ACET2

cobas®

ONLINE TDM Acetaminophen Gen.2

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
06769942190	06769942500	ONLINE TDM Acetaminophen Gen.2 (150 tests)	System-ID 07 7551 7	**cobas c** 311, **cobas c** 501/502, COBAS INTEGRA 400 plus

Materials required (but not provided):

		cobas c 311, **cobas c** 501/502	COBAS INTEGRA 400 plus
07007515190	ACET2 calibrator (1 x 2 mL)	Code 670	System-ID 07 7564 9
04521536190	TDM Control Set Level I (2 x 5 mL) Level II (2 x 5 mL) Level III (2 x 5 mL)	 Code 310 Code 311 Code 312	 System-ID 07 6900 2 System-ID 07 6901 0 System-ID 07 6902 9
04489357190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	n.a.
20756350322	Diluent NaCl 9 %	n.a.	System-ID 07 5635 0

English

Intended use

In vitro diagnostic test for the quantitative determination of acetaminophen overdose in serum and plasma on **cobas c** and COBAS INTEGRA systems.

Summary

Acetaminophen measurements performed with this assay, in human serum and plasma, are used as an aid in identifying acetaminophen intoxication, determining the need for treatment with N-Acetylcysteine to minimize toxic drug effects.

Acetaminophen is a widely used analgesic and antipyretic found in a number of over-the-counter and prescription products. The pharmacologic actions of acetaminophen are related to its nonselective inhibition of cyclooxygenase enzymes (COX), resulting in decreased production of prostaglandins, mediators of inflammation, pain (low to moderate), and fever.[1] In normal doses, acetaminophen is safe and effective, but when consumed in overdose quantities it may cause severe liver and, less frequently, kidney damage, or death.[1] The patient may have mild or no symptoms early after acute overdose of acetaminophen. Other than what can be found in the patient's history, the only reliable early diagnostic indicator is provided by a quantitative measurement of the serum acetaminophen level.[2] The prophylactic antidote, N-acetylcysteine, is highly effective in preventing liver damage if administered 8 to 10 hours after acetaminophen ingestion; if administered 12 to 16 hours after ingestion it is less effective, but should still be given because it improves survival in patients with hepatic failure.[2] Clinical evidence of liver and kidney damage is usually delayed for 24 hours or more after ingestion, well after the time that N-acetylcysteine can be effectively administered.[2] Therefore, assessment of serum acetaminophen concentration is one of the key elements to ensure appropriate and timely overdose management.[3,4,5]

Test principle

The assay is based on a homogeneous enzyme immunoassay technique used for the quantitative analysis of acetaminophen in human serum or plasma. The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for antibody binding sites. Enzyme activity decreases upon binding to the antibody, so the drug concentration in the sample can be measured in terms of enzyme activity. Active enzyme converts oxidized nicotinamide adenine dinucleotide (NAD^+) to NADH, resulting in an absorbance change that is measured spectrophotometrically. Endogenous serum G6PDH does not interfere because the coenzyme functions only with the bacterial (*Leuconostoc mesenteroides*) enzyme employed in the assay.

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.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Warning

H317	May cause an allergic skin reaction.
H412	Harmful to aquatic life with long lasting effects.

Prevention:

P261	Avoid breathing mist or vapours.
P273	Avoid release to the environment.
P280	Wear protective gloves.

Response:

P333 + P313	If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364	Take off contaminated clothing and wash it before reuse.

Disposal:

P501	Dispose of contents/container to an approved waste disposal plant.

Product safety labeling follows EU GHS guidance.
Contact phone: all countries: +49-621-7590

Reagent handling

Ready for use

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: Collect serum using standard sampling tubes.
Plasma: K_2- or K_3-EDTA, or lithium heparinized plasma.

Sample collection tubes containing separating gel have not been verified for use.

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.

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

Stability:	24 hours capped at RT
	7 days capped at 2-8 °C
	6 months capped at -20 °C (± 5 °C)

Freeze only once.

