OPI2

cobas®

ONLINE DAT Opiates II

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08058113190	08058113500	ONLINE DAT Opiates II (700 tests)	System-ID 2095 001	**cobas c** 303, **cobas c** 503

Materials required (but not provided):

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	
04590856190	C.f.a.s. DAT Qualitative Plus Clinical (3 x 5 mL)	Code 20699	
03312950190	Control Set DAT I (for 2000 ng/mL assay) PreciPos DAT Set I (2 x 10 mL) PreciNeg DAT Set I (2 x 10 mL)		
03312968190	Control Set DAT II (for 300 ng/mL assay) PreciPos DAT Set II (2 x 10 mL) PreciNeg DAT Set II (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

OP3Q2: ACN 20952 (Urine): for qualitative assay, 300 ng/mL

OP3QC: ACN 20954 (Urine): for qualitative assay, 300 ng/mL; using C.f.a.s. DAT Qualitative Plus Clinical

OP3S2: ACN 20953 (Urine): for semiquantitative assay, 300 ng/mL

OP2Q2: ACN 20950 (Urine): for qualitative assay, 2000 ng/mL

OP2S2: ACN 20951 (Urine): for semiquantitative assay, 2000 ng/mL

Intended use

Opiates II (OPI2) is an in vitro diagnostic test for the qualitative and semiquantitative detection of morphine and its metabolites in human urine on **cobas c** systems at cutoff concentrations of 300 ng/mL and 2000 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).

Opiates 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.

Summary

Detection of morphine and its metabolites in human urine with this assay is used as an aid in monitoring adherence to treatment in patients under pain treatment with opiates and for presumptive testing of illicit use of opiates in individuals with suspected exposure.

The term opiates refers to naturally occurring alkaloids (morphine and codeine) obtained from the opium poppy and semisynthetic alkaloids that are partially derived from the opium poppy. The term opioids includes both opiates and opioids. Opioids are a group of compounds that have pharmacological properties similar to morphine and have affinity toward the opiate receptors in the brain.[2] Opiates can be administered through various routes, including orally, intravenously or subcutaneously, but can also be smoked or sniffed.[3,4] Upon entering the circulation, they tend to concentrate in the lungs, spleen, kidneys, and liver; lower concentrations are found in the body's musculature and central nervous system.[4] Morphine is the archetypical opiate, its major metabolites are glucuronide conjugates, including inactive morphine-3-glucuronide (M3G; < 60 % of metabolites), active morphine-6-glucuronide (M6G; < 10 % of metabolites) and a small amount of morphine-3,6-diglucuronide. Under long-term administration or high morphine concentrations also hydromorphone is formed.[5] Morphine is excreted in the urine as M3G, M6G, unchanged free morphine, and other minor metabolites.[6] Morphine may also be detected after poppy seeds ingestion or codeine and heroin administration.[5,7] Codeine is one of the most frequently prescribed opiates in the world because of its antitussive and analgesic properties. It has only about one tenth the analgesic potency of morphine and is metabolized into morphine. Both codeine and morphine may be detected in urine following codeine ingestion; however, after 30 hours only morphine may be detectable.[5] Heroin is metabolized by esterases into 6-acetylmorphine (6-MAM), then into morphine[7]and has an analgesic potency two to three times that of morphine.[5]

Opiates, including heroin, can be used illicitly. The main pharmacological effects of the opiates include reduction of sensitivity to physical and psychological stimuli, mitigation of pain, fear and anxiety.[8] Opiate users may present with pupil constriction, itching, constipation, nausea, vomiting, and respiratory depression.[9,10,11,12] Death by overdose, usually resulting from dose miscalculation or dose-strength variability, is caused by respiratory failure.[12] Heroin use is associated with far more accidental overdoses and fatal poisonings than any other scheduled substance.[13]

The opiates produce strong physical dependence; withdrawal symptoms can begin to appear within a few hours of the last dose and may continue for 5-10 days. The addict may pursue continued opiate use as much to avoid the discomfort of withdrawal as to achieve the desired insensate euphoria.[14,15]

Opiates, such as morphine, codeine and hydromorphone, can be prescribed in pain management due to their analgesic effect for treating acute needs such as postsurgical analgesia, and in relieving moderate to severe chronic pain (e.g. cancer-related pain). Nevertheless, because of the addictive capacity leading to abuse and misuse, treatment adherence monitoring including periodic urine testing is considered necessary.[16]

Distinguishing between illicit and prescription use can be difficult due to variable cross-reactivity[2] (for further details see "Analytical specificity" section). 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).[2,5,17,18]

Test principle

The assay is based on the kinetic interaction of microparticles in a solution (KIMS)[19,20] 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 urine 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.[21]

Reagents - working solutions

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

R3 Microparticles attached to morphine 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:	26 weeks

Do not freeze.

