COC2

cobas®

ONLINE DAT Cocaine II

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08057508190	08057508500	ONLINE DAT Cocaine II (850 tests)	System-ID 2045 001	**cobas c** 303, **cobas c** 503, **cobas c** 703

Materials required (but not provided):

Serum/plasma		
03304671190	Preciset DAT Plus I CAL 6 (1 x 5 mL)	Code 20436
07978766190	Serum DAT Control Low (ACQ Partner Channel*)	
09543112190	Serum DAT Control Set	
07978740190	Serum DAT Control High (ACQ Partner Channel*)	
08063494190	NaCl Diluent 9 % (123 mL)	System-ID 2906 001

*Roche does not hold the product registration for Partner Channels. The legal manufacturer indicated on the kit is solely responsible for all of the design, legal, and regulatory aspects of the product.

Urine		
03304671190	Preciset DAT Plus I CAL 1-6 (6 x 5 mL)	Codes 20431-20436
03304698190	C.f.a.s. DAT Qualitative Plus (6 x 5 mL)	Code 20698
04590856190	C.f.a.s. DAT Qualitative Plus Clinical (3 x 5 mL)	Code 20699
03312950190	Control Set DAT I (for 150 ng/mL assay) PreciPos DAT Set I (2 x 10 mL) PreciNeg DAT Set I (2 x 10 mL)	
03312976190	Control Set DAT III (for 300 ng/mL assay) PreciPos DAT Set III (2 x 10 mL) PreciNeg DAT Set III (2 x 10 mL)	
04500873190	Control Set DAT Clinical (for 300 ng/mL assay) PreciPos DAT Clinical (2 x 10 mL) PreciNeg DAT Clinical (2 x 10 mL)	

English

System information

COQ3S: ACN 20455 (Serum/plasma): for qualitative assay, 300 ng/mL

CO1Q2: ACN 20450 (Urine): for qualitative assay, 150 ng/mL

CO3Q2: ACN 20451 (Urine): for qualitative assay, 300 ng/mL

CO1S2: ACN 20452 (Urine): for semiquantitative assay, 150 ng/mL

CO3S2: ACN 20453 (Urine): for semiquantitative assay, 300 ng/mL

CO3QC: ACN 20454 (Urine): for qualitative assay, 300 ng/mL; using C.f.a.s. DAT Qualitative Plus Clinical

CO1-QP: ACN 20456 (Urine): for qualitative assay, 150 ng/mL; using C.f.a.s. DAT Qualitative Plus

Intended use

Application in urine

Cocaine II (COC2) is an in vitro diagnostic test for the qualitative and semiquantitative detection of benzoylecgonine, the primary metabolite of cocaine, in human urine on **cobas c** systems at cutoff concentrations of 150 and 300 ng/mL. Semiquantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality control program. Semiquantitative assays are intended to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas chromatography/mass spectrometry (GC-MS).

Cocaine II provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. GC-MS is the preferred confirmatory method.[1] Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

*Application in serum and plasma**

**not available in all countries*

Cocaine II (COC2) is an in vitro diagnostic test for the qualitative detection of benzoylecgonine, the primary metabolite of cocaine, in human serum and plasma on **cobas c** systems at a cutoff concentration of 300 ng/mL. Cocaine II provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC-MS) or Liquid Chromatography coupled with Tandem Mass Spectrometry (LC-MS/MS) is the preferred confirmatory method.[1] Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

Summary

Detection of cocaine with this assay in human serum, plasma and urine is used for presumptive testing of exposure to cocaine in individuals with suspected exposure, in individuals under pain management treatments and in individuals under rehabilitation programs.