Invert thawed specimens several times prior to testing.

Do not induce foaming of specimens.

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.

Calculation

The systems automatically calculate the analyte concentration of each sample.

Conversion factor: µg/mL x 6.62 = µmol/L[6]

Expected values

Normal therapeutic doses of acetaminophen result in serum concentrations of 10-30 µg/mL (66-199 µmol/L) in healthy adults.[7]

The concentration of acetaminophen in serum or plasma depends on the time of drug ingestion; concomitant drug therapy; sample condition; time of sample collection; and individual variations in absorption, distribution, biotransformation, and excretion. These parameters must be considered when interpreting results.

In acute acetaminophen overdose, a single serum or plasma level determination, plotted on the Rumack-Matthew nomogram[8,9], provides a good indication of whether overdose therapy is required.[2]

Alcoholics are at risk for toxicity at lower doses. Enhanced susceptibility to toxic effects has also been reported in persons receiving long-term anticonvulsant therapy and patients taking isoniazid.[2]

Toxic manifestations have been observed at serum concentrations > 100 µg/mL (> 662 µmol/L), however the toxic range is generally reported at > 200 µg/mL (> 1324 µmol/L). Toxic concentrations can be more effectively related to post dose interval; > 200, > 100, and > 50 µg/mL (> 1324, > 662, and > 331 µmol/L) serum concentrations correspond to toxic concentrations at 4, 8, and 12 hours post dose, respectively.[9]

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

Expected values reflect the data and information provided in the reference and do not necessarily represent therapeutic recommendations and/or dosage instructions. For therapeutic recommendations and dosage instructions refer to applicable guidelines and the full prescription information of the drug.

cobas c systems

System information

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

ACET2: ACN 172

For **cobas c** 502 analyzers:

ACET2: ACN 8172

Reagents - working solutions

R1 Anti-acetaminophen antibody (sheep polyclonal), G6P, NAD, bovine serum albumin, preservatives and stabilizers

R2 Acetaminophen labeled with bacterial G6PDH, Tris buffer, preservatives, bovine serum albumin, and stabilizers

R1 is in position A and R2 is in position C. Position B contains H_2O for technical reasons.

Storage and stability

Shelf life at 2-8° C:	See expiration date on **cobas c** pack label
Do not freeze.	
On-board in use and refrigerated on the analyzer:	12 weeks

Application for serum and plasma

cobas c 311 **test definition**

Assay type	Rate-A		
Reaction time / Assay points	10 / 14-26		
Wavelength (sub/main)	415 / 340 nm		
Reaction direction	Increase		
Units	µg/mL (µmol/L)		
Reagent pipetting		Diluent (H_2O)	
R1	100 µL	–	
R2	50 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	2 µL	30 µL	120 µL
Increased	2 µL	–	–

cobas c 501/502 **test definition**

Assay type	Rate-A		
Reaction time / Assay points	10 / 21-39		
Wavelength (sub/main)	415 / 340 nm		
Reaction direction	Increase		
Units	µg/mL (µmol/L)		
Reagent pipetting		Diluent (H_2O)	
R1	100 µL	–	
R2	50 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2 µL	–	–
Decreased	2 µL	30 µL	120 µL
Increased	2 µL	–	–

Calibration

Calibrators	S1: H_2O
	S2-S6: ACET2 calibrator, dilution by instrument
Calibration mode	RCM
Calibration frequency	full calibration - after reagent lot change - as required following quality control procedures

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against USP reference standards. The calibrator is prepared to contain a known quantity of acetaminophen in buffer.

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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 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.

Limitations - interference

Criterion: Interference is defined as not significant when recovery observed is within ± 1 µg/mL (6.6 µmol/L) of initial value at an acetaminophen level of approximately 5 µg/mL (33.1 µmol/L) and recovery within ± 10 % of initial value at an acetaminophen level of approximately 30 µg/mL (199 µmol/L).

