MM

cobas®

Methadone Metabolite

Order information

REF	CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
05178576 190	DRI® Methadone Metabolite, 100 tests	System-ID 07 7440 5	Roche/Hitachi **cobas c** 311, **cobas c** 501/502
05393663 190	DRI Methadone Metabolite Calibrator 0 (1 x 10 mL)	Code 940	
05178584 190	DRI Methadone Metabolite Calibrator 100 (1 x 10 mL)	Code 936	
05178592 190	DRI Methadone Metabolite Calibrator 300 (1 x 10 mL)	Code 937	
05178606 190	DRI Methadone Metabolite Calibrator 500 (1 x 10 mL)	Code 938	
05178614 190	DRI Methadone Metabolite Calibrator 1000 (1 x 10 mL)	Code 939	
05218225 190	DRI Methadone Metabolite Control Set 100 Positive Control 125 ng/mL (1 x 10 mL) Negative Control 75 ng/mL (1 x 10 mL)		
05218233 190	DRI Methadone Metabolite Control Set 300 Positive Control 375 ng/mL (1 x 10 mL) Negative Control 225 ng/mL (1 x 10 mL)		
04908856 160[a]	Open/Close tool (5 pieces)		

a) Catalog number is for USA only. Open/Close tool is available upon request in other countries.

English

System information

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

MM1Q: ACN 449: for qualitative assay, 100 ng/mL

MM3Q: ACN 455: for qualitative assay, 300 ng/mL

MM1S: ACN 460: for semiquantitative assay, 100 ng/mL

MM3S: ACN 504: for semiquantitative assay, 300 ng/mL

For **cobas c** 502 analyzer:

MM1Q: ACN 8449: for qualitative assay, 100 ng/mL

MM3Q: ACN 8455: for qualitative assay, 300 ng/mL

MM1S: ACN 8460: for semiquantitative assay, 100 ng/mL

MM3S: ACN 8504: for semiquantitative assay, 300 ng/mL

Intended use

DRI Methadone Metabolite assay (MM) is an in vitro diagnostic test for the qualitative and semiquantitative detection of methadone metabolite (2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine or EDDP) in human urine on Roche/Hitachi **cobas c** systems at cutoff concentrations of 100 ng/mL 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).

DRI Methadone Metabolite 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.

Tests for methadone metabolite cannot distinguish between abused drugs and certain prescribed medications. Certain foods or medications may interfere with tests for methadone metabolite and cause false positive results.

Summary

Methadone is a synthetic opiate that effectively suppresses the craving for heroin without the euphoric effects of heroin. Methadone is commonly used in treatment facilities to detoxify and maintain heroin addicts. Methadone treatment compliance is essential and can be effectively monitored by urine screening of methadone and its metabolite.

The mechanism of methadone metabolism is commonly understood. Once administered, methadone is quickly metabolized by the liver into normethadone by N-demethylation. Normethadone is rarely detected, because it readily dehydrates to form EDDP,[2,3] the primary metabolite of methadone. Further demethylation of EDDP forms 2-ethyl-5-methyl-3,3-diphenyl-1-pyrroline (EMDP), the secondary metabolite of methadone, which is present in lower concentrations.[4]

Various immunoassay techniques are currently available for methadone compliance monitoring.[5,6] However, these tests measure only the parent drug, i.e., methadone, and thus are subject to “false positives” from addicts who add a portion of their methadone directly into the urine sample. As a result, confirmation of the presence of EDDP by thin layer chromatography (TLC) or gas chromatography (GC) is often required. Both TLC and GC methods are laborious and subject to considerable interference.[6] An immunoassay that detects the presence of EDDP in urine makes possible the widespread testing for compliance and rules out the possibility of adding methadone to urine in clinics where unsupervised urine collections are permitted.[7]

