

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

A. 510(k) Number:

k080467

B. Purpose for Submission:

Amphetamine, Barbiturates, Benzodiazepines, Cocaine, Marijuana, Morphine 2000, Methamphetamine, Methadone, Phencyclidine, Nortriptyline were previously cleared for professional laboratory use (k061005) and are being cleared for point of care (POC) use in this submission. In addition, 4 new analytes (MDMA, EDDP, BUP and MOR 300) are being cleared for professional POC use.

C. Measurand:

Amphetamine, Barbiturates, Benzodiazepines, Cocaine, Marijuana, Morphine 2000, Methamphetamine, Methadone, Phencyclidine, Nortriptyline, Ecstasy, EDDP, Buprenorphine, and Morphine 300

D. Type of Test:

Qualitative lateral flow immunochromatographic test

E. Applicant:

Applied DNA Technologies Inc.

F. Proprietary and Established Names:

BionexiaTM Single and Multi-Strip DOA Cassette and Dipstick Screen Panels

G. Regulatory Information:

1. Regulation section:

21 CFR §862.3100: Amphetamine Test System

21 CFR §862.3150: Barbiturate Test System

21 CFR §862.3170: Benzodiazepine Test System

21 CFR §862.3250: Cocaine and Cocaine Metabolites Test System

21 CFR §862.3870: Cannabinoids Test System

21 CFR §862.3640: Morphine test system

21 CFR §862.3610: Methamphetamine Test System

21 CFR §862.3620: Methadone test system

Unclassified, 510(k) required: Phencyclidine Test System

21 CFR §862.3650: Opiates Test System,

21 CFR §862.3910: Tricyclic Antidepressant Drugs Test System

2. Classification:

Class II

3. Product code:

LDJ (THC), DIO (COC), DNK (MOR), DKZ (AMP), DJC (MET), DIS (BAR),

JXM (BZO), DJR (MTD), LFG (NOR), DJC (MDMA), DJR (EDDP), DJG (BUP), and LCM (PCP).

4. Panel:
Toxicology (91)

H. Intended Use:

1. Intended use(s):
See Indications for use below.
2. Indication(s) for use:
The Applied DNA Technologies Bionexia™ DOA Panels are rapid chromatographic immunoassays for the qualitative and simultaneous detection of one to thirteen of the following drugs in a variety of combinations in human urine. The designed cutoff concentrations and direct calibrator for these drugs are as follows:

Analyte	Abbreviation	Calibrator	Cutoff concentration
Amphetamine	AMP	Amphetamine	1000 ng/ml
Barbiturate	BAR	Secobarbital	300 ng/ml
Benzodiazepines	BZO	Oxazepam	300 ng/ml
Cocaine	COC	Benzoylecgonine	300 ng/ml
Marijuana	THC	11-nor- Δ^9 -THC9-COOH	50 ng/ml
Methamphetamine	MET	Methamphetamine	1000 ng/ml
Methadone	MTD	Methadone	300 ng/ml
Morphine	MOR	Morphine	2000 ng/ml
Morphine	MOR	Morphine	300 ng/ml
Phencyclidine	PCP	Phencyclidine	25 ng/ml
Nortriptyline	NOR	Nortriptyline	1000 ng/ml
Ecstasy	MDMA	3,4-Methylenedioxy-MET	500 ng/ml
Buprenorphine	BUP	BUP-3-D-Glucuronide	10 ng/ml
EDDP	EDDP	2-ethylidene-1,5-dimethyl-3,3-diphenylpyrrolidine	100 ng/ml

For health care professionals use including professionals at point of care sites (POC) to assist in the determination of drug compliance.

This assay provided only a preliminary analytical test result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas Chromatography / Mass Spectrometry (GC/MS) or Liquid Chromatography / Mass Spectrometry (LC/MS) are 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 prescription use only.

4. Special instrument requirements:

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

I. Device Description:

BionexiaTM Single and Multi-Strip DOA test has two formats: cassette and dipstick. These two formats are manufactured with the same formulation, components, and manufacturing processes. The Cassette contains a test in a plastic housing with a specimen well and a window to read the test results. A specimen pipette is included with the Test Device, but a specimen collection container is not included with either test format. Amphetamine, Barbiturates, Benzodiazepines, Cocaine, Marijuana, Morphine 2000, Methamphetamine, Methadone, Phencyclidine, Nortriptyline were previously cleared for professional laboratory use (k061005) and are being cleared for point of care (POC) use in this submission. In addition, 4 new analytes (MDMA, EDDP, BUP and MOR 300) are being cleared for professional POC use.

