest Detectable Level is estimated at 2 U/l (0.03 µkat/l).
Precision:

	Intra-assay			Inter-assay		
N=20	Mean (U/L)	SD	%CV	Mean (U/L)	SD	%CV
level 1	172.1	4.88	2.83	165.4	5.58	3.37
level 2	776.4	13.46	1.73	740.2	15.26	2.06

Method comparison:
Using 50 samples, a comparison, between this CK MB test (y) and another commercially available test (x), gave the following results:
y = 0.976x – 0.269
r = 0.999
Sample range: 0 to 329 U/l

References:

1. Stein W. Med Weit. 1985, 36:572 & Burtis CA, Ashwood ER. Tietz Fund. Of Clin. Chem. 5th ed. 30-54, 352-390 and 974-975
2. GuderWG, NarayananS, WisserH, ZawtaB. List of Anal; Preanal Variables. From the Patient to the Laboratory. Darmstdt:GIT Verlag 1996.
3. Wurzburg U, Hennrich N, Lang H, Prellwitz W, Neumeier D, Knedel M. Klin. Wschr. 1976: 54 and 357.
4. Szasz G, Busch EW. Third European Congress of Clinical Chemistry, Brighton, England, 3-8 June 1979 (abstract).

Creatinine

Enzymatic colorimetric

CE

Quantitative determination of creatinine concentration
Only for in vitro use in the clinical laboratory. Store at 2-8ºC .

REF: CRE-035B1 / CRE-035B2

Summary:

Creatinine measurements are used in the diagnosis and treatment of renal diseases, in monitoring renal dialysis, and as a calculation basis for measuring other urine analytes.
Clinical diagnosis should not be made on the findings of a single test result, but should integrate both clinical and laboratory data.

Principle:

In the first reaction, creatinase and sarcosine oxidase are used in the enzymatic hydrolysis of endogenous creatine to produce hydrogen peroxide, directly eliminated by catalase. In the second reaction, the catalase is inhibited by sodium azide, and creatininase and 4-aminoantipyrine (4-AA) were added.The creatine generated from creatinine by creatininase is hydrolyzed sequentially by creatinase and sarcosine oxidase to produce hydrogen peroxide. This newly-formed hydrogen peroxide was measured in a coupled reaction catalyzed by peroxidase.

Composition:

R1: MOPS - 25 mmol/L, TOPS - 0.5 mmol/L, Creatinase - 10 KU/L, sarcosine oxidase - 5 KU/L, Catalase - 3 KU/L, EDTA - 1 mmol/L, pH 7.5
R2: MOPS - 90 mmol/L, Creatininase - 30 KU/L, peroxidase - 5 KU/L, sodium azide - 0.5 g/L, pH 7.5

Preparation:

R1 and R2 are ready to use.

Storage and Stability:

All the components of the kit are stable until the expiration date on the label when stored tightly closed at 2-8ºC, protected from light and contaminations prevented during their use.
R1 and R2 are stable 8 weeks after opening bottle.

Samples:

Serum, plasma or urine. Dilute fresh urine 1/50 with distilled water before measurement.
Creatinine is stable 1 day at 2-8ºC.

Equipment:

- Spectrophotometer or photometer measuring at 545±20 nm, with cell holder thermostatable at 37ºC.
- General laboratory equipment.

Procedure:

1. Assay conditions:
Wavelength: . . . . .545 ±20 nm
Temperature . . . . . .37ºC (±0.1°C)
2. Bring the reagents and the instrument to 37ºC (±0.1ºC).
3. Pipette into a thermostatized cuvette:

	Blank	Calibrator	Sample
R1 (µL)	270	207	270
H2O/Cal/Sample (µL)	6	6	6

4. Mix and incubate 5 minutes
5. Read the absorbance (A1) of the calibrator and the samples, at 545 nm against the blank.
6: Add:

	Blank	Calibrator	Sample
R2 (µL)	90	90	90

7. Mix and incubate 5 minutes.
8. Read the absorbance (A2) of the calibrator and the sample, at 545 nm against the blank.

Calculations:

$$\frac{(A2s - A1s) - (A2b - A1b) \times K}{(A2s - A1s) - (A2b - A1b) \times K} \times \text{Concentration of Calibrator.} = \text{Creatinine}$$

K = 0.754 = 276 µL/366 µL

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

	Men	Women	
Serum or plasma	0.9 - 1.3	0.6 - 1.1	mg/dL
Urine	14 - 16	11 - 20	mg/Kg/24h

These values are for orientation purpose; each laboratory should establish its own reference range.

Performance characteristics:

Measuring range:
Measuring range: from detection limit of 0.05 mg/dL to linearity limit of 200 mg/dL. If the results obtained were greater than linearity limit, dilute the sample 1/2 with NaCl 9 g/L and multiply the result by 2.
Precision:

	Intra-assay		Inter-assay	
N=20	Mean (mg/L)	%CV	Mean (mg/L)	%CV
level 1	1.11	0.8	1.09	1.2
level 2	5.73	0.4	5.76	0.4

Accuracy:
Results obtained using these reagents did not show systematic differences when compared with other commercial reagents or with HPLC method. Details of the comparison experiments are available on request.
Interferences:
No interferences were observed with hemoglobin until 5 g/L, bilirubin 40 mg/dL. Other drugs and substances may interfere.

The results of the performance characteristics depend on the analyzer used.

Notes:

1. Calibration with an aqueous standard may cause matrix related bias, it is recommended to calibrate using a serum based calibrator.
2. Urine: multiply the result by 50 (sample dilution factor).

References:

1. Fossati et al. Clin Chem 1983; 29: 1494-1496.
2. Tietz Textbook of Clinical Chemistry, 3rd edition. Burtis CA, Ashwood ER. WB Saunders Co., 1999.
3. Young DS. Effects of drugs on Clinical Lab. Tests, 4th ed AACC Press, 1995.
4. Young DS. Effects of disease on Clinical Lab. Tests, 4th ed AACC 2001.

Copper

Color Di Br-PAESA. Liquid Reagent

CE

In vitro diagnostic reagent for quantitative determination of copper in serum or plasma.
Store at 2-8 °C.

REF: RCO-100

Summary:

The major functions of copper metalloproteins involve oxidation-reduction; most known copper containing enzymes bind and react directly with molecular oxygen. Specific diseases associated with copper include head disease, bone and joint osteoarthritis and osteoporosis and Menkes syndrome, Wilson's disease and others. Elevated levels of copper can also be toxic.

Principle:

In a pH 4.7 buffer system, copper is released from its carrier protein, the ceruloplasmin, and forms with the specific complexant 3,5-DiBr-PAESA a stable coloured complex. The colour intensity of this complex is proportional to the amount of copper in the sample.

Composition:

R1: Acetate buffer pH 5.0 - 0.2 mol/l,
3,5-DiBr-PAESA - N-ethyl-N-sulfopropylaniline - 0.02 mmol/l, Standard - 100 µg/dl (15.73 µmol/l)

Reagent Stability And Storage:

The sealed reagent is stable up to the indicated expiry date if stored at 4°C.

Samples:

Serum, Plasma

Procedure:

1. Assay conditions:
Wavelength: . . . . . 580 nm
Cuvette: . . . . . .1 cm. light path
Temperature . . . . . .+ 37°C

	Standard	Sample
R1 (µL)	1000	1000
Serum or Plasma (µL)	-	50
Standard (µL)	50	-

2.Mix and incubate for 5 minutes at 37°C.
Measure the absorbance of the sample $A_{(S)}$ and of the standard $A_{(STD)}$ against the reagent blank $A_{(RBL)}$

$\Delta A_{(S)} = A_{(S)} - A_{(RBL)}$

$\Delta A_{(STD)} = A_{(STD)} - A_{(RBL)}$

Calculations:

$$\frac{\Delta A \text{sample}}{\Delta A \text{standard}} \times 100 = \mu g/dl \text{ copper}$$

$$\frac{\Delta A \text{sample}}{\Delta A \text{standard}} \times 15.71 = \mu mol/l \text{ copper}$$

Calibration Frequency:
Two-point calibration is recommended:
- after reagent lot change
- as required following quality control procedures

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference Values:

Male: 70-140 µg/dl (11.0 -22.0 µmol/l)
Female: 80 -155 µg/dl (12.6 -24.4 µmol/l)

Performance characteristics:

Measuring and reportable range:

3 – 500 µg/dl. Samples with copper concentration higher than 500 µg/dl (78.65 µmol/l) must be diluted 1:10 with normal saline and result multiplied by 10.

Linearity:

Up to 500 µg/dl (78.65 µmol/l)

Precision:

	Intra-assay			Inter-assay		
	Mean (µg/dL)	SD	%CV	Mean (µg/dL)	SD	%CV
L1	72.60	1.66	2.28	101.7	2.78	2.73
L2	121.20	1.19	0.98	111.9	3.06	2.73
L3	170	1.52	0.89	N/A	N/A	N/A

Method comparison:

A comparison of the mti-diagnostics Copper LS (y) with a commercial obtainable assay (x) gave the following result:
$y = 1.003x + 1.9621$
$R^2 = 0.9977$

Sensitivity (LOD):

0.3 µg/dl
The lower detection limit represents the lowest measurable copper concentration that can be distinguished from zero.

Interferences:

The test is not affected by the presence of conjugated and non-conjugated bilirubin up to 15 mg/dl, hemoglobin up to 0.5 g/dl and triglycerides up to 1000 mg/dl.

Notes:

For in vitro diagnostic use.
Please follow the normal precautions required for handling all laboratory reagents.
Use disposable test tubes and glassware washed with hydrochloric acid 1N solution and distilled water.
Working solution must be limpid; do not use if turbid
R1 contains urea as additive. In the sample order setting, do not input urea test immediately after copper in "random access" automatic analyzers.
In addition to the possible risk indications regarding the reactive components such as preservatives (i.e. sodium azide or other) and detergents. The total concentration of these components is lower than the limits reported by the 67/548/EED and 88/379/EEC directives and following modifications and amendments about classification, labelling and packaging of dangerous preparations (reagents). However, it is recommended to handle reagents carefully, to avoid ingestion and contact with eyes, skin and mucous membranes and to use laboratory reagents according to good laboratory practice

References:

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2. Guder, W.; Zawta, B.: Die Qualität diagnostischer Proben, Empf. der Arbeitsgr. Präanalytik der DGKC und der DGLM 2002, 3. Aufl.
3. Abe A., Yamashita S., Noma A.: Clin. Chem., 35 (1989) 552-554.

D-Dimer

Liquid Reagent

CE

Quantitative measurement of D-dimer in human plasma or serum.
Store at 2-8 °C.

REF: DDM-010

Summary:

D-dimer is a type of fibrin degradation products composed of stable fibrin degraded by plasmin. Stable fibrin is crosslinked by the action of coagulation factor XIII in the blood coagulation and fibrinolysis system. Increasing in the level of D-dimer in the blood are linked to thrombus production, as well as the efficacy of fibrinolysis. Increasing in the level of D-dimer is also known to be associated with various diseases, including malignant tumors, obstetric diseases, vascular lesions, and DIC (disseminated intravascular coagulation syndrome).

Principle:

The D-dimer contained in the sample reacts with the latex sensitized with anti-human D-dimer monoclonal antibody (mouse) and forms aggregates, which are determined optically for calculation of D-dimer concentration.

Composition:

R1: Buffer Reagent
R2: Latex coated with anti-human D-dimer monoclonal antibody

Instruments:

Instrument applications are available upon request.

Preparation:

Reagent is ready for use.
If stored at 2-8°C and handled properly, component is stable until expiry date stated on the label.

On-board, in use and refrigerated on the analyser: 4 weeks.

- Store the reagents according to the specified storage method, and do not use a batch passing the expiry date.
- Never freeze latex solution.
- Be sure not to mix reagents of different lots. Use the same lot of reagents when creating a calibration curve and assaying a sample.
- Avoid mixing the remaining reagents into new one, as this may cause contamination or deterioration of the reagents.
- Upon completion of assay, the reagents should be capped and then stored according to the specified storage method.
- After removing from a refrigerator, Latex reagents should be fully mixed prior to use.
- Do not allow dust or foreign substances to get mixed into reagents or cuvettes.

Samples:

For specimen collection and preparation, collect it in citrate. The plasma, separated by centrifugation as soon as possible after collection, may be stored for up to a week at 4°C, or 2 months at –80°C. Samples may be frozen and thawed three times with no detrimental effect. Serum separated by centrifugation as soon as possible after collection with collecting tube dedicated to FDP containing thrombin and aprotinin may have stability similar to that of citrated plasma.

Equipment:

- D-Dimer Controls
- D-Dimer Calibrator
- General Laboratory Equipment

Procedure:

The operating methods are different depending on the type of automatic analyser. The detailed operating methods and the parameters for each type of automatic analyser are available.
[Hitachi 7100 as an example]

1. Reagent Preparation
- R1: ready to use
- R2: ready to use
- Calibrator: prepare according to the instruction manual
- Diluent: ready to use

2. Supplemental remarks
- Calibrator (optional)

3. Assay procedure
Add 180uL of R1 to 4uL of the sample, warm the mixture to 37°C for 5 minutes, and then add 60uL of R2. Determine the absorbance of the mixture while warming to 37°C, 5 minutes after mixing at 700 nm of main-wavelength. Proceed similarly with the calibrator, and compare the absorbance values for calculation of the D-dimer concentration in the sample.