Test principle

The assay utilizes liquid ready-to-use reagents and calibrators.[8] The assay uses specific antibodies that can detect EDDP in human urine without cross-reactivity to the parent drug methadone. The assay is based on competition between a drug labeled with glucose-6-phosphate dehydrogenase (G6PDH) and free drug from the sample for a fixed number of specific antibody binding sites. In the presence of free drug from the sample, the free drug occupies the antibody binding sites, allowing the drug-labeled G6PDH to interact with the substrate, resulting in enzyme activity. In the absence of free drug from the sample, the specific antibody binds the drug labeled with G6PDH and causes a decrease in enzyme activity. This phenomenon creates a direct relationship between drug concentration in urine and enzyme activity. This enzyme activity is determined spectrophotometrically at 340 nm by measuring its ability to convert nicotinamide adenine dinucleotide (NAD) to NADH.

Reagents - working solutions

R1 Anti-EDDP antibody (mouse monoclonal), glucose-6-phosphate (G6P), and nicotinamide adenine dinucleotide (NAD) in Tris buffer with sodium azide as a preservative

R2 EDDP derivative labeled with glucose-6-phosphate dehydrogenase (G6PDH) in Tris buffer with sodium azide as a preservative

Precautions and warnings

For in vitro diagnostic use.
Exercise the normal precautions required for handling all laboratory reagents.
Reagents from different kit lots must not be interchanged. Reagents within kit lots have been matched to ensure optimum test performance.
Disposal of all waste material should be in accordance with local guidelines.
Safety data sheet available for professional user on request.

For USA: For prescription use only.

Reagent preparation and cobas c pack MULTI assembly

Reagent handling

Ready for use

Labeling the **cobas c** *pack MULTI*

Turn the barcode labeled side of a new **cobas c** pack MULTI toward you. Affix the supplied MM barcode label directly over the existing barcode label.

MM

Methadone Metabolite

Filling the **cobas c** *pack MULTI*

1. Turn the **cobas c** pack MULTI toward you as shown above.
2. Position A of the **cobas c** pack is now in the center, position B on the left side, position C on the right side of the **cobas c** pack.
3. Unscrew the screw cap of the bottle in position B on the left side of the **cobas c** pack MULTI using the Open/Close tool.
4. Pour the content of bottle 1 (18 mL) into the opened bottle of the **cobas c** pack (position B).
5. Close the bottle tightly using the Open/Close tool.
6. Unscrew the screw cap of the bottle in position C on the right side of the **cobas c** pack MULTI using the Open/Close tool.
7. Pour the content of bottle 2 (9 mL) into the opened bottle of the **cobas c** pack (position C).
8. Close the bottle tightly using the Open/Close tool.
9. Leave position A empty.

The MM **cobas c** pack is now ready for use.

NOTE: Solutions must be at the reagent compartment storage temperature of the analyzer before performing assays.

Note

Use only the **cobas c** *pack MULTI. Always use a new* **cobas c** *pack MULTI when preparing fresh reagent. Never reuse accessories designed for single use, as this may result in reagent contamination and could affect test results. If the* **cobas c** *pack MULTI bottles are not filled correctly, this may result in faulty reagent pipetting and could cause erroneous results.*

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

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 within the pH range of 4-11 are suitable for testing with this assay. 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.[9]

For prolonged storage, freezing of the sample is recommended.

Centrifuge highly turbid specimens before 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*.[10]

CAUTION: Specimen dilutions should only be used to interpret results of Calc.?, Samp.?, and >Abs 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.

Three barcode labels: one to overlabel the existing barcode of the **cobas c** pack MULTI. Two extra labels are supplied if needed.
cobas c pack MULTI
Funnels

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.

