MM

Methadone Metabolite

cobas®

Drug abuse testing

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	COBAS INTEGRA 400 plus COBAS INTEGRA 800
05393663 190	DRI Methadone Metabolite Calibrator 0 (1 x 10 mL)		
05178584 190	DRI Methadone Metabolite Calibrator 100 (1 x 10 mL)		
05178592 190	DRI Methadone Metabolite Calibrator 300 (1 x 10 mL)		
05178606 190	DRI Methadone Metabolite Calibrator 500 (1 x 10 mL)		
05178614 190	DRI Methadone Metabolite Calibrator 1000 (1 x 10 mL)		
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

Test MM1S, test ID 0-384 for semiquantitative assay, 100 ng/mL

Test MM3S, test ID 0-385 for semiquantitative assay, 300 ng/mL

Test MM1Q, test ID 0-382 for qualitative assay, 100 ng/mL

Test MM3Q, test ID 0-383 for qualitative assay, 300 ng/mL

Intended use

DRI Methadone Metabolite assay (MM) is an in vitro diagnostic test for the semiquantitative and qualitative detection of methadone metabolite (2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine or EDDP) in human urine at cutoff concentrations of 100 ng/mL and 300 ng/mL on COBAS INTEGRA systems.

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

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

Precautions and warnings

Pay attention to all precautions and warnings listed in Section 1 / Introduction of this Method Manual.

For USA: For prescription use only.

Reagent preparation and cobas c pack MULTI assembly

Reagent handling

MM

Methadone Metabolite

cobas®

Drug abuse testing

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.

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
COBAS INTEGRA 400 plus analyzer	
On-board in use at 10-15 °C	8 weeks
COBAS INTEGRA 800 analyzer	
On-board in use at 8 °C	8 weeks

The on-board in use stability period begins at the time of **cobas c** pack puncture. Do not freeze reagents. Reagents that have been frozen should be discarded.

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 samples do not require any special handling or pretreatment, but an effort should be made to keep pipetted samples free of gross debris. Samples within a 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 HIGH ABS alarms or as an estimation for GC/MS and 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

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.

Applications for urine

COBAS INTEGRA 400 plus test definition

	100 ng/mL and 300 ng/mL cutoffs	
	Semiquantitative	*Qualitative*
Measuring mode	Absorbance	Absorbance
Abs. calculation mode	Kinetic	Kinetic
Reaction mode	R1-S-SR	R1-S-SR
Reaction direction	Increase	Increase
Reaction start	SR	SR
Wavelength A/B	340/409 nm	340/409 nm
Test range	0-1000 ng/mL	0-4000 *MM1Q* 0-2000 *MM3Q*
Calc. first/last	39/44	39/44
Unit	ng/mL	

Pipetting parameters

		Diluent (H_2O)
R1	120 µL	5 µL
Sample	50 µL	5 µL
SR	50 µL	5 µL
Total volume	235 µL	

COBAS INTEGRA 800 test definition

	100 ng/mL and 300 ng/mL cutoffs	
	Semiquantitative	*Qualitative*
Measuring mode	Absorbance	Absorbance
Abs. calculation mode	Kinetic	Kinetic
Reaction mode	R1-S-SR	R1-S-SR
Reaction direction	Increase	Increase
Reaction start	SR	SR
Wavelength A/B	340/409 nm	340/409 nm
Test range	0-1000 ng/mL	0-4000 *MM1Q* 0-2000 *MM3Q*
Calc. first/last	53/62	53/62
Unit	ng/mL	

Pipetting parameters

		Diluent (H_2O)
R1	120 µL	5 µL
Sample	50 µL	5 µL
SR	50 µL	5 µL
Total volume	235 µL	

Calibration

Calibrators

Semiquantitative applications

MM1S, 0-384; MM3S, 0-385

DRI Methadone Metabolite Calibrator 0,
DRI Methadone Metabolite Calibrator 100,
DRI Methadone Metabolite Calibrator 300,
DRI Methadone Metabolite Calibrator 500,
and
DRI Methadone Metabolite Calibrator 1000
0, 100, 300, 500, 1000 ng/mL
(MMSQ, system-ID 07 7444 8)

Qualitative applications

MM1Q, 0-382

DRI Methadone Metabolite Calibrator 0
0 ng/mL
and
DRI Methadone Metabolite Calibrator 100
100 ng/mL
(100 cutoff, MMQ1, system-ID 07 7441 3)
For qualitative applications, the cutoff of 100 ng/mL is assigned a value of 1000.