Specimen collection and preparation

Only the specimens listed below were tested and found acceptable.

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.[22]

For prolonged storage, freezing of the sample is recommended.[22]

Freeze only once.

Invert thawed specimens several times prior to testing.

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*.[23]

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 urine

Test definition - 300 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	65 µL		–
R3	27 µL		–
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (H_2O)*
Normal	3.9 µL	–	–
Decreased	3.9 µL	–	–
Increased	3.9 µL	–	–

Test definition - 2000 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	65 µL		–
R3	27 µL		–
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (H_2O)*
Normal	1.3 µL	–	–
Decreased	1.3 µL	–	–
Increased	1.3 µL	–	–

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

Calibration

Semiquantitative applications

Calibrators	*300 ng/mL cutoff assay*
	S1-6: Preciset DAT Plus II, CAL 1-6
	0, 150, 300, 600, 1000, 2000 ng/mL
	2000 ng/mL cutoff assay
	S1-6: Preciset DAT Plus I, CAL 1-6
	0, 600, 1000, 2000, 4000, 8000 ng/mL
Calibration mode	Result Calculation Mode (RCM)[a]
Calibration frequency	Full calibration - after reagent lot change - every 17 weeks on-board - as required following quality control procedures

Qualitative applications

Calibrators	*300 ng/mL cutoff assay*
	S1: C.f.a.s. DAT Qualitative Plus Clinical or Preciset DAT Plus II, CAL 3
	300 ng/mL
	2000 ng/mL cutoff assay

	S1: Preciset DAT Plus I, CAL 4 2000 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 17 weeks on-board - as required following quality control procedures

a) See Results section.

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.

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 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 opiates and/or their metabolites in urine. It does not measure the level of intoxication.

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

Substance	Concentration tested	% Morphine recovery
Acetone	1 %	98
Ascorbic acid	1.5 %	97
Bilirubin	0.25 mg/mL	95
Creatinine	5 mg/mL	95
Ethanol	1 %	100
Glucose	2 %	97
Hemoglobin	7.5 g/L	99
Human albumin	0.5 %	96
Oxalic acid	2 mg/mL	93
Sodium chloride	0.5 M	84
Sodium chloride	1 M	78
Urea	6 %	94

Urine levels of $MgSO_4$ greater than 400 mg/dL (33.2 mmol/L) were found to interfere with the assay. The results were obtained on a **cobas c** 501 analyzer.

Interfering substances were added to drug free urine at the concentration listed below. These samples were then spiked to 2000 ng/mL using a morphine stock solution. Samples were tested on a Roche/Hitachi 917 analyzer and the following results were obtained:

Substance	Concentration tested	% Morphine recovery
Acetone	1 %	99
Ascorbic acid	1.5 %	96
Bilirubin	0.25 mg/mL	98
Creatinine	5 mg/mL	100
Ethanol	1 %	96
Glucose	2 %	98
Hemoglobin	7.5 g/L	101
Human albumin	0.5 %	96
Oxalic acid	2 mg/mL	96
Sodium chloride	0.5 M	95
Sodium chloride	1 M	91
Urea	6 %	97

Urine levels of $MgSO_4$ up to 600 mg/dL (49.9 mmol/L) do not interfere with the assay. The results were obtained on a **cobas c** 501 analyzer.

