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

A. 510(k) Number:
k063015

B. Purpose of the Submission:
New device

C. Analyte:
Buprenorphine, Propoxyphene, and Cocaine metabolite

D. Type of Test:
Qualitative lateral flow immunochromatographic test, visually read

E. Applicant:
Ameditech, Inc.

F. Proprietary and Established Names:
ImmuTest Multi-Drug Screen BUP/PPX/COC150 (card, cassette, and cup format)

G. Regulatory Information:

1 Regulation section:
862.3650, Enzyme Immunoassay, Opiate test system
862.3700, Enzyme Immunoassay, Propoxyphene test system
862.3250, Enzyme Immunoassay, Cocaine and Cocaine metabolite test system

2 Classification:
Class II, DJG, JXN, DIO

3. Panel:
Toxicology (91)

H. Intended Use:

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

2. Indication(s) for use:
The Ameditech ImmuTest Multi-Drug Screen BUP/PPX/COC150 is an *in vitro* screen test device for the qualitative detection of multi-drugs in human urine. The cutoff concentrations for this panel test are as follows:

Test name	Calibrator	Cutoff (ng/ml)
Buprenorphine (BUP)	Buprenorphine	10
Propoxyphene (PPX)	Propoxyphene	300

Cocaine metabolite (COC150)	Benzoylecgonine	150

This test uses multiple test strips in card format (test strips are placed in a card strip holder), cassette format (test strips are placed in a cassette strip holder), and cup format (test strips are placed in a lid strip holder).
This test is used to obtain a visual, qualitative result and is intended for professional and laboratory use.

This assay provides only a preliminary result. Clinical consideration and professional judgment must be applied to any drug of abuse test result, particularly in evaluating a preliminary positive result. In order to obtain a confirmed analytical result, a more specific alternate chemical method is needed. Gas Chromatography/Mass Spectroscopy (GC/MS) is the preferred confirmation method.

3. Special condition for use statement(s):
For prescription use only

4. Special instrument Requirements:
Not applicable, as the device is a visually read single-use device.

I. Device Description:

The ImmuTest Multi-Drug Screen BUP/PPX/COC150 consists of drug test strips and a plastic test strip holder. Each test strip detects one drug. The ImmuTest Multi-Drug Screen BUP/PPX/COC150 has three types of test formats: card format (test strips are placed in card strip holders), cassette (test strips are placed in cassette strip holders) and cup format (test strips are placed in lid strip holders). The length of the test strips is 59 mm for cassette and card format, and 50 mm for cup format.

J. Substantial Equivalence Information:

1. Predicate device name(s):
QuikStrip OneStep Buprenorphine Test
ACON One-Step Propoxyphene Test Device
ACON One-Step Cocaine-150 Test Strip

2. Predicate K number(s):
k042988, k040445 and k032903

3. Comparison with predicate:
The device is similar to or the same as the previously cleared predicate(s) in the following ways: test principles, indication for use, cut-off concentrations(s), used in a professional and point-of-care setting and sample matrix. The candidate device and the predicates are both visually-read single use devices.

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

The sponsor did not reference any standards or guidance documents in this submission.

L. Test Principle:

The device employs lateral flow immunochromatographic technology and is based on the principle of competitive binding. Drugs, if present in concentrations below the cutoff level, will not saturate the binding sites of the antibody coated particles on the drug specific test strips. The antibody-coated particles will then be captured by immobilized drug-specific conjugate and a colored line will appear in the control region and the test region. If the sample contains drugs above the cutoff level, a colored line will not appear in the strips test region. Binding of drug in the sample causes the absence of a line at the test area, i.e., a positive result. When drug is not present in the sample, the drug-labeled conjugate binds at the test line, resulting in formation of a line, i.e., a negative result. Formation of a colored line in the control region indicates that the proper volume of urine has been added. If a colored line does not appear in the controls region, the test result is inconclusive and should be repeated. The absence or presence of the line is determined visually by the operator.

M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

a. Precision/Reproducibility:

Precision was determined by conducting a lot-to-lot precision study and also by conducting a four site precision study.

