

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

A. 510(k) Number:

k100951

B. Purpose for Submission:

New device

C. Measurand:

Buprenorphine

D. Type of Test:

Qualitative immunochromatographic assay

E. Applicant:

Medtox Diagnostics Inc.

F. Proprietary and Established Names:

Medtox Buprenorphine Test

G. Regulatory Information:

1. Regulation section: 21 CFR 862.3650, Opiate Test System
2. Classification: Class II
3. Product code: DJG
4. Panel: 91, Toxicology

H. Intended Use:

1. Intended use(s):
See Indications for use, below.
2. Indication(s) for use:

The MEDTOX Buprenorphine Test uses immunochromatographic test strips for the rapid, qualitative detection of buprenorphine and its metabolites in human urine. It is intended for prescription use only. The MEDTOX Buprenorphine Test is not for over the-counter sale. It is not intended for use in point-of-care settings.

MEDTOX Buprenorphine detects buprenorphine and its metabolites at the following cutoff concentrations:

BUP Buprenorphine (Buprenorphine) 10 ng/mL

The MEDTOX Buprenorphine Test provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Liquid chromatography/tandem mass spectrometry (LC/MS/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any test result.

3. Special conditions for use statement(s):

As noted in the indications for use, the device is not intended for over the counter sale and is not intended for use in point of care settings.

Tests for buprenorphine cannot distinguish between abused drugs and certain prescribed medications.

4. Special instrument requirements:

None

I. Device Description:

The MEDTOX Buprenorphine Test contains a device with competitive, membrane-based immunochromatographic test strips, a cup and a lid. Each test strip contains mouse monoclonal antibody-colloidal gold, a drug conjugate and an internal procedural control line. Each Test Kit contains all the reagents necessary to test one urine sample for buprenorphine. A bag contains 25 test kits.

J. Substantial Equivalence Information:

1. Predicate device name(s): Acon BUP One Step Buprenorphine Test

2. Predicate 510(k) number(s): k060466

3. Comparison with predicate:

The intended use and method principles are the same as that of the predicate. The specific reagents (e.g., antibodies) and details of the procedure (e.g., read time) differ.

Similarities		
Item	New device	Predicate
Intended use	Determines a preliminary qualitative positive or negative result for the presence of buprenorphine and its metabolite sin human urine.	Same
Cutoff	10 ng/mL	Same
Measurement method	Visually read	Same
Results	Provides preliminary results. Results must be confirmed by a more specific analytical method	Same
Difference		
Sample application	Urine is applied by tilting the cup	Strip is dipped into urine

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

None referenced.

L. Test Principle:

When the test system cup is tipped urine flows into the sample pads of the device, the dried antibody-colloidal gold on the sample pad dissolves and the urine wicks up the white test strips carrying the red antibody colloidal gold with it. When a drug is present in the sample the antibody-colloidal gold binds the drug before it migrates up the test strip. However, when the antibody-colloidal gold bind the drug in the urine, the antibody-colloidal gold cannot bind to the drug conjugate immobilized on the test strip. When the drug concentration is at or above the cutoff concentration, the majority of the antibody colloidal gold is bound to the drug from the urine. Therefore, as drug bound antibody-colloidal gold migrates up the test strip, it is unable to bind to the drug conjugate immobilized on the membrane. Therefore no line is generated at the “T” location on the device for a non-negative sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Samples containing commercial buprenorphine calibrator spiked into a drug-free urine pool to the concentrations shown in the table below were tested with the MEDTOX Buprenorphine Test. Sample concentrations > 5 ng/mL were also confirmed by LCMS. Reproducibility testing was performed by three operators. Each ran masked randomized samples across five days, using one lot, 3 operators;

3 samples; 5 days = 45 reps per level. Results are tabulated below, and demonstrate that test results at concentrations 50% above and 50% below the cutoff were all consistently correct.