Cocaine, a natural product present in the leaves of *Erythroxylon coca*, is a potent central nervous system (CNS) stimulant, an effective local anesthetic and a vasoconstrictor of mucous membranes. Its pharmacological effects are similar to those of amphetamines, but of shorter duration of action. Cocaine is one of the most common illicit drugs of abuse.[2] It is through its interaction with the dopamine and the limbic reward system that cocaine produces positive reinforcing effects.[3] For most individuals, the subjective experience of the acute effects includes a generalized state of euphoria in combination with feelings of increased energy, talkativeness, mental alertness, and hypersensitivity to sight, sound, and touch. These psychological effects are accompanied by increased body temperature, pulse and blood pressure, as well as fatigue, dilation of pupils and in some cases tremors, dizziness and muscle twitching can occur.[3] The “crash” following a cocaine “high” is characterized by dysphoria, anxiety, and

agitation, frequently leading to recurrent substance use. Anxiety and agitation are accompanied by a period of fatigue, increasing depression, and decreased mental and physical energy.[3] Users may resort to other drugs at this time to relieve the depressive effects of the "crash".[3] Tolerance has been observed with chronic, high-dose users.[4]

Cocaine is most commonly taken by nasal insufflation (snorting), intravenous injection, or inhalation of smoke vapors (smoking/inhalation).[3] Absorption and bioavailability depend on the administration route. Cocaine is rapidly hydrolyzed into ecgonine methyl ester or into benzoylecgonine; both of these metabolites may be further hydrolyzed to ecgonine.[4] Unmetabolized cocaine has a fast disposal to the tissues; cocaine metabolites, however, are more water soluble and are readily excreted in the urine along with some portion of unchanged drug.[4] The prominent benzoylecgonine metabolite is the primary urinary marker for detecting cocaine use.[2]

Cocaine testing is recommended also in pain management patients, and individuals under rehabilitation programs, to identify its illicit use and to monitor abstinence while the patients are under rehabilitation treatment.[5,6] In the context of drug screening, samples that test negative on initial screening tests can be reported as negative and disposed of as planned. Otherwise, depending on the situation, presence of the drugs indicated by a positive screening result may need to be confirmed using a suitable confirmatory technique (e.g., GC-MS or LC-MS).[5,6,7,8]

Test principle

The assay is based on the kinetic interaction of microparticles in a solution (KIMS)[9,10] as measured by changes in light transmission. In the absence of sample drug, soluble drug conjugates bind to antibody-bound microparticles, causing the formation of particle aggregates. As the aggregation reaction proceeds in the absence of sample drug, the absorbance increases.

When a sample contains the drug in question, this drug competes with the drug derivative conjugate for microparticle-bound antibody. Antibody bound to sample drug is no longer available to promote particle aggregation, and subsequent particle lattice formation is inhibited. The presence of sample drug diminishes the increasing absorbance in proportion to the concentration of drug in the sample. Sample drug content is determined relative to the value obtained for a known cutoff concentration of drug.[11]

Reagents - working solutions

R1 Conjugated benzoylecgonine derivative; buffer; bovine serum albumin; 0.09 % sodium azide

R3 Microparticles attached to benzoylecgonine antibody (mouse monoclonal); buffer; bovine serum albumin; 0.09 % sodium azide

R1 is in position B and R3 is in position C.

Precautions and warnings

For in vitro diagnostic use for laboratory 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

Carefully invert reagent container several times prior to use to ensure that the reagent components are mixed.

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:	26 weeks

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: Serum tubes with and without separating gel.
Plasma: K_2- or K_3-EDTA, lithium 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.

Stability in serum/plasma:

4 hours capped at 15-25 °C

4 days capped at 2-8 °C

6 months capped at -20 °C (± 5 °C)

Specimens can be repeatedly frozen and thawed up to 3 times.

Invert thawed specimens several times prior to testing.

Urine: Collect urine samples in clean glass or plastic containers. Fresh urine specimens do not require any special handling or pretreatment, but an effort should be made to keep pipetted samples free of gross debris. Samples should be within the normal physiological pH range of 5-8. No additives or preservatives are required. It is recommended that urine specimens be stored at 2-8 °C and tested within 5 days of collection.[12]

For prolonged storage, freezing of the sample is recommended.[12]

Freeze only once.

Adulteration or dilution of the sample can cause erroneous results. If adulteration is suspected, another sample should be collected. Specimen validity testing is required for specimens collected under the *Mandatory Guidelines for Federal Workplace Drug Testing Programs*.[13]

Centrifuge highly turbid specimens or samples containing precipitates before performing the assay.