The lot-to-lot precision study used drug free urine and urine samples containing drug at the cutoff, 50% below the cutoff, 25% below the cutoff, 25% above the cutoff and 50% above the cutoff. The samples were tested with three lots of the ImmuTest Multi-Drug Screen BUP/PPX/COC150 test format (cassette, card and cup formats) for 3 consecutive days. 10 samples for each of the 6 concentrations were tested daily for each lot. One lot per day for 3 days produced a total of 540 specimens per drug. All samples used were drug free urine spiked with the drugs listed below in the chart. All sample concentrations were confirmed by GC/MS. The results are summarized in the table below:

Table 1: Lot-to-lot assay precision:

Drug	Conc.	Card format			Cassette format			Cup format		
	(ng/ml)	Lot 1 (+/-)	Lot 2 (+/-)	Lot 3 (+/-)	Lot 1 (+/-)	Lot 2 (+/-)	Lot 3 (+/-)	Lot 1 (+/-)	Lot2 (+/-)	Lot 3 (+/-)
BUP Cut-off	0	0/30	0/30	0/30	0/30	0/30	0/30	0/30	0/30	0/30
	5	0/30	0/30	0/30	0/30	0/30	0/30	0/30	0/30	0/30
	7.5	6/24	8/22	9/21	7/23	8/11	6/24	7/23	9/21	6/24
	10	17/13	18/12	16/14	17/13	20/10	17/13	19/11	16/14	18/12
	12.5	24/6	22/8	21/9	24/6	26/4	23/7	22/8	24/6	23/7
	15	30/0	30/0	30/0	30/0	30/0	30/0	30/0	30/0	30/0
	0	0/30	0/30	0/30	0/30	0/30	0/30	0/30	0/30	0/30

PPX Cut-off	150	0/30	0/30	0/30	0/30	0/30	0/30	0/30	0/30	0/30
	225	8/22	6/24	9/21	8/22	7/23	8/22	8/22	6/24	9/21
	300	17/13	15/15	19/11	19/11	19/11	18/12	17/13	18/12	16/14
	375	22/8	23/7	25/5	22/8	23/7	24/6	24/6	23/7	25/5
	450	30/0	30/0	30/0	30/0	30/0	30/0	30/0	30/0	30/0
COC150 Cut-off	0	0/30	0/30	0/30	0/30	0/30	0/30	0/30	0/30	0/30
	75	0/30	0/30	0/30	0/30	0/30	0/30	0/30	0/30	0/30
	112.5	9/21	7/23	8/22	9/21	8/22	10/20	8/22	9/21	6/24
	150	19/11	1614	17/13	19/11	17/13	16/14	16/14	19/11	17/13
	187.5	23/7	24/6	25/5	23/7	24/6	23/7	23/7	224/6	26/4
	225	30/0	30/0	30/0	30/0	30/0	30/0	30/0	30/0	30/0

The results from this study showed that the sample solutions at 0 ng/ml (drug-free urine sample) and 50% below cut-off were all identified as negatives and the sample solutions at 50% above cut-off were all identified as positives. The results demonstrated that the performance for the cup and cassette devices were same as that for card device.

The assay precision of the ImmuTest Multi-drug screen was also evaluated by different users from 4 sites. Three sites were external and one site was in-house at Ameditech. The testing was conducted for 3 days and totaled 90 samples per drug. All samples used were drug free urine spiked with the drugs listed below in the chart. All sample concentrations were confirmed by GC/MS. The results are summarized in the table below:

Table 2: Four sites precision study

Drug	Conc.	VH (+/-)	PVH (+/-)	SM (+/-)	Ameditech (+/-)	Total (+/-)
Buprenorphine	0	0/15	0/15	0/15	0/90	0/135
BUP	5	0/15	0/15	0/15	0/90	0/135
	7.5	3/12	5/10	2/13	22/68	30/105
Cut-off	10	6/9	9/6	7/8	46/44	69/66
	12.5	11/4	12/3	11/4	66/24	98/37
	15	15/0	15/0	15/0	90/0	135/0
Propoxyphene	0	0/15	0/15	0/15	0/90	0/135
PPX	150	0/15	0/15	0/15	0/90	0/135
	225	4/11	3/12	4/11	20/70	31/104
Cut-off	300	9/6	9/6	7/8	48/42	74/61
	375	12/3	11/4	10/5	63/27	100/35
	450	15/0	15/0	15/0	90/0	135/0
Cocaine metabolite	0	0/15	0/15	0/15	0/90	0/135
COC150	75	0/15	0/15	0/15	0/90	0/135

	112.5	2/13	4/11	3/12	20/70	27/108
Cut-off	150	6/9	8/7	9/6	53/37	72/63
	187.5	10/5	11/4	12/13	66/24	101/34
	225	15/0	15/0	15/0	90/0	135/0

The results from this study showed that the sample solutions at 0 ng/ml (drug-free urine sample) and 50% below cut-off were all identified as negatives and the sample solutions at 50% above cut-off were all identified as positives by all study sites.

b. Linearity/assay reportable range:

Not applicable. The assay is intended for qualitative use.

c. Traceability (controls, calibrators, or method):

This device has internal process controls. A visible line appearing in the control region confirms that sufficient sample volume and that the correct technique has been used. In the labeling, users are instructed not to interpret the test if a visible line failed to appear in the control region. Controls are not supplied with this device. The presence of the control line serves as a built-in control, which indicates that the proper sample volume has been used and the reagents are migrating properly.