Icterus:[10] No significant interference up to an I index of 30 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 510 µmol/L or 30 mg/dL).

Hemolysis:[10] No significant interference up to an H index of 800 (approximate hemoglobin concentration: 496 µmol/L or 800 mg/dL).

Lipemia (Intralipid):[10] No significant interference up to an L index of 400. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

No significant interference from triglycerides from Intralipid up to 650 mg/dL if the L-index is below 400.

There is the possibility that other substances and/or factors may interfere with the test and cause unreliable 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. 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 required in certain cases.

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

Measuring range

5-200 µg/mL (33.1-1324 µmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 5.

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 1.5 µg/mL (9.9 µmol/L)

Limit of Detection = 3 µg/mL (20 µmol/L)

Limit of Quantitation = 5 µg/mL (33 µmol/L)

The Limit of Blank and Limit of Detection were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 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 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a total error of 20 %. It has been determined using low concentration acetaminophen samples.

Specific performance data

Representative performance data on a **cobas c** analyzer are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP5-A2 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). The following results were obtained on the **cobas c** 501 analyzer:

Repeatability	**Mean**		**SD**		**CV**
	µg/mL	µmol/L	µg/mL	µmol/L	%
Control 1	15.3	101	0.4	3	2.5
Control 2	34.9	231	0.9	6	2.5
Control 3	106	700	2	15	2.2
HS 1	7.7	50.9	0.2	1	2.9
HS 2	73.2	485	1.7	11	2.3
HS 3	130	859	4	23	2.7
HS 4	168	1115	4	28	2.5
HS 5	184	1221	4	28	2.3

Intermediate precision	**Mean**		**SD**		**CV**
	µg/mL	µmol/L	µg/mL	µmol/L	**%**
Control 1	15.3	101	0.5	3	3.2
Control 2	34.9	231	1.0	7	2.8
Control 3	106	700	3	21	3.0
HS 1	7.4	48.9	0.3	2	3.5
HS 2	73.2	485	1.9	13	2.7
HS 3	130	859	4	28	3.2
HS 4	168	1115	5	35	3.2
HS 5	185	1225	6	36	3.0

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

Method comparison

Acetaminophen values for human serum samples obtained on a **cobas c** 501 analyzer (y) were compared with those determined using the Emit® tox™ Acetaminophen assay on Olympus AU5400 analyzer (x).

Sample size (n) = 105

Deming Regression Weighted[12]

y = 1.02x - 0.699 µg/mL

r = 0.997

The sample concentrations were between 5.2 and 198 µg/mL (34.4 and 1310 µmol/L).

Acetaminophen values for human serum samples obtained on a **cobas c** 501 analyzer (y) were compared with those determined using LC-MS/MS (x).[13]

Sample size (n) = 105

Deming Regression Weighted[12]

y = 0.984x - 0.116 µg/mL

r = 0.996

The sample concentrations were between 5.2 and 198 µg/mL (34.4 and 1310 µmol/L).

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

Analytical specificity

The following compounds were tested for cross-reactivity:

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Compound	Compound Concentration [µg/mL]	Concentration Acet-aminophen [µg/mL]	% Cross-reactivity
Acetaminophen cysteine	100	6.1	0.5
Acetaminophen glucuronide	1000	5.2	n.d.*
Acetaminophen mercapturate	300	5.4	0.2
Acetaminophen sulfate	200	6.1	n.d.*
Cysteine	1300	5.8	n.d.*
N-Acetylcysteine	1663	6.3	n.d.*
Phenacetin	500	6.7	0.5

Compound	Compound Concentration [µg/mL]	Concentration Acet-aminophen [µg/mL]	% Cross-reactivity
Acetaminophen cysteine	100	29.2	-0.3
Acetaminophen glucuronide	1000	25.4	-0.1
Acetaminophen mercapturate	300	25.9	0.2
Acetaminophen sulfate	200	27.8	0.1
Cysteine	1300	29.0	n.d.*
N-Acetylcysteine	1663	28.5	n.d.*
Phenacetin	500	29.3	1.3

* n.d. = not detectable

The following 24 drugs were tested for interference. No significant interference with the assay was found.

