ETOH2

cobas®

Ethanol Gen.2

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
03183777190	03183777500	Ethanol Gen.2 (100 tests)	System-ID 07 6611 9	**cobas c** 311, **cobas c** 501/502, COBAS INTEGRA 400 plus

Materials required (but not provided):

		cobas c 311, **cobas c** 501/502	COBAS INTEGRA 400 plus
20751995190	Ammonia/Ethanol/CO2 Calibrator (2 x 4 mL)	Code 688	System-ID 07 5199 5
20752401190	Ammonia/Ethanol/CO2 Control Normal (5 x 4 mL)	Code 100	System-ID 07 5240 1
20753009190	Ammonia/Ethanol/CO2 Control Abnormal (5 x 4 mL)	Code 101	System-ID 07 5300 9

English

Intended use

In vitro test for the quantitative determination of ethanol in human serum, plasma and urine on **cobas c** and COBAS INTEGRA systems.

Summary

Detection of ethanol in human serum, plasma and urine with this assay is used as an aid in the diagnosis and treatment of alcohol intoxication or poisoning in individuals with suspected exposure.

Ethanol (EtOH) is the most widely used and often abused addictive substance and therefore ethyl alcohol determinations are among the most frequent analyses required in the forensic and clinical toxicology laboratory.[1] Alcohol consumption is a causal factor in more than 60 types of diseases and injuries resulting in approximately 2.5 million deaths worldwide each year.[2]

After ingestion, ethanol is absorbed by the oral, gastric and small intestinal mucosa. Detoxification of EtOH starts in the stomach and is facilitated by alcohol dehydrogenase (ADH). The majority of EtOH is metabolized in the liver to acetaldehyde by ADH, the catalase and the microsomal ethanol oxidizing system. Acetaldehyde is further metabolized to acetic acid via acetaldehyde dehydrogenase.[3] A part of the remaining ingested ethanol undergoes non-oxidative metabolism resulting in the following metabolites: ethyl glucuronide (EtG), ethyl sulfate (EtS), fatty acid ethyl esters (FAEEs) and phosphatidylethanol (PEth).[4,5] The elimination rate varies among individuals and is influenced by drinking practices (heavy drinkers have an increased elimination rate due to enzyme induction).[1]

Compared to other alcohol biomarkers ethyl glucuronide (EtG)/Ethyl sulphate (EtS) or phosphatidylethanols (PEth), ethanol has a short window of detection and is therefore useful for detection of recent alcohol consumption and alcohol intoxication.[6]

Test principle

Enzymatic method with alcohol dehydrogenase.

Ethyl alcohol and NAD are converted to acetaldehyde and NADH by ADH.

$$\text{Ethyl alcohol} + NAD^+ \xrightarrow{ADH} \text{acetaldehyde} + NADH + H^+$$

The NADH formed during the reaction, measured photometrically as a rate of change in absorbance, is directly proportional to the ethyl alcohol concentration.

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.

Reagent handling

Ready for use

Specimen collection and preparation[7,8]

Do not use alcohol or other volatile disinfectants at the site of venipuncture. Aqueous Zephiran (benzalkonium chloride), aqueous Merthiolate (thimerosal), or povidone-iodine may be used.

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 and K_2-EDTA

Stability:[9]	2 days at 20 °C (± 5 °C)
	2 weeks at 2-8 °C
	4 weeks at -20 °C (± 5 °C)

Freeze only once.

Plasma: NaF/Na_2-EDTA and NaF/K-Oxalate

Stability:[9]	2 weeks at 20 °C (± 5 °C)
	3 months at 2-8 °C
	6 months at -20 °C (± 5 °C)

Freeze only once.

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.

Urine: Use random urine.

Stability:[10]	30 days at 2-8 °C

Freeze only once.

Storage: Samples must be tightly closed.

Centrifuge samples containing precipitates before performing the assay.

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

Each laboratory should establish guidelines for determining acceptability of specimens and the corrective action to be taken if a specimen is considered unacceptable.

With respect to specimens procured for medicolegal purposes, each legal jurisdiction may have specific requirements concerning the collection and storage of specimens from living subjects, which should be followed as rigorously as possible.[11]

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.