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

CAUTION: Specimen dilutions should only be used to interpret results of Calc.? and Samp.? alarms, or when estimating concentration in preparation for GC-MS or LC-MS/MS. Dilution results are not intended for patient values. Dilution procedures, when used, should be validated.

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

Test definition

	Qualitative
Reporting time	10 min
Wavelength (sub/main)	– /546 nm
Reagent pipetting	
R1	61 µL
R3	27 µL
Sample volumes	*Sample*
300 ng/mL cutoff	
Normal	3.7 µL
Decreased	3.7 µL

Increased	3.7 µL	

Application for urine

Test definition - 150 and 300 ng/mL cutoff assays

	Semi-quantitative	Qualitative
Reporting time	10 min	10 min
Wavelength (sub/main)	– /546 nm	– /546 nm
Reagent pipetting		Diluent (H_2O)
R1	61 µL	–
R3	27 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	3.7 µL	–	–
Decreased	3.7 µL	–	–
Increased	3.7 µL	–	–

For further information about the assay test definitions refer to the application parameters setting screen of the corresponding analyzer and assay.

Calibration

Serum/plasma

Qualitative application

Calibrators	*300 ng/mL cutoff assay* S1-6: Preciset DAT Plus I, CAL 1-6, 5000 ng/mL with automatic pre-dilution
Cutoff calibrator	A value of “0” is encoded in the e-barcode in order to ensure flagging of positive samples with >Test and negative absorbance values for negative samples.
Calibration K factor	The K factor of -1000 is predefined in the application settings.
Calibration mode	Linear
Calibration frequency	Full calibration - after reagent lot change - as required following quality control procedures

Urine

Semiquantitative applications

Calibrators	*150 and 300 ng/mL cutoff assays* S1-6: Preciset DAT Plus I, CAL 1-6 0, 75, 150, 300, 1000, 5000 ng/mL
Calibration mode	Non-linear
Calibration frequency	Full calibration - after reagent lot change - every 13 weeks on-board - as required following quality control procedures

Qualitative application

Calibrators	*150 ng/mL cutoff assay* S1: C.f.a.s. DAT Qualitative Plus or Preciset DAT Plus I, CAL 3 150 ng/mL *300 ng/mL cutoff assay* S1: C.f.a.s. DAT Qualitative Plus Clinical or Preciset DAT Plus I, CAL 4 300 ng/mL
Cutoff calibrator	A value of “0” is encoded in the e-barcode in order to ensure flagging of positive samples with >Test and negative absorbance values for negative samples.
Calibration K factor	The K factor of -1000 is predefined in the application settings.
Calibration mode	Linear
Calibration frequency	Full calibration - after reagent lot change - every 13 weeks on-board - as required following quality control procedures

The drug concentrations of the calibrators have been verified by GC-MS.

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

Traceability: This method has been standardized against a primary reference method (GC-MS).

Quality control

For quality control, use control materials as listed in the “Order information” section. In addition, other suitable control material can be used.

Drug concentrations of Control Set DAT I, III, Clinical and the high and low controls have been verified by GC-MS.

The control intervals and limits should be adapted to each laboratory’s individual requirements. It is recommended to perform quality control always after lot calibration and subsequently at least every 26 weeks.

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.

Results

For the qualitative assay, the cutoff calibrator is used as a reference in distinguishing between preliminary positive and negative samples. Samples producing a positive or “0” absorbance value are considered preliminary positive. Preliminary positive samples are flagged with >Test. Samples producing a negative absorbance value are considered negative. Negative samples are preceded by a minus sign.

For the semiquantitative applications **cobas c** systems automatically calculate the drug or metabolite concentration of each sample in the unit ng/mL. Results equal to or greater than the respective cutoff value are considered preliminary positive. Concentration values below the respective cutoff indicate a negative result.

The semiquantitation of preliminary positive results should only be used by laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as GC-MS. It also permits the laboratory to establish quality control procedures and assess control performance.

