THC2

cobas®

ONLINE DAT Cannabinoids II

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08058644190	08058644500	ONLINE DAT Cannabinoids II (850 tests)	System-ID 2107 001	**cobas c** 303, **cobas c** 503
08771669190	08058644500	ONLINE DAT Cannabinoids II (150 tests)	System-ID 2107 002	**cobas c** 303, **cobas c** 503

Materials required (but not provided):

Serum/plasma		
03304671190	Preciset DAT Plus I CAL 5	Code 20435
07978766190	Serum DAT Control Low (ACQ Partner Channel*)	
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
03304680190	Preciset DAT Plus II CAL 1-6 (6 x 5 mL)	Codes 20437-20442
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 50 ng/mL assay) PreciPos DAT Set I (2 x 10 mL) PreciNeg DAT Set I (2 x 10 mL)	
04500873190	Control Set DAT Clinical (for 50 ng/mL assay) PreciPos DAT Clinical (2 x 10 mL) PreciNeg DAT Clinical (2 x 10 mL)	
03312968190	Control Set DAT II (for 20 ng/mL assay) PreciPos DAT Set II (2 x 10 mL) PreciNeg DAT Set II (2 x 10 mL)	
03312976190	Control Set DAT III (for 100 ng/mL assay) PreciPos DAT Set III (2 x 10 mL) PreciNeg DAT Set III (2 x 10 mL)	

English

System information

THQ5S: ACN 21077 (Serum/plasma): for qualitative assay, 50 ng/mL

TH2Q2: ACN 21070 (Urine): for qualitative assay, 20 ng/mL

TH5Q2: ACN 21071 (Urine): for qualitative assay, 50 ng/mL

TH1Q2: ACN 21072 (Urine): for qualitative assay, 100 ng/mL

TH2S2: ACN 21073 (Urine): for semiquantitative assay, 20 ng/mL

TH5S2: ACN 21074 (Urine): for semiquantitative assay, 50 ng/mL

TH1S2: ACN 21075 (Urine): for semiquantitative assay, 100 ng/mL

TH5QC: ACN 21076 (Urine): for qualitative assay, 50 ng/mL; using C.f.a.s. DAT Qualitative Plus Clinical

TH5-QP: ACN 21078 (Urine): for qualitative assay, 50 ng/mL; using C.f.a.s. DAT Qualitative Plus

Intended use

Application in urine

Cannabinoids II (THC2) is an in vitro diagnostic test for the qualitative and semiquantitative detection of cannabinoids in human urine on **cobas c** systems at cutoff concentrations of 20 ng/mL, 50 ng/mL and 100 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). Cannabinoids 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*

Cannabinoids II (THC2) is an in vitro diagnostic test for the qualitative detection of cannabinoids in human serum and plasma on **cobas c** systems at a cutoff concentration of 50 ng/mL. Cannabinoids 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 cannabinoids in human serum, plasma and urine with this assay is used for presumptive testing of exposure to cannabinoids in individuals with suspected exposure, in individuals under pain management treatments and in individuals under rehabilitation programs.

Cannabinoids are obtained from the plants *Cannabis sativa* and *Cannabis indica* and constitute the active ingredient in marijuana and hashish.[2] The principal psychoactive component of the Cannabis plant is generally accepted to be Δ^9 tetrahydrocannabinol (Δ^9 THC), although it contains more than 60 cannabinoids.[2,3] The effects of cannabis include feelings of

euphoria and elation, altered time perception, lack of concentration, impaired learning and memory, and mood changes such as paranoia, psychosis, and panic attacks. Physiological effects include rapid changes in heart rate and diastolic blood pressure, conjunctival suffusion, dry mouth and throat, increased appetite, vasodilatation and decreased respiratory rate.[4] Although cannabinoids are frequently used as illicit drugs, they also have some limited legitimate medicinal use, for example to treat anorexia and nausea, for multiple sclerosis, certain types of pain and other neurological conditions.[4,5,6,7]

Marijuana is commonly smoked. Hashish has been mixed into foods, brewed as a tea, or inhaled as a vapor. Hemp oil is used in soaps, body care products, and dietary supplements due to its high essential fatty acid content, but negligible THC content.[4] Legitimate use of cannabinoids could lead to positive test results, therefore, caution should be taken in the interpretation of the results.[8]