Acetyl cysteine	Phenylbutazone
Acetylsalicylic acid	Rifampicin
Ampicillin-sodium	Theophylline
Ascorbic acid	Amitriptylline
Cefoxitin	Caffeine
Cyclosporine	Codeine
Doxycycline	Diazepam
Heparin	Methionine
Ibuprofen	Phenylephrine
Levodopa	Propoxyphene
Methyldopa + 1.5 H_2O	Salicylate
Metronidazole	Secobarbital

COBAS INTEGRA systems

System information

ACET2: Test ID 0-040.

Reagents - working solutions

R1 Anti-acetaminophen antibody (sheep polyclonal), G6P, NAD, bovine serum albumin, preservatives and stabilizers

SR Acetaminophen labeled with bacterial G6PDH, Tris buffer, preservatives, bovine serum albumin, and stabilizers

R1 is in position A and SR is in position C. Position B contains H_2O for technical reasons.

Storage and stability

Shelf life at 2-8 °C	See expiration date on **cobas c** pack label
Do not freeze.	
On board in use at 10-15 °C	12 weeks

Application for serum and plasma

Test definition

Measuring mode	Absorbance
Abs. calculation mode	Kinetic
Reaction mode	R1-S-SR
Reaction direction	Increase
Wavelength A	340/409 nm
Calc. first/last	42/59
Unit	µg/mL

Pipetting parameters

		Diluent (H_2O)
R1	100 µL	
SR	50 µL	
Sample	3 µL	5 µL
Total volume	158 µL	

Calibration

Calibrator	ACET2 calibrator, dilution performed automatically by instrument Enter the assigned ACET2 calibrator values for all 6 calibrator points stated in the ACET2 Calibrator Value Sheet.
Calibration mode	logit/log 4
Calibration replicate	Duplicate recommended
Calibration interval	After reagent lot change, every 4 weeks, and as required following quality control procedures.

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against USP reference standards. The calibrator is prepared to contain a known quantity of acetaminophen in buffer.

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 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.

Limitations - interference

Criterion: Interference is defined as not significant when recovery observed is within ± 1 µg/mL (6.6 µmol/L) of initial value at an acetaminophen level of approximately 5 µg/mL (33.1 µmol/L) and recovery within ± 10 % of initial value at an acetaminophen level of approximately 30 µg/mL (199 µmol/L).

Icterus:[10] No significant interference up to an I index of 30 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 510 µmol/L or 30 mg/dL).

Hemolysis:[10] No significant interference up to an H index of 800 (approximate hemoglobin concentration 496 µmol/L or 800 mg/dL).

Lipemia (Intralipid):[10] No significant interference up to an L Index of 400. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

No significant interference from triglycerides from Intralipid up to 650 mg/dL if the L index is below 400.

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 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.

Limits and ranges

Measuring range

5-200 µg/mL (33.1-1324 µmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 5.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation

Limit of Blank = 1.5 µg/mL (9.9 µmol/L)

Limit of Detection = 3 µg/mL (20 µmol/L)

Limit of Quantitation = 5 µg/mL (33 µmol/L)

The Limit of Blank and Limit of Detection were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 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 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a total error of 20 %. It has been determined using low concentration acetaminophen samples.

