

REF	CONTENT	System-ID	Analyzers on which cobas c pack can be used
20753602 122	Abuscreen OnLine Propoxyphene (200 tests)	07 5360 2	COBAS INTEGRA 400 plus COBAS INTEGRA 800
03304671 190	Preciset DAT Plus I CAL 1-6 (6 × 5 mL)		
03304698 190	C.f.a.s. DAT Qualitative Plus (6 × 5 mL)		
04590856 190	C.f.a.s. DAT Qualitative Plus Clinical (3 × 5 mL)		
03312950 190	Control Set DAT I PreciPos DAT Set I (2 × 10 mL) PreciNeg DAT Set I (2 × 10 mL)		
04500873 190	Control Set DAT Clinical PreciPos DAT Clinical (2 × 10 mL) PreciNeg DAT Clinical (2 × 10 mL)		

English

System information

Test PPXS, test-ID 0-508 for semiquantitative assay

Test PPXQL, test-ID 0-608 for qualitative assay

Test PPXQC, test-ID 0-361 for qualitative assay; using C.f.a.s. DAT Qualitative Plus Clinical

Intended use

Propoxyphene (PPX) is an in vitro diagnostic test for the semiquantitative and qualitative detection of propoxyphene and its metabolites in human urine at a cutoff concentration of 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. Measurements obtained by this device are used in the diagnosis of propoxyphene use or abuse and do not measure a level of toxicity. 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).

Propoxyphene 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 judgement should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

Summary

Propoxyphene, either as a hydrochloride or napsylate salt, is administered orally and is used in the treatment of mild to moderate pain disorders.^{2,3,4,5} Propoxyphene is structurally similar to methadone, binds to the opioid receptors, and has similar analgesic effects to those seen with morphine-like opioids. When administered, it is less potent than codeine and when given in combination with aspirin or acetaminophen produces a synergistic effect.^{2,3,4,5} Propoxyphene may cause some mild adverse side effects including gastrointestinal pain, vertigo, drowsiness, nausea, constipation, and anorexia. The drug is irritating when administered either intravenously or subcutaneously and abuse by these routes results in damage to veins and soft tissues.^{2,5}

Propoxyphene by itself or in conjunction with other drugs, including alcohol, can be toxic and cause fatal results.^{5,6} In addition, other toxic effects have been reported such as: pulmonary edema, respiratory depression, cardiotoxicity, hallucinations, and convulsions.^{2,4} Once propoxyphene is ingested it is absorbed from the gastrointestinal tract and is metabolized in the liver. The metabolism is extensive with the primary route of metabolism being N-demethylation to form N-norpropoxyphene.⁷ Norpropoxyphene is one-fourth to one-half as active an analgesic as propoxyphene but it tends to accumulate in plasma due to a longer half-life.⁴ The primary route of release of these metabolites from the human body is through urine and modulations of urinary propoxyphene excretion by urinary pH have been reported.⁸

This assay not only detects propoxyphene, but also has cross-reactivity to the major metabolite norpropoxyphene.^{9,10}

Test principle

Kinetic interaction of microparticles in a solution (KIMS)^{9,10} as measured by changes in light transmission.

In the absence of sample drug, free antibody binds to drug-microparticle conjugates 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 particle-bound drug derivative for free 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.

Reagents - working solutions

Sample Diluent (SD)	Buffer containing stabilizer and 0.09 % sodium azide.
Antibody Reagent (AB)	Propoxyphene antibody (goat polyclonal) in buffer and 0.09 % sodium azide.
Microparticle Reagent (MP)	Conjugated propoxyphene derivative microparticles in buffer and 0.09 % sodium azide.

SD is in position A, AB is in position B and MP is in position C.

Pipetting Sequence

COBAS INTEGRA 400 plus analyzer	R1 = AB R2 = SD R3 (SR) = MP
COBAS INTEGRA 800 analyzer	R1 = SD R2 = AB R3 (SR) = MP

Precautions and warnings

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

For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

Reagent handling

COBAS INTEGRA 400 plus analyzer

Mix all new (non-punctured) **cobas c** packs for 1 minute on a cassette mixer before loading on the analyzer. All in-use **cobas c** packs must also be mixed in the same manner at the beginning of each week (once a week).