NOTE: If a result of Calc.? or Samp.? alarm is obtained, review the Reaction Monitor data for the sample and compare with the Reaction Monitor data for the highest calibrator. The most likely cause is a high concentration of the analyte in the sample, in which case the absorbance value for the sample will be less than that of the highest calibrator. Make an appropriate dilution of the sample using the 0 ng/mL calibrator and rerun the sample. A normal drug-free urine may be substituted for the 0 ng/mL calibrator if the urine and procedure have been validated by the laboratory. To ensure that the sample was not over-diluted, the diluted result, prior to multiplying by the dilution factor, must be at least half the analyte cutoff value. If the diluted result falls below half the analyte cutoff value, repeat the sample with a smaller dilution. A dilution that produces a result closest to the analyte cutoff is the most accurate estimation. To estimate the preliminary positive sample’s concentration, multiply the result by the appropriate dilution factor. Dilutions should only be used to interpret results of Calc.? or Samp.? alarms, or when estimating concentration in preparation for GC-MS or LC-MS/MS.

Use caution when reporting results as there are various factors that influence a urine test result, such as fluid intake and other biological factors.

As with any sensitive test for drugs of abuse on automated clinical chemistry analyzers, the possibility exists for analyte carry-over from a sample with an extremely high concentration to a normal (negative) sample which immediately follows it.

Preliminary positive results should be confirmed by another method.

Limitations - interference

See the "Specific performance data" section of this document for information on substances tested with this assay. There is the possibility that other substances and/or factors may interfere with the test and cause erroneous results (e.g., technical or procedural errors).

A preliminary positive result with this assay indicates the presence of benzoylecgonine and/or its metabolites in the sample. It does not measure the level of intoxication.

Serum/plasma

Criterion: No cross-over at initial values of samples of 150 ng/mL and 450 ng/mL (control levels).

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: 622 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[14] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Rheumatoid factors: No significant interference from rheumatoid factors up to a concentration of 450 IU/mL.

Immunoglobulins: No significant interference from immunoglobulins up to a concentration of 16 g/L (simulated by human immunoglobulin A), up to a concentration of 70 g/L (simulated by human immunoglobulin G) and up to a concentration of 10 g/L (simulated by human immunoglobulin M).

Albumin: No significant interference from human serum albumin up to a concentration of 70 g/L.

As with any assay employing mouse antibodies, the possibility exists for interference by human anti-mouse antibodies (HAMA) in the sample, which could cause falsely lowered results.

Urine

Interfering substances were added to drug free urine at the concentration listed below. These samples were then spiked to 150 ng/mL using a benzoylecgonine stock solution. Samples were tested on a Roche/Hitachi 917 analyzer and the following results were obtained:

Substance	Concentration tested	% Cocaine recovery
Acetone	1 %	96
Ascorbic acid	1.5 %	106
Bilirubin	0.25 mg/mL	99
Creatinine	5 mg/mL	97
Ethanol	1 %	99
Glucose	2 %	99
Hemoglobin	7.5 g/L	97
Human albumin	0.5 %	94
Oxalic acid	2 mg/mL	94
Sodium chloride	0.5 M	91
Sodium chloride	1 M	90
Urea	6 %	104

Interfering substances were added to drug free urine at the concentration listed below. These samples were then spiked to 300 ng/mL using a benzoylecgonine stock solution. Samples were tested on a Roche/Hitachi 917 analyzer and the following results were obtained:

Substance	Concentration tested	% Cocaine recovery
Acetone	1 %	104
Ascorbic acid	1.5 %	113
Bilirubin	0.25 mg/mL	112
Creatinine	5 mg/mL	104
Ethanol	1 %	103
Glucose	2 %	104
Hemoglobin	7.5 g/L	107
Human albumin	0.5 %	105
Oxalic acid	2 mg/mL	105
Sodium chloride	0.5 M	103
Sodium chloride	1 M	103
Urea	6 %	103

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.[15]

ACTION REQUIRED

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

Expected values

Serum/plasma

Qualitative assay

Results of this assay distinguish preliminary positive (≥ 300 ng/mL) from negative samples only. The amount of drug detected in a preliminary positive sample cannot be estimated.