Specific performance data

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

Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP5-A3 requirements. The following results were obtained on the COBAS INTEGRA 400 plus analyzer with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days):

Repeatability	*Mean µg/mL (µmol/L)*	*SD µg/mL (µmol/L)*	*CV %*
Control 1	15.8 (105)	0.6 (4)	3.8
Control 2	34.2 (226)	1.2 (8)	3.4
Control 3	107 (708)	4 (28)	4.0
HS 1	7.6 (50.0)	0.4 (2.6)	5.1
HS 2	77.1 (510)	2.6 (17)	3.3
HS 3	139 (920)	6 (39)	4.2
HS 4	184 (1218)	7 (48)	3.9
HS 5	193 (1278)	7 (47)	3.7

Intermediate precision	*Mean µg/mL (µmol/L)*	*SD µg/mL (µmol/L)*	*CV %*
Control 1	15.8 (105)	1.0 (7)	6.5
Control 2	35.5 (235)	2.4 (16)	6.6
Control 3	111 (735)	8 (50)	6.8
HS 1	7.6 (50.0)	0.5 (3.1)	6.1
HS 2	78.1 (517)	4.7 (31)	6.0
HS 3	138 (914)	8 (53)	5.8
HS 4	185 (1225)	13 (85)	7.0
HS 5	193 (1278)	12 (77)	6.0

Method comparison

Acetaminophen values for human serum samples obtained on a COBAS INTEGRA 400 plus analyzer (y) were compared with those determined with the Emit® tox™ Acetaminophen assay on Olympus AU5400 analyzer (x).

Sample size (n) = 106

Deming Regression Weighted[12]

y = 1.01x - 0.957 µg/mL

r = 0.993

The sample concentrations were between 5.1 and 198 µg/mL (34.0 and 1311 µmol/L).

Acetaminophen values for human serum samples obtained on a COBAS INTEGRA 400 plus analyzer (y) were compared with those determined with LC-MS/MS (x).[13]

Sample size (n) = 106

Deming Regression Weighted[12]

y = 0.973x - 0.380 µg/mL

r = 0.993

The sample concentrations were between 5.1 and 198 µg/mL (34.0 and 1311 µmol/L).

Analytical specificity

The following compounds were tested for cross-reactivity:

Compound	Compound Conc. [µg/mL]	Conc. Acetaminophen [µg/mL]	Cross-reactivity %
Acetaminophen cysteine	100	7.1	0.4
Acetaminphen glucuronide	1000	5.8	ND
Acetaminophen mercapturate	300	5.5	0.1
Acetaminophen sulfate	200	6.7	ND
Cysteine	1300	6.4	ND
N-Acetylcysteine	1663	6.4	ND
Phenacetin	500	7.2	0.6

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Compound	Compound Conc. [µg/mL]	Conc. Acetaminophen [µg/mL]	Cross-reactivity %
Acetaminophen cysteine	100	29.6	1.0
Acetaminphen glucuronide	1000	26.0	ND
Acetaminophen mercapturate	300	25.1	0.2
Acetaminophen sulfate	200	29.9	0.2
Cysteine	1300	29.0	0.1
N-Acetylcysteine	1663	30.3	ND
Phenacetin	500	32.4	1.4

ND = not detectable

Tests were performed on 24 drugs. No significant interference with the assay was found.

Acetyl cysteine	Phenylbutazone
Acetylsalicylic acid	Rifampicin
Ampicillin-sodium	Theophylline
Ascorbic acid	Amitriptyline
Cefoxitin	Caffeine
Cyclosporine	Codeine
Doxycycline	Diazepam
Heparin	Methionine
Ibuprofen	Phenylephrine
Levodopa	Propoxyphene
Methyldopa + 1.5 H_2O	Salicylate
Metronidazole	Secobarbital

References

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8 Rumack BH, Matthew H. Acetaminophen Poisoning and Toxicity. Pediatrics 1975 Jun;55(6):871-876.

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13 Bylda C, Thiele R, Kobold U, et al. Simultaneous quantification of acetaminophen and structurally related compounds in human serum and plasma. Drug Test Anal 2014 May;6(5):451-460 (JCTLM C11RMP8).

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.

The Summary of Safety & Performance Report can be found here: https://ec.europa.eu/tools/eudamed

Symbols

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

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.

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

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CE 0123

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