Applications for urine

Deselect Automatic Rerun for these applications in the Utility menu, Application screen, Range tab.

cobas c 311 **test definition - 100 ng/mL and 300 ng/mL cutoff assays**

	Semiquantitative	Qualitative
Assay type	Rate A	Rate A
Reaction time / Assay points	10 / 28-34	10 / 28-34
Wavelength (sub/main)	415/340 nm	415/340 nm
Reaction direction	Increase	Increase
Unit	ng/mL	mAbs
Reagent pipetting		Diluent (H_2O)
R1	120 µL	–
R3	40 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	35.0 µL	–	–
Decreased	35.0 µL	–	–
Increased	35.0 µL	–	–

cobas c 501/502 **test definition - 100 ng/mL and 300 ng/mL cutoff assays**

	Semiquantitative	Qualitative
Assay type	Rate A	Rate A
Reaction time / Assay points	10 / 42-49	10 / 42-49
Wavelength (sub/main)	415/340 nm	415/340 nm
Reaction direction	Increase	Increase
Unit	ng/mL	mAbs
Reagent pipetting		Diluent (H_2O)
R1	120 µL	–
R3	40 µL	–

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	35.0 µL	–	–
Decreased	35.0 µL	–	–
Increased	35.0 µL	–	–

MM

Methadone Metabolite

cobas®

Calibration

Calibrators	*Semiquantitative applications*
	100 ng/mL and 300 ng/mL cutoff assays
	S1: DRI Methadone Metabolite Calibrator 0
	S2: DRI Methadone Metabolite Calibrator 100
	S3: DRI Methadone Metabolite Calibrator 300
	S4: DRI Methadone Metabolite Calibrator 500
	S5: DRI Methadone Metabolite Calibrator 1000
	0, 100, 300, 500, 1000 ng/mL
	Qualitative applications
	100 ng/mL cutoff assay
	S1: DRI Methadone Metabolite Calibrator 100
	100 ng/mL
	300 ng/mL cutoff assay
	S1: DRI Methadone Metabolite Calibrator 300
	300 ng/mL
	The drug concentrations of the calibrators have been verified by GC/MS.
Calibration K Factor	For the qualitative applications, enter the K Factor as positive 1000 into the Calibration menu, Status screen, Calibration Result window.
Calibration mode	*Semiquantitative applications*
	Result Calculation Mode (RCM)[b]
	Qualitative applications
	Linear
Calibration frequency	Full (semiquantitative) or blank (qualitative) calibration • every 14 days • after reagent lot change • as required following quality control procedures

b) See Results section

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 DRI Methadone Metabolite Control Set 100 and 300 have been verified by GC/MS.

The control intervals and limits should be adapted to each laboratory’s individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

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.

For the semiquantitative assay, the analyzer computer constructs a calibration curve from absorbance measurements of the standards using a 4 parameter logit-log fitting function (RCM). The logit-log function fits a smooth line through the data points. The analyzer computer uses absorbance measurements of samples to calculate drug or drug metabolite concentration by interpolation of the logit-log fitting function.

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 greater than that of the highest calibrator. Make an appropriate dilution of the sample using the 0 ng/mL calibrator and rerun the sample. 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.
NOTE: If a result of >Abs alarm is obtained, the cause is either the presence of a high concentration of a 340 nm light absorbing compound or the presence of a high concentration of the analyte in the sample (see "Limitations - interference" section). Make an appropriate dilution of the sample using the 0 ng/mL calibrator and rerun the sample. When running in the semiquantitative mode, multiply the result by the dilution factor. In case of a near cutoff result, once the dilution factor is applied, the result should be assessed in terms of dilution and accuracy of the assay.

Dilutions should only be used to interpret results of Calc.?, Samp.?, and >Abs alarms, or when estimating concentration in preparation for GC/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.

Confirm all preliminary positive results by another method.

Limitations - interference

See the "Analytical specificity" section of this document for information on substances tested with this assay. There is the possibility that other substances and/or factors, especially substances that absorb light at 340 nm, may interfere with the test and cause >Abs alarms or erroneous results (e.g., technical or procedural errors). Samples flagged with >Abs alarms should be manually diluted (see "Results" section).

