THC2

cobas®

ONLINE DAT Cannabinoids II

Order information

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

Materials required (but not provided):

03304671190	Preciset DAT Plus I calibrator 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.

English

System information

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

Intended use

Cannabinoids II (THCII) is an in vitro diagnostic test for the qualitative detection of cannabinoids in human serum and plasma on Roche/Hitachi **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

The principal psychoactive component of the hemp plant, *Cannabis sativa,* is generally accepted to be Δ^9 tetrahydrocannabinol (Δ^9 THC), although other cannabinoids may contribute to the psychological and physiological actions of marijuana. The acute effects of marijuana use, concomitant with the desired "high", are memory impairment, time confusion, interference with learning, impaired motor skills and depersonalization.[2,3,4] These effects are also manifested in chronic users in addition to cardiovascular, pulmonary, and reproductive effects. Marijuana is usually smoked, but may be ingested, either incorporated into food or as a liquid extract (tea). It is 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.[5]

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.[1] 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.

Test principle

The assay is based on the kinetic interaction of microparticles in a solution (KIMS)[6,7] 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 serum 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.[8]

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.

Stability:	5 days capped at 15-25 °C
	14 days capped at 2-8 °C
	6 months capped at -20 °C

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

Centrifuge samples containing precipitates before performing the assay.

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

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

Invert thawed specimens several times prior to testing.

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.

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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.[9] 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.

Calibration

Calibrators	*Qualitative application* *50 ng/mL cutoff assay* S1: Preciset DAT Plus I calibrator - CAL 5, 200 ng/mL with automatic pre-dilution The drug concentration of the calibrator has been verified by GC-MS.
Calibration K factor	For the qualitative application a K factor of -1000 is predefined in the application settings.
Calibration mode	*Qualitative application* Linear
Calibration frequency	Full calibration - after reagent lot change - as required following quality control procedures

For the 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 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 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 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

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.

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

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

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. It does not measure the level of intoxication.

Icterus:[10] 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:[10] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 622 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[10] 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.

In very rare cases, gammopathy, in particular type IgM (Waldenström’s macroglobulinemia), may cause unreliable results.[11]

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

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on **cobas c** systems. 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 information. For further instructions refer to the operator’s manual.

Expected values

Qualitative assay

Results of this assay distinguish preliminary positive (≥ 50 ng/mL) from negative samples only. The amount of drug detected in a preliminary positive sample cannot be estimated.

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

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).

Accuracy

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

Analytical specificity

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

Drug interference

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

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References

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

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

Symbols

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

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number

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

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