BUP (10)

ng/ml	%		Operator #1	Operator #2	Operator #3	All Operators	Precision
0	NEG	#Pos	0	0	0	0	
		#Neg	15	15	15	45	
		%Neg	100%	100%	100%	100%	100%
2.5	25%	#Pos	0	0	0	0	
		#Neg	15	15	15	45	
		%Neg	100%	100%	100%	100%	100%
5	50%	#Pos	0	0	0	0	
		#Neg	15	15	15	45	
		%Neg	100%	100%	100%	100%	100%
7.5	75%	#Pos	7	4	6	17	
		#Neg	8	11	9	28	
		%Neg	53%	73%	60%	62%	78%
12.5	125%	#Pos	14	15	12	41	
		#Neg	1	0	3	4	
		%Pos	93%	100%	80%	91%	91%
15	150%	#Pos	15	15	15	45	
		#Neg	0	0	0	0	
		%Pos	100%	100%	100%	100%	100%

b. Linearity/assay reportable range:

Not applicable. This is a qualitative test. There is no high dose hook effect with the MEDTOX Buprenorphine Test. Testing with spiked samples demonstrated that the MEDTOX Buprenorphine Test provides positive results at concentrations above those attainable in human urine.

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

Both real time and accelerated stability studies were performed. The manufacturer's acceptance criteria require that the control materials, including those containing 5 and 15 ng/mL buprenorphine, must give the expected qualitative result at the expiration date under the recommended storage conditions (25 degrees C). Controls are prepared by adding known quantities of drug or metabolite to a stabilized urine matrix. Levels of drug in each lot of controls are confirmed by GC/MS or LC/MS/MS methods.

Control materials are listed as required but are not included with the kit.

d. Detection limit:

Evaluations were performed to determine the test detection limit, using multiple lots and operators.

Buprenorphine (with purity certified by the manufacturer) was spiked into a negative urine pool to the concentration levels shown in the table below. Each concentration was tested 30 times in each of three lots by a total of 10 operators. Results across lots are similar to those observed for the precision study (above).

Bup concentration (ng/mL)	# Positive results/# total results			All lots - results combined
	Lot 1	Lot 2	Lot 3	
0	0/30	0/30	0/30	0/90
2.5	0/30	0/30	0/30	0/90
5	1/30	0/30	0/30	1/90
7.5	10/30	2/30	9/30	21/90
10	16/30	14/30	19/30	49/90
12.5	28/30	27/30	26/30	81/90
15	30/30	30/30	30/30	90/90

e. Analytical specificity:

Studies were performed to test the effect of (1) potentially cross reactive compounds and (2) potentially interfering endogenous and exogenous substances. All compounds tested were obtained from commercial suppliers.

Potential Cross-reacting compounds:

The following potential cross-reactants and metabolites were prepared in negative urine samples. Results are expressed as the minimum concentration expected to produce a positive result in the indicated assay. The non-reacting opiate compounds were also tested in the presence of 5 ng/mL (50% of the cutoff) and 15 ng/mL (150% of the cutoff) of Buprenorphine. Samples were evaluated in triplicate by in-house operators. None of the nonreactive opiate listed in the following table affected the expected results.

Buprenorphine (BUP) (<i>Buprenorphine</i>) 10 ng/mL		
Compound	Result	% Cross-Reactive
Buprenorphine-	Positive at 7.5 ng/mL	133%

glucuronide		
Norbuprenorphine	Positive at 50 ng/mL	20%
Norbuprenorphine-glucuronide	Positive at 75 ng/mL	13%
Codeine	Negative at 100,000 ng/mL	None Detected
Diacetylmorphine	Negative at 100,000 ng/mL	None Detected
Hydrocodone	Negative at 100,000 ng/mL	None Detected
Hydromorphone	Negative at 100,000 ng/mL	None Detected
Levorphanol	Negative at 50,000 ng/mL	None Detected
6-Monoacetylmorphine	Negative at 100,000 ng/mL	None Detected
Morphine	Negative at 100,000 ng/mL	None Detected
Naloxone	Negative at 100,000 ng/mL	None Detected
Naltrexone	Negative at 100,000 ng/mL	None Detected
Oxycodone	Negative at 100,000 ng/mL	None Detected
Oxymorphone	Negative at 100,000 ng/mL	None Detected
Thebaine	Negative at 100,000 ng/mL	None Detected

Endogenous Compounds:

Interference by endogenous compound was evaluated in the presence of 5 ng/mL and 15 ng/mL buprenorphine. Most of the compounds were evaluated for interference at 100 µg/mL (albumin was evaluated at 20 mg/mL and bilirubin was evaluated at 200 µg/mL). Samples were evaluated in triplicate by in-house operators. None of the endogenous compounds listed below affected the expected results.