A preliminary positive result with this assay indicates the presence of methadone metabolite in urine. It does not measure the level of intoxication.

The potential effect of endogenous and exogenous urine substances and pH on the recovery of methadone metabolite using the DRI Methadone Metabolite assay was assessed by spiking known amounts of potentially interfering substances into the negative and positive levels (± 25 % of cutoff) for both cutoffs. The compounds were determined to not interfere with the assay if the rate of each negative sample was below its cutoff rate, and if all samples were recovered within 20 % error of their expected concentrations. No interference was observed, on a Roche/Hitachi 917 analyzer, by the addition of the compounds up to the concentrations listed below.

Qualitative (NEG/POS)		100 ng/mL Cutoff		300 ng/mL Cutoff	
Compound	**Concentration**	**Neg Level**	**Pos Level**	**Neg Level**	**Pos Level**
Acetaminophen	100 µg/mL	NEG	POS	NEG	POS
Acetone	1 g/dL	NEG	POS	NEG	POS
Ascorbic Acid	250 mg/dL	NEG	POS	NEG	POS
Aspirin	100 µg/mL	NEG	POS	NEG	POS
Caffeine	100 µg/mL	NEG	POS	NEG	POS
Creatinine	500 mg/dL	NEG	POS	NEG	POS
Ethanol	1 g/dL	NEG	POS	NEG	POS
Galactose	10 mg/dL	NEG	POS	NEG	POS
γ-Globulin	500 mg/dL	NEG	POS	NEG	POS

Qualitative (NEG/POS)		100 ng/mL Cutoff		300 ng/mL Cutoff	
Compound	**Concentration**	**Neg Level**	**Pos Level**	**Neg Level**	**Pos Level**
Glucose	3 g/dL	NEG	POS	NEG	POS
Hemoglobin	150 mg/dL	NEG	POS	NEG	POS
Human serum albumin	500 mg/dL	NEG	POS	NEG	POS
Ibuprofen	100 µg/mL	NEG	POS	NEG	POS
Oxalic Acid	100 mg/dL	NEG	POS	NEG	POS
pH Range	4-11	NEG	POS	NEG	POS
Riboflavin	7.5 mg/dL	NEG	POS	NEG	POS
Sodium Chloride	900 mg/dL	NEG	POS	NEG	POS
Specific Gravity Range	1.004-1.035	NEG	POS	NEG	POS
Urea	1.25 g/dL	NEG	POS	NEG	POS

Semiquantitative (ng/mL)		100 ng/mL Cutoff		300 ng/mL Cutoff	
Compound	**Concentration**	**Neg Level**	**Pos Level**	**Neg Level**	**Pos Level**
Acetaminophen	100 µg/mL	74 (NEG)	128 (POS)	229 (NEG)	357 (POS)
Acetone	1 g/dL	76 (NEG)	127 (POS)	229 (NEG)	358 (POS)
Ascorbic Acid	250 mg/dL	60 (NEG)	110 (POS)	214 (NEG)	343 (POS)
Aspirin	100 µg/mL	74 (NEG)	128 (POS)	222 (NEG)	353 (POS)
Caffeine	100 µg/mL	76 (NEG)	130 (POS)	231 (NEG)	362 (POS)
Creatinine	500 mg/dL	81 (NEG)	131 (POS)	226 (NEG)	355 (POS)
Ethanol	1 g/dL	74 (NEG)	126 (POS)	223 (NEG)	349 (POS)
Galactose	10 mg/dL	69 (NEG)	125 (POS)	220 (NEG)	358 (POS)
γ-Globulin	500 mg/dL	75 (NEG)	129 (POS)	230 (NEG)	368 (POS)
Glucose	3 g/dL	75 (NEG)	126 (POS)	223 (NEG)	361 (POS)
Hemoglobin	150 mg/dL	85 (NEG)	141 (POS)	247 (NEG)	388 (POS)
Human serum albumin	500 mg/dL	80 (NEG)	131 (POS)	236 (NEG)	374 (POS)
Ibuprofen	100 µg/mL	73 (NEG)	127 (POS)	222 (NEG)	350 (POS)
Oxalic Acid	100 mg/dL	74 (NEG)	128 (POS)	227 (NEG)	359 (POS)
pH Range	4-11	60 (NEG)	123 (POS)	219 (NEG)	350 (POS)
Riboflavin	7.5 mg/dL	76 (NEG)	128 (POS)	228 (NEG)	355 (POS)
Sodium Chloride	900 mg/dL	63 (NEG)	119 (POS)	217 (NEG)	347 (POS)
Specific Gravity Range	1.004-1.035	74 (NEG)	124 (POS)	218 (NEG)	346 (POS)