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

Measuring range: 1.0 ug/mL or less

Performance characteristics:

Performance results can vary with the instrument used. Data obtained in each individual laboratory may differ from these values.

Specificity:
When assaying control samples of known concentration, the assay values are within ± 15% of the known concentration.

Interfering substances:
Bilirubin: No significant interference up to 18mg/dl.
Lipemia (Intralipid): No significant interference up to 2000 mg/dl.
Hemolysis: No significant interference up to 500mg/dl.

Sensitivity:
When the calibrator containing D-dimer at a concentration of 0 ug/mL and 0.5 ug/mL are assayed 10 times each consecutively, MEAN ± 2SD of the assayed absorbance of each sample is not overlapped.

Reproducibility:
When a control sample is assayed 5 times consecutively, CV is 10% or less.

Assay Range:
From 0.5 to 30ug/Ml (on Hitachi).

Measuring Ranges:

1.0ug/mL or less

The reference value range will possibly be different depending on various conditions of individual laboratories, so set the reference value range suitable to each laboratory.

1. Some samples may consist of substances which cause non-specific reaction or interfering reaction. When assay values and results are questionable, validate it through re-testing by dilution or assaying by other test kit.
2. Note that Prozone (PZ) remark may be indicated for samples with target substance of beyond calibration range. However, samples with extremely high-level substance may show low values.
3. Note that samples with high-level (beyond calibration range) substance may affect the assay results of succeeding samples by carryover.
4. Note that serum separating agents in blood collection tubes may affect the assay result.
5. The responsible physician should make a clinical diagnosis comprehensively based on the assay results, clinical symptoms, and other results.

References:

1. Rylatt D.B.,et al: An immunoassay for human D dimmer using monoclonal antibodies. Thromb. Res., 31(6):767,1983.

HOMOCYSTEINE

Liquid Reagent

CE

In Vitro Diagnostic reagent for the quantitative determination of Homocysteine (HCY) in serum and plasma. Store at 2-8°C .

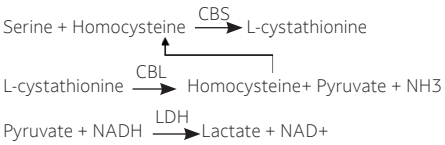
REF: HCY-010B1 / HCY-010B2

Summary:

Homocysteine (Hyc) is a thiol-containing amino acid produced by the intracellular demethylation of methionine. Total homocysteine (tHcy) represents the sum of oxidised, protein bound and free forms of Hcy.
Elevated levels of tHcy have emerged as an important risk factor in the assessment of cardiovascular disease. Excess Hcy in the blood stream may cause injury to arterial vessels due to its irritant nature, and result in inflammation and plaque formation, which may eventually cause blockage of blood flow to the heart.
Elevated levels of tHcy are also linked with Alzheimers disease and osteoporosis.

Principle:

Oxidised homocysteine is reduced to free homocysteine. Free HCY is converted to cystathionine by the use of CBS (cystathionine beta-synthase) and excess serine. The cystathionine is then broken down to homocysteine, pyruvate and ammonia. Pyruvate is converted to lactate via lactate dehydrogenase with NADH as coenzyme. The rate of NADH conversion to NAD+ (Δ A340 nm) is directly proportional to the concentration of homocysteine.



Composition of the reagent(s):

R1 Enzymes: Tris Buffer, LDH - 35KU/L, L-Serine - 0.76 mmol/L, TCEP - 0.5 mmol/L, NADH - 0.47 mmol/L, PRESERVATIVES
R2 Enzymes: Tris Buffer, Cystathionine β-Synthase - 20KU/L, Cystathionine β-lyase - 10KU/L, L-Serinelyase - 20KU/L, PRESERVATIVES

Precautions:

For In Vitro Diagnostics Use Only - For Professional Use Only
Carefully read instructions for use. Deviations from this procedure may alter performance of the assay.
Components Colour and Appearance:
Reagent 1: Clear, colourless liquid, Reagent 2: Clear, light yellow liquid.
Any significant changes could indicate that the assay might be compromised. Refer to Laboratory's QC program for actions to be taken. In case of serious damage to the bottle and/or cap, resulting in product leakage and/or contamination, do not use the reagent pack and contact your distributor.
Safety precautions:
This product is not hazardous under EU specifications. Contains Sodium Azide. Material Safety Data Sheet is available upon request.
Handling precautions:
- Take the necessary precautions required for handling all laboratory reagents.
- Do not use components past the expiry date stated on the Bottles.
- Do not Freeze Reagents.
- Do not use components for any purpose other than described in the "Intended Use" section.
- Do not interchange caps among components as contamination may occur and compromise test results.
- Refer to local legal requirements for safe waste disposal.
- Carbamazepine, methotrexate, phenytoin, nitrous oxide, or 6-azauridine triacetate may affect the homocysteine concentration.

Instruments:

This assay is designed to run on clinical chemistry analysers. Refer to relevant user's manual or Laboratory internal practice for routine maintenance procedures. Instrument applications are available upon request.

Preparation:

- **R1 and R2** are ready to use.
Before use, mix reagent by gently inverting each bottle.
If stored and handled properly, unopened components are stable until the expiry date stated on the label.

Samples:

Use serum or heparin plasma as specimen.
It is recommended to follow NCCLS procedures (or similar standardised conditions) regarding specimen handling. Specimen should be collected in an appropriate sample container, with proper specimen identification.
- Serum/plasma should be separated from cells within 8 hours after collection.
Stability: 2 weeks at 2-8°C.

Equipment:

- HCY Calibrator and Controls
- General Laboratory Equipment

Procedure:

1. Assay conditions:
Wavelength: . . . . . 340 nm
Cuvette: . . . . . 1 cm. light path
Temperature . . . . . .30°C or 37°C

2. Standard procedure:

	Blank	Calibrator	Sample
R1 (µL)	960	960	960
Sample (µL)	-	-	-
Calibrator (µL)	-	52	-

4. Gently mix and Incubate at 37°C for 5 minutes.
5. Add:

R2(µL)	260	260	260

6. Gently mix and Incubate at 37°C for 1 minute.
7. measure the change of Optical Density per minute (ΔOD/min) over the next 2 minutes.

Using recommended Calibrator, calibrate the assay:
- When using a new reagent kit or changing lot number.
- Following preventive maintenance or replacement of a critical part of the photometer used.
- When Quality Controls are out of range.

Calculations:

$$\frac{\Delta Abs/min Sample}{\Delta Abs/min Calibrator} \times \text{Concentration of Calibrator.} = \text{Concentration}$$

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

Adult: ≤15µmol/L
Elder population ≥ 60 years: 15 - 20µmol/L
Each laboratory should establish its own reference range. Amylase results should always be reviewed with the patient's medical examination and history.

Performance characteristics:

Performance results can vary with the instrument used. Data obtained in each individual laboratory may differ from these values.
Linearity:
This assay is linear up to 50µmol/L.
For samples with a higher concentration, dilute 1:1 with 0.9% NaCl (9g/l) and re-assay. Multiply result by 2.
Interfering substances:
Results of study are as follows:
Bilirubin (mixed isomers): Less than 10% interference up to 600 µmol/l Bilirubin
Haemolysis: Less than 10% interference up to 500 mg/dl Haemoglobin
Lipemia: Less than 10% interference up to 500 mg/dl Lipemia
Sensitivity:
The Lower Detectable Level was estimated at 0.7µmol/L.
Precision:

	Intra-assay			Inter-assay		
N=20	Mean (µmol/L)	SD	%CV	Mean (µmol/L)	SD	%CV
level 1	12.1	1.02	2.62	12.9	0.96	2.68
level 2	25.6	2.42	1.78	2.4	3.84	1.92

Method comparison:
Using 23 samples, a comparison, between this HCY test (y) and another commercially available test (x), gave the following results:
y = 0.97x – 3.67
r = 0.997
Sample range: 3 to 36µmol/L

References:

1. Ueland PM. Homocysteine Species as Components of Plasma Redox Thiol Status. Clin Chem 1995;41:340-342
2. Perry IJ, Refsum H, Morris RW, et al. Prospective Study of Serum Total Homocysteine Concentration and Risk of Stroke in Middle-aged British Men. The Lancet 1995;346:1395-1398
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5. Mudd SH, Levy HL, Skovby F. Disorders of Transsulfuration. In: Scriver CR, Beaudet AL, Sly WS, et al., eds The Metabolic and Molecular Basis of Inherited Disease. New York: McGraw-Hill, 1995;1279-1327
6. Ueland PM, Refsum H, Stabler SP, et al. Total Homocysteine in Plasma or Serum: Methods and Clinical Applications. Clin Chem 1993;39:1764-1779

HDL Direct Cholesterol

CE

Reagent for direct measurement of HDL Cholesterol concentration in human serum and plasma. For in Vitro Diagnostic Use. Do not freeze. Store at 2-8ºC .

REF: RHDL-10JA / RHDL-10JB

Summary:

This reagent is designed for quantitative determination of HDL Cholesterol (HDL-C) concentration in human serum and plasma.
High-density lipoproteins are one of the major classes of plasma lipoproteins. HDL Cholesterol is known as "good cholesterol" because high levels can help to lower the risk of heart disease and coronary artery disease (CHD).
A low HDL-C level, is considered as a greater heart disease risk.
Accurate measurement of HDL-C is a key parameter when assessing patient risk from CHD.

Principle:

After addition of magnesium ions, dextran sulfate selectively forms water-soluble complexes with LDL, VLDL and chylomicrons which are resistant to PEG-modified enzymes.
HDL-C in human serum is dissolved with a specific detergent, and makes color reactions with Cholesterol esterase, Cholesterol oxidase and Peroxidase.
Non-HDL-Lipoproteins such as chylomicron (CM), low density lipoprotein (LDL), very low density lipoprotein (VLDL) are inhibited by detergents so they don't react with the mentioned enzymes.
HDL Cholesterol concentration is determined by color intensity following Trinder's reaction.

Test Parameters

Method: Colorimetric, End Point Reaction
Wavelength: Main: 604 - 700 nm
Temperature: 37°C
Sample: Serum
Linearity: 3 mg/dL - 200 mg/dL

Composition:

R1: Dextran Sulfate - ≤ 10 gr/dL, Magnesium Chloride Hegzahydrate - ≤ 5 gr/dL, Preservative, Brij 35 - ≤ 10 gr/dL
R2: Detergent - ≤ 2 %, PEG - Cholesterol Esterase - ≤ 5 KU/L, PEG - Cholesterol Oxidase - ≤ 5 KU/L, 4 AAP - ≤ 1 gr/dL, Peroxidase - ≤ 8000 U/L

Reagent Stability And Storage:

Stability: up to expiration date on labels at 2-8°C.
Once opened vials are stable minimum 30 days at 2-80C at optimum conditions. There is a strong relation between on board stability and auto analysers cooling specification and carry-over values.

Precautions:

Product to be used in professional laboratories by professional operators.
Components from human origin have been tested and found to be negative for the presence of HBsAg, HCV, and antibody to HIV (1/2). However handle cautiously as potentially infectious.

Preparation:

Reagents are ready to use, liquid.

Samples:

Fresh Serum, or EDTA and heparinized plasma. Samples are collected by standard procedures.
Note: Separate the serum or plasma as soon as possible after collection (within 3 hours). Store serum no more than 12 hours at room temperature, no more 7 days at 2-8 ºC. HDL in sample is stable for 30 days at – 70 ºC.

Procedure:

Mix well and incubate 10 minutes at 37°C.
Read Calibrator blank tube absorbance (A_{BCAL}) and Calibrator tube absorbance (A_{CAL}).
Then read sample blank tube absorbance (A_{SB}) and Sample tube absorbance (A_S).
$\Delta A\ Cal = (A_{CAL}-A_{BCAL})$ $\Delta A\ Sample = (A_B-A_{SB})$
Calibration stability: >30 days

Different incubation time gives differents absorbance values. Incubation time of sample and calibrator always have the same time duration.
Test time: 10 seconds

Calculations:

$$\frac{\Delta A\text{sample}}{\Delta A\text{CAL}} \times \text{Conc.Cal (mg/dL)} = \text{HDL Direct (mg/dL)}$$

Unit Conversion:
mmol/L*38.67= mg/dL
mg/dL*0.02586=mmol/L

Reference Intervals (Normal Values):

National Cholesterol Education Program (NCEP) guidelines:
<40 mg/dL: Low HDL (major risk factor for CHD)
≥60 mg/dL: High HDL ("negative" risk factor for CHD)

HDL-cholesterol is affected by a number of factors, e.g. smoking, exercises, hormones, sex and age.
It is recommended that each laboratory establishes its own normal range.

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Performance characteristics:

Low Linearity (LOQ):
(Values are based on CV%≤ 20%): 3 mg/dL HDL Cholesterol.

High Linearity:
The test is linear up to 200 mg/dL.

Precision:
(Based on CLSI EP05A3 Doc.):

Intra-assay			Inter-assay		
Mean (mg/dL)	%CV	n	Mean (mg/dL)	%CV	n
106	1.70	20	80	1.90	20
22	2.80	20	22	2.95	20

Sensitivity (LOD):
2.7 mg/dL.

Accuracy:
No systematic differences seen in results obtained with this reagent when compared with reference reagents. It's available to get details of comparison experiments in case of requirement.