COBAS INTEGRA 800 analyzer

Ready for use. After **cobas c** pack puncture, the analyzer automatically mixes the reagent for 1 minute and for half a minute during Begin of Day.

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 83 days

COBAS INTEGRA 800 analyzer

On-board in use at 8 °C 83 days

| 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 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.¹¹

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*.¹²

Caution: Specimen dilutions should only be used 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.

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.

Application for urine

| COBAS INTEGRA 400 plus test definition

	<i>Semiquantitative</i>	<i>Qualitative</i>
Measuring mode	Absorbance	Absorbance
Abs. calculation mode	Endpoint	Endpoint
Reaction mode	R1-R2-S-SR	R1-R2-S-SR
Reaction direction	Increase	Increase
Reaction start	SR	SR
Wavelength A	520 nm	520 nm
Test range	0-600 ng/mL	0-2000
with postdilution	0-6000 ng/mL	
Postdilution factor	10 recommended ^{a)}	No
Calc. first/last	49/63	49/63
Unit	ng/mL	

a) For use when estimating concentration in preparation for GC/MS analysis.

Pipetting parameters

		Diluent (H ₂ O)
R1	53 µL	8 µL
R2	50 µL	15 µL
Sample	5 µL	10 µL
SR	15 µL	8 µL
Total volume	164 µL	

COBAS INTEGRA 800 test definition

	<i>Semiquantitative</i>	<i>Qualitative</i>
Measuring mode	Absorbance	Absorbance

Abs. calculation mode	Endpoint	Endpoint
Reaction mode	R1-R2-S-SR	R1-R2-S-SR
Reaction direction	Increase	Increase
Reaction start	SR	SR
Wavelength A	520 nm	520 nm
Test range	0-600 ng/mL	0-2000
with postdilution	0-6000 ng/mL	
Postdilution factor	10 recommended ^{b)}	No
Calc. first/last	44/78	44/78
Unit	ng/mL	

b) For use when estimating concentration in preparation for GC/MS analysis.

Pipetting parameters

		Diluent (H ₂ O)
R1	50 µL	8 µL
R2	53 µL	5 µL
Sample	3.75 µL	3.75 µL
SR	13 µL	6 µL
Total volume	142.5 µL	

Calibration

Calibrators	<i>Semiquantitative application</i>
<i>PPXS, 0-508</i>	Preciset DAT Plus I calibrators, CAL1-4 0, 150, 300, 600 ng/mL propoxyphene (DATS9, system-ID 07 6798 0)
	<i>Qualitative applications</i>
<i>PPXQL, 0-608</i>	Preciset DAT Plus I calibrators, CAL 1 0 ng/mL or deionized water and Preciset DAT Plus I calibrators, CAL 3 ^{c)} or C.f.a.s. DAT Qualitative Plus 300 ng/mL (DATQ1, system-ID 07 6744 1)
<i>PPXQC, 0-361</i>	Preciset DAT Plus I or II ^{d)} calibrators, CAL 1 0 ng/mL or deionized water and C.f.a.s. DAT Qualitative Plus Clinical 300 ng/mL (DATQ5, system-ID 07 6880 4)
	For qualitative applications, the cutoff value is assigned as 1000.

c) Do not use Preciset DAT Plus I, CAL 3 if calibrating the Opiates 300/2000 qualitative 2000 ng/mL assay (test OP2QL, test-ID 0-410).

d) Preciset DAT Plus II, CAL 1, while generally not required for the calibration of Propoxyphene, may be used as an alternative 0 ng/mL level for DATQ5, system-ID 07 6880 4.

Calibration mode	<i>Semiquantitative application</i>
	Linear interpolation
	<i>Qualitative applications</i>
	Linear regression
Calibration replicate	Duplicate recommended
Calibration interval	COBAS INTEGRA 400 plus analyzer: Each lot, every 12 weeks, and as required following quality control procedures COBAS INTEGRA 800 analyzer: Each lot, every 6 weeks, and as required following quality control procedures

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

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 system and recalled for later use.

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

Quality control

Quality control	Control Set DAT I
	PreciPos DAT Set I (DAT1P, system-ID 07 6753 0)
	PreciNeg DAT Set I (DAT1N, system-ID 07 6754 9)
	or
	Control Set DAT Clinical
	PreciPos DAT Clinical (DATCP, system-ID 07 6879 0)
	PreciNeg DAT Clinical (DATCN, system-ID 07 6878 2)

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 Control Set DAT I and Clinical 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

Flag	COBAS INTEGRA	Value range
No flag	Negative	< 300 ng/mL
<TEST RNG	Negative	< 0 ng/mL
>TEST RNG	Positive	> 600 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

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.