J. Substantial Equivalence Information:

1. Predicate device name(s):

ACON One Step Ecstasy Screen Test

ACON One Step Morphine 300 Test

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

k022589, k013380

3. Comparison with predicate:

The device is similar to or the same as to the previously cleared predicate(s) in the following ways: test principles, indication for use, cut-off concentration(s), use in a professional setting, sample matrix, endpoint, and test time.

The devices differ by manufacturer, specific monoclonal antibodies used, the analytes detected, and the proposed device is cleared for use in point-of-care settings.

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

None referenced by the manufacturer.

L. Test Principle:

The BionexiaTM DOA Screen Panels are immunoassays in which chemically labeled drugs (drug-protein conjugates) compete for limited antibody binding sites with drugs which may be present in urine. The test device contains membrane strips which are pre-coated with drug-protein conjugates on the test band(s). On each strip, the drug antibody-colloidal gold conjugate pad is placed at one end of the membrane. In the absence of drug in the urine, the solution of the colored antibody-colloidal gold conjugate move along with the sample solution upward chromatographically by capillary action across the membrane to the immobilized drug-protein conjugate zone on the test band region. The colored antibody-gold conjugate then attaches to the drug-protein conjugates to form visible lines as the antibody complex with the drug conjugate. Therefore, the formation of the visible line in the test zone occurs when the test urine is negative for the drug. When the drug is present in the urine, the

drug/metabolite antigen competes with drug-protein conjugate on the test band region for the limited antibody. When a sufficient concentration of the drug is present, it will fill the limited antibody binding sites. This will prevent attachment of the colored antibody (drug-protein conjugate)-colloidal gold conjugate to the drug-protein conjugate zone on the test band region. Therefore, absence of the color band on the test region indicates a positive result.

A control band with a different antigen/antibody reaction is added to the immunochromatographic membrane strip at the control region (C) to indicate that sufficient sample volume has been added. This control line should always appear regardless of the presence of drug or metabolite. If the control line does not appear the test device should be considered invalid.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The point of care (POC) precision study was conducted at three physician's office sites by untrained operators. 3 different lots (one lot per site) of product (Dipstick (strip) for all 13 analytes; Cassette and Dipstick for MOR 300) were used to demonstrate the within run, between run and between operator precision. Each product lot was tested by using GC/MS confirmed controls (LC/MS confirmed controls for BUP) at concentration levels of negative, 50%, 75%, 125%, and 150% of the cutoff. Each concentration level was tested 5 times a day for 3 days continuously. There was no significant difference in precision between the two lots or between the readers:

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
MOR 2000		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	15	0	45	0

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
PCP		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	14	1	44	1

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
MTD		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	15	0	45	0

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
BAR		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	15	0	45	0

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
COC		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	15	0	45	0

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
MET		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	15	0	45	0

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
AMP		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	15	0	45	0

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
TCA		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	15	0	45	0

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
BZO		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	15	0	45	0

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
THC		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	13	0	43
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	14	0	44	0

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
BUP		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	15	0	45	0

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
EDDP		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	15	0	45	0

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
MDMA		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	15	0	45	0

Drug Con.	No. tested	Site 1		Site 2		Site 3		Total	
MOR 300		+	-	+	-	+	-	+	-
Negative	45	0	15	0	15	0	15	0	45
50% of cutoff	45	0	15	0	15	0	15	0	45
75% of cutoff	45	0	15	0	15	0	15	0	45
125% of cutoff	45	15	0	15	0	15	0	45	0
150% of cutoff	45	15	0	15	0	15	0	45	0

b. *Linearity/assay reportable range:*

Not applicable. The assay is intended for qualitative use.

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

This device has internal process controls. A red line appearing in the control region confirms sufficient sample volume and adequate membrane wicking. Users are informed not to interpret the test if no line forms in the control region.

Control standards are not supplied with this device; however it is good laboratory practice to confirm the test procedure and to verify proper test performance. Users should follow all applicable guidelines for testing QC materials.

d. *Detection limit:*

Analytical performance of the device around the cutoff is described in Section 1.M.f below.

e. *Analytical specificity:*

The specificity of the new Bionexia™ DOA Screen tests (MDMA, EDDP, BUP, and MOR 300) was evaluated by adding various drugs, drug metabolites, and other structurally similar compounds that are likely to be present in drug-free normal human urine. To evaluate the positive cross-reactivity concentration of the substance, tested substances were added into commercial negative normal urine control to verify the lowest concentrations which indicate a positive result. The following compounds were tested for cross-reactivity in the drug strip and found to be positive if the levels were greater than the following listed concentrations (in ng/ml).