Interferences:
No interferences were observed to bilirubin T. and D. up to 60 mg/dL, hemoglobin up to 30 g/L or lipemia up to 2500 mg/dL.
A list of drugs and other interfering substances with HDL cholesterol determination has been reported by Young et. al.

Notes

1. For in vitro diagnostic use only. Do not pipette by mouth. Avoid contact with skin and mucous membranes.
2. All the calibrators, controls and some reagents must be considered as human & animal sample, so potentially infectious; all the protection actions must be applied to avoid any potential biological risk.
3. Material safety data sheet will be supplied on request.
4. Exercise the normal precautions required for handling laboratory reagents.
5. Caps of the reagents bottles cannot be used between two different kind of reagent and between R1&R2.
6. Reagents with different lot numbers should not be interchanged or mixed.
7. The reagents contain sodium azide (< 0.1%) as a preservative.

References:

1. Young DS. Effects of drugs on clinical laboratory tests, 4th ed. AACC Press, 1995.
2. Expected Values Handbook of Laboratory Medicine, Li-hua Zhu 1998
3. Third Report of the Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III), NIH Publication No. 01-3670, May 2001.
4. Tietz NW. Clinical guide to laboratory tests, 2nd ed. Saunders Co, 1991.1988;26:783-790
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9. Sonntag O, Scholer A. Drug interferences in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001; 38:376-385.
10. Report on the Symposium "Drug effects in clinical chemistry methods", Breuer J, Eur J Clin Chem Clin Biochem 1996;34:385-386.
11. Sugiuchi H. History of development and technical details of the homogeneous assay for HDL and LDL cholesterol. The Fats of Life 2005; IX No. 1:4-11.
12. Third Report of the National Cholesterol Education Programme (NCEP) Expert Panel on Detection, Evaluation and treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). JAMA Publication, Vol 285, No. 19, P2486 - 2497; 2001.

LDL Direct Cholesterol

CE

Reagent for direct measurement of LDL Cholesterol concentration in human serum and plasma. For in Vitro Diagnostic Use. Do not freeze. Store at 2-8ºC .

REF: LDL-1000A / LDL-1000B

Summary:

This reagent is designed for quantitative determination of LDL Cholesterol (LDL-C) concentration in human serum and plasma.
The LDL-C particles are lipoproteins that transport cholesterol to the cells. Often called "bad cholesterol" because high levels are risk factor for coronary heart disease and are associated with obesity, diabetes and nephrosis.

Principle:

The specific detergent present in Reagent 1 solubilizes only the non-LDL lipoprotein particles (CM, HDL, VLDL). The cholesterol released will be used up by enzymatic reagent in a non-color forming reaction.
Another specific detergent present in Reagent 2 solubilizes LDL-C.
LDL Cholesterol concentration is determined by color intensity following Trinder's reaction.

Test Parameters

Method: Colorimetric
Wavelenght: Main 572-600 nm /Sub 700-750 nm
Temperature: 37 °C
Sample: Serum, plasma
Linearity: 5-600 mg/dL

Composition:

R1: Polyaniondetergent 1, Cholesterol esterase - ≤ 200.000 U/L, Cholesterol oxidase - ≤ 200.000 U/L, Peroxidase - ≤ 200.000 U/L, 4-aminoantipyrine, TOOS
R2: Detergent 2, TOOS, Tris Buffer

Testing of human serum used in the preparation of the standard is resulted as negative for the presence of antibodies anti-HIV and anti-HCV, beside for HBs antigen. Because of the possibility of being infectious, standard should be used cautiously and with GLP rules.

Reagent Stability And Storage:

Store at 2-8ºC. Reagents are stable till the expiry date stated on the label when they stored in closed vials and avoiding contamination during their usage.
There is a strong relation between on board stability and auto analysers cooling specification and carry-over values.

Precautions:

Product to be used in professional laboratories by professional operators.
Components from human origin have been tested and found to be negative for the presence of HBsAg, HCV, and antibody to HIV (1/2). However handle cautiously as potentially infectious.

Preparation:

Reagents are ready to use, liquid.

Samples:

Fresh Serum or EDTA and heparinized plasma.
Note: Separate the serum or plasma as soon as possible after collection (within 3 hours). Store serum no more than 12 hours at room temperature, no more 7 days at 2-8 °C. Serum is stable for 30 days at (-60)-(-80)°C.

Procedure:

Mix well and incubate 10 minutes at 37°C.
Read Calibrator blank tube absorbance (ABCAL) and Calibrator tube absorbance (ACAL).
Then read sample blank tube absorbance (ASB) and Sample tube absorbance (AS).
ΔA Cal = (ACAL-ABCAL) ΔA Sample = (AB-ASB)
Calibration stability: >30 days

Different incubation time gives differents absorbance values. Incubation time of sample and calibrator always have the same time duration.
Test time: 10 seconds

Calculations:

$$\frac{\Delta A \text{sample}}{\Delta A \text{CAL}} \times \text{Conc. Cal (mg/dL)} = \text{LDL Direct (mg/dL)}$$

Unit Conversion:
mmol/Lx38.61=mg/dL

Reference Intervals (Normal Values):

Optimal: <100 mg/dL (<2.59 mmol/L)
Near optimal,
Above optimal: 100 – 129mg/dL (2.59 – 3.34 mmol/L)
Borderline high: 130 - 159 mg/dL (3.37 – 4,12 mmol/L)
High: 160 – 189 mg/dL (4,14 – 4,89 mmol/L)
Very high: ≥ 190 mg/dL (≥4,92 mmol/L)

It is recommended that each laboratory establish its own reference range.

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Performance characteristics:

Low Linearity (LOQ):
(LOQ values are based on CV% ≤ 20%): 5 mg/dL.
High Linearity:
The test is linear up to 600 mg/dL.
Precision:
(Based on CLSI EP05A3 Doc.):

Intra-assay			Inter-assay		
Mean (mg/dL)	%CV	n	Mean (mg/dL)	%CV	n
45	4.6	20	45	4.2	25
65	3.4	20	65	3.9	25

Sensitivity (LOD):
4.5 mg/dL.
Accuracy:
No systematic differences seen in results obtained with this reagent when compared with reference reagents. It's available to get details of comparison experiments in case of requirement.
Interferences:
No interferences were observed to bilirubin T. and D. up to 15 mg/dL, hemoglobin up to 10 g/L or lipemia up to 2500 mg/dL.
A list of drugs and other interfering substances with HDL cholesterol determination has been reported by Young et. al.

Notes:

1. For in vitro diagnostic use only. Do not pipette by mouth. Avoid contact with skin and mucous membranes.
2. All the calibrators, controls and some reagents must be considered as human & animal sample, so potentially infectious; all the protection actions must be applied to avoid any potential biological risk.
3. Material safety data sheet will be supplied on request.
4. Exercise the normal precautions required for handling laboratory reagents.
5. Caps of the reagents bottles cannot be used between two different kind of reagent and between R1&R2.
6. Reagents with different lot numbers should not be interchanged or mixed.
7. The reagents contain sodium azide (< 0.1%) as a preservative.

References:

1. Young DS. Effects of drugs on clinical laboratory tests, 4thed. AACC Press, 1995.
2. Tietz NW. Clinical guide to laboratory tests, 2nd ed. Saunders Co, 1991.1988;26:783-790
3. Rifai N, Warnick GR, McNamara JR, Belcher JD, Grinstead GF, Expected Values Handbook of Laboratory Medicine, Li-hua Zhu 1998
4. Frantz Jr ID. Measurement of Low-Density-Lipoprotein Cholesterol in Serum: a Status Report. Clin Chem 1992; 38:150-160.
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6. Bachoric P. Measurement of Low-Density-Lipoprotein. 245-263. In: Handbook of Lipoprotein Testing (eds. Rifai, Warnick and Dominiczak), 2nd edition, AACC press, 2000.
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11. Westgard, J.O., Carey, R.N., Wold, S., Criteria for judging precision and accuracy in method development and evaluation. ClinicalChemistry1974:20:825-833.
12. Armstrong V, Seidel D. Evaluation of a Commercial Kit for the Determination of LDL-Cholesterol in Serum Based on Precipitationof LDL with Dextran Sulfate. Ärztl. Lab. 1985; 31:325-330.
13. National Institutes on Health Publicationno. 93-3095, September 1993.

Lipase
Color Liquid

CE

Kinetic colorimetric direct determination of lipase activity in serum and plasma.
Store at 2-8°C .

REF: LIP-027B

Summary:
Lipase enzymes are produced in the pancreas and also secreted in small amounts by the salivary glands as well as by gastric, pulmonary and intestinal mucosa. Determination of lipase is used for diagnosis and treatment of diseases of pancreas such as acute and chronic pancreatitis and obstruction of the pancreatic duct.

Principle:
The method for the determination of lipase is based on the cleavage of specific chromogenic lipase substrate 1,2-O-dilauryl-rac-glycero-3-glutaric acid-(6'-methylresorufin)-ester emulsified in stabilized microparticles. In the presence of specific activators of pancreatic lipase as colipase, calcium ions and bile acids, the substrate is converted in 1,2-O-dilauryl-rac-glycerol and glutaric acid-6'-methylresorufin-ester which decomposes spontaneously in glutaric acid and methylresorufin. The increase of absorbance, due to methylresorufin formation, is proportional to the activity of lipase in the sample.

Composition:
The components of the kit, stored at 2-8 °C in unopened vials, are stable up to the expiry date indicated on the package.
R1: tris buffer - 40 mmol/L pH 8.3, colipase - ≥ 1 mg/L, desoxycholate - ≥ 1.8 mmol/L, taurodesoxycholate - ≥ 7.0 mmol/L
R2: tartrate buffer - 15 mmol/L pH 4.0, lipase substrate - ≥ 0.7 mmol/L, calcium ions - ≥ 1 mmol/L

Precautions:
- For in vitro diagnostic use.
- Do not use components beyond the expiration date.
- Do not mix materials from different kit lot numbers.
- Safety Data Sheets are available

Instruments:
Instrument applications are available upon request.

Preparation:
R1 and R2 are ready to use.
Reagent 1 is in a clear liquid form, discard if turbid.
Reagent 2 is a turbid orange-colored micro-emulsion, discard if turning to red. In some storage conditions (i.e. storage at a temperature lower than the one indicated) a precipitate may appear in the vial that will not influence the reagent performance; however, it is recommended to resuspend the product with a slight rotation of the vial before carrying out the analysis.

Stability:
On Board: 30 days, if contamination is avoided.
Calibration: 30 days. Repeat the calibration at any variation in the reagent lot.

Samples:
Serum or plasma (EDTA or heparin).
Stability: 7 days at 2-8 °C or 12 months at -20 °C.

Equipment:
General Laboratory Equipment
Calibrator
Control Serum (normal and pathologic)

Procedure:
1. Assay conditions:
Wavelength: . . . . . 570 nm (main)
. . . . . 800 nm (reference)
Cuvette: . . . . . 1 cm. light path
Temperature: . . . . . 37°C
Sample/R1/R2: 1/100/200
Reaction: . . . . . Fixed time (increase)

Allow reagents to reach working temperature before using.
A proportional variation of the indicated reaction volumes does not change the results.
Example of analytical procedure on automated intruments
Time 0
Calibrator/Controls/Sample = 3 µL
R1 = 300 µL
After 300 sec
Addition of R2 = 60 µL
After 150 sec
Reading 1
After 150 sec
Reading 2

Calculations:
1. Plot a calibration curve on a graph paper by tracing absorbance (y axis) according to corresponding U/L activity (x axis) for each Calibrator.
2. Indicate on the calibration curve the absorbance value obtained for Samples and Controls.
3. Extrapolate the U/L value for Samples and Controls from the calibration curve.

Conversion factor: LPS [U/L] x 0. 01667 = LPS [µkat/L]

Lipase activity (reported on the CALIBRATOR TcA) in U/L methylresorufin method at 37 °C, can be converted in turbidimetric U/L at 37 °C with triolein substrate (Roche turbidimetric) multiplying the LPS value in TcA by the calculated factor of 6.2.

Quality control:
All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:
Lipase in normal subjects
(U/L methylresorufin at 37 °C): ≤ 38 U/L
It is recommended that each laboratory establish its own expected range.

Performance characteristics:
Sensitivity:
5.0 U/L. Sensitivity was calculated on 20 replicates of normal saline and reported as the «mean zero value + 3 SD»
y = 1.015x + 7.690
r = 0.991
Sample range: 12 to 124 U/l

Precision:

Determined from 1x3x20 tests (day x run x rep) on 2 commercial controls (L1/L2) and a human sera pool (L3).

	Intra-assay		
U/L	L1	L2	L3
Mean	36.8	64.8	12.8
SD	0.37	0.40	0.24
CV%	1.0	0.6	1.9

Determined from 10x2x2 tests (day x run x rep) on 3 commercial controls (L1/L2/L3).

	Inter-assay						
	Mean	Total Imprecision		Between Days		Repeatability	
	U/L	SD	CV%	SD	CV%	SD	CV%
L1	18.0	0.88	4.9	0.49	2.7	0.74	4.1
L2	33.6	0.85	2.5	0.47	1.4	0.68	2.0
L3	95.1	1.55	1.6	1.18	1.2	0.73	0.8

Method comparison:
Accuracy:
this test (y) was compared with a commercially methylresorufin available method (x).
The results were as follows:
N= 101
r = 0.997
y = 0.50 x + 3.94
this test (y) was compared with a commercially 1,2-digliceride available method (x).
The results were as follows:
N = 52
r = 0.996
y = 0.63 x + 6.62

Interferences:
The test is not affected by the presence of haemoglobin up to 500 mg/dL, bilirubin up to 60 mg/dL and lipids (intralipid) up to 300 mg/dL.