ETOH2

Ethanol Gen.2

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

Repeat assays must be performed on freshly poured cups, due to evaporation of alcohol.

When using Ammonia/Ethanol/CO2 Calibrator: Do not leave calibrator cups open for longer than 30 minutes at 15-25 °C.

When using Ammonia/Ethanol/CO2 Controls: Do not leave control cups open for longer than 1 hour at 15-25 °C.

Calculation[12]

The systems automatically calculate the analyte concentration of each sample in the unit mmol/L (g/L, mg/dL, ‰).

Conversion factors:	mmol/L x 0.04608 = g/L
	mmol/L x 4.608 = mg/dL
	mmol/L x 0.0374 = ‰

Expected values

Serum/plasma[12]

10.9-21.7 mmol/L (0.5-1 g/L, 50-100 mg/dL)	Flushing, slowing of reflexes, impaired visual acuity
> 21.7 mmol/L (> 1 g/L, > 100 mg/dL)	Depression of CNS
> 86.8 mmol/L (> 4 g/L, > 400 mg/dL)	Fatalities reported

Urine

The ratio of the urinary ethanol concentration to blood ethanol concentration is often reported as 1.3:1. However other lower or higher ratios might be used depending on the patient population and related factors such as the volume of urine that is produced and excreted.[13]

The legal definition of intoxication varies according to local law. Each laboratory should establish an acceptable reporting format and identify procedures for the reporting of abnormal results. Clinical consideration and professional judgment should be applied to the interpretation of any alcohol test results.

cobas c systems

System information

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

ETOH2: ACN 703

SETH2: ACN 671 (STAT, reaction time: 5)

For **cobas c** 502 analyzer:

ETOH2: ACN 8703

SETH2: ACN 8671 (STAT, reaction time: 5)

Reagents - working solutions

R1 Buffer; preservatives

R2 NAD (yeast): ≥ 3 mmol/L; ADH (EC 1.1.1.1; yeast; 25 °C): ≥ 617 µkat/L (37 U/mL); stabilizers; preservatives

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

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

Application for serum, plasma and urine

cobas c 311 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 14-23 (STAT 5 / 14-23)
Wavelength (sub/main)	700/340 nm
Reaction direction	Increase
Units	mmol/L (g/L, mg/dL)

Reagent pipetting		Diluent (H_2O)
R1	50 µL	–
R2	50 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	4 µL	–	–
Decreased	2 µL	–	–
Increased	4 µL	–	–

cobas c 501 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 21-33 (STAT 5 / 21-33)
Wavelength (sub/main)	700/340 nm
Reaction direction	Increase
Units	mmol/L (g/L, mg/dL)

Reagent pipetting		Diluent (H_2O)
R1	50 µL	–
R2	50 µL	-

Sample volumes	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	4 µL	–	–
Decreased	2 µL	–	–
Increased	4 µL	–	–

cobas c 502 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 21-33 (STAT 5 / 21-33)
Wavelength (sub/main)	700/340 nm
Reaction direction	Increase
Units	mmol/L (g/L, mg/dL)

Reagent pipetting		Diluent (H_2O)
R1	50 µL	–
R2	50 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	Diluent (H_2O)
Normal	4 µL	–	–
Decreased	2 µL	–	–
Increased	8 µL	–	–

Calibration

Calibrators	S1: H_2O
	S2: Ammonia/Ethanol/CO2 Calibrator
Calibration mode	Linear
Calibration frequency	2-point calibration - after reagent lot change - every 6 weeks on board - 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 NIST-traceable materials.

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.

Limitations - interference

Criterion: Recovery within ± 2.2 mmol/L of initial values of samples ≤ 21.7 mmol/L and within ± 10 % for samples > 21.7 mmol/L.

Serum/plasma

Icterus:[14] No significant interference up to an I index of 30 for conjugated bilirubin and 60 for unconjugated bilirubin (approximate conjugated bilirubin concentration: 513 µmol/L or 30 mg/dL; approximate unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[14] No significant interference up to an H index of 200 (approximate hemoglobin concentration: 124.2 µmol/L or 200 mg/dL).