Semiquantitative (ng/mL)		100 ng/mL Cutoff		300 ng/mL Cutoff	
Compound	**Concentration**	**Neg Level**	**Pos Level**	**Neg Level**	**Pos Level**
Urea	1.25 g/dL	73 (NEG)	123 (POS)	219 (NEG)	343 (POS)

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 Roche/Hitachi **cobas c** systems. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is not required.

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

Expected values

Qualitative assay

Results of this assay distinguish preliminary positive (≥ 100 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 a Roche/Hitachi analyzer are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined in an internal protocol by running 6 replicates of each level of control and cutoff calibrator. The samples were measured in random order, twice a day, for 5 days, for a total of 10 runs (n = 60). The following results were obtained on a Roche/Hitachi **cobas c** 501 analyzer.

Semiquantitative precision - 100 ng/mL			
Repeatability	*Mean ng/mL*	*SD ng/mL*	*CV %*
Level 1	70	1.9	2.7
Level 2	97	2.5	2.6
Level 3	125	2.9	2.3

Intermediate precision	*Mean ng/mL*	*SD ng/mL*	*CV %*
Level 1	70	2.4	3.4
Level 2	97	2.8	2.9
Level 3	125	3.1	2.5

Qualitative precision - 100 ng/mL			
Cutoff (100)	Number tested	Correct results	Confidence level
0.75x	60	60	> 90 % negative reading
1.25x	60	60	> 90 % positive reading

Semiquantitative precision - 300 ng/mL			
Repeatability	*Mean ng/mL*	*SD ng/mL*	*CV %*
Level 1	235	4.2	1.8
Level 2	316	5.2	1.6
Level 3	377	5.0	1.3

Intermediate precision	*Mean ng/mL*	*SD ng/mL*	*CV %*
Level 1	235	5.5	2.3
Level 2	316	7.4	2.3
Level 3	377	6.4	1.7

Qualitative precision - 300 ng/mL			
Cutoff (300)	Number tested	Correct results	Confidence level
0.75x	60	60	> 90 % negative reading
1.25x	60	60	> 90 % positive reading

Limit of Blank

4.2 ng/mL

The Limit of Blank was determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A requirements.

The Limit of Blank is the 95th percentile value from n ≥ 20 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

Accuracy

Qualitative assay

A total of 190 urine samples were assayed with the DRI Methadone Metabolite assay on the Roche/Hitachi 917 and the **cobas c** 501 analyzers. A sensitivity of 99.1 % (105 out of 106 preliminary positive samples) and a specificity of 98.8 % (83 out of 84 negative samples) were observed between the two analyzers.

100 ng/mL cutoff			
		cobas c 501 analyzer	
		+	-
Roche/Hitachi 917 analyzer	+	105	1
	-	1	83

A total of 190 urine samples were assayed with the DRI Methadone Metabolite assay on the Roche/Hitachi 917 and the **cobas c** 501 analyzers. A sensitivity of 98.5 % (65 out of 66 preliminary positive samples) and a specificity of 98.4 % (122 out of 124 negative samples) were observed between the two analyzers.

