PROC2

cobas®

ONLINE TDM Procainamide

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
04490975190	04490975500	ONLINE TDM Procainamide (100 Tests)	System-ID 07 6983 5	**cobas c** 311, **cobas c** 501/502

Materials required (but not provided):

03375781190	Preciset TDM II CAL A-F (1 x 5 mL) Diluent (1 x 10 mL)	Codes 743-748	
04521536190	TDM Control Set Level I (2 x 5 mL) Level II (2 x 5 mL) Level III (2 x 5 mL)	Code 310 Code 311 Code 312	

English

System information

For **cobas c** 311/501 analyzers:
PROC2: ACN 619

For **cobas c** 502 analyzer:
PROC2: ACN 8619

Intended use

In vitro test for the quantitative determination of procainamide in serum and plasma on **cobas c** systems.

Summary

Procainamide measurements, performed with this assay in human serum and plasma, are used to monitor procainamide therapy to ensure appropriate therapy.

Procainamide is a Class IA antiarrhythmic agent mainly used to manage and treat ventricular arrhythmias.[1,2,3,4,5,6] Procainamide shows a large variability between dose and plasma concentration.[7] Increased procainamide serum and plasma levels are associated with an increased risk of drug toxicity.[2] A significant fraction of the circulating procainamide is metabolized in hepatocytes to N-acetylprocainamide (NAPA), ranging from 16 to 21 percent of an administered dose in “slow acetylators” to 24 to 33 percent in “fast-acetylators”.[1] This metabolite is pharmacologically active but with lower potency than procainamide and has qualitatively different cardiac actions.[7,8] Both procainamide and NAPA are chiefly eliminated by the kidneys, resulting in the need for dose adjustment of procainamide when used in patients with impaired renal function.[9] NAPA has slower renal clearance compared to procainamide and can accumulate rapidly in the presence of renal or circulatory impairment. Hepatic acetylation rate capability, renal function, as well as age, affect the half-life and clearance of procainamide and the NAPA derivative.[1,2,7] Serum concentrations of both procainamide and NAPA can be monitored during therapy, especially in patients with renal or hepatic insufficiency or in patients with potential adverse effects.[9,10,11]

Test principle

The assay is based on a homogeneous enzyme immunoassay technique used for the quantitative analysis of procainamide in human serum or plasma.[12,13] The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for antibody binding sites. Enzyme activity decreases upon binding to the antibody, so the drug concentration in the sample can be measured in terms of enzyme activity. Active enzyme converts oxidized nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that is measured spectrophotometrically. Endogenous serum G6PDH does not interfere because the coenzyme functions only with the bacterial *(Leuconostoc mesenteroides)* enzyme employed in the assay.

Reagents - working solutions

R1 Anti-procainamide antibody (mouse monoclonal), G6P, NAD, preservatives and stabilizers

R2 Procainamide labeled with bacterial G6PDH in buffer

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

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317	May cause an allergic skin reaction.
Prevention:	
P261	Avoid breathing mist or vapours.
P272	Contaminated work clothing should not be allowed out of the workplace.
P280	Wear protective gloves.
Response:	
P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.
Disposal:	
P501	Dispose of contents/container to an approved waste disposal plant.
EUH 208	Contains reaction mass of: 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1). May produce an allergic reaction.

Product safety labeling primarily follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

Reagent handling

Ready for use

Mix reagents by gentle inversion numerous times before placing on-board the analyzer.

Storage and stability

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

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Do not freeze.

Specimen collection and preparation

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

Only the specimens listed below were tested and found acceptable.

Serum: Collect serum using standard sampling tubes.

Plasma: K_2- or K_3-EDTA, citrate, oxalate, or sodium or lithium heparinized plasma.

Stability:[14]	2 weeks capped at 2-8 °C 6 months capped at -20 °C (± 5 °C)

Freeze only once.

Do not induce foaming of specimens.

Invert thawed specimens several times prior to testing.

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.