Lipemia (Intralipid):[14] No significant interference up to an L index of 500. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[15,16]

LDH/lactic acid (using a dose-response curve with purified LDH fractions added to a 30 mmol/L lactic acid solution): No significant interference up to 2000 U/L LDH.

Urine

Glucose: No significant interference from glucose up to a concentration of 111 mmol/L (2000 mg/dL).

Urea: No significant interference from urea up to a concentration of 1800 mmol/L (10811 mg/dL).

Creatinine: No significant interference from creatinine up to a concentration of 22.1 mmol/L (250 mg/dL).
CAUTION: Urine containing sugars and contaminated with microorganisms may yield a false positive result due to fermentation of sugar to alcohol.
CAUTION: Do not use volatile solvents in the work area when performing assays. Do not perform sample preparation (especially spiking of pools) in the immediate work area. Vapor contamination of reagents can impact calibration stability.

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

Serum/plasma/urine

The **cobas c** Ethanol Gen.2 reagent is specific for ethanol. The following cross-reactants were measured at 2000 mg/dL:

Compound	% cross-reactivity (serum)	% cross-reactivity (urine)
n-Propanol	8.0	9.9
n-Butanol	2.8	1.5
Isopropanol	0.2	0.5
Acetone	0.0	0.2
Ethylene glycol	0.0	0.2
Methanol	-0.1	0.2
Acetaldehyde	-1.1	-0.3

$$\frac{\text{mg/dL apparent ethanol}}{\text{mg/dL cross-reactant in sample}} \times 100 = \%\ \text{cross-reactivity}$$

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

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[17]

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 and urine

2.20-108 mmol/L (0.101-4.98 g/L, 10.1-498 mg/dL)

Specimen dilution

NOTE: Do not use automatic rerun.

Determine samples with higher concentrations via the decreased sample volume function. Use a fresh aliquot from a sample stored tightly closed. Reduction of sample volume via the decreased sample volume function represents a 1:2 dilution. These results are automatically multiplied by a factor of 2.

Lower limits of measurement

Lower detection limit

2.20 mmol/L (0.101 g/L, 10.1 mg/dL)

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

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 on the **cobas c** 501 analyzer:

Serum/plasma

Repeatability	*Mean*	*SD*	*CV*
	mmol/L (g/L, mg/dL)	*mmol/L (g/L, mg/dL)*	*%*
AEC Control N	10.9 (0.502, 50.2)	0.2 (0.009, 0.9)	1.6
AEC Control A	32.5 (1.50, 150)	0.3 (0.01, 1)	0.9
Human serum 1	19.7 (0.908, 90.8)	0.2 (0.009, 0.9)	1.2
Human serum 2	75.8 (3.49, 349)	0.8 (0.04, 4)	1.1
Intermediate precision	*Mean*	*SD*	*CV*
	mmol/L (g/L, mg/dL)	*mmol/L (g/L, mg/dL)*	*%*
AEC Control N	11.1 (0.511, 51.1)	0.3 (0.01, 1)	2.4
AEC Control A	31.6 (1.46, 146)	0.4 (0.02, 2)	1.2
Human serum 3	26.9 (1.24, 124)	0.6 (0.03, 3)	2.0
Human serum 4	68.4 (3.15, 315)	0.8 (0.04, 4)	1.2

Urine

Repeatability	*Mean*	*SD*	*CV*
	mmol/L (g/L, mg/dL)	*mmol/L (g/L, mg/dL)*	*%*
AEC Control N	10.9 (0.502, 50.2)	0.2 (0.009, 0.9)	1.6

AEC Control A	32.5 (1.50, 150)	0.3 (0.01, 1)	0.9
Human urine 1	21.0 (0.968, 96.8)	0.3 (0.01, 1)	1.4
Human urine 2	76.5 (3.53, 353)	0.6 (0.03, 3)	0.8

Intermediate precision	*Mean*	*SD*	*CV*
	mmol/L (g/L, mg/dL)	*mmol/L (g/L, mg/dL)*	*%*
AEC Control N	11.1 (0.511, 51.1)	0.3 (0.01, 1)	2.4
AEC Control A	31.6 (1.46, 146)	0.4 (0.02, 2)	1.2
Human urine 3	19.0 (0.876, 87.6)	0.4 (0.02, 2)	1.9
Human urine 4	34.5 (1.59, 159)	0.6 (0.03, 3)	1.8

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

Method comparison

Ethanol values for human serum, plasma and urine samples obtained on a **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) = 72

Passing/Bablok[18]	Linear regression
y = 1.023x + 0.090 mmol/L	y = 1.020x + 0.248 mmol/L
τ = 0.988	r = 1.000

The sample concentrations were between 2.67 and 94.1 mmol/L (0.123 and 4.34 g/L, 12.3 and 434 mg/dL).