External controls are available from commercial sources to ensure proper kit performance. In the labeling the sponsor recommends that the external control values are within established limits and if the values of external control do not fall within established limits, the test results are invalid.

d. Detection limit:

Sensitivity of this assay is characterized by validating performance around the claimed cutoff concentration of the assay, including a determination of the lowest concentration of drug that is capable of producing a positive result. The sponsor tested the device to determine the analytical sensitivity at and around the designated cutoff concentrations. Drug free urine and urine samples containing drug at the cutoff, 50% below the cutoff, 25% below the cutoff, 25% above the cutoff and 50% above the cutoff were tested with three lots of the ImmuTest Multi-Drug Screen BUP/PPX/COC150 test format (Cassette card and cup formats) for 3 consecutive days. 10 samples for each of the 6 concentrations were tested daily for each lot. A total of 540 specimens cups were used for three lots, three days testing. All sample concentrations were confirmed by GC/MS analysis. The test results were independently interpreted by two readers. The results are summarized in the table below:

Drug	Conc. (ng/ml)	# Tested	Card Format		Cassette Format		Cup Format	
			A (+/-)	B (+/-)	A (+/-)	B (+/-)	A (+/-)	B (+/-)
Buprenorphine BUP	0	90	0/90	0/90	0/90	0/90	0/90	0/90
	5	90	0/90	0/90	0/90	0/90	0/90	0/90
	7.5	90	23/67	24/66	21/69	24/66	22/68	24/66
Cut-off	10	90	51/39	54/36	54/36	51/39	53/37	52/38
	12.5	90	67/23	75/15	73/17	71/19	69/21	70/20
	15	90	90/0	90/0	90/0	90/0	90/0	90/0
Propoxyphene PPX	0	90	0/90	0/90	0/90	0/90	0/90	0/90
	150	90	0/90	0/90	0/90	0/90	0/90	0/90
	225	90	23/67	22/68	23/67	25/65	25/65	21/69
Cut-off	300	90	52/38	50/40	56/34	50/40	51/39	54/36
	375	90	70/20	71/19	69/21	66/24	72/18	69/21
	450	90	90/0	90/0	90/0	90/0	90/0	90/0
Cocaine metabolite COC150	0	90	0/90	0/90	0/90	0/90	0/90	0/90
	75	90	0/90	0/90	0/90	0/90	0/90	0/90
	112.5	90	24/66	23/67	27/63	24/66	23/67	22/68
Cut-off	150	90	52/38	52/38	52/38	54/36	52/38	56/34
	187.5	90	72/18	73/17	70/20	66/24	73/17	71/19
	225	90	90/0	90/0	90/0	90/0	90/0	90/0

e. Analytical specificity:

The specificity for the ImmuTest Multi-Drug Screen BUP/PPX/COC150 (cassette format) was determined by testing various drugs, drug metabolites, and other compounds that are likely to be present in urine. All compounds were prepared in drug-free normal human urine.

The following compounds produce positive results when tested at levels greater than the concentrations listed below.

Compound	**Concentration (ng/ml)**
Buprenorphine	
Buprenorphine	10
Buprenorphine-3-beta-D-glucuronide	7.5
Norbuprenorphine	25,000
Norbuprenorphine-3-beta-D-glucuronide	150
Codeine	>100,000
Morphine	>100,000

Nalorphine	10,000
Propoxyphene	
D-Propoxyphene	300
D-Norpropoxyphene	300
Cocaine Metabolite	
Benzoylecgonine	150
Cocaine	5,000
Ecgonine	>100,000
Cocaethylene	>100,000
Ecgonine methyl esters	>100,000

Interference Studies:

The following compounds were evaluated for potential positive and/or negative interference with the Multi-Drug Screen BUP/PPX/COC150 (cassette format). Drug controls at 50% below and 50% above cutoff levels, prepared in the Sensitivity Study section, were used in this study. All compounds were dissolved in the 50% below and 50% above cutoff controls and tested with ImmuTest Multi-Drug Screen BUP//PPX/COC150. An unaltered sample was used as a control. The interferents tested were at concentrations up to 100 μg/mL. The results of the interference study were showed in the tables below.