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 and plasma

Deselect Automatic Rerun for these applications in the Utility menu, Application screen, Range tab.

cobas c 311 **test definition**

Assay type	Rate-A assay		
Reaction time /Assay points:	10 / 21-29		
Wavelength (sub/main)	415/340 nm		
Reaction direction	Increase		
Unit	µg/mL		
Reagent pipetting		Diluent (H_2O)	
R1	133 µL	–	
R2	67 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2.6 µL	–	–
Decreased	2.6 µL	–	–
Increased	2.6 µL	–	–

cobas c 501/502 **test definition**

Assay type	Rate-A assay		
Reaction time /Assay points:	10 / 30-44		
Wavelength (sub/main)	415/340 nm		
Reaction direction	Increase		
Unit	µg/mL		
Reagent pipetting		Diluent (H_2O)	
R1	133 µL	–	
R2	67 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2.6 µL	–	–
Decreased	2.6 µL	–	–
Increased	2.6 µL	–	–

Calibration

Calibrator	S1-6: Preciset TDM II Calibrators
Calibration mode	RCM
Calibration frequency	6-point calibration - after reagent lot change - every 6 weeks - as required following quality control procedures

Traceability: This method has been standardized against USP reference standards. The calibrators are prepared to contain known quantities of procainamide in normal human serum.

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

cobas c systems automatically calculate the analyte concentration of each sample in the unit µg/mL (µmol/L).

Conversion factor:[15] µg/mL x 4.23 = µmol/L

Limitations - interference

Criterion: Recovery within ± 10 % of initial value at procainamide levels of approximately 4 and 10 µg/mL (16.9 and 42.3 µmol/L).

Icterus:[16] No significant interference up to an I index of 30 for conjugated bilirubin and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 513 µmol/L or 30 mg/dL).

Hemolysis:[16] No significant interference up to an H index of 800 (approximate hemoglobin concentration: 800 mg/dL or 497 µmol/L).

Lipemia (Intralipid):[16] No significant interference up to an L index of 500. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Criterion: Recovery within ± 10 % of initial value at a procainamide level of approximately 4 µg/mL (16.9 µmol/L).

No significant interference from triglycerides up to 1000 mg/dL (11.3 mmol/L).

Rheumatoid factors: No significant interference from rheumatoid factors up to 100 IU/mL.

Total protein: No interference from total protein from 2-12 g/dL.

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[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 **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: 0.53-14 µg/mL (2.24-59.22 µmol/L)

Specimen dilution

Manually dilute samples above the measuring range 1 + 1 with Preciset TDM II Diluent (0 µg/mL) and reassay. Multiply the result by 2 to obtain the specimen value.

Lower limits of measurement

Lower detection limit of the test

0.53 µg/mL (2.24 µmol/L)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 2 standard deviations above that of the lowest standard (standard 1 + 2 SD, repeatability, n = 21).

Expected values

The commonly accepted therapeutic range for procainamide is 4-10 µg/mL (16.9-42.3 µmol/L) and the sum of procainamide and N-acetylprocainamide is 5-30 µg/mL (21.2-126.9 µmol/L). Procainamide is thought to be toxic at levels greater than 16 µg/mL (> 67.7 µmol/L). For effective treatment, some patients may require serum or plasma procainamide levels outside these ranges. These ranges are, therefore, provided only as a guide for interpretation along with other clinical symptoms and clinical history.[18,19,15]

The factors that can influence the relationship between procainamide serum or plasma concentrations and clinical response include renal and circulatory function, rate of acetylation, the severity and type of cardiac arrhythmia, general state of health, and use of other drugs. The concentration of procainamide in serum or plasma depends on the time of the last drug dose; mode of administration; concomitant drug therapy; sample condition; time of sample collection; and individual variations in absorption, biotransformation, distribution, and excretion. These parameters must be considered when interpreting results.[15]

Expected values reflect the data and information provided in the reference and do not necessarily represent therapeutic recommendations and/or dosage instructions. For therapeutic recommendations and dosage instructions refer to applicable guidelines and the full prescription information of the drug.