Analytical Range:
5.0 - 250 U/L.
Samples with values higher than 250 U/L must be diluted 1:10 with normal saline and the result multiplied by 10.

Waste Management:
Reagents must be disposed of in accordance with local regulations.

References:

1. NCCLS Procedures for the Collection of Diagnostic Blood Specimens by Venipuncture; Approved Standard - Fifth Edition (H3-A5). Wayne, PA: The National Committee for Clinical Laboratory Standards, 2003.
2. US Department of Labor, Occupational Safety and Health Administration. 29 CFR Part 1910.1030. Bloodborne Pathogens.
3. US Department of Health and Human Services. Biosafety in Microbiological and Biomedical Laboratories, 5th Ed. Washington,DC: US Government Printing Office, January 2007.
4. World Health Organization. Laboratory Biosafety Manual, 3rd ed.Geneva: World Health Organization, 2004.
5. Sewell DL, Bove KE, Callihan DR, et al. Protection of Laboratory Workers from Occupationally Acquired Infections; Approved Guideline — Third Edition (M29-A3). Wayne, PA: Clinical and Laboratory Standards Institute, 2005.
6. Pesce, A.J., Kaplan, L.A.: "Methods in Clinical Chemistry", Mosby Ed. (1987).
7. Burtis C.A., Ashwood E.R.: "Tietz Textbook of Clinical Chemistry", W.B. Saunders Company Ed. (3rd edition, 1999).

Zinc

Color 5 Br-PAPS

CE

In vitro diagnostic reagent for direct colorimetric determination of zinc in serum, plasma and urin. Store at room temperature.

REF: ZIN-032B

Summary:

Zinc is necessary for cell replication. Deficiency is characterized by growth retardation in children and adolescents, hypogonadism in males, mild dermatitis, poor appetite, delayed wound healing, abnormal dark adaptation, and mental lethargy and impaired immune responses.

Principle:

Direct colorimetric mesurement without deproteinization of the sample. Zinc forms a stable colored complex with 5-Br-PAPS which colour intensity is proportional to the amount of Zinc in the sample.

Composition:

R1: 5-Br-PAPS - 0.02 mmol/l, Bicarbonate buffer pH 9.8 - 200 mmol/l, Sodium citrate - 170 mmol/l, Dimethylglyoxime - 4 mmol/l, Detergent - 1%
Zinc standard: 200 µg/dl (30.6µ mol/l)

Reagent Stability And Storage:

The sealed reagent is stable up to the indicated expiry date if stored at +18° to +22°C. The reagent can be stored at 2-8°C after opening.

Precautions:

In addition to the possible risk indications regarding the reactive components, reagents may contain non-reactive components such as preservatives (i.e. sodium azide of other) and detergents.

Samples:

Serum, Plasma, Urine

Equipment:

Usual laboratory equipment

Procedure:

1. Assay conditions:
Wavelength: . . . . 546 nm
Cuvette: . . . .1 cm. light path
Temperature . . . . . .+ 25°C / + 37°C

	Standard	Sample
R1 (µL)	1000	1000
Serum or Plasma (µL)	-	50
Standard (µL)	50	-

2.Mix and incubate for 10 minutes at 25°C or 5 minutes at 37°C. Measure the absorbance of the sample $A_{(S)}$ and of the standard $A_{(STD)}$ against the reagent blank $A_{(RBL)}$

$\Delta A_{(S)} = A_{(S)} - A_{(RBL)}$

$\Delta A_{(STD)} = A_{(STD)} - S_{(RBL)}$

Calculations:

$$\frac{\Delta A\text{sample}}{\Delta A\text{standard}} \times 200 = \text{Conc. g/dl zinc}$$

$$\frac{\Delta A\text{sample}}{\Delta A\text{standard}} \times 30.6 = \text{Conc. mol/l zinc}$$

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program. Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference Values:

Expected range:
Men: 72.6 - 127µg/dl (11.1-19.5µmol/l)
Women: 70.0 - 114µg/dl (10.7-17.5µmol/l)
During pregnancy and menstruation the concentration of zinc could be low.
Children: 63.8 - 110µg/dl (9.8-16.8µmol/l)
New born: 49.5 - 99.7µg/dl (7.6-15.3µmol/l)
Urine: 300 - 800mg/24h

Performance characteristics:

Measuring and reportable range:

4 - 2000 µg/dl. Samples with zinc concentration higher than 2000 µg/dl (306 µmol/l) must be diluted 1:10 with normal saline and result multiplied by 10.

Linearity:

Up to 2000 g/dl (306 µmol/l)

Precision:

	Intra-assay			Inter-assay		
	Mean (µg/dL)	SD	%CV	Mean (µg/dL)	SD	%CV
L1	70.70	1.94	2.74	120.90	1.13	0.93
L2	112.50	4.08	3.62	176.80	3.20	1.81
L3	172.50	2.77	1.61	N/A	N/A	N/A

Sensitivity (Lower detection limit):

Detection limit: 4 µg/dl
The lower detection limit represents the lowest measurable zinc activity that can be distinguished from zero.

Interferences:

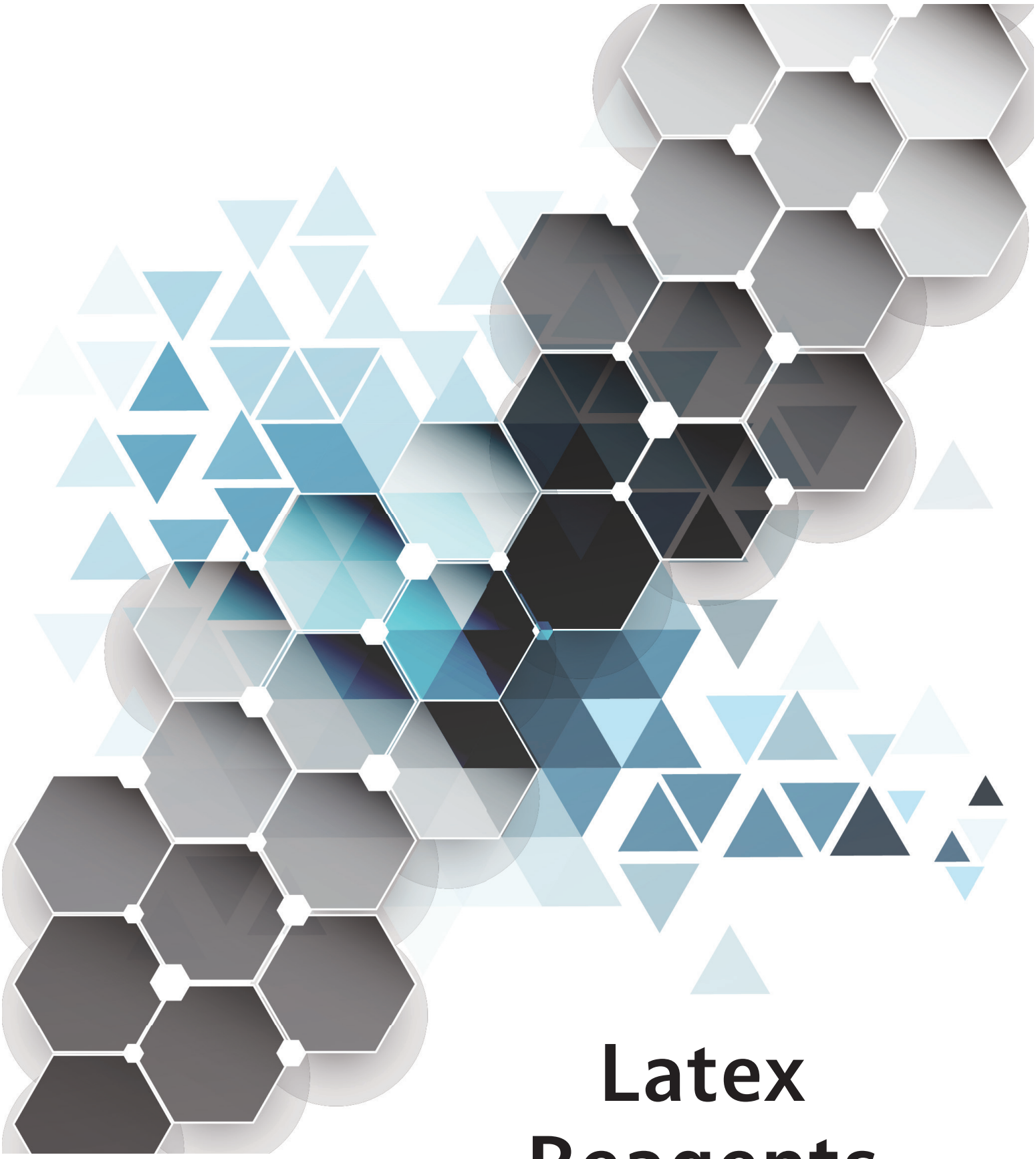
EDTA anticoagulant masks zinc to 5-Br-PAPS chromogenic system. The test is not affected by the presence of conjugated and non-conjugated bilirubin up to 15 mg/dl, hemoglobin up to 500 mg/dl and triglycerides up to 1000 mg/dl.

Notes:

For in vitro diagnostic use.
Use disposable test tubes and glassware washed with hydrochloric acid 1N solution and distilled water.
The Standard value is verified using a NIST (National Institute of Standards and Technology) traceable reference standard.
Working solution must be limpid; do not use if turbid.
R1 contains urea as additive. In the sample order setting, do not input urea test immediately after zinc in "random access" automatic analyzers.

References:

1. Johnsen and R.Eliasson: Evaluation of a commercially available kit for the colorimetric determination of zinc. International Journal of Andrology, 1987, April 10 (2): 435-440.



Latex Reagents

ASO-latex

Slide agglutination

CE

Qualitative determination of anti-streptolysin O (ASO)
IVD Store at 2-8ºC.

REF: KASO-001B

Summary:

Streptolysin O is a toxic immunogenic exoenzyme produced by β-heamolitic Streptococci of groups A, C and G. Measuring the ASO antibodies are useful for the diagnostic of rheumatoid fever, acute glomerulonephritis and streptococcal infections. Rheumatic fever is an inflammatory disease affecting connective tissue from several parts of human body as (skin, heart, joints, etc…) and acute glomerulonephritis is a renal infection that affects mainly to renal glommerulus.

Principle:

The ASO-latex is a slide agglutination test for the qualitative and semiquantitative detection of anti-streptolysin O (ASO) in human serum. Latex particles coated with streptolysin O (SLO) are agglutinated when mixed with samples containing ASO.

Composition:

Latex: Latex particles coated with streptolysin O, pH, 8,2. Preservative
Control + Red cap: Human serum with an ASO concentration > 200 IU/mL, Preservative
Control - Blue cap: Animal serum, Preservative

Precautions:

Components from human origin have been tested and found to be negative for the presence of HBsAg, HCV, and antibody to HIV (1/2).
However handle cautiously as potentially infectious.

Calibration:

The ASO-latex sensitivity is calibrated against the ASO International Standard from NIBSC ASO.

Storage and stability:

All the kit components are ready to use, and will remain stable until the expiration date printed on the label, when stored tightly closed at 2-8ºC and contaminations are prevented during their use. Do not freeze: frozen reagents could change the functionality of the test.
Mix reagents gently before use.
Reagents deterioration: Presence of particles and turbidity.

Samples:

Fresh serum. Stable 7 days at 2-8ºC or 3 months at –20ºC.
Samples with presence of fibrin should be centrifuged.
Do not use highly hemolized or lipemic samples.

Equipment:

- Mechanical rotator with adjustable speed at 80-100 r.p.m.
- Vortex mixer.
- Pipettes 50 µL.

Procedure:

Qualitative method

1. Allow the reagents and samples to reach room temperature. The sensitivity of the test may be reduced at low temperatures.
2. Place 50 µL of the sample and one drop of each Positive and Negative controls into separate circles on the slide test.
3. Mix the ASO-latex reagent vigorously or on a vortex mixer before using and add one drop (50 µL) next to the sample to be tested.
4. Mix the drops with a stirrer, spreading them over the entire surface of the circle. Use different stirrers for each sample.
5. Place the slide on a mechanical rotator at 80-100 r.p.m. for 2 minutes. False positive results could appear if the test is read later than two minutes.

Semi-quantitative method

1. Make serial two fold dilutions of the sample in 9 g/L saline solution.
2. Proceed for each dilution as in the qualitative method.

Reading and Interpretation:

Examine macroscopically the presence or absence of visible agglutination immediately after removing the slide from the rotator.
The presence of agglutination indicates an ASO concentration equal or greater than 200 IU/mL.
The titer, in the semi-quantitative method, is defined as the highest dilution showing a positive result.

Calculations:

The approximate ASO concentration in the patient sample is calculated as follows:
200 x ASO Titer = IU/mL

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

Up to 200 IU/mL(adults) and 100 IU/mL (children < 5 years old).
Each laboratory should establish its own reference range.

Performance characteristics:

Prozone effect:
No prozone effect was detected up to 1500 IU/mL.

