0003183742122c501V10.0

# AMYL2

cobas®

**α-Amylase EPS ver.2**

**Order information**

| REF | CONTENT | | Analyzer(s) on which **cobas c** pack(s) can be used |
|---|---|---|---|
| **03183742** 122 | α-Amylase EPS ver.2 (300 tests) | System-ID 07 6609 7 | Roche/Hitachi **cobas c** 311, **cobas c** 501/502 |
| **10759350** 190 | Calibrator f.a.s. (12 x 3 mL) | Code 401 | |
| **10759350** 360 | Calibrator f.a.s. (12 x 3 mL, for USA) | Code 401 | |
| **12149435** 122 | Precinorm U plus (10 x 3 mL) | Code 300 | |
| **12149435** 160 | Precinorm U plus (10 x 3 mL, for USA) | Code 300 | |
| **12149443** 122 | Precipath U plus (10 x 3 mL) | Code 301 | |
| **12149443** 160 | Precipath U plus (10 x 3 mL, for USA) | Code 301 | |
| **10171743** 122 | Precinorm U (20 x 5 mL) | Code 300 | |
| **10171735** 122 | Precinorm U (4 × 5 mL) | Code 300 | |
| **10171778** 122 | Precipath U (20 x 5 mL) | Code 301 | |
| **10171760** 122 | Precipath U (4 × 5 mL) | Code 301 | |
| **05117003** 190 | PreciControl ClinChem Multi 1 (20 x 5 mL) | Code 391 | |
| **05947626** 190 | PreciControl ClinChem Multi 1 (4 x 5 mL) | Code 391 | |
| **05947626** 160 | PreciControl ClinChem Multi 1 (4 x 5 mL, for USA) | Code 391 | |
| **05117216** 190 | PreciControl ClinChem Multi 2 (20 x 5 mL) | Code 392 | |
| **05947774** 190 | PreciControl ClinChem Multi 2 (4 x 5 mL) | Code 392 | |
| **05947774** 160 | PreciControl ClinChem Multi 2 (4 x 5 mL, for USA) | Code 392 | |
| **04489357** 190 | Diluent NaCl 9 % (50 mL) | System-ID 07 6869 3 | |

## English

### System information

For **cobas c** 311/501 analyzers:

**AMYL2:** ACN 570

**SAMY2:** ACN 566 (STAT, reaction time: 7)

For **cobas c** 502 analyzer:

**AMYL2:** ACN 8570

**SAMY2:** ACN 8566 (STAT, reaction time: 7)

### Intended use

In vitro test for the quantitative determination of α-amylase in human serum, plasma and urine on Roche/Hitachi **cobas c** systems.

### Summary[1,2,3,4,5,6,7,8,9]

The α-amylases (1,4-α-D-glucanohydrolases, EC 3.2.1.1) catalyze the hydrolytic degradation of polymeric carbohydrates such as amylose, amylopectin and glycogen by cleaving 1,4-α-glucosidic bonds. In polysaccharides and oligosaccharides, several glycosidic bonds are hydrolyzed simultaneously. Maltotriose, the smallest such unit, is converted into maltose and glucose, albeit very slowly. Two types of α-amylases can be distinguished, the pancreatic type (P-type) and the salivary type (S-type). Whereas the P-type can be attributed almost exclusively to the pancreas and is therefore organ-specific, the S-type can originate from a number of sites. As well as appearing in the salivary glands it can also be found in tears, sweat, human milk, amniotic fluid, the lungs, testes and the epithelium of the fallopian tube.

Because of the sparsity of specific clinical symptoms of pancreatic diseases, α-amylase determinations are of considerable importance in pancreatic diagnostics. They are mainly used in the diagnosis and monitoring of acute pancreatitis. Hyperamylasemia does not, however, only occur with acute pancreatitis or in the inflammatory phase of chronic pancreatitis, but also in renal failure (reduced glomerular filtration), tumors of the lungs or ovaries, pulmonary inflammation, diseases of the salivary gland, diabetic ketoacidosis, cerebral trauma, surgical interventions or in the case of macroamylasemia. To confirm pancreatic specificity, it is recommended that an additional pancreas-specific enzyme - lipase or pancreatic-α-amylase - also be determined.