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 a modified NCCLS EP5-T2 protocol (repeatability n = 63, intermediate precision n = 63). The following results were obtained on a **cobas c** 501 analyzer.

Repeatability	*Mean*		*SD*		*CV*
	µg/mL	*µmol/L*	*µg/mL*	*µmol/L*	*%*
Control 1	1.74	7.36	0.03	0.13	1.6
Control 2	7.02	29.6	0.11	0.5	1.6
Control 3	10.8	45.7	0.4	1.7	3.3
HS 1	4.04	16.9	0.04	0.2	1.0
HS 2	10.7	45.3	0.4	1.7	3.6

Intermediate precision	*Mean*		*SD*		*CV*
	µg/mL	*µmol/L*	*µg/mL*	*µmol/L*	*%*
Control 1	1.74	7.36	0.08	0.34	4.7
Control 2	7.02	29.6	0.20	0.9	2.8
Control 3	10.8	45.7	0.5	2.1	4.7
HS 1	4.04	16.9	0.09	0.4	2.2
HS 2	10.7	45.3	0.5	2.1	4.5

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

Method comparison

Procainamide values for human serum and plasma samples obtained on a **cobas c** 501 analyzer (y) were compared with those determined with the corresponding reagent on a Roche/Hitachi 917 analyzer (x) and on a COBAS INTEGRA 700 analyzer (x).

Roche/Hitachi 917 analyzer	Sample size (n) = 75
Passing/Bablok[20]	Linear regression
y = 1.021x - 0.034 µg/mL	y = 1.032x - 0.062 µg/mL
τ = 0.976	r = 0.997

The sample concentrations were between 0.680 and 11.8 µg/mL (2.88 and 49.9 µmol/L).

COBAS INTEGRA 700 analyzer	Sample size (n) = 75
Passing/Bablok[20]	Linear regression
y = 0.995x + 0.253 µg/mL	y = 0.990x + 0.309 µg/mL
τ = 0.959	r = 0.996

The sample concentrations were between 0.400 and 11.3 µg/mL (1.69 and 47.8 µmol/L).

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

Analytical specificity

The following compounds were tested for cross-reactivity in normal human serum spiked with procainamide at approximately 5 µg/mL (21.2 µmol/L).

Compound	**Concentration Tested (µg/mL)**	**% Cross-reactivity**
Acetaminophen	100	ND
Desethyl-N-acetylprocainamide (DENAPA)	100	ND
Digoxin	0.1	ND
Diphenylhydantoin	100	ND
Disopyramide	100	ND
Ephedrine	100	ND
Furosemide	100	ND
Glycinexylidide (GX)	100	ND
Hydrochlorothiazide	100	ND
Isoproterenol	100	ND
Lidocaine	100	ND
Monoethylglycinexylidide (MEGX)	100	ND
N-Acetylprocainamide	40	ND
N-(2-Diethylaminoethyl) isonicotinamide	100	ND

p-Acetamidobenzoic acid	100	ND
p-Aminobenzoic acid (PABA)	100	ND
Procaine	100	ND
Propanolol	100	ND
Quinidine	100	ND
Tocainide	100	ND

Cross-reactivity was designated as “Not Detectable” (ND) if the obtained value was less than the sensitivity of the assay.

Tests were performed on 16 drugs. No significant interference with the assay was found.

Acetaminophen	Doxycycline (Tetracycline)
Acetyl cysteine	Ibuprofen
Acetylsalicylic acid	Levodopa
Ampicillin-Na	Methyldopa+1.5 H_2O
Ascorbic acid	Metronidazole
Ca-Dobesilate	Phenylbutazone
Cefoxitin	Rifampicin
Cyclosporine	Theophylline

References

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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.

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

The Summary of Safety & Performance Report can be found here: https://ec.europa.eu/tools/eudamed

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

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