Sensitivity:
200 (± 50) IU/mL, under the described assay conditions

Diagnostic Sensitivity:
98 %

Diagnostic specificity:
97 %

Interferences:

Bilirubin (20 mg/dL), hemoglobin (10 g/L), lipids (10 g/L), rheumatoid factors (300 IU/mL) do not interfere. Other substances may interfere.

Limitations:

- False positive results may be obtained in conditions such as, reumatoide arthritis, scarlet fever, tonsilitis, several streptococcal infections and healthy carriers.
- Early infections and children from 6 months to 5 years may cause false negative results.
- A single ASO determination does not produce much information about the actual state of the disease. Titrations at biweekly intervals during 4 or 6 weeks are advisable to follow the disease evolution.
- Clinical diagnosis should not be made on findings of a single test result, but should integrate both clinical and laboratory data.

References:

1. Haffejee . Quarterly Journal of Medicine 1992. New series 84; 305: 641-658.
2. Ahmed Samir et al. Pediatric Annals 1992; 21: 835-842.
3. Spaun J et al. Bull Wld Hlth Org 1961; 24: 271-279.
4. The association of Clinical Pathologists 1961. Broadsheet 34.
5. Picard B et al. La Presse Medicale 1983; 23: 2-6.
6. Klein GC. Applied Microbiology 1971; 21: 999-1001.
7. Young DS. Effects of drugs on clinical laboratory test, 4th ed. AACC Press, 1995.

CRP-latex

Slide agglutination

CE

Qualitative determination of C-Reactive Protein (CRP)
IVD Store at 2-8ºC.

REF: KCRP-004B

Summary:

CRP is an acute-phase protein present in normal serum, which increases significantly after most forms of tissue injuries, bacterial and virus infections, inflammation and malignant neoplasia. During tissue necrosis and inflammation resulting from microbial infections, the CRP concentration can rise up to 300 mg/L in 12-24 hours.

Principle:

The CRP-latex is a slide agglutination test for the qualitative and semiquantitative detection of C- Reactive Protein (CRP) in human serum. Latex particles coated with goat IgG anti-human CRP are agglutinated when mixed with samples containing CRP.

Composition:

Latex: Latex particles coated with goat IgG anti-human CRP, pH, 8,2. Preservative
Control + Red cap: Human serum with a CRP concentration > 20 mg/L, Preservative
Control - Blue cap: Animal serum, Preservative

Precautions:

Components from human origin have been tested and found to be negative for the presence of HBsAg, HCV, and antibody to HIV (1/2).
However handle cautiously as potentially infectious.

Calibration:

The CRP-latex sensitivity is calibrated to the Reference Material ERMDA 474/IFCC.

Storage and stability:

All the kit components are ready to use, and will remain stable until the expiration date printed on the label, when stored tightly closed at 2-8ºC and contaminations are prevented during their use. Do not freeze: frozen reagents could change the functionality of the test.
Mix reagents gently before use.
Reagents deterioration: Presence of particles and turbidity.

Samples:

Fresh serum. Stable 7 days at 2-8ºC or 3 months at –20ºC.
Samples with presence of fibrin should be centrifuged before testing.
Do not use highly hemolysed or lipemic samples.

Equipment:

- Mechanical rotator with adjustable speed at 80-100 r.p.m.
- Vortex mixer.
- Pipettes 50 µL.

Procedure:

Qualitative method
1. Allow the reagents and samples to reach room temperature. The sensitivity of the test may be reduced at low temperatures.
2. Place 50 µL of the sample (Note 1) and one drop of each Positive and Negative controls into separate circles on the slide test.
3. Mix the CRP-latex reagent vigorously or on a vortex mixer before using and add one drop (50 µL) next to the samples to be tested.
4. Mix the drops with a stirrer, spreading them over the entire surface of the circle. Use different stirrers for each sample.
5. Place the slide on a mechanical rotator at 80-100 r.p.m. for 2 minutes. False positive results could appear if the test is read later than two minutes.

Semi-quantitative method
1. Make serial two fold dilutions of the sample in 9 g/L saline solution.
2. Proceed for each dilution as in the qualitative method.

Reading and Interpretation:

Examine macroscopically the presence or absence of visible agglutination immediately after removing the slide from the rotator.
The presence of agglutination indicates a CRP concentration equal or greater than 6 mg/L (Note 2 and 3).
The titer, in semi-quantitative method, is defined as the highest dilution showing a positive result.

Calculations:

The approximate CRP concentration in the patient sample is calculated as follow:
6 x CRP Titer = mg/L

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

Up to 6 mg/L. Each laboratory should establish its own reference range.

Performance characteristics:

Prozone effect:
No prozone effect was detected up to 1600 mg/L.

Sensitivity:
6 (5-10) mg/L, under the described assay conditions

Diagnostic Sensitivity:
95.6 %

Diagnostic specificity:
96.2 %

Interferences:

Bilirubin (20 mg/dL), hemoglobin (10 g/L), and lipids (10 g/L), do not interfere. Rheumatoid factors (100 IU/mL), interfere. Other substances may interfere.

Notes:

1. High CRP concentration samples may give negative results (prozone effect). Re-test the sample again using a drop of 20 µL.
2. The strength of agglutination is not indicative of the CRP concentration in the samples tested.
3. Clinical diagnosis should not be made on findings of a single test result, but should integrate both clinical and laboratory data.

References:

1. Lars-Olof Hanson et al. Current Opinion in Infectious diseases 1997; 10: 196-201.
2. M.M. Pepys. The Lancet 1981; March 21: 653 – 656.
3. Chetana Vaishnavi. Immunology and Infectious Diseases 1996; 6: 139 – 144.
4. Yoshitsugy Hokama et al. Journal of Clinical Laboratory Status 1987; 1: 15 – 27.
5. Yamamoto S et al. Veterinary Immunology and Immunopathology 1993; 36: 257 – 264.
6. Charles Wadsworth et al. Clinica Chimica Acta; 1984: 138: 309 – 318.
7. Young DS. Effects of drugs on clinical laboratory test, 4th ed. AACC Press, 1995.

RF-latex

Slide agglutination

CE

Qualitative determination of Rheumatoid Factors (RF)
IVD Store at 2-8ºC.

REF: KRFL-007B

Summary:

Rheumatoid factors are a group of antibodies directed to determinants in the Fc portion of the immunoglobulin G molecule. Although rheumatoid factors are found in a number of rheumatoid disorders, such as systemic lupus erythematosus (SLE) and Sjögren's syndrome, as well as in nonrheumatic conditions, its central role in clinic lies its utility as an aid in the diagnosis of rheumatoid arthritis (RA).
A study of the "American College of Rheumatology" shows that the 80,4% of RA patients were RF positive.

Principle:

The RF-latex is a slide agglutination test for the qualitative and semiquantitative detection of RF in human serum. Latex particles coated with human gammaglobulin are agglutinated when mixed with samples containing RF.

Composition:

Latex: Latex particles coated with human gamma-globulin, pH 8,2. Preservative
Control + Red cap: Human serum with a RF concentration > 30 IU/mL. Preservative
Control - Blue cap: Animal serum, Preservative

Precautions:

Components from human origin have been tested and found to be negative for the presence of HBsAg, HCV, and antibody to HIV (1/2).
However handle cautiously as potentially infectious.

Calibration:

The RF-latex sensitivity is calibrated against the RF International Standard from NIBSC 64/002.

Storage and stability:

All the kit components are ready to use, and will remain stable until the expiration date printed on the label, when stored tightly closed at 2-8ºC and contaminations are prevented during their use. Do not freeze: frozen reagents could change the functionality of the test.
Mix reagents gently before use.
Reagents deterioration: Presence of particles and turbidity.

Samples:

Fresh serum. Stable 7 days at 2-8ºC or 3 months at –20ºC.
Samples with presence of fibrin should be centrifuged before testing. Do not use highly haemolized or lipemic samples.

Equipment:

- Mechanical rotator with adjustable speed at 80-100 r.p.m.
- Vortex mixer.
- Pipettes 50 µL.

Procedure:

Qualitative method

1. Allow the reagents and samples to reach room temperature. The sensitivity of the test may be reduced at low temperatures.
2. Place 50 µL of the sample and one drop of each Positive and Negative controls into separate circles on the slide test.
3. Mix the RF-latex reagent rigorously or on a vortex mixer before using and add one drop (50 µL) next to the sample to be tested.
4. Mix the drops with a stirrer, spreading them over the entire surface of the circle. Use different stirrers for each sample.
5. Place the slide on a mechanical rotator at 80-100 r.p.m. for 2 minutes. False positive results could appear if the test is read later than two minutes.

Semi-quantitative method

1. Make serial two fold dilutions of the sample in 9 g/L saline solution.
2. Proceed for each dilution as in the qualitative method.

Reading and Interpretation:

Examine macroscopically the presence or absence of visible agglutination immediately after removing the slide from the rotator.
The presence of agglutination indicates a RF concentration equal or greater than 8 IU/mL (Note 1).
The titer, in the semi-quantitative method, is defined as the highest dilution showing a positive result.

Calculations:

The approximate CRP concentration in the patient sample is calculated as follow:
6 x CRP Titer = mg/L

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

Up to 8 IU/mL. Each laboratory should establish its own reference range.

Performance characteristics:

Prozone effect:
No prozone effect was detected up to 1500 IU/mL.

Sensitivity:
8 (6-16) IU/mL, under the described assay conditions

Diagnostic Sensitivity:
100 %

Diagnostic specificity:
100 %

Interferences:

Bilirubin (20 mg/dL), hemoglobin (10 g/L), and lipids (10 g/L), do not interfere. Other substances may interfere.

Notes:

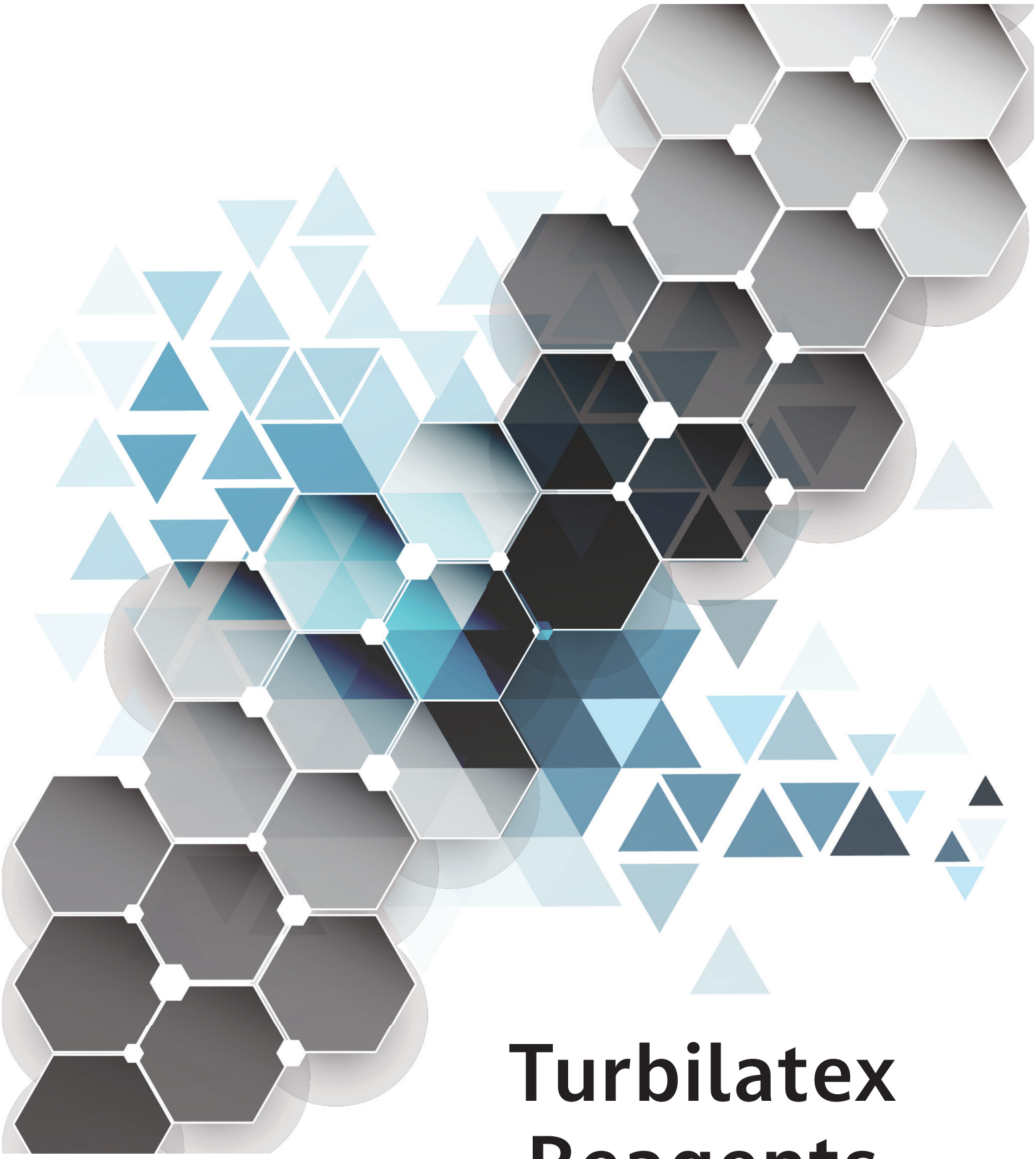
- The incidence of false positive results is about 3-5 %. Individuals suffering from infectious mononucleosis, hepatitis, syphilis as well as elderly people may give positive results.
- Diagnosis should not be solely based on the results of latex method but also should be complemented with a Waaler Rose test along with the clinical examination.

