

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k043303

B. Purpose for Submission:

New submission because of modifications to the device.

C. Measurand:

Propoxyphene in urine

D. Type of Test:

Qualitative and Semi-Quantitative

KIMS Immunoassay (Kinetic Interaction of Microparticles in Solution)

E. Applicant:

Roche, Diagnostics

F. Proprietary and Established Names:

ONLINE DAT Propoxyphene Plus

G. Regulatory Information:

1. Regulation section:
862.3700, Enzyme Immunoassay, Propoxyphene
2. Classification: Class II
3. Product code: JXN
4. Panel: 91 (Toxicology)

H. Intended Use:

1. Intended use(s):
Refer to Indications for use.
2. Indication(s) for use:
Propoxyphene Plus is an in vitro diagnostic test for the qualitative and semi-quantitative detection of propoxyphene and its metabolites in human urine on the Roche Hitachi automated clinical chemistry family of analyzers at a cutoff of 300 ng/ml. Semi-quantitative 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.

Propoxyphene Plus screening test provides only a preliminary analytical test result. To confirm a presumptive screen positive result, a more specific alternate chemical method, such as gas chromatograph - mass spectrometer (GC/MS) should be used. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are obtained

The device is for in vitro diagnostic use.

3. Special conditions for use statement(s):

The assay is for Rx use.

Semi-quantitative results may be helpful in estimating the concentrations of drug(s) in samples to prepare dilutions for further GC/MS testing or to monitor quality control.

4. Special instrument requirements:

The assay is to be used on the Hitachi family of instruments.

Performance was demonstrated in this submission on the Hitachi 917 analyzer, although they are claiming the Hitachi family of analyzers.

I. Device Description:

This assay is a wet chemistry system, consisting of two reagents:

R1 Reagent: an antibody working solution, Propoxyphene antibody (goat polyclonal) in buffer with BSA and 0.09% NaAzide.

R2 Reagent: the microparticle working solution, conjugated propoxyphene derivative microparticles in buffer and 0.09% NaAzide.

Previously cleared calibrators and controls are used with the assay.

Human Source Material: The sponsor indicates there are no human source materials in this device. Additionally, they have provided adequate documentation concerning the safety of the BSA component.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Abuscreen OnLine Propoxyphene Assay

2. Predicate 510(k) number(s):

k983700

3. Comparison with predicate:

Both devices are for measurement of the same analyte(s) in the same matrix, have the same intended use (for the qualitative and semi-quantitative use of

propoxyphene), utilize the same test methodology (KIMS) and cutoff concentration. Both are for use on automated analyzers.

The reagent formulations vary slightly between the two devices. The candidate has a lower sensitivity claim, i.e., 19 versus 40 ng/mL.

K. Standard/Guidance Document Referenced (if applicable):

None referenced

L. Test Principle:

The ONLINE DAT Propoxyphene Plus assay is based on the kinetic interaction of microparticles in a solution (KIMS technology). Assay measurement is based on measurable changes in light transmission related to the interaction of microparticles in a solution and the sample drug of interest, if present. Propoxyphene drug derivative is conjugated to microparticles in solution, and propoxyphene polyclonal antibody (goat) is solubilized in buffer. 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.

Negative Sample

drug-conjugated microparticles + free antibody = particle aggregates
(↑ absorbance)

Positive Sample

sample drug + drug-conjugated microparticle = particle aggregation inhibited
drug-conjugated microparticles + free antibody = particle aggregates

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

Performance was established on the Hitachi 917 analyzer unless otherwise noted.

a. *Precision/Reproducibility:*

The imprecision of the ONLINE DAT Propoxyphene Plus assay was determined by running a series of calibrators and controls in replicates of 20 per day for five days on a Hitachi 911 analyzer.

The results of the study are presented below. The numbers

appearing in the tables below, represent the median values for each level, chosen from one of the five days.

Within-run Imprecision (N=20)

Cals/Controls (ng/ml)	Semi-quantitative		Qualitative	
	Mean (ng/ml)	CV %	Mean (mAbs)	CV %
.50X (150)	173.0	5.0	515.3	2.8
.75X (225)	228.8	3.9	442.6	3.0
Cutoff (300)	308.6	3.2	358.9	3.0
1.25X (375)	392.5	3.0	303.5	2.7
1.5 X (450)	494.2	2.2	239.5	2.6

Day-to-day Imprecision (N=100)

Cals/Controls (ng/ml)	Semi-quantitative		Qualitative	
	Mean (ng/ml)	CV %	Mean (mAbs)	CV %
.50X (150)	173.7	5.4	523.0	3.2
.75X (225)	230.3	4.9	444.7	3.0
Cutoff (300)	306.3	3.7	362.2	3.4
1.25X (375)	390.5	4.0	299.4	3.0
1.5 X (450)	494.0	3.3	243.5	2.7

Near Cutoff Imprecision

Controls (ng/ml)	Number Tested	Correct Results
.75X (225)	100	100
1.25X (375)	100	100

b. Linearity/assay reportable range:

Although this is a semi-quantitative range, the precision study data demonstrates adequate accuracy for the claims being made, i.e., for estimating dilutions and for monitoring QC.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The sponsor makes no claims for traceability of their assay.