<u>MDMA related compounds</u>	<u>Concentration (ng/ml)</u>
3,4-Methylenedioxy-methamphetamine (MDMA)	500
3,4-Methylenedioxyamphetamine (MDA)	1,000
3,4-Methylenedioxyethylamphetamine (MDEA)	300
d-Amphetamine	>100,000
d-Methamphetamine	>100,000
Paramethoxyamphetamine (PMA)	5,000
<u>EDDP related compounds</u>	<u>Concentration (ng/ml)</u>
EDDP	100
	>1,000,000
Doxylamine	00
Methadone	>10,000
Methadol	>10,000
<u>BUP related compounds</u>	<u>Concentration (ng/ml)</u>
Buprenorphine 3 – D – Glucuronide	10
Buprenorphine	15
Codeine	25,000
Morphine	50,000
Nalorphine	2,000
Norbuprenorphine	>1,000
Norbuprenorphine 3 – D – Glucuronide	>1,000
<u>Morphine 300 related compounds</u>	<u>Concentration (ng/ml)</u>
Morphine	300
Codeine	300
Diacetyl Morphin (Heroin)	300
Ethylmorphine	300
Hydromorphone	1,500
Hydrocodone	1,500
Merperidine	>100,000
6-Monoacetylmorphine	300
Morphine-3-glucuronid	6,000
Oxycodone	>20,000
Oxymorphone	>20,000
Rifampicine	25,000
Thebaine	2,500
Promethazine	>250,00
Trimipramine	>20,000

Non Cross-Reacting Compounds

Potential interferences to the Bionexia drugs of abuse tests were evaluated by adding various drugs, drug metabolites, and other compounds that are commonly found in the urine which may interfere with test result. All compounds were prepared in drug free pooled human urine or GC/MS confirmed urine controls. The following compounds were found not to cross-react when tested at concentrations at 100 µg/ml.

Acetaminophen	Furosemide
Acetone	Guaiacol Glyceryl Ether
Albumin	Hemoglobin
Amitriptyline	Ibuprofen
Ampicillin	Imipramine (Except TCA)
Aspartame	(+/-)-Isoproterenol
Aspirin	Lidocaine
Atropine	N-Methyl-Ephedrine
Benzocaine	(+)-Naproxen
Bilirubin	Oxalic Acid
Caffeine	Penicillin-G
Chloroquine	Pheniramine
Chlorpheniramine	Phenothiazine
Creatine	L-Phenylephrine
Dextrophan tartrate	β-Phenylethylamine
4-Dimethylaminoantipyrine	Procaine
Dopamine	Quinidine
(+/-)-Ephedrine	Ranitidine
(-)-Ephedrine	Sulindac
Erythromycin	Tyramine
Ethanol	Vitamin C

To evaluate the effect of pH value on the test results, GC/MS confirmed urine controls at zero concentration, 75%, 125%, and 3X of cutoff were used. Each control level was adjusted by either 7N NaOH or 7N HCl to the pH level at 3, 5, 6.5, 7.5 and 8.5. For evaluate specific gravity effect, negative urine samples containing low to high specific gravity levels were collected and pooled to prepared the following levels: 1.00, 1.01, 1.02 and 1.03. The target drug was added to the pooled urines at the following drug levels: negative, -25%, +25% and 3X of cutoff. The Bionexia™ DOA Screen Panels performances at cutoff point are not affected by pH range of urine specimens of 3.0 to 8.5 or a specific gravity range of 1.005 to 1.03.

f. Assay cut-off:

The cutoff of Bionexia™ DOA Screen Panels (MDMA, EDDP, BUP, and MOR 300) were determined by testing GC/MS confirmed controls to the concentrations at negative, -50% cutoff,

-25% cutoff, cutoff, +25% cutoff, +50% cutoff and 3 times the cutoff. Both the cassette and dipstick versions of the test were evaluated. The results are summarized below:

Drug Con.	n	MDMA		EDDP		BUP		MOR 300	
		-	+	-	+	-	+	-	+
-	50	50		25		50		50	
-50	50	50		25		50		50	
-25	50	50		25		50		50	
C/O	50	25	25	23	27	22	28	18	32
+25	50		50		50		50		50
+50	50		50		50		50		50
3X	50		50		50		50		50

2. Comparison studies:

a. *Method comparison with predicate device:*

Performance of the Bionexia™ DOA Screen panels was established by comparing the results of unaltered urine samples against GC/MS (LC/MS for BUP). Both the cassette and dipstick versions of the test were evaluated.