Notes:

Results obtained with a latex method do not compare with those obtained with Waaler Rose test. Differences in the results between methods do not reflect differences in the ability to detect rheumatoid factors.

References:

1. Robert W Dorner et al. Clinica Chimica Acta 1987; 167: 1 – 21.
2. Frederick Wolfe et al. Arthritis and Rheumatism 1991; 34: 951- 960.
3. Robert H Shmerling et al. The American Journal of Medicine 1991; 91: 528 – 534.
4. Adalbert F S et al. The New England Journal of Medicine 1959; 261: 363 – 368.
5. Charles M. Plotz 1956; American Journal of Medicine; 21:893 – 896.
6. Young DS. Effects of drugs on clinical laboratory test, 4th ed. AACC Press, 1995.



Turbilatex Reagents

ASO-turbilatex

Latex turbidimetry

CE

Determination of ASO in human serum or plasma.
Store at 2-8 °C

REF: KASO-T41B14 / KASO-T41B24

Summary:

SLO is a toxic immunogenic exoenzyme produced by ß-heamolitic Streptococci of groups A, C and G. Measuring the ASO antibodies are useful for the diagnostic of rheumatoid fever, acute glomerulonephritis and streptococcal infections. Rheumatic fever is an inflammatory disease affecting connective tissue from several parts of human body as skin, heart, joints etc… and acute glomerulonephritis is a renal infection that affects mainly to renal glommerulus.

Principle:

Latex particles coated with streptolysin O (SLO) are agglutinated when mixed with samples containing ASO. The agglutination causes an absorbance change, dependent upon the ASO contents of the patient sample that can be quantified by comparison from a calibrator of known ASO concentration.

Composition:

R1 (diluent): Tris buffer - 20 mmol/L, pH 8,2. Preservative
R1 (Latex): Latex particles coated with streptolysin O, pH 10,0. Preservative
ASO-CAL: Calibrator. Human serum. ASO concentration is stated on the vial label.

Precautions:

Components from human origin have been tested and found to be negative for the presence of HBsAg, HCV, and antibody to HIV (1/2). However handle cautiously as potentially infectious.

Calibration:

Use ASO Calibrator.
The sensitivity of the assay and the target value of the calibrator have been standardized against the ASO International Standard from NIBSC ASO.
The calibration is stable for 3 weeks.
Recalibrate when control results are out of specified tolerances, when using different lot of reagent and when the instrument is adjusted.

Preparation:

ASO Calibrator: Reconstitute (→) with 1,0 mL of distilled water. Mix gently and incubate at room temperature for 10 minutes before use.

Storage and Stability:

All the components of the kit are stable until the expiration date on the label when stored tightly closed at 2-8ºC and contaminations prevented during their use. Do not use reagents over the expiration date. Do not freeze; frozen Latex or Diluent could change the functionality of the test.
Reagent deterioration: Presence of particles and turbidity.
ASO Calibrator: Stable for 1 month at 2-8ºC or 3 months at –20ºC.

Samples:

Fresh serum. Stable 7 days at 2-8ºC or 3 months at –20ºC.
Samples with presence of fibrin should be centrifuged before testing.
Do not use highly hemolized or lipemic samples.

Equipment:

- Thermostatic bath at 37ºC.
- Spectrophotometer or photometer thermostatable at 37ºC with a 540 nm filter.

Procedure:

1. Bring the reagents and the photometer (cuvette holder) to 37ºC.

2. Assay conditions:
Wavelength: . . . . 540 nm (530-550)
Cuvette: . . . . .1 cm. light path
Temperature 37ºC

3. Adjust the instrument to zero with distilled water.

4. Pipette into a cuvette:
Diluent R1: 800 µL
Latex R2: 200 µL
Calibrator or sample: 10 µL
5. Mix and read the absorbance immediately (A1) and after 2 minutes (A2) of the sample addition.

Calculations:

$$\frac{(A2\text{-}A1)\ \text{Sample}}{(A2\text{-}A1)\ \text{calibrator}} \times \text{Concentration of Calibrator.} = \text{IU/mL ASO}$$

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

Normal values up to 200 IU/mL (adults) and 100 IU/mL (children < 5 years old).
Each laboratory should establish its own reference range.

Performance characteristics:

Linearity:
Up to 800 IU/mL, under the described assay conditions.
Samples with higher concentrations, should be diluted 1/3 in NaCl 9 g/L and retested again. The linearity limit depends on the sample-reagent ratio, as well the analyzer used. It will be higher by decreasing the sample volume, although the sensitivity of the test will be proportionally decreased.

Detection limit:
Values less than 20 IU/mL give non-reproducible results.

Prozone effect:
No prozone effect was detected up to 1000 IU/mL.

Sensitivity:
Δ0,73 mA. IU/mL.

Precision:
The reagent has been tested for 20 days, using three different ASO concentrations in a EP5-based study.

EP5	%CV		
	+/- 100 IU/mL	+/- 200 IU/mL	+/- 400 IU/mL
Total	6.4	5.7	5.1
Intra-assay	2.4	1.7	1.4
Inter-assay	3.6	4.2	4.9
Inter-day	4.7	3.5	0.7

Accuracy:
Results obtained using this reagent (y) were compared to those obtained using a commercial reagent (x) with similar characteristics. 60 samples of different concentrations of ASO were assayed. The correlation coefficient (r) was 0.99 and the regression equation:
y = 0,915x –4,844.
The results of the performance characteristics depend on the analyzer used.

Interferences:

Bilirrubin (20 mg/dL), hemoglobin (10 g/L), lipemia (10 g/L) and rheumatoid factors (600 IU/mL), do not interfere. Other substances may interfere.

Notes:

Clinical diagnosis should not be made on findings of a single test result, butshould integrate both clinical and laboratory data.

References:

1. Haffejee I, Quarterly Journal of Medicine 1992, New series 84; 305: 641 –658.
2. Alouf Jodeph E. Pharma Ther 1980; 11: 661-717.
3. M Fasani et al. Eur J Lab Med 1994; vol2.nº1: 67.
4. Todd E W. J Exp Med 1932; 55: 267 - 280.
5. Klein, GC. Applied Microbiology 1970; 19:60-61.
6. Klein GC. Applied Microbiology 1971; 21: 999-1001.
7. Young DS. Effects of drugs on clinical laboratory test, 4th ed. AACC Press, 1995

CRP-turbilatex

Latex turbidimetry

CE

Determination of CRP in human serum or plasma.
Store at 2-8 °C.

REF: KCRP-T43B14 / KCRP-T43B24

Summary:

CRP is an acute-phase protein present in normal serum, which increases significantly after most forms of tissue injuries, bacterial and virus infections, inflammation and malignant neoplasia. During tissue necrosis and inflammation resulting from microbial infections, the CRP concentration can rise up to 300 mg/L in 12-24 hours.

Principle:

Latex particles coated with specific anti- human CRP are agglutinated when mixed with samples containing CRP. The agglutination causes an absorbance change, dependent upon the CRP contents of the patient sample that can be quantified by comparison from a calibrator of known CRP concentration.

Composition:

R1 (diluent): Tris buffer - 20 mmol/L, pH 8,2. Preservative
R1 (Latex): Latex particles coated with goat IgG anti-human CRP, pH 7,3. Preservative.
CRP-CAL: Calibrator. C-Reactive protein concentration is stated on the vial label.

Precautions:

Components from human origin have been tested and found to be negative for the presence of HBsAg, HCV, and antibody to HIV (1/2). However handle cautiously as potentially infectious.

Calibration:

Use CRP Calibrator.
The sensitivity of the assay and the target value of the calibrator have been standardized against the Reference Material ERM-DA 474/IFCC.
The calibration is stable for 1 month.
Recalibrate when control results are out of specified tolerances, when using different lot of reagent and when the instrument is adjusted.

Preparation:

CRP Calibrator: Reconstitute (→) with 1,0 mL of distilled water. Mix gently and incubate at room temperature for 10 minutes before use.

Storage and Stability:

All the components of the kit are stable until the expiration date on the label when stored tightly closed at 2-8°C and contaminations prevented during their use. Reagents should not be left inside the analyzer after use, they must be stored refrigerated at 2-8°C. Latex may sediment. Mix reagents gently before use. Do not use reagents over the expiration date. Do not freeze; frozen Latex or Diluent could change the functionality of the test.
Reagent deterioration: Presence of particles and turbidity.
ASO Calibrator: Stable for 1 month at 2-8°C or 3 months at –20°C.

Samples:

Fresh serum. Stable 7 days at 2-8°C or 3 months at –20°C.
Samples with presence of fibrin should be centrifuged before testing.
Do not use highly hemolized or lipemic samples.

Equipment:

- Thermostatic bath at 37°C.
- Spectrophotometer or photometer thermostatable at 37°C with a 540 nm filter.

Procedure:

1. Bring the reagents and the photometer (cuvette holder) to 37°C.

2. Assay conditions:
Wavelength: . . . . . 540 nm (530-550)
Cuvette: . . . . . 1 cm. light path
Temperature: . . . . . 37°C

3. Adjust the instrument to zero with distilled water.

4. Pipette into a cuvette:
Diluent R1: 800 µL
Latex R2: 200 µL
Calibrator or sample: 5 µL
5. Mix and read the absorbance immediately (A1) and after 2 minutes (A2) of the sample addition.

Calculations:

$$\frac{(A2\text{-}A1)\ \text{Sample}}{(A2\text{-}A1)\ \text{calibrator}} \times \text{Concentration of Calibrator} = \text{mg/L CRP}$$

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

Normal values up to 6 mg/L.
Each laboratory should establish its own reference range.

Performance characteristics:

Linearity:
Up to 150 mg/L, under the described assay conditions.
Samples with higher concentrations should be diluted 1/5 in NaCl 9 g/L and retested again. The linearity limit depends on the sample / reagent ratio, as well as the analyzer used. It will be higher by decreasing the sample volume, although the sensitivity of the test will be proportionally decreased.

Detection limit:
Values less than 1 mg/L give non-reproducible results.

Prozone effect:
No prozone effect was detected upon 800 mg/L.

Sensitivity:
Δ 4,2 mA.mg/L.

Precision:
The reagent has been tested for 20 days, using three different CRP concentrations in a EP5-based study.

EP5	%CV		
	9,2 mg/L	16,8 mg/L	57,97 mg/L
Total	7.3	6.9	5.9
Intra-assay	2.8	3.1	2.9
Inter-assay	6.1	4.7	3.9
Inter-day	3	4	3.4

Accuracy:
Results obtained using this reagent (y) were compared to those obtained using a commercial reagent (x) with similar characteristics. 50 samples of different concentrations of CRP were assayed. The correlation coefficient (r)2 was 0,99 and the regression equation:
y = 1,101x + 2,518.
The results of the performance characteristics depend on the analyzer used.

Interferences:

Bilirubin (20 mg/dL) and lipemia (10 g/L) do not interfere. Hemoglobin (≥ 5 g/L), interferes. Other substances may interfere.

Notes:

Clinical diagnosis should not be made on findings of a single test result, but should integrate both clinical and laboratory data.

References:

1. Lars-Olof Hanson et al. Current Opinion in Infect Diseases 1997; 10: 196-201.
2. Chetana Vaishnavi. Immunology and Infectious Diseases 1996; 6: 139 – 144.
3. Yoshitsugy Hokama et al. Journal of Clinical Lab. Status 1987; 1: 15 – 27.
4. Kari Pulki et al. Sacand J Clin Lab Invest 1986; 46: 606 – 607.
5. Werner Müller et al. Journal of Immunological Methods 1985; 80: 77 – 90.
6. Shogo Otsuji et al. Clin Chem 1982; 28/10: 2121 – 2124.
7. Young DS. Effects of drugs on clinical laboratory test, 4th ed. AACC Press, 1995.

RF-turbilatex

Latex turbidimetry

CE

Determination of Rheumatoid Factors in human serum or plasma.
Store at 2-8 °C

REF: KRF-T42B14 / KRF-T42B24

Summary:

Rheumatoid factors are a group of antibodies directed to determinants in the Fc portion of the immunoglobulin G molecule. Although rheumatoid factors are found in a number of rheumatoid disorders, such as systemic lupus erythematosus (SLE) and Sjögren's syndrome, as well as in nonrheumatic conditions, its central role in clinic lies its utility as an aid in the diagnosis of rheumatoid arthritis (RA).
A study of the "American College of Rheumatology" shows that the 80,4% of RA patients were RF positive.

Principle:

Latex particles coated with human gammaglobulin are agglutinated when mixed with samples containing RF. The agglutination causes an absorbance change, dependent upon the RF contents of sample that can be quantified by comparison from a calibrator of known RF concentration.

Composition:

R1 (diluent): Tris buffer - 20 mmol/L, pH 8,2. Preservative
R1 (Latex): Latex particles coated with human gammaglobulin, pH 7,4.Preservative.
RF-CAL: Calibrator. Human serum. The RF concentration is stated on the vial label.

Precautions:

Components from human origin have been tested and found to be negative for the presence of HBsAg, HCV, and antibody to HIV (1/2). However handle cautiously as potentially infectious.