Urine

Qualitative assay

Results of this assay distinguish preliminary positive (≥ 150 ng/mL or ≥ 300 ng/mL depending on the cutoff) from negative samples only. The amount of drug detected in a preliminary positive sample cannot be estimated.

Semiquantitative assay

Results of this assay yield only approximate cumulative concentrations of the drug and its metabolites (see Analytical specificity section).

Specific performance data

Representative performance data on the analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

Precision

Serum/plasma

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). Results for repeatability and intermediate precision were obtained on the **cobas c** 503 analyzer.

Drug	Concentration of sample	Number of determinations	Results # Neg / # Pos
Benzoylecgonine	-75 %	84	84 Neg / 0 Pos
Benzoylecgonine	-50 %	84	84 Neg / 0 Pos
Benzoylecgonine	Cutoff	n.a.**	n.a.**

COC2

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Drug	Concentration of sample	Number of determinations	Results # Neg / # Pos
Benzoylecgonine	+50 %	84	0 Neg / 84 Pos
Benzoylecgonine	+75 %	84	0 Neg / 84 Pos

**n.a. = not applicable

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

Urine

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). Results for repeatability and intermediate precision were obtained on the **cobas c** 503 analyzer.

Semiquantitative precision - 150 ng/mL

Repeatability	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	82.5	4.15	5.0
DAT1N	120	3.95	3.3
Cutoff urine	163	5.21	3.2
DAT1P	188	3.48	1.9
Urine +50 %	231	6.51	2.8

Intermediate precision	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	82.5	4.90	5.9
DAT1N	120	4.15	3.5
Cutoff urine	163	6.32	3.9
DAT1P	188	4.77	2.5
Urine +50 %	231	7.79	3.4

Qualitative precision - 150 ng/mL

Cutoff (150)	Number tested	Correct results	Confidence level
Urine -50 %	84	84	>95 % negative reading
DAT1N	84	84	>95 % negative reading
Cutoff urine	84	n.a.*	n.a.*
DAT1P	84	84	>95 % positive reading
Urine +50 %	84	84	>95 % positive reading

*n.a. = not applicable

Semiquantitative precision - 300 ng/mL

Repeatability	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	162	4.01	2.5
DAT3N	223	4.55	2.0
Cutoff urine	312	5.90	1.9
DAT3P	367	5.88	1.6
Urine +50 %	473	6.94	1.5

Intermediate precision	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	162	4.68	2.9
DAT3N	223	5.49	2.5
Cutoff urine	312	6.62	2.1
DAT3P	367	6.50	1.8
Urine +50 %	473	6.94	1.5

Qualitative precision - 300 ng/mL

Cutoff (300)	Number tested	Correct results	Confidence level
Urine -50 %	84	84	>95 % negative reading
DAT3N	84	84	>95 % negative reading
Cutoff urine	84	n.a.*	n.a.*
DAT3P	84	84	>95 % positive reading
Urine +50 %	84	84	>95 % positive reading

*n.a. = not applicable

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

Accuracy

Serum/plasma

110 serum samples screened negative for benzoylecgonine on a **cobas c** 501 analyzer were evaluated with the Cocaine II assay on a **cobas c** 503 analyzer. 100 % of these normal serum samples were negative with the Cocaine II assay on a **cobas c** 503 analyzer. 50 serum samples screened positive for benzoylecgonine relative to the 300 ng/mL cutoff on a **cobas c** 501 analyzer were evaluated with the Cocaine II assay on a **cobas c** 503 analyzer. At the 300 ng/mL cutoff, 100 % of the samples were positive on both the **cobas c** 501 analyzer and the **cobas c** 503 analyzer.

Cocaine II correlation (cutoff = 300 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 503 analyzer	+	50	0
	-	0	110

50 serum samples screened negative for benzoylecgonine on a **cobas c** 501 analyzer were evaluated with the Cocaine II assay on a **cobas c** 303 analyzer. 100 % of these normal serum samples were negative with the Cocaine II assay on a **cobas c** 303 analyzer. 50 serum samples screened positive for benzoylecgonine relative to the 300 ng/mL cutoff on a **cobas c** 501 analyzer were evaluated with the Cocaine II assay on a **cobas c** 303 analyzer. At the 300 ng/mL cutoff, 100 % of the samples were positive on both the **cobas c** 501 analyzer and the **cobas c** 303 analyzer.