Numerous methods have been described for the determination of α-amylase. These either determine the decrease in the amount of substrate viscometrically, turbidimetrically, nephelometrically and amyloclastically or measure the formation of degradation products saccharogenically or kinetically with the aid of enzyme-catalyzed subsequent reactions. The kinetic method described here is based on the well-proven cleavage of 4,6-ethylidene-($G_7$)-1,4-nitrophenyl-($G_1$)-α,D-maltoheptaoside (Ethylidene Protected Substrate = EPS) by α-amylase and subsequent hydrolysis of all the degradation products to p-nitrophenol with the aid of α-glucosidase (100 % chromophore liberation). The results of this method correlate with those obtained by HPLC. This assay follows the recommendation of the IFCC, but was optimized for performance and stability.

### Test principle[10,11]

Enzymatic colorimetric assay acc. to IFCC.

Defined oligosaccharides such as 4,6-ethylidene-($G_7$) p-nitrophenyl-($G_1$)-α-D-maltoheptaoside (ethylidene-$G_7$PNP) are cleaved under the catalytic action of α-amylases. The $G_2$PNP, $G_3$PNP and $G_4$PNP fragments so formed are completely hydrolyzed to p-nitrophenol and glucose by α-glucosidase.

Simplified reaction scheme:

$$5\ \text{ethylidene-G}_7\text{PNP}^{a)} + 5\ H_2O \xrightarrow{\alpha\text{-amylase}} 2\ \text{ethylidene-G}_5 + 2\ G_2\text{PNP} + 2\ \text{ethylidene-G}_4 + 2\ G_3\text{PNP} + \text{ethylidene-G}_3 + G_4\text{PNP}$$

$$2\ G_2\text{PNP} + 2\ G_3\text{PNP} + G_4\text{PNP} + 14\ H_2O \xrightarrow{\alpha\text{-glucosidase}} 5\ \text{PNP} + 14\ G^{b)}$$

a) PNP ≙ p-nitrophenol

b) G ≙ Glucose

The color intensity of the p-nitrophenol formed is directly proportional to the α-amylase activity. It is determined by measuring the increase in absorbance.

### Reagents - working solutions

**R1** HEPES: 52.4 mmol/L; sodium chloride: 87 mmol/L; calcium chloride: 0.08 mmol/L; magnesium chloride: 12.6 mmol/L; α-glucosidase (microbial): ≥ 66.8 µkat/L; pH 7.0 (37 °C); preservatives; stabilizers

**R2** HEPES: 52.4 mmol/L; ethylidene-$G_7$-PNP: 22 mmol/L; pH 7.0 (37 °C); preservatives; stabilizers

R1 is in position B and R2 is in position C.

### Precautions and warnings

For in vitro diagnostic use.

Exercise the normal precautions required for handling all laboratory

reagents.
Disposal of all waste material should be in accordance with local guidelines. Safety data sheet available for professional user on request.

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

**Reagent handling**

Ready for use

**Storage and stability**

| | |
|---|---|
| *AMYL2* | |
| Shelf life at 2‑8 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 12 weeks |
| *Diluent NaCl 9 %* | |
| Shelf life at 2‑8 °C: | See expiration date on **cobas c** pack label. |
| On-board in use and refrigerated on the analyzer: | 12 weeks |

**Specimen collection and preparation**[9,12]

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.
Serum
Plasma: Li-heparin plasma.

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

See the limitations and interferences section for details about possible sample interferences.

Sample stability claims were established by experimental data by the manufacturer or based on reference literature and only for the temperatures/time frames as stated in the method sheet. It is the responsibility of the individual laboratory to use all available references and/or its own studies to determine specific stability criteria for its laboratory.

Urine: Collect urine without additives. α-Amylase is unstable in acid urine. Assay promptly or adjust pH to alkaline range (just above pH 7) before storage.[13]

| | |
|---|---|
| Stability in *serum or plasma:*[13] | 7 days at 15‑25 °C<br>1 month at 2‑8 °C |
| Stability in *urine:*[14] | 2 days at 15‑25 °C<br>10 days at 2‑8 °C |

**Materials provided**

See “Reagents – working solutions” section for reagents.

**Materials required (but not provided)**

- See “Order information” section
- General laboratory equipment

**Assay**

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator’s manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

**Application for serum, plasma and urine**

**cobas c** 311 **test definition**

| | | | |
|---|---|---|---|
| Assay type | Rate A | | |
| Reaction time / Assay points | 10 / 22‑32 (STAT 7/ 22‑32) | | |
| Wavelength (sub/main) | 700/415 nm | | |
| Reaction direction | Increase | | |
| Unit | U/L (µkat/L) | | |
| Reagent pipetting | | Diluent ($H_2O$) | |
| R1 | 100 µL | – | |
| R2 | 20 µL | – | |
| *Sample volumes* | *Sample* | *Sample dilution* | |
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 4 µL | – | – |
| Decreased | 8 µL | 15 µL | 135 µL |
| Increased | 4 µL | – | – |