When smoked or inhaled, cannabinoids are rapidly absorbed from the lungs into the blood with rapid onset of effects; the onset is slower but prolonged when ingested. The natural cannabinoids and their metabolic products are fat soluble and are stored in the body's fatty tissues, including brain tissue, for prolonged periods after use.[9] Cannabinoid metabolites are found in blood, bile, feces, and urine and may be detected in urine within hours of exposure. Because of their fat solubility, they also remain in the body's fatty tissues with slow release and subsequent urinary excretion for days, weeks, and even months after the last exposure, depending on the intensity and frequency of use. The prominent Δ^9 THC metabolite, 11-nor-Δ^9 THC-9-carboxylic acid (Δ^9 COOH-THC), is the primary urinary marker for detecting marijuana use.[2]

In the context of drug screening (presumptive testing in individuals with suspected exposure, in individuals under pain management treatments and in individuals under rehabilitation programs), 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).[3,4,10,11,12]

Test principle

The assay is based on the kinetic interaction of microparticles in a solution (KIMS)[13,14] 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.[15]

Reagents - working solutions

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

R3 Microparticles attached to cannabinoid 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 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

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:	8 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.

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:	5 days capped at 15-25 °C
	14 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.[16]

For prolonged storage, freezing of the sample is recommended.[16]

Freeze only once.

It has been reported that THC and its derivatives may adsorb onto plastics used for sample collection containers, effectively lowering the drug concentration of the sample.[17]

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.*[18]

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. 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

THC and its derivatives may adsorb onto plastics.[17] To minimize the potential for lowering the drug concentration of any sample containing THC, the following is recommended:

1. Dispense > 0.5 mL of each sample (calibrators, controls and patient specimens) into separate analyzer sample cups by pouring over from the primary container or by dispensing with a glass pipette.
2. Avoid the use of plastic pipettes and/or tips due to the potential for adsorbance and possible decrease of THC concentration.
3. Assay the samples within 2 hours of dispensing into the sample cup.

4. Do not return any unused material back into the original sample container.

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

Test definition

	Qualitative		
Reporting time	10 min		
Wavelength (sub/main)	– /570 nm		
Reagent pipetting			Diluent (H_2O)
R1	64 µL		-
R3	28 µL		-
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	1.8 µL	-	-
Decreased	1.8 µL	-	-
Increased	1.8 µL	-	-

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

For **cobas c** 503 an instrument specific application correction factor B of +30 is predefined in the application settings.

Application for urine

Test definition - 20 ng/mL cutoff assay

	Semiquantitative		Qualitative
Reporting time	10 min		10 min
Wavelength (sub/main)	– /570 nm		– /570 nm
Reagent pipetting			Diluent (H_2O)
R1	64 µL		–
R3	28 µL		–
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	3.2 µL	–	–
Decreased	3.2 µL	–	–
Increased	3.2 µL	–	–

Test definition - 50 ng/mL cutoff assay

	Semiquantitative		Qualitative
Reporting time	10 min		10 min
Wavelength (sub/main)	– /570 nm		– /570 nm
Reagent pipetting			Diluent (H_2O)
R1	64 µL		–
R3	28 µL		–
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	1.8 µL	–	–
Decreased	1.8 µL	–	–
Increased	1.8 µL	–	–

Test definition - 100 ng/mL cutoff assay

	Semiquantitative		Qualitative
Reporting time	10 min		10 min
Wavelength (sub/main)	– /570 nm		– /570 nm
Reagent pipetting			Diluent (H_2O)
R1	64 µL		–
R3	28 µL		–
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	1.4 µL	–	–
Decreased	1.4 µL	–	–
Increased	1.4 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

Calibrator	*50 ng/mL cutoff assay* S1: Preciset DAT Plus I, CAL 5, 200 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 application

Calibrators	*20 ng/mL cutoff assay* S1-5: Preciset DAT Plus II, CAL 1-5 0, 10, 20, 40, 100 ng/mL *50 ng/mL cutoff assay* S1-5: Preciset DAT Plus I, CAL 1-4, 6 0, 20, 50, 100, 300 ng/mL *100 ng/mL cutoff assay* S1-5: Preciset DAT Plus I, CAL 1, 3-6 0, 50, 100, 200, 300 ng/mL
Calibration mode	Non-linear
Calibration frequency	Full calibration - after reagent lot change - as required following quality control procedures

Qualitative application

Calibrators	*20 ng/mL cutoff assay* S1: Preciset DAT II, CAL 3 20 ng/mL *50 ng/mL cutoff assay* S1: C.f.a.s. DAT Qualitative Plus, C.f.a.s. DAT

	Qualitative Plus Clinical, or Preciset DAT Plus I, CAL 3
	50 ng/mL
	100 ng/mL cutoff assay
	S1: Preciset DAT Plus I, CAL 4
	100 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 - 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: These methods have 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.