Urine

Sample size (n) = 73

Passing/Bablok[18]	Linear regression
y = 1.008x + 0.288 mmol/L	y = 1.007x + 0.261 mmol/L
τ = 0.982	r = 1.000

The sample concentrations were between 2.85 and 97.1 mmol/L (0.131 and 4.47 g/L, 13.1 and 447 mg/dL).

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

COBAS INTEGRA systems

System information

ETOH2: Test ID 0-611 (serum, plasma)

ETOU2: Test ID 0-511 (urine)

Reagents - working solutions

R1 Buffer; preservatives

SR NAD (yeast): ≥ 3 mmol/L; ADH (EC 1.1.1.1; yeast; 25 °C): ≥ 617 µkat/L (37 U/mL); stabilizers; preservatives

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

Storage and stability

Shelf life at 2-8 °C	See expiration date on **cobas c** pack label
On-board in use at 10-15 °C	4 weeks

Application for serum, plasma and urine

Test definition

Measuring mode	Absorbance
Abs. calculation mode	Kinetic
Reaction mode	R1-S-SR
Reaction direction	Increase
Wavelength A/B	340/659 nm
Calc. first/last	44/54
Unit	mmol/L

Pipetting parameters

Serum, plasma, urine		Diluent (H_2O)
R1	50 µL	-
Sample	4 µL	16 µL
SR	50 µL	-
Total volume	120 µL	

Calibration

Calibrators	S1: H_2O S2: Ammonia/Ethanol/CO2 Calibrator
Calibration mode	Linear regression
Calibration replicate	Duplicate recommended
Calibration frequency	- after reagent lot change - 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 NIST-traceable standard materials.

Quality control

Quality control	Ammonia/Ethanol/CO_2 Control Normal and Abnormal
Control interval	8 hours recommended
Control sequence	User defined
Control after calibration	Recommended

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.

Limitations - interference

Do not use volatile solvents in the work area when performing assays. Do not perform sample preparation (especially spiking of pools) in the immediate work area. Vapor contamination of reagents can impact calibration stability.

Criterion: Recovery within ± 2.2 mmol/L of initial values of samples ≤ 21.7 mmol/L and within ± 10 % for samples > 21.7 mmol/L.

Serum/plasma

Icterus:[14] 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:[14] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[14] No significant interference up to an L index of 1200. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[15,16]

LDH/lactic acid (using a dose-response curve with purified LDH fractions added to 30 mmol/L lactic acid solution): No significant interference up to 2000 U/L LDH.

Urine

Glucose: No significant interference from glucose up to a concentration of 111 mmol/L (2000 mg/dL).

Urea: No significant interference from urea up to a concentration of 1800 mmol/L (10811 mg/dL).

Creatinine: No significant interference from creatinine up to a concentration of 22.1 mmol/L (250 mg/dL).

Drugs: No interference was found at therapeutic concentrations using common drug panels.[16] Exception: No significant interference from salicyluric acid up to a concentration of 600 mg/L.

Urines containing sugars and contaminated with microorganisms may yield a false positive result due to fermentation of sugar to alcohol.

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

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[17]

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on COBAS INTEGRA analyzers. Refer to the CLEAN Method Sheet for further instructions and for the latest version of the Extra wash cycle list.

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

Limits and ranges

Measuring range

2.17-108 mmol/L (10.0-498 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:3 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 3.