Cocaine II correlation (cutoff = 300 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 303 analyzer	+	50	0
	-	0	50

51 serum samples screened negative for benzoylecgonine on a **cobas c** 503 analyzer were evaluated with the Cocaine II assay on a **cobas c** 703 analyzer. 100 % of these normal serum samples were negative with the Cocaine II assay on a **cobas c** 703 analyzer. 50 serum samples screened positive for benzoylecgonine relative to the 300 ng/mL cutoff on a **cobas c** 503 analyzer were evaluated with the Cocaine II assay on a **cobas c** 703 analyzer. At the 300 ng/mL cutoff, 100 % of the samples were positive on both the **cobas c** 503 analyzer and the **cobas c** 703 analyzer.

Cocaine II correlation (cutoff = 300 ng/mL)			
		cobas c 503 analyzer	
		+	-
cobas c 703 analyzer	+	50	0
	-	0	51

Urine

100 urine samples, obtained from a clinical laboratory where they screened negative in a drug test panel, were evaluated with the Cocaine II assay. 100 % of these normal urines were negative relative to the 150 ng/mL and

300 ng/mL cutoffs. 50 samples obtained from a clinical laboratory, where they screened preliminary positive with a commercially available immunoassay and were subsequently confirmed positive by GC-MS, were evaluated with the Cocaine II assay. 100 % of these samples were positive relative to the 150 ng/mL cutoff. 50 samples obtained from a clinical laboratory, where they screened preliminary positive with a commercially available immunoassay and were subsequently confirmed positive by GC-MS, were evaluated with the Cocaine II assay. 100 % of these samples were positive relative to the 300 ng/mL cutoff. In addition, 10 samples were diluted to a benzoylecgonine concentration of 75-100 % of the cutoff concentration for each cutoff; and 10 samples were diluted to a benzoylecgonine concentration of 100-125 % of the cutoff concentration for each cutoff. Data from the accuracy studies described above that fell within the near cutoff value ranges were combined with data generated from diluted positive samples. The following results were obtained with the Cocaine II assay on the Roche/Hitachi 917 analyzer relative to the GC-MS values.

Cocaine II correlation (cutoff = 150 ng/mL)

		Negative samples	GC-MS values (ng/mL)		
			Near cutoff		Positive samples
			113	188	344-106072
Roche/Hitachi 917 analyzer	+	0	0	10	50
	-	100	10	0	0

Cocaine II correlation (cutoff = 300 ng/mL)

		Negative samples	GC-MS values (ng/mL)		
			Near cutoff		Positive samples
			225	309-402	428-106072
Roche/Hitachi 917 analyzer	+	0	0	11	49
	-	100	10	0	0

109 urine samples screened negative for benzoylecgonine on a **cobas c** 501 analyzer were evaluated with the Cocaine II assay on a **cobas c** 503 analyzer. 100 % of these normal urines were negative for both cutoffs with the Cocaine II assay on a **cobas c** 503 analyzer. 55 urine samples screened positive for benzoylecgonine relative to the corresponding cutoff on a **cobas c** 501 analyzer and subsequently confirmed by GC-MS, were evaluated with the Cocaine II assay on a **cobas c** 503 analyzer. For both cutoffs 100 % of the samples were positive on both the **cobas c** 501 analyzer and the **cobas c** 503 analyzer.