Semiquantitative result reporting

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: When using the post-dilution function (1:10 dilution), to ensure the sample was not over-diluted, the diluted result must be at least half the

analyte cutoff value times 10. If the diluted result falls below half the analyte cutoff value times 10, 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 as an estimation for GC/MS.

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 propoxyphene in urine. It does not measure the level of intoxication.

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 propoxyphene controls in replicates of 20, once a day, for 5 days on 2 analyzers. The following results were obtained on the COBAS INTEGRA 700 analyzer.

Semiquantitative precision

Repeatability	Mean ng/mL	SD ng/mL	CV %
Level 1	151	10.4	6.9
Level 2	247	11.2	4.6
Level 3	313	14.5	4.6
Level 4	399	14.5	3.6

Intermediate precision	Mean ng/mL	SD ng/mL	CV %
Level 1	151	12.7	8.4
Level 2	247	14.3	5.8
Level 3	313	19.4	6.2
Level 4	399	18.0	4.5

Qualitative precision

Cutoff (x)	Number tested	Correct results	Confidence level
0.8x	200	200	> 95 % negative reading
1.2x	200	200	> 95 % positive reading

Lower detection limit of the test

10 ng/mL

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 2 standard deviations above that of the zero calibrator (zero calibrator + 2 SD, repeatability, n = 40).

Accuracy

100 urine samples, obtained from a clinical laboratory where they screened negative in a drug test panel by another technology, were evaluated for

Abuscreen OnLine Propoxyphene

propoxyphene on the COBAS INTEGRA systems. All 100 clinical samples were negative relative to the 300 ng/mL cutoff.

50 urine samples, obtained from clinical laboratories where they screened preliminary positive by a commercially available enzyme immunoassay and confirmed positive for propoxyphene by GC/MS, were also evaluated on a COBAS INTEGRA 400 analyzer. All 50 samples were positive with the COBAS INTEGRA Propoxyphene assay relative to the 300 ng/mL cutoff.

		GC/MS	
		+	-
COBAS INTEGRA 400 analyzer	+	50	0
	-	0	0

Analytical specificity

The specificity of the COBAS INTEGRA Propoxyphene 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 the 300 ng/mL propoxyphene assay cutoff.

Compound	Approximate ng/mL equivalent to 300 ng/mL of propoxyphene	Approximate percent cross-reactivity
Norpropoxyphene	436	69
<i>p</i> -Hydroxypropoxyphene	836	36
Methadone	890208	0.03

Drug interference

The following compounds were added to aliquots of pooled normal human urine at a concentration of 100000 ng/mL. None of these compounds gave values in the assay that were equal to or greater than 0.1 % cross reactivity.

Acetaminophen	Ketamine
Acetylsalicylic acid	Lidocaine
Aminopyrine	LSD
Amitriptyline	MDA
Amobarbital	MDMA
<i>d</i> -Amphetamine	Melanin
<i>l</i> -Amphetamine	Meperidine
Ampicillin	<i>d</i> -Methamphetamine
Ascorbic acid	<i>l</i> -Methamphetamine
Aspartame	Methapyrilene
Atropine	Methaqualone
Benzocaine	Methylphenidate
Benzoylcegonine (cocaine metabolite)	Methypylon
Benzphetamine	Morphine sulfate
(±)Brompheniramine	Naloxone
Butabarbital	Naltrexone
Caffeine	Naproxen
Calcium hypochlorite	Niacinamide
Chlordiazepoxide	Nordiazepam
Chloroquine	Norethindrone
(+)Chlorpheniramine	<i>l</i> -Norpseudoephedrine
(±)Chlorpheniramine	Nortriptyline
Chlorpromazine	Oxazepam
Clemastine	Penicillin G
	Pentobarbital