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.[24]

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 (≥ 300 ng/mL or ≥ 2000 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

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 - 300 ng/mL

Repeatability	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	163	2.88	1.8
DATCN	242	3.72	1.5
DAT2N	240	3.77	1.6
Cutoff urine	304	3.54	1.2
DAT2P	395	5.08	1.3
DATCP	397	4.48	1.1
Urine +50 %	471	5.82	1.2

Intermediate precision	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	163	5.47	3.4
DATCN	242	6.58	2.7
DAT2N	240	6.84	2.9
Cutoff urine	304	7.93	2.6
DAT2P	395	9.45	2.4
DATCP	397	8.06	2.0
Urine +50 %	471	10.2	2.2

Qualitative precision - 300 ng/mL

Cutoff (300)	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 - 2000 ng/mL

Repeatability	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	1126	11.7	1.0
DAT1N	1572	28.1	1.8
Cutoff urine	2005	25.2	1.3
DAT1P	2526	27.9	1.1
Urine +50 %	3003	51.1	1.7

Intermediate precision	*Mean ng/mL*	*SD ng/mL*	*CV %*
Urine -50 %	1126	23.8	2.1
DAT1N	1572	37.6	2.4
Cutoff urine	2005	33.5	1.7
DAT1P	2526	44.0	1.7
Urine +50 %	3003	56.0	1.9

Qualitative precision - 2000 ng/mL

Cutoff (2000)	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

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

Accuracy

100 urine samples, obtained from a clinical laboratory where they screened negative in a drug test panel, were evaluated with the Opiates II assay. 100 % of these normal urines were negative relative to the 300 ng/mL and 2000 ng/mL cutoffs. 70 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 Opiates II assay. 100 % of these samples were positive relative to the 300 ng/mL cutoff. 54 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 Opiates II assay. 100 % of these samples were positive relative to the 2000 ng/mL cutoff. In addition, positive urine samples were diluted with drug-free urine. For each cutoff (300 ng/mL and 2000 ng/mL), 10 positive samples were diluted to obtain drug concentrations less than the respective cutoffs. For each cutoff (300 ng/mL and 2000 ng/mL), the same 10 positive samples were diluted to obtain drug concentrations greater than the respective cutoffs. 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 Opiates II assay on the Roche/Hitachi 917 analyzer relative to the GC-MS values.

Opiates II clinical correlation (cutoff = 300 ng/mL)

		Negative samples	GC-MS values (ng/mL)[a]		
			Near cutoff		Positive samples
			40-253	301-794	825-48247
Roche/Hitachi 917 analyzer	+	0	5	7	68
	-	100	8	2	0

a) GC-MS values are represented by the sum of morphine and codeine and do not include all metabolites.

Opiates II clinical correlation (cutoff = 2000 ng/mL)

		Negative samples	GC-MS values (ng/mL)[a]		
			Near cutoff		Positive samples
			153-1982	2051-3220	3254-48247
Roche/Hitachi 917 analyzer	+	0	4	18	42
	-	100	10	0	0

a) GC-MS values are represented by the sum of morphine and codeine and do not include all metabolites.

Additional clinical samples were evaluated with this assay on a **cobas c** 503 analyzer and on a **cobas c** 501 analyzer. 110 urine samples screened negative for opiates on a **cobas c** 501 analyzer were evaluated with the Opiates II assay on a **cobas c** 503 analyzer. 100 % of these normal urines were negative for all cutoffs with the Opiates II assay on a **cobas c** 503 analyzer. 55 urine samples for the 300 ng/mL and 2000 ng/mL cutoffs, screened positive for opiates relative to the corresponding cutoff on a **cobas c** 501 analyzer and subsequently confirmed by GC-MS, were evaluated with the Opiates II assay on a **cobas c** 503 analyzer. At the 300 ng/mL and 2000 ng/mL cutoffs, 100 % of the samples were positive on both the **cobas c** 501 analyzer and the **cobas c** 503 analyzer.

Opiates II correlation (cutoff = 300 ng/mL)

		cobas c 501 analyzer	
		+	-
cobas c 503 analyzer	+	55	0
	-	0	110

Opiates II correlation (cutoff = 2000 ng/mL)

		cobas c 501 analyzer	
		+	-
cobas c 503 analyzer	+	55	0
	-	0	110

Additional clinical samples were evaluated with this assay on a **cobas c** 303 analyzer and on a **cobas c** 501 analyzer. 100 urine samples screened negative for opiates on a **cobas c** 501 analyzer were evaluated with the Opiates II assay on a **cobas c** 303 analyzer. 100 % of these normal urines were negative for all cutoffs with the Opiates II assay on a **cobas c** 303 analyzer. 50 urine samples for the 300 ng/mL and 2000 ng/mL cutoffs, screened positive for opiates relative to the corresponding cutoff on a **cobas c** 501 analyzer and subsequently confirmed by GC-MS, were evaluated with the Opiates II assay on a **cobas c** 303 analyzer. At the 300 ng/mL and 2000 ng/mL cutoffs, 100 % of the samples were positive on both the **cobas c** 501 analyzer and the **cobas c** 303 analyzer.