Cocaine II correlation (cutoff = 150 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 503 analyzer	+	55	0
	-	0	109

Cocaine II correlation (cutoff = 300 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 503 analyzer	+	55	0
	-	0	109

100 urine samples screened negative for benzoylecgonine on a **cobas c** 501 analyzer were evaluated with the Cocaine II assay on a **cobas c** 303 analyzer. 100 % of these normal urines were negative for both cutoffs with the Cocaine II assay on a **cobas c** 303 analyzer. 50 urine samples screened positive for benzoylecgonine relative to the corresponding cutoff on a **cobas c** 501 analyzer and subsequently confirmed by GC-MS, were evaluated with the Cocaine II assay on a **cobas c** 303 analyzer. For both cutoffs 100 % of the samples were positive on both the **cobas c** 501 analyzer and the **cobas c** 303 analyzer.

Cocaine II correlation (cutoff = 150 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 303 analyzer	+	50	0
	-	0	100

Cocaine II correlation (cutoff = 300 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 303 analyzer	+	50	0
	-	0	100

100 urine samples screened negative for benzoylecgonine on a **cobas c** 503 analyzer were evaluated with the Cocaine II assay on a **cobas c** 703 analyzer. 100 % of these normal urines were negative for both cutoffs with the Cocaine II assay on a **cobas c** 703 analyzer. 52 urine samples screened positive for benzoylecgonine relative to the corresponding cutoff on a **cobas c** 503 analyzer and subsequently confirmed by GC-MS, were evaluated with the Cocaine II assay on a **cobas c** 703 analyzer. For both cutoffs 100 % of the samples were positive on both the **cobas c** 503 analyzer and the **cobas c** 703 analyzer.

Cocaine II correlation (cutoff = 150 ng/mL)			
		cobas c 503 analyzer	
		+	-
cobas c 703 analyzer	+	52	0
	-	0	100

Cocaine II correlation (cutoff = 300 ng/mL)			
		cobas c 503 analyzer	
		+	-
cobas c 703 analyzer	+	52	0
	-	0	100

Analytical specificity

Serum/plasma

The specificity of this assay for cocaine and its metabolites was determined by generating inhibition curves for each of the compounds listed and determining the approximate quantity of each compound that is equivalent in assay reactivity to a 300 ng/mL benzoylecgonine assay cutoff. The following results were obtained on a **cobas c** 501 analyzer.

Compound	**ng/mL Equivalent to 300 ng/mL benzoylecgonine**	**Approximate % cross-reactivity**
Benzoylecgonine	254	118
Cocaethylene	49453	0.61
Cocaine	7084	4.23
Ecgonine	> 100000	n.d.
Ecgonine methyl ester	> 100000	n.d.

n.d. = not detectable

Urine

The specificity of this assay for cocaine and its metabolites was determined by generating inhibition curves for each of the compounds listed and determining the approximate quantity of each compound that is equivalent in assay reactivity to a 150 ng/mL and a 300 ng/mL benzoylecgonine assay cutoff. The following results were obtained on a Roche/Hitachi 917 analyzer.

Compound	ng/mL Equivalent to 150 ng/mL benzoylecgonine	Approximate % cross-reactivity
Cocaine	7733	1.9
Cocaethylene	34933	0.4

Compound	ng/mL Equivalent to 300 ng/mL benzoylecgonine	Approximate % cross-reactivity
Cocaine	18132	1.7
Cocaethylene	67435	0.4

Additionally, the following compounds were tested at a concentration of 100000 ng/mL in pooled normal human urine and shown to have cross-reactivity values of less than 0.05 %.

Ecgonine	Ecgonine methyl ester	Norcocaine

Drug interference

Serum/plasma

Interfering substances were added to serum containing benzoylecgonine at -50 % and +50 % of the cutoff level at the concentration listed below. Samples were tested and the following results were obtained on a **cobas c** 501 analyzer.