MM3Q, 0-383

DRI Methadone Metabolite Calibrator 0
0 ng/mL
and
DRI Methadone Metabolite Calibrator 300
300 ng/mL
(300 cutoff, MMQ3, system-ID 07 7442 1)
For qualitative applications, the cutoff of 300 ng/mL is assigned a value of 1000.

Calibration mode

Semiquantitative applications
Logit/Log 4
Qualitative applications
Linear regression

Calibration replicate: Duplicate recommended

Calibration interval: COBAS INTEGRA 400 plus analyzer: Each lot, every 14 days, and as required following quality control procedures

COBAS INTEGRA 800 analyzer: Each lot, every 14 days, and as required following quality control procedures

A calibration curve is generated using the calibrators. Calibrators must be placed from the highest concentration first to the lowest last on the CAL/QC rack. This curve is retained in memory by the COBAS INTEGRA systems and recalled for later use.

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

Quality control

Quality control

100 ng/mL cutoff
DRI Methadone Metabolite Control Set 100
Positive Control 125 ng/mL
(MM1P, system-ID 07 7449 9)
Negative Control 75 ng/mL
(MM1N, system-ID 07 7450 2)

300 ng/mL cutoff
DRI Methadone Metabolite Control Set 300
Positive Control 375 ng/mL
(MM3P, system-ID 07 7451 0)
Negative Control 225 ng/mL
(MM3N, system-ID 07 7452 9)

Control sequence: User defined

Control after calibration: Recommended

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

COBAS INTEGRA systems report results with the following test flags:

Semiquantitative result reporting

MM1S (100 ng/mL cutoff)		
Flag	COBAS INTEGRA	Value range
No flag	Negative	< 100 ng/mL
<TEST RNG	Negative	< 0 ng/mL
>TEST RNG	Positive	> 1000 ng/mL
POS 100	Positive	≥ 100 ng/mL

Value ranges listed above are based on a cutoff value of 100 ng/mL.

MM3S (300 ng/mL cutoff)		
Flag	COBAS INTEGRA	Value range
No flag	Negative	< 300 ng/mL
<TEST RNG	Negative	< 0 ng/mL
>TEST RNG	Positive	> 1000 ng/mL
POS 300	Positive	≥ 300 ng/mL

Value ranges listed above are based on a cutoff value of 300 ng/mL.

Qualitative result reporting

MM1Q (100 ng/mL cutoff)		
Flag	COBAS INTEGRA	Value range
No flag	Negative	< 1000
<TEST RNG	Negative	< 0
>TEST RNG	Positive	> 4000
POS 1000	Positive	≥ 1000

Value ranges above are based on assigning the cutoff of 100 ng/mL a value of 1000.

MM3Q (300 ng/mL cutoff)		
Flag	COBAS INTEGRA	Value range
No flag	Negative	< 1000
<TEST RNG	Negative	< 0
>TEST RNG	Positive	> 2000
POS 1000	Positive	≥ 1000

Value ranges above are based on assigning the cutoff of 300 ng/mL a value of 1000.

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 HIGH 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 HIGH ABS alarms or when estimating concentration in preparation for GC/MS.

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 HIGH ABS alarms or erroneous results (e.g., technical or procedural errors). Samples flagged with HIGH 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
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)

Semiquantitative (ng/mL)		100 ng/mL Cutoff		300 ng/mL Cutoff	
Compound	**Concentration**	**Neg Level**	**Pos Level**	**Neg Level**	**Pos Level**
Specific Gravity Range	1.004-1.035	74 (NEG)	124 (POS)	218 (NEG)	346 (POS)
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 COBAS INTEGRA analyzers. Refer to the CLEAN Method Sheet for further instructions and for the latest version of the Extra wash cycle list.