Acetaldehyde	Creatinine	Sodium Chloride
Acetone	Epinephrine	Tetrahydrocortisone
Albumin, human	B-estradiol	d,1-Thyroxine Uric Acid
Ascorbic Acid	Estriol	Uric Acid
Bilirubin	Glucose Std. Solution	
Cholesterol	Hemoglobin, Human	

Common prescription and OTC medications

Potential interference from common drugs was evaluated by adding 100,000 ng/mL of each drug tested into urine containing reference calibrator at buprenorphine levels of 50% of cutoff and 150% of the cutoff concentration (5 and 15 ng/mL). Samples were evaluated in triplicate. None of the common drugs listed in the table below affected the expected results.

Acetylsalicylic Acid	Cocaine	Phenobarbital
----------------------	---------	---------------

Acetaminophen	Dextromethorphan	d-Pseudoephedrine
Amitriptyline	Diphenylhydantoin	Rifampin
Brompheniramine maleate	Doxylamine	Salicylic Acid
Caffeine	Fluoxetine	Vancomycin
Carbamazepine	Ibuprophen	
Chlorpheniramine	Morphine	

pH and specific gravity:

Interference from pH was tested fortifying negative urine samples adjusted to pH 5.0, 6.0, 7.0 and 8.0 (± 0.1) with buprenorphine added at the 5 ng/mL of cutoff and 15 ng/mL. These buprenorphine levels correspond to those at which >95% negative and >95% positive results were observed, respectively. Interference from specific gravity was tested by fortifying three negative urine samples, adjusted to specific gravity values of 1.003, 1.015, and 1.030 ± 0.001 , with buprenorphine added at concentrations of 5 ng/mL and 15 ng/mL.

All samples were assayed in triplicate. No effect of pH or specific gravity was observed in this evaluation.

f. Assay cut-off:

See Detection Limit Section, above.

2. Comparison studies:

a. Method comparison with predicate device:

Samples used in the method comparison studies were leftover (de-linked) and randomized clinical urine samples that had been submitted for drug testing and contained varying concentrations of buprenorphine. Samples were assayed and selected using both screening and confirmatory (LC/MS/MS) methods. All samples containing buprenorphine (whether above or below the cutoff concentration), were confirmed by LC/MS/MS. The LC/MS/MS determination included buprenorphine and norbuprenorphine. There was one specimen obtained per patient and one measurement taken per specimen.

The MEDTOX Buprenorphine Tests results were interpreted at both 5 minutes and 15 minutes (covering the recommended read-time range), and identical results were obtained at both time intervals.

The operator who performed the method comparison testing was representative of those expected to perform such testing at the intended use sites, including reference laboratories.

Results are shown in the table below:

Clinical Samples - Method Comparison

Concentration determined by LC/MS/MS		No Drug	Near Cutoff Negative (between - 50% and cutoff)	Near Cutoff Positive (between cutoff and +50%)	High Positive (greater than +50%)	# Correct/ # Observed	Score 95% Confidence Limits
Medtox result BUP (10)	Positive	0	3	8	72	80/80	95.4% - 100%
	Negative	70	4	0	0	74/77	89.2% - 98.7%

The three discrepant samples shown in the table had concentrations between 50% below the cutoff concentration (5 ng/mL) and the cutoff concentration (10 ng/mL) according to LC/MS/MS. The total buprenorphine concentrations determined by LC/MS/MS for these three samples were 5, 7, and 9 ng/mL.

b. Matrix comparison:

Not applicable. The test is only for urine specimens.

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):

Not applicable

4. Clinical cut-off:

Not applicable; the device is for determining positive or negative. See Section above on Detection Limits and Precision for analytical cutoff information.

5. Expected values/Reference range:

Not applicable.

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.