Results of the positive interference study are presented below:

Compound	**BUP**	**PPX**	**COC150**
Unaltered Drug Control	-	-	-
Acetaminophen	-	-	-
Acetone	-	-	-
Albumin	-	-	-
Ampicillin	-	-	-
Ascorbic Acid	-	-	-
Aspartame	-	-	-
Aspirin	-	-	-
Atropine	-	-	-
Benzocaine	-	-	-
Bilirubin	-	-	-
Caffeine	-	-	-
Chloroquine	-	-	-
(+)-Chlorpheniramine	-	-	-
(+/-)-Chlorpheniramine	-	-	-
Creatine	-	-	-
Dexbrompheniramine	-	-	-
Dextromethorphan	-	-	-

Compound	BUP	PPX	COC150
4-Dimethylaminoantipyrine	-	-	-
Diphenhydramine	-	-	-
Dopamine	-	-	-
(+/-)-Ephedrine	-	-	-
Erythromycin	-	-	-
Ethanol	-	-	-
Furosemide	-	-	-
Glucose	-	-	-
Guaiacol Glyceryl Ether	-	-	-
Hemoglobin	-	-	-
Ibuprofen	-	-	-
(+/-)-Isoproterenol	-	-	-
Ketamine	-	-	-
Levorphanol	-	-	-
Lidocaine	-	-	-
(1R,2S)-(-)-N-Methyl-Ephedrine	-	-	-
(+)-Naproxen	-	-	-
Niacinamide	-	-	-
Nicotine	-	-	-
(+/-)-Norephedrine	-	-	-
Oxalic acid	-	-	-
Penicillin-G	-	-	-
Pheniramine	-	-	-
Phenothiazine	-	-	-
l-Phenylephrine	-	-	-
ß-phenylethylamine	-	-	-
Procaine	-	-	-
Quinidine	-	-	-
Ranitidine	-	-	-
Riboflavin	-	-	-
Sodium Chloride	-	-	-
Sulindac	-	-	-
Theophylline	-	-	-
Tyramine	-	-	-

Results of the negative interference study are presented below:

Compound	BUP	PPX	COC150
Unaltered Drug Control	+	+	+
Acetaminophen	+	+	+
Acetone	+	+	+

Compound	BUP	PPX	COC150
Albumin	+	+	+
Ampicillin	+	+	+
Ascorbic Acid	+	+	+
Aspartame	+	+	+
Aspirin	+	+	+
Atropine	+	+	+
Benzocaine	+	+	+
Bilirubin	+	+	+
Caffeine	+	+	+
Chloroquine	+	+	+
(+)-Chlorpheniramine	+	+	+
(+/-)-Chlorpheniramine	+	+	+
Creatine	+	+	+
Dexbrompheniramine	+	+	+
Dextromethorphan	+	+	+
4-Dimethylaminoantipyrine	+	+	+
Diphenhydramine	+	+	+
Dopamine	+	+	+
(+/-)-Ephedrine	+	+	+
Erythromycin	+	+	+
Ethanol	+	+	+
Furosemide	+	+	+
Glucose	+	+	+
Guaiacol Glyceryl Ether	+	+	+
Hemoglobin	+	+	+
Ibuprofen	+	+	+
(+/-)-Isoproterenol	+	+	+
Ketamine	+	+	+
Levorphanol	+	+	+
Lidocaine	+	+	+
(1R,2S)-(-)-N-Methyl-Ephedrine	+	+	+
(+)-Naproxen	+	+	+
Niacinamide	+	+	+
Nicotine	+	+	+
(+/-)-Norephedrine	+	+	+
Oxalic acid	+	+	+
Penicillin-G	+	+	+
Pheniramine	+	+	+
Phenothiazine	+	+	+
l-Phenylephrine	+	+	+
ß-phenylethylamine	+	+	+

Compound	BUP	PPX	COC150
Procaine	+	+	+
Quinidine	+	+	+
Ranitidine	+	+	+
Riboflavin	+	+	+
Sodium Chloride	+	+	+
Sulindac	+	+	+
Theophylline	+	+	+
Tyramine	+	+	+

Urinary pH studies:

Sample solutions containing drug concentrations that were 50% above and 50% below the cutoff used in the sensitivity studies were adjusted for pH between the range of 4 to 9 in 1.0 increments using either 1.0 N HCl or 1.0 N NaOH solution. The pH adjusted sample solutions were tested in triplicate with the ImmuTest Multi-Drug Screen BUP//PPX/COC150. An unaltered sample was used as a control. The results are summarized in the table below:

Drug		Unaltered (+/-)	pH 4 (+/-)	pH 5 (+/-)	pH 6 (+/-)	pH 7 (+/-)	pH 8 (+/-)	pH 9 (+/-)
BUP	(-50%)	0/3	0/3	0/3	0/3	0/3	0/3	0/3
	(+50%)	3/0	3/0	3/0	3/0	3/0	3/0	3/0
PPX	(-50%)	0/3	0/3	0/3	0/3	0/3	0/3	0/3
	(+50%)	3/0	3/0	3/0	3/0	3/0	3/0	3/0
COC 150	(-50%)	0/3	0/3	0/3	0/3	0/3	0/3	0/3
	(+50%)	3/0	3/0	3/0	3/0	3/0	3/0	3/0

Urinary Specific Gravity studies:

Sample solutions containing drug concentrations that were 50% above and 50% below the cutoff used in the sensitivity studies were adjusted to specific gravities that ranged from 1.003 to 1.04. Specific Gravity was determined by the weight of the sample solution divided by the volume (g/mL). The specific gravity adjusted samples were tested in triplicate with the ImmuTest Multi-Drug Screen BUP/PPX/COC150. An unaltered sample was used as a control. The results are summarized in the table below:

Drug		Unaltered (+/-)	SG 1.003 (+/-)	SG 1.02 (+/-)	SG 1.03 (+/-)	SG 1.04 (+/-)
BUP	(-50%)	0/3	0/3	0/3	0/3	0/3
	(+50%)	3/0	3/0	3/0	3/0	3/0
PPX	(-50%)	0/3	0/3	0/3	0/3	0/3

	(+50%)	3/0	3/0	3/0	3/0	3/0
COC150	(-50%)	0/3	0/3	0/3	0/3	0/3
	(+50%)	3/0	3/0	3/0	3/0	3/0

f. Assay cut-off:

The Substance Abuse and Mental Health Services Administration (SAMHSA) has not recommended a cut-off concentration for Buprenorphine and Propoxyphene. The cut-offs for those drugs were chosen based on the levels used by predicate devices. SAMHSA has recommended a cutoff concentration for cocaine metabolite at 300 ng/mL and the ImmuTest Multi-Drug Screen BUP/PPX/COC150 has a cutoff at 150ng/mL for cocaine metabolite. Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision section above.

2. <u>Comparison studies:</u>

a. Method comparison with predicate device and GC/MS:

The ImmuTest Multi-Drug Screen BUP/PPX/COC150 device was compared to the commercially available drug screen tests (New Bay Bioresearch QuikStrip One Step BUP test, ACON One-step PPX test, and ACON COC150 One Step Cocaine test). Sixty (60) negative urine samples collected from presumed non-user volunteers were tested by both ImmuTest Multi-Drug Screen BUP/PPX/COC150 and commercially available drug screen tests. Of these negative urine samples tested, all were found negatives by both methods. In a separate study, clinical urine samples obtained from clinical testing laboratories where they were analyzed by GC/MS were tested by both Multi-Drug Screen BUP/PPX/COC150 device and commercially available drug screen tests.

A total of 270 samples were obtained from clinical testing laboratories. An additional 39 diluted samples were also included and were prepared by diluting positive samples with negative urine. This was done in order to obtain more samples near the cutoff concentrations. The results are summarized in the tables below:

<u>Candidate device vs. Predicate device:</u>

			Predicate device		% Agreement with Predicate device
Test			Positive	Negative	
BUP	ImmuTest	Positive	43	0	100
		Negative	0	85	100
PPX	ImmuTest	Positive	68	2	100

		Negative	0	74	97.5
COC150	ImmuTest	Positive	68	0	98.6
		Negative	1	84	100

Candidate device vs. GC/MS:

ImmuTest Multi-Drug Screen BUP/PPX/COC150	GC/MS Negative	GC/MS Near Cutoff Negative (between –50% Cutoff and Cutoff)	GC/MS Near Cutoff Positive (between Cutoff and +50% Cutoff)	GC/MS Positive (greater than +50% Cutoff)	Percent Agreement with GC/MS
BUP	0	5-8 ng/mL	11-15 ng/mL	16-890 ng/mL	% Agreement
Positive	0	0	8	35	97.7
Negative	18	6	1	0	100
PPX	0	150-250 ng/mL	310-445 ng/mL	500-55,752 ng/mL	% Agreement
Positive	0	0	6	64	98.6
Negative	10	7	1	0	100
COC150	0	75-140 ng/mL	170-223 ng/mL	228-33,770 ng/mL	% Agreement
Positive	0	1	7	60	100
Negative	15	10	0	0	96.2

b. Matrix comparison:

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

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:

No elicit drugs should be present in urine.

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.