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

Specific performance data

Representative performance data on the COBAS INTEGRA analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined in an internal protocol using a series of methadone metabolite calibrator and controls in replicates of 6, twice a day, for 5 days. The following results were obtained on a COBAS INTEGRA 800 analyzer.

Semiquantitative precision - 100 ng/mL cutoff			
Repeatability	Mean ng/mL	SD ng/mL	CV %
Level 1 (75 ng/mL)	64	2	3.1
Level 2 (100 ng/mL)	91	3	3.2
Level 3 (125 ng/mL)	117	4	3.1

Intermediate precision	Mean ng/mL	SD ng/mL	CV %
Level 1 (75 ng/mL)	64	3	5.3
Level 2 (100 ng/mL)	91	5	5.3
Level 3 (125 ng/mL)	117	5	4.5

Semiquantitative precision - 300 ng/mL cutoff			
Repeatability	Mean ng/mL	SD ng/mL	CV %
Level 1 (225 ng/mL)	219	4	1.9
Level 2 (300 ng/mL)	294	6	2.0
Level 3 (375 ng/mL)	351	7	1.9

Intermediate precision	Mean ng/mL	SD ng/mL	CV %
Level 1 (225 ng/mL)	219	6	2.7
Level 2 (300 ng/mL)	294	8	2.6
Level 3 (375 ng/mL)	351	9	2.7

Qualitative precision ***100 ng/mL cutoff*** ***300 ng/mL cutoff***			
Cutoff (x)	Number tested	Correct results	Confidence level
0.75x	60	60	> 95 % negative reading
1.25x	60	60	> 95 % positive reading

Limit of Blank

5.8 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 ≥ 21 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 145 urine samples were assayed with the DRI Methadone Metabolite assay on the Roche/Hitachi 917 and the COBAS INTEGRA 800 analyzers. A sensitivity of 98.8 % (85 out of 86 preliminary positive samples) and a specificity of 100 % (59 out of 59 negative samples) were observed between the two analyzers.

100 ng/mL cutoff			
		COBAS INTEGRA 800 analyzer	
		+	-
Roche/Hitachi 917 analyzer	+	85	1
	-	0	59

A total of 145 urine samples were assayed with the DRI Methadone Metabolite assay on the Roche/Hitachi 917 and the COBAS INTEGRA 800 analyzers. A sensitivity of 100 % (48 out of 48 preliminary positive samples) and a specificity of 99 % (96 out of 97 negative samples) were observed between the two analyzers.

300 ng/mL cutoff			
		COBAS INTEGRA 800 analyzer	
		+	-
Roche/Hitachi 917 analyzer	+	48	0
	-	1	96

Semiquantitative assay

A total of 145 urine samples were assayed with the DRI Methadone Metabolite assay on the Roche/Hitachi 917 and the COBAS INTEGRA 800 analyzers. A sensitivity of 97.7 % (84 out of 86 preliminary positive samples) and a specificity of 100 % (59 out of 59 negative samples) were observed between the two analyzers.

100 ng/mL cutoff			
		COBAS INTEGRA 800 analyzer	
		+	-
Roche/Hitachi 917 analyzer	+	84	2
	-	0	59

A total of 145 urine samples were assayed with the DRI Methadone Metabolite assay on the Roche/Hitachi 917 and the COBAS INTEGRA 800 analyzers. A sensitivity of 100 % (49 out of 49 preliminary positive samples) and a specificity of 100 % (96 out of 96 negative samples) were observed between the two analyzers.

300 ng/mL cutoff			
		COBAS INTEGRA 800 analyzer	
		+	-
Roche/Hitachi 917 analyzer	+	49	0
	-	0	96

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 the 100 ng/mL cutoff calibrator, 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	100 ng/mL Cutoff 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-COOH	10000
Thebaine	100000
Thioridazine	150000
Tramadol	500000

Any modification of the instrument as set forth in this labeling requires validation by the laboratory.

References

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8 Rubenstein KE, Schneider RS, Ullman EF. "Homogenous Enzyme Immunoassay: A New Immunochemical Technique". Biochem Biophis Res Commun 1972;47:846.

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

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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