Compound	Comp. conc. mg/L	Neg. level	Pos. level
Acetaminophen	200	neg	pos
Acetylcysteine	1660	neg	pos
Acetylsalicylic acid	1000	neg	pos
Amitriptyline	1.00	neg	pos
Ampicillin-Na	1000	neg	pos
Ascorbic acid	300	neg	pos
Caffeine	59.8	neg	pos
Cefoxitin	2500	neg	pos
Chlorpromazine	2.01	neg	pos
Cyclosporine	5.00	neg	pos
d-Amphetamine	1.36	neg	pos
Dextromethorphan	1.00	neg	pos
Diphenhydramine	5.00	neg	pos
Doxycycline	50.0	neg	pos
d-Pseudoephedrine	9.98	neg	pos
Erythromycin	59.9	neg	pos
Fenoprofen	195	neg	pos
Furosemide	59.9	neg	pos
Gentisic acid	18.0	neg	pos
Heparin	5000 U/L	neg	pos
Hydrochlorothiazide	6.02	neg	pos
l-Amphetamine	1.00	neg	pos
Ibuprofen	500	neg	pos
Imipramine	0.70	neg	pos
Ketamine	10.0	neg	pos
Levodopa	20.0	neg	pos
Lidocaine	12.0	neg	pos
Methadone	2.00	neg	pos
Methyldopa + 1.5 H_2O	20.0	neg	pos
Metronidazole	200	neg	pos
Naproxen	499	neg	pos
Phenylbutazone	400	neg	pos
Procaine	39.9	neg	pos
Promethazine	1.20	neg	pos
Quinidine	12.0	neg	pos
Quinine	48.0	neg	pos
Rifampicin	60.0	neg	pos
Tetracycline	15.1	neg	pos
Theophylline	100	neg	pos
Trifluoperazine hydrochloride	1.00	neg	pos
Verapamil	2.00	neg	pos

Urine

The following compounds were prepared in aliquots of pooled normal human urine to yield a final concentration of 100000 ng/mL. None of these compounds gave values in the assay that were greater than 0.05 % cross-reactivity.

Acetaminophen	LSD
Acetylsalicylic acid	Maprotiline
Aminopyrine	MDA
Amitriptyline	MDMA
Amobarbital	Melanin
d-Amphetamine	Meperidine
l-Amphetamine	Methadol
Ampicillin	Methadone
Ascorbic acid	*d*-Methamphetamine
Aspartame	*l*-Methamphetamine
Atropine	Methaqualone
Benzocaine	Methotrimeprazine
Benzphetamine	Methylphenidate
Butabarbital	Methyprylon
Caffeine	Mianserin
Calcium hypochlorite	Morphine sulfate
Cannabidiol	Naloxone
Carbamazepine	Naltrexone
Chlordiazepoxide	Naproxen
Chloroquine	Niacinamide
Chlorpheniramine	Nicotine
Chlorpromazine	Nordiazepam
Chlorprothixene	Nordoxepin
Clomipramine	Norethindrone
Codeine	*l*-Norpseudoephedrine
Cotinine	Nortriptyline
Cyclobenzaprine	Orphenadrine
Cyproheptadine	Oxazepam
Desipramine	Oxycodone
Dextromethorphan	Penicillin G
Dextropropoxyphene	Pentobarbital
Diazepam	Perphenazine

Diphenhydramine	Phencyclidine
Diphenylhydantoin	*β*-Phenethylamine
Disopyramide	Phenobarbital
Dopamine	Phenothiazine
Doxepin	Phentermine
Doxylamine	Phenylbutazone
d-Ephedrine	Phenylpropanolamine
d,l-Ephedrine	*d*-Phenylpropanolamine
l-Ephedrine	Phendimetrazine
Epinephrine	Procaine
EDDP	Promazine
EMDP	Promethazine
Erythromycin	Propoxyphene
Estriol	Protriptyline
Fenoprofen	*d*-Pseudoephedrine
Fluconazole	*l*-Pseudoephedrine
Fluoxetine	Quinidine
Furosemide	Quinine
Gentisic acid	Secobarbital
Glutethimide	Sulindac
Guaiacol glycerol ether	Tetracycline
Haloperidol	Δ^9 THC-9-carboxylic acid
Hydrochlorothiazide	Tetrahydrozoline
Hydroxymethadone	Thioridazine
Ibuprofen	Thiothixene
Imipramine	Trifluoperazine
Isoproterenol	Trimipramine
Ketamine	Tyramine
LAAM	Verapamil
Lidocaine	Zomepirac

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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.

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.

Additions, deletions or changes are indicated by a change bar in the margin.

CE 0123

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