Calibrators and controls are required with this assay, and are specifically identified in the labeling. They are provided separately.

STABILITY

The sponsor has described the stability studies for their assay as follows:

Product shelf-life claims for the both reagents will be established based on real-time stability studies. At least one lot of reagent will be tested up to or exceeding the expiration date before commercializing the product.

Reagents are stored at 2 – 8 °C over the claimed shelf life. Each is tested at time 0, and at approximately 50%, 75% and 100% of the shelf life claim. Testing includes $\leq 5\%$ crossovers at the cutoff when tested at 0.75x and 1.25x relative to the 300 ng/ml cutoff.

Users are instructed to follow federal, state, and local guidelines concerning when to run external controls.

d. Detection limit:

Sensitivity of the assay is 18.7 ng/mL.

The limit of detection (or analytical sensitivity) of ONLINE DAT Propoxyphene Plus was performed by testing 21 replicates of the 0 ng/ml standard. Two standard deviations above the mean yields a limit of detection of 18.7 ng/ml propoxyphene.

e. Analytical specificity:

The percent cross-reactivity of structurally related compounds relative to the 300 ng/ml cutoff was estimated as follows. A linear regression line between two concentrations of a cross-reactant spiked into drug-free human urine which produced responses closely below and above the response by the propoxyphene 300 ng/ml cutoff was first generated. By interpolating against this line, the cross-reactant concentration which gave a response equal to that of the cutoff was then estimated. The percent cross-reactivity was calculated by dividing the propoxyphene cutoff concentration by the cross-reactant concentration, multiplied by 100.

**SPECIFICITY of STRUCTURALLY RELATED COMPOUNDS for
Propoxyphene Plus, 300 ng/mL Cutoff,
on the Roche/Hitachi 917 System**

COMPOUND	Concentrations Tested (ng/mL)	Roche/Hitachi 917 (ng/mL)	APPROXIMATE CROSS REACTIVITY	ng/mL Equivalent to 300 ng/mL Propoxyphene
p-Hydroxypropoxyphene	800	264	32.1%	933
	1200	372		
Methadone	100000	117	0.1%	>100,000 ng/mL
Norpropoxyphene	300	211	70.7%	424
	500	354		

Additionally, an extensive list (104 compounds) were prepared in aliquots of pooled normal human urine to yield a final concentration of 100,000 ng/ml. None of these compounds gave values in the assay that were greater than 0.133 % cross-reactivity or the assay cutoff.

Endogenous compounds were added to a drug free urine at appropriately challenging concentrations. These samples were then spiked to 300 ng/ml propoxyphene. Samples were tested and did not demonstrate any remarkable findings. They appear in the package insert.

There is the possibility that other substances and/or factors not listed above may interfere with the test and cause false results, e.g., technical or procedural errors.

f. Assay cut-off:

The identified cutoff concentration of the assay is commonly found in industry. There are no recommended cutoffs for this assay by the Substance Abuse and Mental Health Services Administration (SAMHSA).

2. Comparison studies:

a. Method comparison with GC/MS:

Because the candidate device was compared to values from a reference method, GC/MS, it was not necessary to compare to the predicate device.

Negative Comparison Study:

One hundred (100) urine samples were evaluated. They were obtained from a clinical laboratory where they had screened negative for propoxyphene by a commercially available screening assay (having the same cutoff concentration). Ten of the samples were

also confirmed negative by GC/MS. Of the 100 samples tested, all 100 were negative by the Propoxyphene Plus assay.

Positive Comparison Study:

Similarly, sixty-nine urine samples were obtained from a clinical laboratory where they were screened positive for propoxyphene using the same commercially available immunoassay. All of the samples were confirmed positive by GC/MS for propoxyphene and/or norpropoxyphene. All 69 samples were positive by the Propoxyphene Plus assay.

Cutoff Challenge:

Performance of the ONLINE DAT Propoxyphene Plus assay was challenged near the 300 ng/ml cutoff using positive clinical samples diluted to approximately +/- 25% of the cutoff with drug free urine.

Pooled Positive and Negative Comparison Studies and the Cutoff Challenge

Candidate Device Results	Negative by Samples	Near Cutoff Negative (Between 221-274 ng/mL)	Near Cutoff Positive (Between 316-382 ng/mL)	High Positive (greater than 431 ng/mL)
Positive	0	0	12	66
Negative	100	10	1	0

GC/MS values used to categorize samples in this table were determined by adding together in an unweighted fashion the propoxyphene and norpropoxephine found in the sample.

- b. *Matrix comparison:*
Not applicable. The assay is intended for only one sample matrix.
- 3. Clinical studies:
 - a. *Clinical Sensitivity:*
Not applicable. Clinical studies are not typically submitted for this device type.
 - b. *Clinical specificity:*
Not applicable. Clinical studies are not typically submitted for this device type.
 - c. Other clinical supportive data (when a. and b. are not applicable):
- 4. Clinical cut-off:
Not applicable.

5. Expected values/Reference range:

Not applicable. There are no recognized reference values for therapeutic or toxic levels of propoxyphene in urine.

N. Proposed Labeling:

The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.