Calibration:

Use RF Calibrator.
The sensitivity of the assay and the target value of the calibrator have been standardized against the International Reference Standard from NIBSC 64/002. The calibration is stable for at least 1 month.
Recalibrate when control results are out of specified tolerances, when using different lot of reagent and when the instrument is adjusted.

Calibration curve:
Prepare the following RF calibrator dilutions in NaCl 9 g/L.
Multiply the concentration of the RF calibrator by the corresponding factor stated in table bellow to obtain the RF concentration of each dilution.

Calibrator dilution	1	2	3	4	5	6
Calibrator FERR (µL) NaCl 9 g/L (µL)	- 400	25 375	50 350	100 300	200 200	400 -
Dilution Factor	0	1/16	1/8	1/4	1/2	1

Preparation:

RF Calibrator: Reconstitute (→) with 2,0 mL of distilled water. Mix gently and bring to room temperature for 10 minutes before use.

Storage and stability:

All the components of the kit are stable until the expiration date on the label when stored tightly closed at 2-8ºC and contaminations are prevented during their use. Reagents should not be left inside the analyzer after use, they must be stored refrigerated at 2-8ºC. Latex may sediment. Mix reagents gently before use. Do not use reagents over the expiration date.
Do not freeze; frozen latex and diluent could change the functionality of the test.
Reagent deterioration: Presence of particles and turbidity.
Reconstituted calibrator: Stable for 1 month at 2-8ºC or 3 months at –20ºC.

Samples:

Fresh serum. Stable 7 days at 2-8ºC or 3 months at –20ºC.
The samples with presence of fibrin should be centrifuged before testing.
Do not use highly hemolized or lipemic samples.

Equipment:

- Thermostatic bath at 37ºC.
- Spectrophotometer or photometer thermostatable at 37ºC with a 650 nm filter.

Procedure:

1. Bring the reagents and the photometer (cuvette holder) to 37ºC.

2. Assay conditions:
Wavelength: . . . . . 650 nm (600-650)
Cuvette: . . . . . .1 cm. light path
Temperature . . . . . .37°C

3. Adjust the instrument to zero with distilled water.

4. Pipette into a cuvette:
Diluent R1: 800 mL
Latex R2: 200 mL
5. Mix and read the absorbance (Blank reagent).

6. Add the sample/ calibrator.

	Blank	Calibrator / Sample
NaCl 9 g/L (µL)	7	-
Calibrator or sample (µL)	-	7

7. Mix and read the absorbance after 2 minutes (A2) of the sample addition.

Calculations:

Calculate the absorbance difference (A_2-$A_{blank\ reagent}$) of each point of the calibration curve and plot the values obtained against the RF concentration of each calibrator dilution. Rheumatoid factor concentration in the sample is calculated by interpolation of its (A_2-$A_{blank\ reagent}$) in the calibration curve.

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

Normal values up to 20 IU/mL.
Each laboratory should establish its own reference range.

Performance characteristics:

Measuring range:
6-160 IU/mL, under the described assay conditions. Samples with higher concentrations should be diluted 1/5 in range depends on the sample to reagent/ratio, as well as the analyzer used. It will be higher by decreasing the sample volume, although the sensitivity of the test will be proportionally decreased.

Detection limit:
Values less than 6 IU/mL give non-reproducible results.

Prozone effect:
No prozone effect was detected upon 800 IU/mL.

Sensitivity:
Δ 3,34 mA. IU/mL.

Precision:
The reagent has been tested for 20 days, using three different FR concentrations in a EP5-based study.

EP5	%CV		
	35,8 IU/mL	78,05 IU/mL	123,26 IU/mL
Total	4.5	4.1	5.9
Intra-ssay	3.3	2.6	3.2
Inter-assay	1.7	2.3	3.4
Inter-day	2.5	2.1	3.6

Accuracy:
Results obtained using this reagent (y) were compared to those obtained using a commercial reagent (x) with similar characteristics. 41 samples of different concentrations of FR were assayed. The correlation coefficient (r)2 was 0,91 and the regression equation:
y = 1,2042x + 3,1344.
The results of the performance characteristics depend on the analyzer used.

Interferences:

Hemoglobin (10 g/L), bilirrubin (20 mg/dL) and lipemia (10 g/L), do not interfere. Other substances may interfere.

Notes:

Clinical diagnosis should not be made on findings of a single test result, but should integrate both clinical and laboratory data.

References:

1. Frederick Wolfe et al. Arthritis and Rheumatism 1991; 34: 951- 960.
2. Robert W Dorner et al. Clinica Chimica Acta 1987; 167: 1-21.
3. Robert H Shmerling et al. The American Journal of Medicine 1991; 91: 528 – 534.
4. Vladimir Muié et al. Scand J Rheumatology 1972; 1: 181 – 187.
5. Paul R et al. Clin Chem 1979; 25/11: 1909 – 1914.
6. Young DS. Effects of drugs on clinical laboratory test, 4th ed. AACC Press, 1995.

Cystatin C

Latex turbidimetry

CE

In Vitro Diagnostic reagent for the quantitative determination of Cystatin C in serum and plasma. Store at 2-8ºC .

REF: CYC-037B

Summary:

Cystatin C is a low molecular weight protein of 13Kda which is produced at a constant rate and is filtered through the glomerular filtration.
Therefore, the plasma concentration of Cystatin C is almost exclusively determined by the glomerular filtration rate (GFR), making Cystatin C an excellent indicator of GFR. Cystatin C is more accurate than plasma creatinine and is more reliable than the 24-h creatinine clearance.
More and more studies suggest that Cystatin C can be used to detect kidney disease at earlier stages than serum creatinine which may help facilitate prevention efforts in the elderly and those with diabetes, hypertension or cardiovascular disease.

Principle:

This test is based on the reaction between Cystatin C and latex covalently bound antibodies against human Cystatin C. Cystatin C values are determined turbidimetrically using fixed-time measurement with sample blank correction. The relationship between absorbance and concentration permits a multipoint calibration with a measuring range of between 0 to 10 mg/L.

Composition:

R1: Tris Buffer pH7.2 with protein stabilisers - 0.1M, Preservative
R2: Glycine Buffer pH8.2 - 0.1M, NaCl - 0.15M, BSA - 0.5%, anti-human Cystatin C antibody, Preservative

Precautions:

Components Colour and Appearance:
Reagent 1: Clear Liquid
Reagent 2: White Liquid
Any significant changes could indicate that the assay might be compromised. Refer to Laboratory's QC program for actions to be taken. In case of serious damage to the bottle and/or cap, resulting in product leakage and/or contamination, do not use the reagent pack and contact your distributor.

Safety precautions:
This product is not hazardous under EU specifications. Contains <1% Sodium Azide. Material Safety Data Sheet is available upon request.

Handling precautions:
- Take the necessary precautions required for handling all laboratory reagents.
- Reagents containing Sodium azide must be handled with precaution. Sodium azide can form explosive azides with lead and copper plumbing.
- Do not ingest
- Avoid contact with skin and eyes.
- Do not use components past the expiry date stated on the Bottles.
- Do not Freeze Reagents.
- Do not use components for any purpose other than described in the "Intended Use" section.
- Do not interchange caps among components as contamination may occur and compromise test results.
- Refer to local legal requirements for safe waste disposal.

Instruments:

This assay is designed to run on clinical chemistry analysers. Refer to relevant user's manual or Laboratory internal practice for routine maintenance procedures. Instrument applications are available upon request.
All information is encoded in the barcode, where applicable. If analyser fails to read or if the barcode is damaged, enter the series of numbers beneath the barcode.

Preparation:

Reagent is ready to use.
Before use, mix reagent by gently inverting each bottle.
If stored and handled properly, component is stable until expiry date stated on the label.

Samples:

Fresh or deep frozen serum can be used. Cystatin C remain stable for 12 days at +2 to +8ºC. If the test should be performed later, it is recommended to freeze the serum. Avoid successive freezing and thawing. Discard haemolysed or contaminated samples.
It is recommended to follow NCCLS procedures (or similar standardised conditions) regarding specimen handling. Specimen should be collected in an appropriate sampling container, with proper specimen identification. Serum/Plasma should be separated from cells within 2 hours after collection.

Equipment:

- Cystatin C Control and Calibrator
- General Laboratory Equipment

Procedure:

1. Assay conditions:
Wavelength: . . . . . .550 nm
Cuvette: . . . . . .1 cm. light path
Temperature 37ºC

	Blank	Calibrator	Sample
R1 (µL)	1000	1000	1000
Sample (µL)	-	-	12
Calibrator (µL)	-	12	-
Gently mix and incubate at 37ºC for 5 minutes			
R2 (µL)	250	250	250

2. Gently mix and Incubate at 37°C, measure the Optical Density (OD1) after 30 sec. Measure the Optical Density (OD2) after further 5 minutes.
3. Calibration: Cystatin C calibrators are provided separately and ready for use. For automated analysers, use the recommended calibrator and calibrate the assay. The calibration curve is stable for up to 14 days after which a new curve must be generated. Recalibrate:
- When using a new reagent kit or changing lot number.
- Following preventive maintenance or replacement of a critical part of the photometer used.
- When Quality Control results are out of range.

Calculations:

The Turbidimetric analysers automatically calculate the Cystatin C concentration of each sample.
Conversion mg/L = µg/ml

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

The reference interval is 0.59 – 1.03 mg/L are considered within the normal range. Each laboratory should establish its own reference range. Results should always be reviewed with the patient's medical examination and history.

Performance characteristics:

Performance results can vary with the instrument used. Data obtained in each individual laboratory may differ from these values.

Linearity:
Linearity was evaluated using serial dilutions, prepared with saline solution, of three pooled samples, which contained values of Cystatin C in the range of analysis ranging from 0.05 to 8mg/L. Linear regression values of Cystatin C mg/L vs concentration yielded correlation coefficients , r>0.999, for all samples. Within the assays measuring range, the deviations of measurement from theoretical values did not exceed the 10% level. In addition, the system did not show prozone phenomenon at least up to 16mg/L.

Interfering substances:
Results of study are as follows:
Bilirubin: Less than 10% interference up to 18 mg/dL
Haemoglobin: Less than 10% interference up to 5g/L

Precision:

	Intra-assay		Inter-assay	
N=80	Mean (mg/L)	%CV	Mean (mg/L)	%CV
level 1	0.86	0.70	0.86	1.54
level 2	5	1.22	5	3.37

Accuracy:
Various concentrations of Cystatin C (0.5 – 8.0mg/L) were added to 43 different serum samples. The linear regression gives correlation of r2 value of 0.98, slope of 0.97 and y intercept of 0.05.

Method comparison:
Analytical characteristics have been obtained in a single experiment in a Cobras-Mira plus analyser. As is well known the analytical characteristics of a clinical chemistry reagent depend on both the reagents and instrument used. Multicenter studies indicate important differences in analytical characteristics among similar instruments. Therefore, the data expressed in the present document should be interpreted as a guide example.

References:

1. A V Lewis, T J James, J B J Mc Guire,and R P Taylor. Improved immunoturbidimetric assay for Cystatin C . Ann Clin Biochem 2001;38: 111-114
2. Mutsumi Tanaka,kenje Matsuo, Masayasu Enomoto and Koji Mizuno. A Sol particle homogenous immunoassay for measuring serum Cystatin C. Cli. Biochem. 37 (2004) 27-35
3. David Massey. Commentary: Clinical diagnostic Use of Cystatin C. Journal of clinical Laboratory Analysis 18:50 – 60 (2004)
4. Michael G. Shilpak and al. Cystatin C and the risk of death and cardiovascular events among elderly persons. NEJM 2005 volume 352:2049-2060
5. David J Newman. Cystatin C. Ann Clin Biochem 2002;39:89 – 104
6. Li Hai, Xu Guo Bing and Xia Tie An. Serum Cystatin C for the detection of early renal impairment in diabetic patients. JCLA 2004;18:31-35
7. Young DS. Effects of Drugs on Clinical Laboratory Test. 5th Edition, AACC Press, 2000

Ferritin-turbilatex

Latex turbidimetry

CE

Determination of Ferritin in human serum or plasma.
Store at 2-8 °C

REF: KFER-T46B1 / KFER-T46B2

Summary:

Serum ferritin concentration usually reflects body iron stores and is considered one of the most reliable indicators of iron status of patients Whereas low serum concentrations of ferritin are always indicative of an iron deficiency, elevated concentrations can occur for variety of reasons. Thus, although elevated concentrations often indicate an excessive iron intake, they are also caused by liver disease, chronic inflammation and malignancies. Pregnant women, blood donors, hemodialysis patients, adolescents and children are groups particularly at risk.

Principle:

Ferritin-turbilatex is a quantitative turbidimetric test for the measurement of ferritin in human serum or plasma.
Latex particles coated with specific anti-human ferritin are agglutinated when mixed with samples containing ferritin. The agglutination causes an absorbance change, dependent upon the ferritin contents of the sample that can be quantified by comparison from a calibrator of known ferritin concentration.

Composition:

R1 (diluent): Tris buffer - 20 mmol/L, pH 8,2. Preservative
R1 (Latex): Latex particles coated with rabbit IgG anti-human ferritin, pH, 8,2. Preservative.
FERR-CAL: Calibrator. Ferritin concentration is stated on the vial.