**cobas c** 501 **test definition**

| | | | |
|---|---|---|---|
| Assay type | Rate A | | |
| Reaction time / Assay points | 10 / 30‑47 (STAT 7 / 30‑47) | | |
| Wavelength (sub/main) | 700/415 nm | | |
| Reaction direction | Increase | | |
| Unit | U/L (µkat/L) | | |
| Reagent pipetting | | Diluent ($H_2O$) | |
| R1 | 100 µL | – | |
| R2 | 20 µL | – | |
| *Sample volumes* | *Sample* | *Sample dilution* | |
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 4 µL | – | – |
| Decreased | 8 µL | 15 µL | 135 µL |
| Increased | 4 µL | – | – |

**cobas c** 502 **test definition**

| | | | |
|---|---|---|---|
| Assay type | Rate A | | |
| Reaction time / Assay points | 10 / 30‑47 (STAT 7 / 30‑47) | | |
| Wavelength (sub/main) | 700/415 nm | | |
| Reaction direction | Increase | | |
| Unit | U/L (µkat/L) | | |
| Reagent pipetting | | Diluent ($H_2O$) | |
| R1 | 100 µL | – | |
| R2 | 20 µL | – | |
| *Sample volumes* | *Sample* | *Sample dilution* | |
| | | *Sample* | *Diluent (NaCl)* |
| Normal | 4 µL | – | – |
| Decreased | 8 µL | 15 µL | 135 µL |
| Increased | 8 µL | – | – |

**Calibration**

| | |
|---|---|
| Calibrators | S1: $H_2O$<br>S2: C.f.a.s. |

| | |
|---|---|
| Calibration mode | Linear |
| Calibration frequency | 2-point calibration<br>• after reagent lot change<br>• as required following quality control procedures |

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against Roche system reagent using calibrated pipettes together with a manual photometer providing absolute values and substrate-specific absorptivity, ε.

### Quality control

For quality control, use control materials as listed in the "Order information" section.

In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

### Calculation

Roche/Hitachi **cobas c** systems automatically calculate the analyte activity of each sample.

Conversion factor: U/L x 0.0167 = µkat/L

### Limitations - interference

A slight change in the yellow coloration of solution 2 does not interfere with the performance of the test.

Do not pipette by mouth, and ensure that the reagent does not come into contact with the skin. **Saliva and sweat** contain α-amylase!

Criterion: Recovery within ± 10 % of initial value at an amylase activity of 100 U/L (1.67 µkat/L).

*Serum/plasma*

Icterus:[15] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[15] No significant interference up to an H index of 500 (approximate hemoglobin concentration: 311 µmol/L or 500 mg/dL).

Lipemia (Intralipid):[15] No significant interference up to an L index of 1500. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

In rare cases, samples with a combination of elevated turbidity (L-index) and high Amylase activity may cause a >React or >Abs flag.

Highly turbid and grossly lipemic samples may cause Abs. flags.

Anticoagulants: Interference was found with citrate, fluoride, and EDTA.[12]

Glucose: No significant interference from glucose up to a concentration of 111 mmol/L (2000 mg/dL). Approximately 10 % higher recovery was found at glucose concentrations of 250 mmol/L (4500 mg/dL).

Ascorbic acid: No significant interference from ascorbic acid up to a concentration of 5.68 mmol/L (100 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.[16,17]

Exception: Icodextrin-based drugs may lead to decreased amylase results.[18]

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[19]

*Urine*

Hemolysis:[15] No significant interference up to a hemoglobin concentration of 311 µmol/L or 500 mg/dL.

Ascorbic acid: No significant interference from ascorbic acid up to a concentration of 2.27 mmol/L (40 mg/dL). Approximately 15 % lower recovery was found at ascorbic acid concentrations of 22.7 mmol/L (400 mg/dL).

Phosphate: No significant interference from phosphate up to a concentration of 70 mmol/L (217 mg/dL).

Urea: No significant interference from urea up to a concentration of 2100 mmol/L (12612 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.[17]

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

**ACTION REQUIRED**
**Special Wash Programming:** The use of special wash steps is mandatory when certain test combinations are run together on Roche/Hitachi **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is required in certain cases.

**Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.**

### Limits and ranges

### Measuring range

*Serum/plasma/urine*

3-1500 U/L (0.05-25.0 µkat/L)

Determine samples having higher activities via the rerun function. Dilution of samples via the rerun function is a 1:5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 5.