Lower limits of measurement

Lower detection limit of the test (serum, plasma, and urine):
2.17 mmol/L (10.0 mg/dL)

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

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 (1 aliquot per run, 1 run per day, 10 days). The following results were obtained on the COBAS INTEGRA 700 analyzer:

Serum/plasma

	Repeatability		*Intermediate precision*	
Sample	*Mean mmol/L (mg/dL)*	*CV %*	*Mean mmol/L (mg/dL)*	*CV %*
Level 1	20.1 (93.0)	1.2	21.8 (100)	2.4
Level 2	42.0 (194)	1.1	42.8 (197)	3.9

Urine

	Repeatability		*Intermediate precision*	
Sample	*Mean mmol/L (mg/dL)*	*CV %*	*Mean mmol/L (mg/dL)*	*CV %*
Level 1	20.1 (93.0)	1.2	24.0 (111)	3.6
Level 2	31.9 (147)	1.7	30.7 (142)	3.3

The data obtained on COBAS INTEGRA 700 analyzer(s) are representative for COBAS INTEGRA 400 analyzer(s).

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (1 aliquot per run, 1 run per day, 21 days). The following results were obtained on the COBAS INTEGRA 400 analyzer:

Serum/plasma

	Repeatability		*Intermediate precision*	
Sample	*Mean mmol/L (mg/dL)*	*CV %*	*Mean mmol/L (mg/dL)*	*CV %*
Level 1	24.2 (111.6)	0.8	23.8 (109.7)	1.0
Level 2	51.5 (237.4)	0.7	51.5 (237.4)	1.0

Method comparison

Serum/plasma

Ethanol values for human serum and plasma samples obtained on a COBAS INTEGRA 400 analyzer using the COBAS INTEGRA Ethanol Gen.2 reagent (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x) and with those determined using the previous reagent (ETOH) on a COBAS INTEGRA 400 analyzer (x).

Roche/Hitachi 917 analyzer	Sample size (n) = 52
Passing/Bablok[18]	Linear regression
y = 0.982x + 0.485 mmol/L	y = 0.980x + 0.534 mmol/L
τ = 0.961	r = 0.998
SD (md 95) = 2.68	Sy.x = 1.43

The sample concentrations were between 8.30 and 106 mmol/L (38.3 and 489 mg/dL).

COBAS INTEGRA 400 analyzer	Sample size (n) = 52
Passing/Bablok[18]	Linear regression
y = 0.991x + 0.296 mmol/L	y = 0.997x + 0.079 mmol/L
τ = 0.989	r = 1.000
SD (md 95) = 0.977	Sy.x = 0.464

The sample concentrations were between 8.30 and 106 mmol/L (38.3 and 489 mg/dL).

Urine

Ethanol values for human urine samples obtained on a COBAS INTEGRA 700 analyzer using the COBAS INTEGRA Ethanol Gen.2 reagent (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x) and with those determined using the previous reagent (ETOH) on a COBAS INTEGRA 700 analyzer (x).

Roche/Hitachi 917 analyzer	Sample size (n) = 60
Passing/Bablok[18]	Linear regression
y = 0.964x - 0.217 mmol/L	y = 0.967x - 0.296 mmol/L
τ = 0.978	r = 0.999
SD (md 95) = 0.936	Sy.x = 0.779

The values were between 0.270 and 111 mmol/L (1.24 and 512 mg/dL).

COBAS INTEGRA 700 analyzer	Sample size (n) = 58
Passing/Bablok[18]	Linear regression
y = 0.997x - 0.235 mmol/L	y = 0.993x - 0.245 mmol/L
τ = 0.979	r = 0.999
SD (md 95) = 1.74	Sy.x = 0.699

The values were between 0.270 and 108 mmol/L (1.24 and 498 mg/dL).

The data obtained on COBAS INTEGRA 700 analyzer(s) are representative for COBAS INTEGRA 400 analyzer(s).

Ethanol values for human urine samples obtained on a COBAS INTEGRA 800 analyzer (y) using the Ethanol Gen.2 reagent were compared with those determined using the corresponding reagent on a COBAS INTEGRA 400 Plus analyzer (x).

ETOH2

Ethanol Gen.2

COBAS INTEGRA 400 Plus analyzer	Sample size (n) = 65
Passing/Bablok[18]	Linear regression
y = 0.979x - 2.20 mmol/L	y = 0.986x - 2.48 mmol/L
τ = 0.974	r = 0.997

The sample concentrations were between 0.24 and 105.1 mmol/L (1.11 and 485 mg/dL).