Opiates II correlation (cutoff = 300 ng/mL)

		cobas c 501 analyzer	
		+	-
cobas c 303 analyzer	+	50	0
	-	0	100

Opiates II correlation (cutoff = 2000 ng/mL)

		cobas c 501 analyzer	
		+	-
cobas c 303 analyzer	+	50	0
	-	0	100

Analytical specificity

The specificity of this assay for structurally similar compounds 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 and a 2000 ng/mL assay cutoff. The following results were obtained on a Roche/Hitachi 917 analyzer.

Compound	**ng/mL Equivalent to 300 ng/mL morphine**	**Approximate % cross-reactivity**
Codeine	224	134
Ethyl morphine	297	101
Diacetylmorphine	366	82
6-Acetylmorphine	386	78
Dihydrocodeine	510	59
Morphine-3-glucuronide	552	54
Dihydromorphine**	937	32
Hydrocodone	1086	28
Thebaine	1210	25
Hydromorphone	1425	21
n-Norcodeine	18590	2
Oxycodone	> 75000	< 0.4
Meperidine	> 100000	< 0.3
Fentanyl**	> 150000	< 0.2

Compound	**ng/mL Equivalent to 2000 ng/mL morphine**	**Approximate % cross-reactivity**
Codeine	1541	130
Ethyl morphine	2474	81
6-Acetylmorphine	2598	77
Diacetylmorphine	2915	69
Dihydrocodeine	3170	63
Morphine-3-glucuronide	3785	53
Hydrocodone	7166	28
Dihydromorphine**	7393	27
Thebaine	7579	26
Hydromorphone	10768	19
n-Norcodeine	99264	2
Oxycodone	> 670000	< 0.3
Meperidine	> 670000	< 0.3
Fentanyl**	> 1000000	< 0.2

** Results were obtained on a **cobas c** 501 analyzer

Drug interference

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 0.5 % cross-reactivity.

Acetaminophen	Ibuprofen
Acetylsalicylic acid	Imipramine
Aminopyrine	Isoproterenol
Amitriptyline	Ketamine
Amobarbital	Lidocaine
d-Amphetamine	LSD[b)]
l-Amphetamine	Melanin
Ampicillin	Methadone
Ascorbic acid	*d*-Methamphetamine
Aspartame	*l*-Methamphetamine
Atropine	Methaqualone
Benzocaine	Methylphenidate
Benzoylecgonine (cocaine metabolite)	Methyprylon
Benzphetamine	Naloxone
Butabarbital	Naltrexone
Caffeine	Naproxen
Calcium hypochlorite	Niacinamide
Cannabidiol	Norethindrone
Chlordiazepoxide	*l*-Norpseudoephedrine
Chloroquine	Oxazepam
Chlorpheniramine	Penicillin G
Chlorpromazine	Pentobarbital
Cocaine	Phencyclidine
Dextromethorphan	Phenobarbital
Dextropropoxyphene	Phenothiazine
Diazepam	Phenylbutazone
Diphenhydramine	*d*-Phenylpropanolamine
Diphenylhydantoin	Phenylpropanolamine
Ecgonine	Procaine
Ecgonine methyl ester	Promethazine
d-Ephedrine	*d*-Pseudoephedrine
d,l-Ephedrine	*l*-Pseudoephedrine
l-Ephedrine	Quinidine
Epinephrine	Quinine
Erythromycin	Secobarbital
Estriol	Sulindac
Fenoprofen	Tetracycline
Furosemide	Δ^9 THC-9-carboxylic acid[c)]
Gentisic acid	Tetrahydrozoline
Glutethimide	Trifluoperazine
Guaiacol glycerol ether	Verapamil
Hydrochlorothiazide	

b) LSD was tested at 2500 ng/mL.

c) Δ9 THC-9-carboxylic acid was tested at 10000 ng/mL.

The cross-reactivity for rifampin was tested with the Opiates II assay. The results obtained were 11.0 % and 15.7 % for the 300 ng/mL and 2000 ng/mL cutoffs, respectively.