The drug concentrations of the 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 8 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.

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.

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.

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 cannabinoids and/or cannabinoid metabolites in serum or urine. It does not measure the level of intoxication.

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

Serum/plasma

Criterion: No cross-over at initial values of samples of 25 ng/mL and 75 ng/mL (control levels).

Icterus:[19] 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:[19] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 622 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[19] No significant interference up to an L index of 900. 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 1200 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

With a low cutoff assay for cannabinoids, it may be possible to obtain a preliminary positive test result from a non-user as a result of passive inhalation. Significant increases in urinary levels of cannabinoids from passive inhalation have been reported to occur only after exposure to extremely high concentrations of marijuana smoke in small unventilated areas.[20] These extreme exposure conditions are not typical of the usual situations in which the drug is used. More recent reports indicate that urine cannabinoid concentrations resulting from passive inhalation are not likely to exceed 20 ng/mL.[20,21,22]

Interfering substances were added to drug free urine at the concentration listed below. These samples were then spiked to 20 ng/mL using a THC stock solution. Samples were tested on a Roche/Hitachi 917 analyzer and the following results were obtained.

Substance	Concentration tested	% THC recovery
Acetone	1 %	98
Ascorbic acid	1.5 %	80
Bilirubin	0.25 mg/mL	111
Creatinine	5 mg/mL	99
Ethanol	1 %	105
Glucose	2 %	101

Hemoglobin	7.5 g/L	95
Human albumin	0.5 %	105
Oxalic acid	2 mg/mL	92
Sodium chloride	0.5 M	100
Sodium chloride	1 M	106
Urea	6 %	100

Interfering substances were added to drug free urine at the concentration listed below. These samples were then spiked to 50 ng/mL using a THC stock solution. Samples were tested on a Roche/Hitachi 917 analyzer and the following results were obtained.

Substance	Concentration tested	% THC recovery
Acetone	1 %	110
Ascorbic acid	1.5 %	105
Bilirubin	0.25 mg/mL	114
Creatinine	5 mg/mL	113
Ethanol	1 %	108
Glucose	2 %	108
Hemoglobin	7.5 g/L	108
Human albumin	0.5 %	107
Oxalic acid	2 mg/mL	113
Sodium chloride	0.5 M	108
Sodium chloride	1 M	110
Urea	6 %	115

Interfering substances were added to drug free urine at the concentration listed below. These samples were then spiked to 100 ng/mL using a THC stock solution. Samples were tested on a Roche/Hitachi 917 analyzer and the following results were obtained.

Substance	Concentration tested	% THC recovery
Acetone	1 %	112
Ascorbic acid	1.5 %	88
Bilirubin	0.25 mg/mL	110
Creatinine	5 mg/mL	101
Ethanol	1 %	107
Glucose	2 %	106
Hemoglobin	7.5 g/L	92
Human albumin	0.5 %	106
Oxalic acid	2 mg/mL	107
Sodium chloride	0.5 M	108
Sodium chloride	1 M	111
Urea	6 %	102

In very rare cases, gammopathy, in particular type IgM (Waldenström's macroglobulinemia), may cause unreliable results.[23]

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

Qualitative assay

Results of this assay distinguish preliminary positive (≥ 20 ng/mL, ≥ 50 ng/mL, or ≥ 100 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.

Qualitative precision - 50 ng/mL

Cutoff (50)	Number tested	Correct results	Confidence level
Serum -75 %	84	84	> 95 % negative reading
ACQ-L	84	84	> 95 % negative reading
Cutoff serum	84	n.a.*	n.a.*
ACQ-H	84	84	> 95 % positive reading
Serum +75 %	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).