Precautions:

Components from human origin have been tested and found to be negative for the presence of HBsAg, HCV, and antibody to HIV (1/2). However handle cautiously as potentially infectious.

Calibration:

Use Ferritin Calibrator.
The sensitivity of the assay and the target value of the calibrator have been standardized against the 3rd International Standard of Ferritin (94/572, 2008 WHO).
The calibration is stable for at least 1 month.
Recalibrate when control results are out of specified values, when using different lot of reagent and when the instrument is adjusted.

Calibration curve:
Prepare the following dilutions of the FERR Calibrator using NaCl 9 g/L. To obtain the concentration of each dilution, multiply using the dilution factor shown in the next table:

Calibrator dilution	1	2	3	4	5	6
Calibrator FERR (µL) NaCl 9 g/L (µL)	- 400	25 375	50 350	100 300	200 200	400 -
Dilution Factor	0	1/16	1/8	1/4	1/2	1

Preparation:

Ferritin Calibrator: Reconstitute (→) with 3,0 mL of distilled water. Mix gently and incubate at room temperature for 10 minutes before use.

Storage and stability:

All the components of the kit are stable until the expiration date on the label when stored tightly closed at 2-8ºC and contaminations are prevented during their use. Reagents should not be left inside the analyzer after use, they must be stored refrigerated at 2-8ºC. Latex may sediment. Mix reagents gently before use. Do not use reagents over the expiration date.
Do not freeze; frozen Latex or Diluent could change the functionality of the test.
Reagent deterioration: Presence of particles and turbidity.

Samples:

Fresh serum. Stable 7 days at 2-8ºC or 3 months at –20ºC.
The samples with presence of fibrin should be centrifuged before testing.
Do not use highly hemolized or lipemic samples.

Equipment:

- Thermostatic bath at 37ºC.
- Spectrophotometer or photometer thermostatable at 37ºC with a 540 nm filter.

Procedure:

1. Bring the reagents and the photometer (cuvette holder) to 37ºC.

2. Assay conditions:
Wavelength: . . . . . 540 nm (530-550)
Cuvette: . . . . . 1 cm. light path
Temperature 37ºC

3. Adjust the instrument to zero with distilled water.

4. Pipette into a cuvette:
Diluent R1: 800 µL
Latex R2: 200 µL
Calibrator or sample: 90 µL
5. Mix and read the absorbance immediately (A1) and after 2 minutes (A2) of the sample addition.

Calculations:

Calculate the absorbance difference (A2-A1) of each point of the calibration curve and plot the values obtained against the Ferritin concentration of each calibrator dilution. Ferritin concentration in the sample is calculated by interpolation of its (A2-A1) in the calibration curve.

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

Reference values:

Men: 30 – 220 µg/L.
Women: 20 – 110 µg/L.
Each laboratory should establish its own reference range.

Performance characteristics:

Measuring range:
Up to 600 µg/L. Samples with higher values should be diluted 1/5 in NaCl 9 g/L and retested. The upper linearity limit increases as the sample volume and the sensitivity decrease.

Detection limit:
5,04 µg/L.

Quantification limit:
Values under 6,6 µg/L may give non-reproducible results.

Prozone effect:
No prozone effect was detected at least up to 9000 µg/L.

Precision:
According to the EP5-A2 standards (CLSI), the reagent has been tested for 20 days, measuring each level per duplicate twice a day (n=80):

	Intra-assay (n=80)			Total (n=80)		
Mean (µg/L)	33.4	114.5	289.8	33.4	114.5	289.8
SD	1.7	1.4	2.4	2.1	3.4	7.5
%CV	5.1	1.2	0.8	6.3	2.9	2.6

Method comparison:
The reagent was compared to another commercially available Ferritin reagent by testing 144 samples (male and female), with concentrations between 6,97 and 730 ug/L. The coefficient of correlation (r) and the equation (y) were:
r = 0,988
y = 0,96x + 1,15
Performance characteristics depend on the analyzer used.

Interferences:

Bilirubin (40 mg/dL), hemoglobin (5 g/L), y and rheumatoid factor (750 UI/mL), do not interfere. Lipids (≥ 2,5 g/L) do interfere. Other substances may interfere.

Notes:

Clinical diagnosis should not be made on findings of a single test result, but should integrate both clinical and laboratory data.

References:

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HbA_1c

Glycated Hemoglobin A1c

CE

Diagnostic liquid bi-reagent for determination of HbA1c concentration. IVD.
Store at 2-8 °C

REF: HBA1-200A

Summary:

Hemoglobin A1c is formed continuously by the addition of glucose to the N-terminal of the hemoglobin beta chain. This process, which is non-enzymatic, reflects the average exposure of hemoglobin to glucose over an extended period. It has been demonstrated that Hemoglobin A1c in diabetic subjects is elevated 2-3 fold over the levels found in normal patients. Several investigators have recommended that Hemoglobin A1c serves as an indicator of metabolic control of the diabetic patients.

Principle:

This reagent uses the interaction of antigen and antibody to directly determine the HbA1c in whole blood. Total hemoglobin and HbA1c have the same unspecific absorption rate to latex particles. When mouse antihuman HbA1c monoclonal antibody is added (R2), latex-HbA1c-mouse anti human HbA1c antibody complex is formed. Agglutination is formed when goat anti-mouse IgG polyclonal antibody interacts with the monoclonal antibody. The amount of agglutination is proportional to the amount of HbA1c absorbed on to the surface of latex particles. The amount of agglutination is measured as absorbance. The HbA1c value is obtained from a calibration curve.

Composition:

Lyse Reagent: Stabilizers, Buffers, lysing agent, water
R1: Latex - < 0, 15 %, Buffer, Stabilizers.
R2: Mouse anti-human HbA1c monoclonal antibody - < 0.06 mg/mL, goat anti-mouse IgG polyclonal antibody - < 0.09 mg/dL, Buffer, Stabilizers.

Reagent Stability And Storage:

Reagents are stable at +2/+8˚C till the expiration date stated on the label which is only for closed vials.
Once opened vials are stable for 30 days at +2/+8°C. On board stability is related to auto analyzers' cooling specification and carry-over values.

Preparation:

Reagents are ready for use.

Samples:

The assay is formulated for use with human whole blood samples. Venous whole blood samples collected with EDTA anticoagulant can be used. It is recommended that samples be used within 7 days of collection when stored refrigerated. Prior to testing, whole blood samples should be mixed by gentle inversion to re-suspend settled erythrocytes.
Auto analyzer usage: Samples should be tested by stat mode (Emergency mode) to avoid precipitation.

Preparation of Hemolysate

1. Whole blood samples are taken to room temperature,
2. Blood samples are mixed in order to mix erythrocytes homogeneously,
3. Using a calibrated pipette, transfer 1000 µL Lyse solution to the sample cup,
4. 30 µL of homogenized blood sample is transferred to the sample cup with Lyse added,
5. Hemolysate is mixed thoroughly, incubated for 5 minutes at room temperature,
6. Hemolysate is ready for use for HbA1c.

Procedure:

1. Assay conditions:
Wavelength: . . . . . 660 (600/660) nm
Cuvette: . . . . . 1 cm. light path
Temperature . . . . . .37°C

2. Adjust the instrument to zero with distilled water.

3. Pipette into a cuvette:

R1 (µL)	360
Sample (µL)	10

4. Mix and incubate 5 minutes.

5. Pipete into the cuvette:

R2 (µL)	120

6. Mix and read the absorbance after 5 minutes (A) of the R2 addition.

Calculations:

HbA1c concentration (%)
Plot (A) obtained against the HbA1c concentration of each calibrator (1 to 4 Level). HbA1c percentage in the sample is calculated by interpolation of its absorbance (A) in the calibration curve.

Quality control:

All clinical laboratories should establish an Internal Quality Control program. Check instrument and reagent performance with recommended controls or similar. The values obtained for QC should fall within manufacturer's acceptable ranges or should be established according to the Laboratory's QC program.
Controls should be assayed:
- Prior reporting patient results.
- Following any maintenance procedure on the photometer used.
- At pre-established intervals following the Q.C. Laboratory recommandations.

The International Federation of Clinical Chemistry (IFCC) values are calculated according to the formula given:

Conversion formula:
NGSP%= [0.09148 x (IFCC)] + 2.152

Reference Intervals (Normal Values):

Expected Values: %4.5 - 6.5 (NGSP/DCCT)
Expected Values: 26 - 48 mmol/mol (IFCC)
Levels above 6.5% HbA1c are suitable for the diagnosis of diabetes mellitus according to the data provided by NGSP. Patients with levels between 39-46 mmol/mol (IFCC) or 5.7% - 6.4% HbA1c (NGSP) have a possibility of developing diabetes risk. It is recommended that each laboratory establish its own normal range.
Reference interval has been verified by using CLSI EP28-A3c protocol.

Limitations:
- The linearity of the assay is up to 15% HbA1c. Samples with values above 15% should not be diluted and retested. Instead the values should be reported as higher than 16% (>16%).
- It has been observed that the patients who have alcoholism, high dose of acetyl salicylic acide, opiate and lead poisoning may lead to inconsistency.
- The assay is formulated for use with human whole blood samples in EDTA.
- Elevated levels of HbF may lead to insufficient evaluation of HbA1c and uremia does not interfere with HbA1c determination by immunoassay.

Performance characteristics:

The following values were obtained by comparing Sorachim reagent to a commercially available HPLC method.

Whole blood application	
n	100
Slope	1.001
Intercept	0.027
Correlation coefficient	0.990
Range of values	5% - 14% HbA1c

Low Linearity (LOQ):
(LoQ values are based on Coefficient of Variation Percentage (CV) ≤ 20%): The limit of detection is 4%.
LoQ value has been verified by using CLSI EP17-A protocol.

High Linearity:
The method is linear up to 15.0%.
Linearity may considerably vary depending on the instrument used.

Precision:

	Intra-assay			Inter-assay		
	Mean (%)	%CV	n	Mean (%)	%CV	n
Low	5.46	1.45	40	5.46	2.81	40
High	10.1	1.73	40	10.1	2.72	80

Precision Studies data have been verified by using CLSI EP05-A3 protocol.

Interferences:
No significant interactions were observed for Conjugated Bilirubin, Triglycerides, Ascorbic Acid, Acetlated Hb, Carbamylated Hb up to the interferent concentration given below:
Ascorbic acid: 40 mg/dL
Total bilirubin: 48 mg/dL
Acetylated Hb: 4.8 mmol/L
Triglycerides: 2000 mg/dL
Carbamylated Hb: 7.3 mmol/L

The acceptable interference limit is set 10% below the highest interference concentration within ± 10% recovery of the target.
Interferences may affect the results due to medication or endogenous substances.
These performance characteristics have been obtained by using an analyzer. Results may vary if a different instrument or a manual procedure is used.

Disposal
Dispose the vials and contents according to the local regulations.

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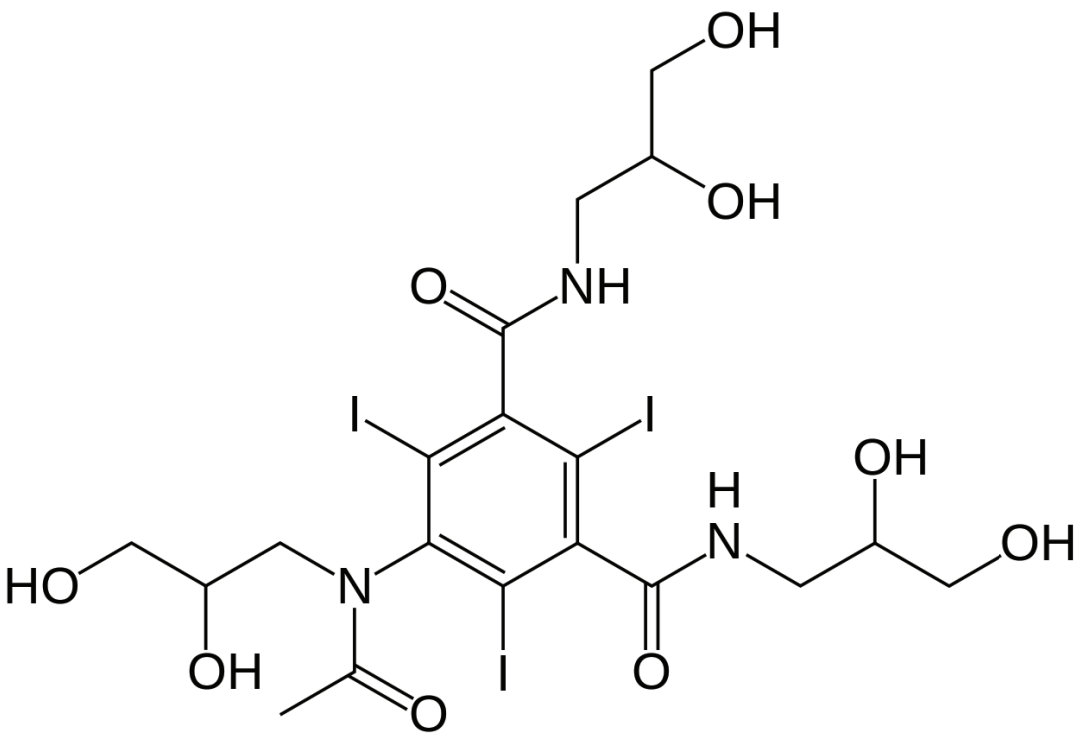

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