

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

A. 510(k) Number:

K043211

B. Purpose for Submission:

New device

C. Measurand:

Barbiturate

D. Type of Test:

Quantitative; Kinetic interaction of microparticles in solution

E. Applicant:

Roche Diagnostics Corporation

F. Proprietary and Established Names:

ONLINE DAT Barbiturates Plus

G. Regulatory Information:

1. Regulation section:

21 CFR 862.3150; Barbiturate test system

2. Classification:

Class II

3. Product code:

DIS

4. Panel:

Toxicology (91)

H. Intended Use:

1. Intended use(s):

Barbiturates Plus (BAR P) is an in vitro diagnostic test for the qualitative and semiquantitative detection of barbiturates in human urine on automated clinical chemistry analyzers at a cutoff of 200 ng/mL. Semiquantitative test results may be obtained that permit laboratories to assess assay performance as part of a quality control program.

Barbiturates Plus provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GS/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

2. Indication(s) for use:

Barbiturates Plus is an in vitro diagnostic test for the qualitative and semi-quantitative detection of barbiturates in human urine on automated clinical chemistry analyzers at a cutoff of 200 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 and treatment of barbiturate use or overdose. Barbiturates Plus provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result.

3. Special conditions for use statement(s):

This product is for prescription use.

4. Special instrument requirements:

Roche/Hitachi 911/912/917/MODULAR (for qualitative assay): ACN 572
Roche/Hitachi 911/912/917/MODULAR (for semiquantitative assay): ACN 573
This assay is not for use on the MODULAR D modules.

I. Device Description:

The Barbiturates Plus assay consist of two bottles (antibody and diluent) that are combined to make R1 and one bottle for R2. R1 is the Antibody Working Solution, which contains secobarbital antibody (sheep polyclonal) in buffer with bovine serum albumin and sodium azide. R2 is the Microparticle Working Solution, which contains conjugated secobarbital derivative microparticles in buffer and sodium azide. These reagents are supplied in four different kit configurations (volumes supplied).

Additional barcode labels are also provided.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Abuscreen OnLine Barbiturates assay

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

K983698

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Qualitative and semiquantitative detection of barbiturates	Same
Sample	Urine	Same
Instruments	Hitachi 911/912/917/MODULAR P & DAT	Same
Methodology	Kinetic interaction of microparticles in a solution	Same
Reagents	Secobarbital polyclonal antibody in buffer; microparticles coated with conjugated secobarbital derivative in buffer	Same
Cutoff	200 ng/mL	Same

Differences		
Item	Device	Predicate
Sensitivity (Limit of Detection)	9 ng/mL	18 ng/mL

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

Replacement Reagent and Instrument Family Policy guidance

L. Test Principle:

ONLINE DAT Plus automated assays are based on the kinetic interaction of microparticles in a solution (KIMS) 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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The imprecision of the ONLINE DAT Barbiturates Plus assay was determined by running a series of calibrators and controls in replicates of 20 per day for five days on a Hitachi 917 analyzer. The following results were obtained for the 200 ng/mL cutoff.

Within-run Imprecision (N = 20)

Calibrators/Controls (ng/mL)	Semi-quantitative		Qualitative	
	Mean (ng/mL)	%CV	Mean (mAbs)	%CV
.50X (100)	103.9	3.2	270.3	1.6
.75X (150)	150.9	2.2	223.0	1.5
Cutoff (200)	204.2	1.9	186.0	1.7
1.25X (250)	257.3	2.2	156.4	1.4
1.5X (300)	339.6	1.9	126.9	1.4

Day-to-day Imprecision (N = 100)

Calibrators/Controls (ng/mL)	Semi-quantitative		Qualitative	
	Mean (ng/mL)	%CV	Mean (mAbs)	%CV
.50X (100)	103.2	7.1	271.9	1.7

.75X (150)	147.2	4.4	224.5	1.6
Cutoff (200)	199.9	2.9	185.0	1.6
1.25X (250)	251.8	2.9	156.3	1.6
1.5X (300)	334.9	2.6	126.9	1.5

Near Cutoff Imprecision

Controls (ng/mL)	Number Tested	Correct Results	Confidence Level
.75X (150)	100	100	>95% negative reading
1.25X (250)	100	100	>95% positive reading

b. *Linearity/assay reportable range:*

Not applicable

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

This method has been standardized against GC/MS.

d. *Detection limit:*

The limit of detection (or analytical sensitivity) of ONLINE DAT Barbiturates Plus is 9 ng/mL. This value represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying two standard deviations above the mean (n = 21) of the lowest standard.

e. *Analytical specificity:*

The specificity of Barbiturates Plus for some common barbiturates and structurally similar compounds was determined by generating inhibition curves for each of the compounds and determining the approximate quantity of each compound that is equivalent in assay reactivity to a secobarbital 200 ng/mL cutoff.

Compound	Approx. % Cross-reactivity
Cyclopentobarbital	101
Aprobarbital	93
Butalbital	71
Allobarbital	71
Butobarbital	37
Pentobarbital	36
Amobarbital	29
<i>p</i> -Hydroxyphenobarbital	22
Barbital	19
1,3-Dimethylbarbituric acid	11

Other common barbiturates and structurally similar compounds tested yielded <0.1 percent cross-reactivity.

Cross-reactivity with unrelated drugs was also evaluated. Eighty-nine (89) compounds were prepared in aliquots of pooled normal human urine to yield a final concentration of 100,000 ng/mL. None of the compounds gave values in the assay that were greater than 0.012% cross-reactivity.

f. Assay cut-off:

See Detection limit above.

2. Comparison studies:

a. Method comparison with predicate device:

See Other clinical supportive data below.

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Accuracy of the ONLINE DAT Barbiturates Plus assay at a 200 ng/mL cutoff was evaluated in method comparison studies between the Barbiturates Plus assay and GC/MS results.

One hundred (100) urine samples, obtained from a clinical laboratory where they screened negative in a drug test panel, were evaluated with Barbiturates Plus. Of the 100 samples evaluated, 100 were negative relative to the 200 ng/mL cutoff.

Fifty-four (54) urine samples, obtained from a clinical laboratory where they were screened positive for barbiturates by a commercially available immunoassay and subsequently confirmed positive by GC/MS for

phenobarbital and/or butalbital, were evaluated with Barbiturates Plus. Of the 54 samples evaluated, 54 were positive relative to the 200 ng/mL cutoff.

In addition, 10 samples were diluted to a barbiturate concentration of approximately 75-100% of the cutoff concentration; and 10 samples were diluted to a barbiturate concentration of approximately 100-125% of the cutoff concentration. Data from the accuracy studies described above that fell within the near cutoff value ranges were combined with data generated from the diluted positive urine samples. The following results were obtained with the Barbiturates Plus assay on the Roche/Hitachi 917 relative to the GC/MS values.

		Negative Samples	GC/MS Values (ng/mL)		
			148-151	248-251	578->7500
ONLINE	+	0	6	10	54
DAT/Hitachi 917	-	100	4	0	0

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Qualitative assay

Results of this assay distinguish positive (≥ 200 ng/mL) from negative samples only. The amount of drug detected in a positive sample cannot be estimated.

Semiquantitative assay

Results of this assay yield only approximate cumulative concentrations of the drug and its metabolites.

N. Proposed Labeling:

The labeling is sufficient and it 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.