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 - 20 ng/mL

Repeatability	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	11.0	0.433	3.9
DAT2N	15.6	0.434	2.8
Cutoff urine	19.7	0.607	3.1
DAT2P	24.3	0.611	2.5
Urine +50 %	28.6	0.530	1.9

Intermediate precision	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	11.0	0.631	5.7
DAT2N	15.6	0.760	4.9
Cutoff urine	19.7	0.799	4.0
DAT2P	24.3	0.840	3.5
Urine +50 %	28.6	0.743	2.6

Qualitative precision - 20 ng/mL

Cutoff (20)	Number tested	Correct results	Confidence level
Urine -50 %	84	84	> 95 % negative reading
DAT2N	84	84	> 95 % negative reading

Cutoff urine	84	n.a.*	n.a.*
DAT2P	84	84	> 95 % positive reading
Urine +50 %	84	84	> 95 % positive reading

*n.a. = not applicable

Semiquantitative precision - 50 ng/mL

Repeatability	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	26.3	0.750	2.8
DAT1N	37.6	1.35	3.6
DATCN	37.8	0.930	2.5
Cutoff urine	49.4	1.15	2.3
DAT1P	63.4	1.52	2.4
DATCP	63.5	1.43	2.3
Urine +50 %	73.7	1.37	1.9

Intermediate precision	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	26.3	1.09	4.2
DAT1N	37.6	1.45	3.9
DATCN	37.8	1.37	3.6
Cutoff urine	49.4	1.98	4.0
DAT1P	63.4	1.84	2.9
DATCP	63.5	1.85	2.9
Urine +50 %	73.7	1.88	2.6

Qualitative precision - 50 ng/mL

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

*n.a. = not applicable

Semiquantitative precision - 100 ng/mL

Repeatability	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	51.5	1.31	2.5
DAT3N	77.0	2.14	2.8
Cutoff urine	103	1.80	1.8
DAT3P	129	2.16	1.7
Urine +50 %	142	3.45	2.4

Intermediate precision	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	51.5	1.70	3.3
DAT3N	77.0	2.34	3.0
Cutoff urine	103	2.12	2.1
DAT3P	129	3.35	2.6
Urine +50 %	142	4.25	3.0

Qualitative precision - 100 ng/mL

Cutoff (100)	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).

Accuracy

Serum/plasma

110 serum samples, screened negative for cannabinoids on a **cobas c** 501 analyzer were evaluated with the Cannabinoids II assay on a **cobas c** 503 analyzer. 100 % of these normal serums were negative for all cutoffs with the Cannabinoids II assay on a **cobas c** 503 analyzer. 54 serum samples screened positive for cannabinoids relative to the 50 ng/mL cutoff on a **cobas c** 501 analyzer were evaluated with the Cannabinoids II assay on a **cobas c** 503 analyzer. At the 50 ng/mL cutoff, 100 % of the samples were positive on both the **cobas c** 501 analyzer and the **cobas c** 503 analyzer.

Cannabinoids II correlation (cutoff = 50 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 503 analyzer	+	54	0
	-	0	110

Additional 110 serum samples, screened negative for cannabinoids on a **cobas c** 501 analyzer were evaluated with the Cannabinoids II assay on a **cobas c** 303 analyzer. 100 % of these normal serums were negative for all cutoffs with the Cannabinoids II assay on a **cobas c** 303 analyzer. 55 serum samples screened positive for cannabinoids relative to the 50 ng/mL cutoff on a **cobas c** 501 analyzer were evaluated with the Cannabinoids II assay on a **cobas c** 303 analyzer. At the 50 ng/mL cutoff, 96.4 % of the samples were positive on the **cobas c** 303 analyzer.

Cannabinoids II correlation (cutoff = 50 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 303 analyzer	+	53	0
	-	2	110

Urine

100 urine samples, obtained from a clinical laboratory where they screened negative in a drug test panel, were evaluated with the Cannabinoids II assay. 100 % of these normal urines were negative relative to the 20 ng/mL, 50 ng/mL and 100 ng/mL cutoffs. 52 samples obtained from a clinical laboratory, where they screened preliminary positive with a commercially available immunoassay and were subsequently confirmed by GC-MS, were evaluated with the Cannabinoids II assay. 100 % of these samples were positive relative to the 20 ng/mL, 50 ng/mL and 100 ng/mL cutoffs. In addition, 10 samples were diluted to a Δ^9 COOH-THC concentration of 75-100 % of the cutoff concentration for each cutoff; and 10 samples were diluted to a Δ^9 COOH-THC 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 urine samples. The following results were obtained with the Cannabinoids II assay on the Roche/Hitachi 917 analyzer relative to the GC-MS values.