### Lower limits of measurement

*Lower detection limit of the test*

3 U/L (0.05 µkat/L)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying three standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

### Expected values[9]

| | | | |
|---|---|---|---|
| Serum/plasma | Men/Women | 0.47-1.67 µkat/L | 28-100 U/L |
| Spontaneously voided urine | Men | 0.27-8.20 µkat/L | 16-491 U/L |
| | Women | 0.35-7.46 µkat/L | 21-447 U/L |
| α-amylase/ creatinine quotient | Men | 0.97-4.73 µkat/g | 58-283 U/g |
| | Women | 1.25-6.51 µkat/g | 75-390 U/g |

*α-Amylase/creatinine quotient*

To allow for fluctuations in the α-amylase activity in urine, it is advisable to determine the α-amylase/creatinine quotient. To do this, determine the α-amylase activity and creatinine concentration in spontaneously voided urine.

$$\text{Quotient [U/g or µkat/mmol]} = \frac{\text{α-amylase [U/L or µkat/L]}}{\text{creatinine [g/L or mmol/L]}}$$

*Amylase/Creatinine Clearance Ratio (ACCR)*[13]

The ACCR is calculated from amylase activity and creatinine concentration. Both the serum and urine samples should be collected at the same time.

$$\text{ACCR [\%]} = \frac{\text{urine amylase [U/L]} \times \text{serum creatinine [mg/L]}}{\text{serum amylase [U/L]} \times \text{urine creatinine [mg/L]}} \times 100$$

The ACCR is approximately equal to 2-5 %.

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

### Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

### Precision

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 21 days). The following results were obtained:

*Serum/plasma*

| *Repeatability* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *U/L (µkat/L)* | *U/L (µkat/L)* | *%* |
| Precinorm U | 83.2 (1.39) | 0.8 (0.01) | 0.9 |
| Precipath U | 182 (3.09) | 1 (0.02) | 0.6 |
| Human serum 1 | 34.5 (0.576) | 0.4 (0.007) | 1.2 |
| Human serum 2 | 97.9 (1.63) | 0.7 (0.01) | 0.7 |

| *Intermediate precision* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *U/L (µkat/L)* | *U/L (µkat/L)* | *%* |
| Precinorm U | 84.0 (1.40) | 1.1 (0.02) | 1.3 |
| Precipath U | 184 (3.08) | 3 (0.05) | 1.5 |
| Human serum 3 | 35.1 (0.586) | 0.9 (0.015) | 2.4 |
| Human serum 4 | 98.9 (1.65) | 1.6 (0.03) | 1.6 |

*Urine*

| *Repeatability* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *U/L (µkat/L)* | *U/L (µkat/L)* | *%* |
| Control level 1 | 50.6 (0.845) | 0.5 (0.008) | 0.9 |
| Control level 2 | 164 (2.74) | 1 (0.02) | 0.6 |
| Urine 1 | 21.4 (0.357) | 0.2 (0.003) | 1.1 |
| Urine 2 | 68.5 (1.14) | 0.7 (0.01) | 0.9 |

| *Intermediate precision* | *Mean* | *SD* | *CV* |
|---|---|---|---|
| | *U/L (µkat/L)* | *U/L (µkat/L)* | *%* |
| Control level 1 | 51.8 (0.865) | 0.9 (0.015) | 1.7 |
| Control level 2 | 168 (2.81) | 2 (0.03) | 1.1 |
| Urine 3 | 24.5 (0.409) | 0.5 (0.008) | 1.9 |
| Urine 4 | 67.0 (1.12) | 2.8 (0.05) | 4.2 |

### Method comparison

Amylase values for human serum, plasma and urine samples obtained on a Roche/Hitachi **cobas c** 501 analyzer (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x).

*Serum/plasma*

Sample size (n) = 79

| Passing/Bablok[20] | Linear regression |
|---|---|
| $y = 0.999x + 2.83$ U/L | $y = 0.998x + 4.75$ U/L |
| $\tau = 0.969$ | $r = 0.998$ |

The sample activities were between 51.7 and 1409 U/L (0.863 and 23.5 µkat/L).

*Urine*

Sample size (n) = 88

| Passing/Bablok[20] | Linear regression |
|---|---|
| $y = 0.986x + 0.423$ U/L | $y = 0.982x + 2.03$ U/L |
| $\tau = 0.987$ | $r = 1.000$ |

The sample activities were between 33.6 and 1248 U/L (0.561 and 20.8 µkat/L).

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A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

### Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard (for USA: see https://usdiagnostics.roche.com for definition of symbols used):

| | |
|---|---|
| CONTENT | Contents of kit |
| → | Volume after reconstitution or mixing |
| GTIN | Global Trade Item Number |

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