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

A. 510(k) Number:

k092048

B. Purpose for Submission:

New device

C. Measurand:

Methadone (EDDP)

D. Type of Test:

Qualitative immunochromatographic assay

E. Applicant:

BioSite, Inc

F. Proprietary and Established Names:

One Step EDDP (Methadone Metabolite) Test Strip

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DJR- Methadone Test System	II	862.3620	91, Toxicology

H. Intended Use:

1. Intended use(s):

   See Indications for Use below

2. Indication(s) for use:

   The One Step EDDP (methadone Metabolite) Test Strip is a rapid immunochromatographic assays, for the qualitative detection of 2-ethylidene-1,5-

dimethyl-3,3-diphenylpyrrolidine (EDDP), an inactive metabolite of methadone, at a designates cutoff concentration of 300 ng/mL. This product is used to obtain a visual, qualitative result and is intended for professional use and professionals at point of care sites.

This assay provides only preliminary results. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/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 indicated.

3. Special conditions for use statement(s):

   For Professional prescription use and point-of-care use

4. Special instrument requirements:

   Not applicable, as the devices are visually-read single-use devices.

I. Device Description:

The One Step EDDP (Methadone Metabolite) Test Strip contains 25 test devices packaged in a desiccant sealed pouch and a package insert (directions for use).

J. Substantial Equivalence Information:

1. Predicate device name(s):

   ACON MTD One Step Methadone Test Strip
   DRI Methadone Metabolite Enzyme Assay, Microgenics Corporation
   Bionexia Single and Multi-Strip Cassette/Dipstick DOA Screen Panels, Applied DNA Technologies Inc.

2. Predicate K number(s):

   k012595, k023617 and k081378 respectively

3. Comparison with predicate:

Similarities/Differences				
Item	Device	ACON MTD strip and device	Bionexia Single and Multi-Strip Cassette/Dipstick	DRI Methadone Metabolite
Intended Use	for the qualitative detection of 2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP), an inactive metabolite of methadone in human urine	Same	Same	Same
Test Principle	Competitive Binding immunoassay	Same	Same	Liquid Homogeneous Enzyme Assay
Sample	Urine	Same	Same	Same
Antibody	Monoclonal	Same	Same	Same
Cutoff	300 ng/mL	Same	100 ng/mL	Same
Tracer	Ab-Colloidal Gold complex	Same	Same	Glucos-6-Phosphate Dehydrogenase
Analyte	2-ethylidene-1,5-dimethyl-3,3-diphenylpyr-rolidine (EDDP)	Methadone	Same	Same

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

None were identified.

L. Test Principle:

The One Step EDDP (Methadone Metabolite) Test Strip is an immunoassay based on the principle of competitive binding. Drugs which may be present in the urine specimen compete against the drug conjugate for binding sites on the antibody. During testing, a urine sample migrates upward by capillary action. EDDP, if present in the urine sample below 300 ng/mL, will not saturate the binding sites of antibody-coated particles in the test strip. The antibody-coated particles will then be captured by immobilized EDDP conjugate and a visible colored line will show up in the test region. The colored line will not form in the test region if the EDDP levels exceed 300 ng/mL because it will saturate all the binding sites of anti-EDDP antibodies.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Precision studies were performed at three Physician's office laboratories using drug free urine spiked to the following concentrations: 0, 150, 225, 375 and 450 ng/mL. The samples were aliquots, coded, randomized and blinded, than given to each site. A total of 45 determinations were made at each concentration. Testing was performed once a day for three days by three operators (1 per site). Three different lot numbers for each device were used for the study. Sample concentrations were confirmed by GC/MS. The results are displayed in the tables below:

	Concentration of sample ng/mL	Number of determinations	EDDP Test Strip Results #Neg/#Pos
Site A	0 (negative)	15	15/0
	150 (-50%)	15	15/0
	225 (-25%)	15	9/6
	375 (+25%)	15	0/15
	450 (+50%)	15	0/15
Site B	0 (negative)	15	15/0
	150 (-50%)	15	15/0
	225 (-25%)	15	8/7
	375 (+25%)	15	3/12
	450 (+50%)	15	0/15
Site C	0 (negative)	15	15/0
	150 (-50%)	15	14/1
	225 (-25%)	15	11/4
	375 (+25%)	15	1/14
	450 (+50%)	15	0/15
Combined	0 (negative)	45	45/0
	150 (-50%)	45	44/1
	225 (-25%)	45	28/17
	375 (+25%)	45	4/41
	450 (+50%)	45	0/45

Reading time:
The sponsor conducted a reading time study to validate the optimal reading time and stability of the test result for both devices. Drug-free urine specimens were spiked with commercially available EDDP to achieve three GC/MS confirmed concentration levels (+/-50% and a negative).
The samples were tested at 3, 4, 5, 6, 7, 10 minutes, 15 minutes, 20 minutes,

30 minutes, 60 minutes, 2 hours, 4 hours, 8 hours and 24 hours. The results support the sponsors reading time of 5 minutes and the stability of the results up to 8 hours for both formats.

b. *Linearity/assay reportable range:*

Not applicable, the device is intended for qualitative use.