Cannabinoids II clinical correlation (cutoff = 20 ng/mL)

		Negative samples	GC-MS values (ng/mL)		
			Near cutoff		Positive samples
			15	20-25	28-981
Roche/Hitachi 917 analyzer	+	0	0	16	46
	-	100	10	0	0

Cannabinoids II clinical correlation (cutoff = 50 ng/mL)

		Negative samples	GC-MS values (ng/mL)		
			Near cutoff		Positive samples
			30-49	50-63	64-338
Roche/Hitachi 917 analyzer	+	0	7	17	38
	-	100	10	0	0

Cannabinoids II clinical correlation (cutoff = 100 ng/mL)

		Negative samples	GC-MS values (ng/mL)		
			Near cutoff		Positive samples
			75	110-125	143-779
Roche/Hitachi 917 analyzer	+	0	0	16	46
	-	100	10	0	0

100 urine samples, screened negative for cannabinoids on a **cobas c** 501 analyzer were evaluated with the Cannabinoids II assay on a **cobas c** 503 analyzer. 100 % of these normal urines were negative for all cutoffs with the Cannabinoids II assay on a **cobas c** 503 analyzer. 50 urine samples for the 20 ng/mL, 50 ng/mL and 100 ng/mL cutoffs, screened positive for cannabinoids relative to the corresponding cutoff on a **cobas c** 501 analyzer and subsequently confirmed by GC-MS, were evaluated with the Cannabinoids II assay on a **cobas c** 503 analyzer. At the 20 ng/mL, 50 ng/mL and 100 ng/mL cutoffs, 100 % of the samples were positive on both the **cobas c** 501 analyzer and the **cobas c** 503 analyzer.

Cannabinoids II correlation (cutoff = 20 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 503 analyzer	+	50	0
	-	0	100

Cannabinoids II correlation (cutoff = 50 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 503 analyzer	+	50	0
	-	0	100

Cannabinoids II correlation (cutoff = 100 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 503 analyzer	+	50	0
	-	0	100

Additional clinical samples were evaluated with this assay on a **cobas c** 303 analyzer and on a **cobas c** 501 analyzer. Urine samples screened negative in a drug test panel, were evaluated with the Cannabinoids II assay (112 samples negative relative to the 20 ng/mL cutoff, 113 samples negative relative to the 50 ng/mL cutoff and 112 samples negative relative to the 100 ng/mL cutoff). 100 % of these normal urines were negative for the 20 ng/mL on the **cobas c** 303 analyzer. For the 50 ng/mL cutoff 98.2 % of these normal urines were negative on the **cobas c** 303 analyzer. For the 100 ng/mL cutoff 99.1 % of these normal urines were negative on the **cobas c** 303 analyzer. Preliminary positive urine samples (53 samples relative to the 20 ng/mL, 52 samples relative to the 50 ng/mL cutoff and 53 samples relative to the 100 ng/mL cutoff) were confirmed by GC-MS. 100 % of these samples were positive for the 20 ng/mL and the 50 ng/mL cutoffs on the **cobas c** 303 analyzer. For the 100 ng/mL cutoff 96.2 % of these samples were positive on the **cobas c** 303 analyzer.

Cannabinoids II correlation (cutoff = 20 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 303 analyzer	+	53	0
	-	0	112

Cannabinoids II correlation (cutoff = 50 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 303 analyzer	+	52	2
	-	0	111

Cannabinoids II correlation (cutoff = 100 ng/mL)			
		cobas c 501 analyzer	
		+	-
cobas c 303 analyzer	+	51	1
	-	2	111

Analytical specificity

Serum/plasma

The specificity of this assay for various cannabinoids and cannabinoid 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 the 50 ng/mL Δ^9 COOH-THC assay cutoff. The following results were obtained on a **cobas c** 501 analyzer.

Compound	**ng/mL Equivalent to 50 ng/mL 11-nor-9-carboxy-THC**	**Approximate % cross-reactivity**
8-β-11-Dihydroxy-Δ9 THC	94.9	52.7
8-α-Hydroxy-Δ9 THC	91.8	54.5
11-Hydroxy-Δ9 THC	327	15.3

Urine

The specificity of this assay for various cannabinoids and cannabinoid 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 the 20 ng/mL, 50 ng/mL and 100 ng/mL Δ^9 COOH-THC assay cutoff. The following results were obtained on a Roche/Hitachi 917 analyzer.