Analytical specificity

COBAS INTEGRA Ethanol Gen.2 reagent is specific for ethanol. The following cross reactants were measured at 2000 mg/dL.

Compound	% Cross-reactivity (serum)	% Cross-reactivity (urine)
n-Propanol	8.5	4.8
n-Butanol	2.9	2.5
Isopropanol	0.5	0.3
Acetone	0.0	0.0
Ethylene glycol	0.0	0.0
Methanol	0.0	0.0
Acetaldehyde	0.0	0.0

$$\frac{\text{mg/dL apparent ethanol}}{\text{mg/dL cross-reactant in sample}} \times 100 = \%\ \text{cross-reactivity}$$

References

1 Langman LJ, Bechtel LK, Holstege CP. Clinical Toxicology. In: Rifai N, Chiu RWK, Young I, Burnham CAD, Wittwer CT, editors. Tietz Textbook of Laboratory Medicine, Saunders Elsevier, Philadelphia, 7th edition, 2023, chapter 43, p. 454-454.e84.

2 Maenhout TM, De Buyzere ML, Delanghe JR. Non-oxidative ethanol metabolites as a measure of alcohol intake. Clin Chim Acta 2013 Jan 16;415:322-329.

3 Staufer K, Yegles M. Biomarkers for detection of alcohol consumption in liver transplantation. World J Gastroenterol 2016 Apr 14;22(14):3725-3734.

4 Kummer N, Lambert WE, Samyn N, Stove CP. Alternative sampling strategies for the assessment of alcohol intake of living persons. Clin Biochem 2016 Sep;49(13-14):1078-1091.

5 Oppolzer D, Barroso M, Gallardo E. Bioanalytical procedures and developments in the determination of alcohol biomarkers in biological specimens. Bioanalysis 2016 Feb;8(3):229-251.

6 Topic A, Djukic M. Diagnostic characteristics and application of alcohol biomarkers. Clin Lab 2013;59(3-4):233-245.

7 Proposed guidelines NCCLS: Blood Alcohol Testing in the Clinical Laboratory. NCCLS Vol. 8 No. 10. December 1988.

8 Tietz NW. Fundamentals of Clinical Chemistry. 3rd ed. Philadelphia: WB Saunder 1987;890.

9 Tietz NW, ed. Clinical Guide to Laboratory Tests, 4th ed. Philadelphia, PA: WB Saunders Company 2006;1344-1346.

10 Levine B, Smith ML. Stability of drugs of abuse in biological specimens. Forensic Sci Rev 1990;2:148-156.

11 Garriott JC, ed. Medicolegal Aspects of Alcohol. 3rd ed. Tucson, AZ: Lawyers & Judges Publishing Co, Inc 1996:262.

12 Tietz NW, ed. Clinical Guide to Laboratory Tests, 3rd ed. Philadelphia, PA: WB Saunders Company 1995;224-225.

13 Jones AW. Reference Limits for Urine/Blood Ratios of Ethanol in Two Successive Voids from Drinking Drivers. J Anal Toxicol 2002;26(Sep):333-339.

14 Glick MR, Ryder KW, Jackson SA. Graphical Comparisons of Interferences in Clinical Chemistry Instrumentation. Clin Chem 1986;32:470-475.

15 Breuer J. Report on the Symposium "Drug effects in Clinical Chemistry Methods". Eur J Clin Chem Clin Biochem 1996;34:385-386.

16 Sonntag O, Scholer A. Drug interference in clinical chemistry: recommendation of drugs and their concentrations to be used in drug interference studies. Ann Clin Biochem 2001;38:376-385.

17 Bakker AJ, Mücke M. Gammopathy interference in clinical chemistry assays: mechanisms, detection and prevention. Clin Chem Lab Med 2007;45(9):1240-1243.

18 Bablok W, Passing H, Bender R, et al. A general regression procedure for method transformation. Application of linear regression procedures for method comparison studies in clinical chemistry, Part III. J Clin Chem Clin Biochem 1988 Nov;26(11):783-790.

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.

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

Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com
+800 5505 6606