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

Procedural controls are included in the test strip and device. A colored line appearing in the control zone is considered as an internal procedural control. It confirms sufficient specimen volume and adequate membrane wicking. Users are informed not to interpret the test if no red line appears in the control zone.

Control standards are not supplied with these tests; however it is recommended that positive and negative controls be tested as a good laboratory practice to confirm the test procedure and to verify proper test performance. User should follow local, state and federal guidelines for testing QC material.

d. *Detection limit:*

To test the analytical sensitivity for EDDP seven different urine samples containing drug concentrations from negative to 3X the cutoff were tested; 30 devices, on three lots for each format were tested. Drug concentrations were confirmed by GC/MS:

EDDP		Strip			
		Lot 1	Lot 2	Lot 3	Total
Conc (ng/mL)	% of Cutoff	Neg/Pos	Neg/Pos	Neg/Pos	Neg/Pos
0	0	30/0	30/0	30/0	90/0
150	50% cutoff	30/0	30/0	30/0	90/0
225	75 % cutoff	30/0	30/0	30/0	90/0
300	Cutoff	18/12	16/14	17/13	51/39
375	125% cutoff	6/24	3/27	5/25	14/76
450	150% cutoff	0/30	0/30	0/30	0/90
900	300% cutoff	0/30	0/30	0/30	0/90

e. Analytical specificity:

Cross-reactivity was established by spiking similarly structured drug compounds to a concentration of 100 µg/mL into urine having concentrations of EDDP at -25% of the cutoff and +25% of the cutoff. These solutions were tested with both devices. The table below summarizes the results:

Compound	Concentration tested	Test Results	
		EDDP Test Strip	
		-25% CO	+25% CO
EDDP	0 µg/mL	Negative	Positive
EDDP	100 µg/mL	Positive	Positive
Doxylamine	100 µg/mL	Negative	Positive
EMDP	100 µg/mL	Negative	Positive
LAAM HCL	100 µg/mL	Negative	Positive
Nor-LAAM HCL	100 µg/mL	Negative	Positive
MDP	100 µg/mL	Negative	Positive
(-) alpha methadol	100 µg/mL	Negative	Positive
Methadone	100 µg/mL	Negative	Positive

Interfering substances to a final concentration of 100 µg/mL for each compound were spiked into a low negative urine and positive urine. The samples were tested with device and showed no interference at the concentration tested. The complete list of the compounds can be found in the package insert.

<u>pH and Specific Gravity:</u>

To test for possible positive and/or negative interference drug free urine were adjusted to the following pH concentrations 4.0, 5.0. 6.0, 7.0, 8.0 and 9.0.

Each of these samples were divided into three aliquots: drug free urine, EDDP was spiked to -25% of the cutoff and EDDP was spiked to 25% of the cutoff. Each sample was assayed in duplicate. No negative or positive interference due to pH was observed.

To test for possible positive and/or negative interference from specific gravity 15 drug free urine samples having specific gravity from 1.000-1.034 were used. Each of these samples were divided into three aliquots: drug free urine, EDDP was spiked to -25% of the cutoff and EDDP was spiked to 25% of the cutoff. Each sample was assayed in duplicate. No negative or positive interference due to specific gravity was observed.

f. Assay cut-off:

Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision section, 1.d, above.

2. Comparison studies:

a. Method comparison with predicate device:

Performance for the EDDP One Step Methadone Metabolite Test Strip was evaluated at two Physician Office Laboratories and one clinical laboratory with a total of nine operators who are typical operators at these sites. Operators ran 183 unaltered clinical urine samples. The samples were blind labeled and compared to GC/MS results. The operators were only provided the labeling to perform the testing. The results are presented in the table below:

EDDP Test Strip		Negative	Negative (<50% cutoff concentration by GC/MS)	Near cutoff negative (-50% to the cutoff concentration)	Near cutoff positive (cutoff to 50%)	High Positive (>50% cutoff)	% Agreement
Site 1	Positive	0	0	3	8	70	98% (180/183)
	Negative	100	1	1	0	0	
Site 2	Positive	0	0	4	8	70	97.8 (179/183)
	Negative	100	1	0	0	0	
Site 3	Positive	0	0	4	8	70	97.8 (179/183)
	Negative	100	1	0	0	0	

b. Matrix comparison:

Not applicable. The assay is intended for only one sample matrix, urine.

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.

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.