Compound	**ng/mL Equivalent to 20 ng/mL Δ^9 COOH-THC**	**Approximate % cross-reactivity**
9-carboxy-11-nor-Δ^8 THC	28	71.9
9-carboxy-11-nor-Δ^9 THC glucuronide	45	44.1
8-β-11-dihydroxy-Δ^9 THC	60	33.9
8-α-hydroxy-Δ^9 THC	154	13.0

11-hydroxy-Δ^9 THC	172	11.6
Cannabinol	3333	0.6
Δ^9 THC	3333	0.6

Compound	ng/mL Equivalent to 50 ng/mL Δ^9 COOH-THC	Approximate % cross-reactivity
9-carboxy-11-nor-Δ^8 THC	73	69.0
9-carboxy-11-nor-Δ^9 THC glucuronide	93	54.0
8-β-11-dihydroxy-Δ^9 THC	162	30.9
8-α-hydroxy-Δ^9 THC	338	14.8
11-hydroxy-Δ^9 THC	376	13.3
Cannabinol	8333	0.6
Δ^9 THC	25000	0.2

Compound	ng/mL Equivalent to 100 ng/mL Δ^9 COOH-THC	Approximate % cross-reactivity
9-carboxy-11-nor-Δ^8 THC	145	68.8
9-carboxy-11-nor-Δ^9 THC glucuronide	174	57.5
8-β-11-dihydroxy-Δ^9 THC	283	35.3
8-α-hydroxy-Δ^9 THC	485	20.6
11-hydroxy-Δ^9 THC	581	17.2
Cannabinol	25000	0.4
Δ^9 THC	33333	0.3

Drug interference

Serum/plasma

Interfering substances were added to serum containing 11-nor-9-carboxy-THC 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
Cyclosporine	5.00	neg	pos
d-Amphetamine	1.36	neg	pos
Doxycycline	50.0	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	50.0	neg	pos
Imipramine	0.70	neg	pos
Ketamine	10.0	neg	pos
Levodopa	20.0	neg	pos
Lidocaine	12.0	neg	pos
Methyldopa + 1.5 H_2O	20.0	neg	pos
Metronidazole	200	neg	pos
Naproxen	499	neg	pos
Phenylbutazone	400	neg	pos
Procaine	20.0	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	1.00	neg	pos

Urine

The following compounds were added to aliquots of pooled normal human urine at a concentration of 100000 ng/mL. None of these compounds gave values in the assay that were equal to or greater than 0.015 % cross-reactivity and no results were greater than the assay cutoffs (20 ng/mL, 50 ng/mL and 100 ng/mL).

Acetaminophen	Ibuprofen
Acetylsalicylic acid	Imipramine
Aminopyrine	Isoproterenol
Amitriptyline	Ketamine
Amobarbital	Lidocaine
Amoxicillin	LSD
d-Amphetamine	Mefloquine
Ampicillin	Melanin
Ascorbic acid	Meperidine
Aspartame	Methadone
Atropine	*d*-Methamphetamine
Benzocaine	Methaqualone
Benzoylecgonine (cocaine metabolite)	Methyprylon
	Morphine sulfate
Benzphetamine	Naloxone
Butabarbital	Naltrexone
Caffeine	Naproxen
Calcium hypochlorite	Niacinamide
Captopril	Nifedipine
Chlordiazepoxide	Norethindrone
Chloroquine	Norpseudoephedrine
Chlorpheniramine	Omeprazole
Chlorpromazine	Oxazepam
Dextromethorphan	Pantoprazole
Dextropropoxyphene	Penicillin G

Diazepam	Pentazocine
Digoxin	Pentobarbital
Diphenhydramine	Phencyclidine
Diphenylhydantoin	Phenobarbital
Dopamine	Phenothiazine
Ecgonine	Phenylbutazone
Ecgonine methyl ester	Phenylpropanolamine
Enalapril	Procaine
Ephedrine	Promethazine
Epinephrine	*d*-Pseudoephedrine
Erythromycin	*l*-Pseudoephedrine
Estriol	Quinidine
Fenoprofen	Quinine
Fluoxetine	Ranitidine
Flurbiprofen	Secobarbital
Furosemide	Sulindac
Gentisic acid	Tetracycline
Glutethimide	Tetrahydrozoline
Guaiacol glycerol ether	Tolmetin
Hydrochlorothiazide	Trifluoperazine
5-Hydroxyindole-3 acetic acid	Verapamil
5-Hydroxyindole-2 carboxylic acid	Zomepirac

For the 20 ng/mL cutoff, the cross-reactivity for niflumic acid, at a concentration of 1250 ng/mL, is 2 %. For the 50 ng/mL cutoff, the cross-reactivity for niflumic acid, at a concentration of 4750 ng/mL, is 1 %. For the 100 ng/mL cutoff, the cross-reactivity for niflumic acid, at a concentration of 10897 ng/mL, is 1 %.

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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.

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