References

1 Karch SB, ed. Drug Abuse Handbook. Boca Raton, FL: CRC Press LLC 1998.

2 Substance Abuse and Mental Health Services Administration. Clinical Drug Testing in Primary Care. Technical Assistance Publication (TAP) 32. HHS Publication No. (SMA) 12-4668. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2012. Available from: https://store.samhsa.gov/sites/default/files/d7/priv/sma12-4668.pdf

3 Gerada C, Ashworth M. ABC of mental health. Addiction and dependence--I: Illicit drugs. BMJ 1997 Aug 2;315(7103):297-300.

4 Way EL, Adler TK. The pharmacological implications of the fate of morphine and its surrogates. Pharmacol Rev 1960 Dec;12:383-446.

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

6 Andersen G, Christrup L, Sjøgren P. Relationships among morphine metabolism, pain and side effects during long-term treatment: an update. J Pain Symptom Manage 2003 Jan;25(1):74-91.

7 SCDAT - Swiss Guidelines Committee for Drugs of Abuse Testing. Guidelines for Drugs of Abuse Testing. Vers EN 2021-03-25 (corrected 2022-12-6). Available from: https://www.scdat.ch/documents/SCDAT_Guidelines_EN_2021_03_25_corr20221206.pdf

8 Nummenmaa L, Tuominen L. Opioid system and human emotions. Br J Pharmacol 2018 Jul;175(14):2737-2749.

9 Pickworth WB, Welch P, Henningfield JE, et al. Opiate-induced pupillary effects in humans. Methods Find Exp Clin Pharmacol 1989 Dec;11(12):759-763.

10 Swegle JM, Logemann C. Management of common opioid-induced adverse effects. Am Fam Physician 2006 Oct 15;74(8):1347-1354.

11 Wood JD, Galligan JJ. Function of opioids in the enteric nervous system. Neurogastroenterol Motil 2004 Oct;16 Suppl 2:17-28.

12 Kiyatkin EA. Respiratory depression and brain hypoxia induced by opioid drugs: Morphine, oxycodone, heroin, and fentanyl. Neuropharmacology 2019 Jun;151:219-226.

13 European Monitoring Centre for Drugs and Drug Addiction. Drug Profiles Heroin. [accessed on Jan 9, 2024]. Available from: http://www.emcdda.europa.eu/publications/drug-profiles/heroin

14 Blum K. Handbook of Abusable Drugs. 1st ed. New York, NY: Gardner Press Inc 1984.

15 Jaffe JH. Drug addiction and drug abuse. In: Goodman L, Gilman A, eds. The Pharmacological Basis of Therapeutics. 4th ed. New York: Macmillan 1970.

16 Jannetto PJ, Bratanow NC, Clark WA, et al. Executive Summary: American Association of Clinical Chemistry Laboratory Medicine Practice Guideline-Using Clinical Laboratory Tests to Monitor Drug Therapy in Pain Management Patients. J Appl Lab Med 2018 Jan 1;2(4):489-526.

17 Taskinen S, Beck O, Bosch T, et al. European guidelines for workplace drug testing in urine. Drug Test Anal 2017 Jun;9(6):853-865.

18 Jarvis M, Williams J, Hurford M, et al. Appropriate Use of Drug Testing in Clinical Addiction Medicine. J Addict Med 2017 May/Jun;11(3):163-173.

19 Armbruster DA, Schwarzhoff RH, Pierce BL, et al. Method comparison of EMIT II and ONLINE with RIA for drug screening. J Forensic Sci 1993;38:1326-1341.

20 Armbruster DA, Schwarzhoff RH, Hubster EC, et al. Enzyme immunoassay, kinetic microparticle immunoassay, radioimmunoassay, and fluorescence polarization immunoassay compared for drugs-of-abuse screening. Clin Chem 1993;39:2137-2146.

21 Bates M, Brandle J, Casaretto E, et al. An Abuscreen immunoassay for opiates in urine on the COBAS MIRA automated analyzer. Amer Acad Forensic Sci. Abstract 1991;37(6):1000.

22 Toxicology and Drug Testing in the Clinical Laboratory; Approved Guideline. 2nd ed. (C52-A2). Clinical and Laboratory Standards Institute 2007;27:33.

23 Mandatory Guidelines for Federal Workplace Drug Testing Programs. Fed Regist 2017 Jan 23;82:7920-7970.

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

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

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

Symbols

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

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

CE 0123

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