300 ng/mL cutoff			
		cobas c 501 analyzer	
		+	-
Roche/Hitachi 917 analyzer	+	65	1
	-	2	122

Semiquantitative assay

A total of 190 urine samples were assayed with the DRI Methadone Metabolite assay on the Roche/Hitachi 917 and the **cobas c** 501 analyzers. A sensitivity of 99.1 % (106 out of 107 preliminary positive samples) and a specificity of 100 % (83 out of 83 negative samples) were observed between the two analyzers.

100 ng/mL cutoff			
		cobas c 501 analyzer	
		+	-
Roche/Hitachi 917 analyzer	+	106	1
	-	0	83

A total of 190 urine samples were assayed with the DRI Methadone Metabolite assay on the Roche/Hitachi 917 and the **cobas c** 501 analyzers. A sensitivity of 98.6 % (68 out of 69 preliminary positive samples) and a specificity of 100 % (121 out of 121 negative samples) were observed between the two analyzers.

300 ng/mL cutoff			
		cobas c 501 analyzer	
		+	-
Roche/Hitachi 917 analyzer	+	68	1
	-	0	121

Analytical specificity

The cross-reactivity of parent drug, metabolites, and drugs commonly found in specimens was evaluated by adding known amounts of each substance to methadone metabolite-free urine. A compound producing negative results, compared to both the 100 ng/mL and 300 ng/mL cutoff calibrators, was considered to have no cross-reactivity.

Methadone, its metabolite, and structurally related compounds produced a negative result, on a Roche/Hitachi 917 analyzer, at the concentrations listed below.

Compound	**Concentration (ng/mL)**
Methadone	500000
EMDP	200000
LAAM HCl	100000
Nor-LAAM HCl	10000

Drug interference

Structurally unrelated compounds and/or concurrently used drugs produced a negative result, on a Roche/Hitachi 917 analyzer, at the concentrations listed below.

Compound	**Concentrations (ng/mL)**
Acetaminophen	1000000
6-Acetyl morphine	500000
Acetylsalicylic acid	1000000
Amitriptyline	100000
Amoxicillin	500000
Amphetamine	1000000
Benzoylecgonine	1000000
Caffeine	100000
Captopril	500000
Carbamazepine	500000
Chlordiazepoxide	100000
Chlorpromazine	100000
Cimetidine	500000
Clomipramine	100000
Cocaine	200000
Codeine	1000000
Desipramine	1000000
Dextromethorphan	30000
Diazepam	30000

Dihydrocodeine	1000000
Diphenhydramine	500000
Disopyramide	1000000
Doxepine	200000
Doxylamine	500000
Ephedrine	2000000
Fentanyl	200000
Fluoxetine	1000000
Fluphenazine	500000
Heroin	1000000
Hydrocodone	200000
Hydromorphone	200000
Ibuprofen	1000000
Imipramine	1000000
Ketamine	400000
Levorphanol	200000
Levothyroxine	500000
Maprotiline	1000000
Meperidine	1000000
d-Methamphetamine	100000
l-Methamphetamine	100000
Metronidazole	250000
Morphine	1000000
Nalbuphine	1000000
Naloxone	3000000
Naltrexone	3000000
Norcodeine	1000000
Normorphine	1000000
Nortriptyline	500000
Oxazepam	500000
Oxycodone	500000
Phencyclidine	50000
Phenobarbital	1000000
Phentermine	1000000
Promethazine	100000
Propoxyphene	50000
Ranitidine	500000
Salicyluric Acid	500000
Secobarbital	1000000
Talwin	500000
11-Nor-Δ^9-THC-9-COOH	10000
Thebaine	100000
Thioridazine	150000
Tramadol	500000

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10 Mandatory Guidelines for Federal Workplace Drug Testing Programs. Fed Regist 2008 Nov 25;73:71858-71907.

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.

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 after reconstitution or mixing
GTIN	Global Trade Item Number

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