MDMA: In this study, one hundred twenty six (126) unaltered negative and positive urine samples (0 to 21616 ng/ml) were tested by cassette and dipstick device and were compared with GC/MS and compared to GC/MS. The results are summarized below:

Positive Agreement: 100% and Negative Agreement: 100%

Bionexia™	No Drug present	Negative (Less than 50% the cutoff concentration by GC/MS analysis)	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration)	High Positive (Greater than 50% above the cutoff concentration)	% Agreement
+	0	0	0	12	63	100 %
-	35	7	9	0	0	100 %
Total	35	7	9	12	63	100 %

EDDP: In this study, one hundred eleven (111) negative and positive unaltered urine samples (0 to 56700 ng/ml) were tested by cassette and dipstick device and compared to GC/MS. The concentration of the discrepant specimen was close to the cutoff value at 104.0 ng/ml. The results are summarized below:

Positive Agreement: 98.6 % and Negative Agreement: 100%

Bionexia™	No Drug present	Negative (Less than 50% the cutoff concentration by GC/MS analysis)	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration)	High Positive (Greater than 50% above the cutoff concentration)	% Agreement
+	0	0	0	3	65	98.6%
-	38	0	4	1	0	100 %
Total	38	0	4	4	65	99.1 %

BUP: In this study, one hundred seventeen (117) negative and positive unaltered urine samples (0 to 1160 ng/ml) were tested by cassette and dipstick device and compared to LC/MS. The results are summarized below:

Positive Agreement: 100% and Negative Agreement: 100%

Bionexia™	No Drug present	Negative (Less than 50% the cutoff concentration by LC/MS analysis)	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration)	High Positive (Greater than 50% above the cutoff concentration)	% Agreement
+	0	0	0	4	72	100 %
-	35	1	5	0	0	100%
Total	35	1	5	4	72	100 %

MOR 300: In this study, one hundred eleven (111) negative and positive unaltered urine samples (0 to 5182 ng/ml) were tested by cassette and dipstick device and were compared to GC/MS. The concentrations of both discrepant specimens close to the cutoff value at 308 and 309 ng/ml. The results are summarized below:

Positive Agreement: 96.8% and Negative Agreement: 97.9%

Bionexia™	No Drug present	Negative (Less than 50% the cutoff concentration by GC/MS analysis)	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration)	High Positive (Greater than 50% above the cutoff concentration)	% Agreement
+	0	0	1	11	50	96.8%
-	35	0	12	2	0	97.9%
Total	35	0	13	13	50	97.3 %

The POC Method Comparison Study was performed at one POC site with 3 operators by evaluating negative and positive clinical urine specimens (including unaltered urine specimens and near cutoff level urine specimens that were diluted by a urine negative control). Approximately 20 to 26 urine samples were tested for each drug/analyte. More than half of tested samples were in between +/-50% of the cutoffs. The results are summarized in the following table.

Drug / Cutoff (ng/ml)	Candidate Device Results	No Drug present	Negative (Less than 50% the cutoff concentration by GC/MS or LC/MS analysis)	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration)	High Positive (Greater than 50% above the cutoff concentration)	% Agreement
AMP	+	0	0	1	7	5	92.3 %
1000	-	0	5	6	1	0	91.7 %
BAR	+	0	0	0	6	5	100 %
300	-	0	5	8	0	0	100 %
BZO	+	0	0	0	9	5	100 %
300	-	0	3	7	0	0	100 %
BUP	+	0	0	0	9	5	100 %
10	-	0	4	6	0	0	100 %
COC	+	0	0	0	6	8	93.3 %
300	-	0	4	6	1	0	100 %
EDDP	+	0	0	0	6	6	100 %
100	-	0	4	8	0	0	100 %
THC	+	0	0	1	9	5	100 %
50	-	0	3	6	0	0	90 %
MET	+	0	0	0	7	5	92.3 %
1000	-	0	5	8	1	0	100 %
MDMA	+	0	0	0	6	5	91.7 %
500	-	0	5	7	1	0	100 %
MOR	+	0	0	0	6	5	91.7 %
300	-	0	4	7	1	0	100 %
MOR	+	0	0	0	9	5	100 %
2000	-	0	5	7	0	0	100 %
MTD	+	0	0	0	8	5	100 %
300	-	0	5	7	0	0	100 %
PCP	+	0	0	1	8	8	100 %
25	-	0	0	7	0	0	87.5 %
NOR	+	0	0	1	5	6	100 %
1000	-	0	0	8	0	0	88.9 %

- b. Matrix comparison:*
Not applicable; these devices are for use with urine only.
- 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):*
- 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.