Cocaine	Phencyclidine
Codeine	<i>β</i> -Phenethylamine
Cyclizine	Phenobarbital
Desipramine	Phenothiazine
Dextromethorphan	Phentermine
Diazepam	Phenylbutazone
Diphenhydramine	<i>d</i> -Phenylpropanolamine
Diphenylhydantoin	Phenylpropanolamine
Dopamine	Phenyltoloxamine
Doxylamine	Procaine
Ecgonine	Promethazine
Ecgonine methyl ester	<i>d</i> -Pseudoephedrine
Ephedrine	<i>l</i> -Pseudoephedrine
<i>d</i> -Ephedrine	Procyclidine
<i>l</i> -Ephedrine	Quinidine
Epinephrine	Quinine
Erythromycin	Secobarbital
Estriol	Sulindac
17-Ethynylestradio1	Tetracycline
Fenoprofen	Δ^9 THC-9-carboxylic acid
Furosemide	Tetrahydrozoline
Gentisic acid	Thioridazine
Glutethimide	Trifluoperazine
Guaiacol glycerol ether	<i>d,l</i> -Trihexyphenidyl
Hydrochlorothiazide	Trimipramine
<i>p</i> -Hydroxyamphetamine	Tripelennamine
Ibuprofen	Tyramine
Imipramine	Verapamil
Isoproterenol	

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

References




- 1 Karch SB, ed. Drug Abuse Handbook. Boca Raton, FL: CRC Press LLC 1998.
- 2 Hardman JG, Limbird LE, Gilman A, eds. Goodman and Gilman's The Pharmacological Basis of Therapeutics. 10th ed. New York, NY: McGraw Hill Pub Co. 2001.
- 3 Nickander RC, Emmerson JL, Hynes MD, et al. Pharmacologic and toxic effects in animals of dextropropoxyphene and its major metabolite norpropoxyphene: A Review. Human Toxicol 1984;3:13S-36S.
- 4 Baselt RC. Disposition of Toxic Drugs and Chemicals in Man. 7th ed. Foster City, CA: Biomedical Publications 2004.
- 5 Miller RR. Propoxyphene: A Review. Am J Hosp Pharm 1977;34:413-423.
- 6 Finkle BS, Caplan YH, Garriott JC, et al. Propoxyphene in postmortem toxicology 1976-1978. J Forensic Sci 1981;26:739-757.
- 7 Due SL, Sullivan HR, McMahon RE. Propoxyphene: pathways of metabolism in man and laboratory animals. Biomed Mass Spectrum 1976;3:217-226.
- 8 Karkkainen S, Neuvonen PJ. Effect of oral charcoal and urine pH on dextropropoxyphene pharmacokinetics. Int J Clin Pharmacol Ther Toxicol 1985;23:219-225.

- 9 McNally AJ, Pilcher I, Wu R, et al. Evaluation of the OnLine Immunoassay for Propoxyphene: Comparison to EMIT II and GC-MS. J Anal Toxicol 1996;20:537-540.
- 10 Wu RS, McNally AJ, Pilcher IA, et al. Synthesis of new d-propoxyphene derivatives and the development of a microparticle-based immunoassay for the detection of propoxyphene and norpropoxyphene Bioconjug Chem 1997;8:385-390.
- 11 Toxicology and Drug Testing in the Clinical Laboratory; Approved Guideline. 2nd ed. (C52-A2). Clinical and Laboratory Standards Institute 2007;27:33.
- 12 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 (for USA: see <https://usdiagnostics.roche.com> for definition of symbols used):

	Contents of kit
	Volume after reconstitution or mixing
	Global Trade Item Number

FOR US CUSTOMERS ONLY: LIMITED WARRANTY

Roche Diagnostics warrants that this product will meet the specifications stated in the labeling when used in accordance with such labeling and will be free from defects in material and workmanship until the expiration date printed on the label. THIS LIMITED WARRANTY IS IN LIEU OF ANY OTHER WARRANTY, EXPRESS OR IMPLIED, INCLUDING ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR PARTICULAR PURPOSE. IN NO EVENT SHALL ROCHE DIAGNOSTICS BE LIABLE FOR INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES.

COBAS, COBAS C, COBAS INTEGRA, ABUSCREEN and PRECISET are trademarks of Roche.

All other product names and trademarks are the property of their respective owners.

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

© 2016, Roche Diagnostics



Roche Diagnostics GmbH, Sandhofer Strasse 116, D-68305 Mannheim
www.roche.com



Distribution in USA by:
 Roche Diagnostics, Indianapolis, IN
 US Customer Technical Support 1-800-428-2336