

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

**A. 510(k) Number:**

k153693

**B. Purpose for Submission:**

New device

**C. Measurand:**

Methamphetamine

**D. Type of Test:**

Homogenous enzyme immunoassay

**E. Applicant:**

Immunoanalysis Corporation

**F. Proprietary and Established Names:**

Immunoanalysis Methamphetamine Urine Enzyme Immunoassay  
Immunoanalysis Multi-Drug Calibrators

**G. Regulatory Information:**

Product Code	Classification	Regulation Section	Panel
LAF	Class II	21 CFR 862.3610, Methamphetamine test system	Toxicology (91)
DLJ	Class II	21 CFR 862.3200, Clinical toxicology calibrator	Toxicology (91)

**H. Intended Use:**

1. Intended use(s):

Refer to Indications for Use below.

2. Indication(s) for use:

The Immunalysis Methamphetamine Urine Enzyme Immunoassay is a homogeneous enzyme immunoassay with dual cutoffs of 500ng/mL and 1000ng/mL. The assay is intended for use in laboratories for the qualitative and semi-quantitative analysis of Methamphetamine in human urine with automated clinical chemistry analyzers. This assay is calibrated against Methamphetamine. This in-vitro diagnostic device is for prescription use only.

The semi-quantitative mode is for purposes of enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as Gas Chromatography/ Mass Spectrometry (GC-MS) or permitting laboratories to establish quality control procedures.

The Immunalysis Methamphetamine Urine Enzyme Immunoassay Kit provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. GC-MS or Liquid Chromatography / Mass Spectrometry (LC/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.

The Immunalysis Multi-Drug Calibrators are intended for in vitro diagnostic use for the calibration of assays for the analytes currently listed in the package insert: Benzoylcegonine, Methamphetamine, Morphine, PCP and Oxazepam. The calibrators are designed for prescription use with immunoassays.

3. Special conditions for use statement(s):

For prescription use only.  
For in vitro diagnostic use only.

4. Special instrument requirements:

The Beckman Coulter AU400e Chemistry Analyzer was used to generate the performance data in this submission. Instruments must be capable of maintaining a constant reaction temperature, pipetting samples and reagents, mixing reagents, timing reactions and measuring enzyme rates precisely.

**I. Device Description:**

The assay consists of antibody/ substrate reagent and enzyme conjugate reagent. The antibody/ substrate reagent includes monoclonal antibodies to Methamphetamine, glucose-6-phosphate (G6P) and nicotinamide adenine dinucleotide (NAD) in Tris buffer with Sodium Azide as a preservative. The enzyme conjugate reagent includes Methamphetamine derivative labeled with glucose-6-phosphate dehydrogenase (G6PDH) in Tris buffer with Sodium Azide

as a preservative.

All of the Immunalysis Multi-Drug Calibrators are liquid and ready to use. Each contains a known concentration of a specific drug analyte as a mixture. The negative calibrator is a processed, drug-free synthetic urine matrix with sodium azide as a preservative. The Level 1, 2, 3 and 4 calibrators are prepared by spiking known concentrations of drug analyte into the negative calibrator matrix. These five calibrators (negative, Level 1, 2, 3 and 4) are sold as individual bottles. The concentration of drug analyte in the corresponding calibrators is summarized as follows:

Analyte	Multi-Drug Calibrators			
	Level 1	Level 2	Level 3	Level 4
Benzoylcegonine	150 ng/mL	300 ng/mL	500 ng/mL	1000 ng/mL
Methamphetamine	500 ng/mL	1000 ng/mL	1500 ng/mL	2000 ng/mL
Morphine	100 ng/mL	300 ng/mL	500 ng/mL	1000 ng/mL
PCP	12.5 ng/mL	25 ng/mL	50 ng/mL	100 ng/mL
Oxazepam	100 ng/mL	200 ng/mL	500 ng/mL	1000 ng/mL

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

Microgenics, Inc. DRI® Methamphetamines Assay  
 Lin-Zhi International Multi-Analyte Urine Drugs of Abuse Calibrators

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

k093114  
 k051088

3. Comparison with predicate:

Similarities - Reagent		
Item	Predicate Device Microgenics, Inc. DRI Methamphetamines Assay k093114	Candidate Device Immunalysis Methamphetamine Urine Enzyme Immunoassay
<b>Intended Use</b>	For the qualitative and semi-quantitative determination of Methamphetamine in human urine	Same
<b>Measured Analytes</b>	Methamphetamine and	Methamphetamine

<b>Similarities - Reagent</b>		
	Amphetamine	
<b>Test Matrix</b>	Urine	Same
<b>Item</b>	Predicate Device Microgenics, Inc. DRI Methamphetamines Assay k093114	Candidate Device Immunoanalysis Methamphetamine Urine Enzyme Immunoassay
<b>Cutoff Levels</b>	500 ng/mL and 1000 ng/mL of Methamphetamine and Amphetamine	500 ng/mL and 1000 ng/mL of Methamphetamine
<b>Methodology</b>	Homogeneous Enzyme Immunoassay	Same
<b>Materials</b>	Liquid Ready-to-Use Two Reagent Assay (R1 and R2)	Antibody/Substrate Reagents and Enzyme Labeled Conjugate
<b>Storage</b>	2 – 8°C until expiration date	Same

<b>Differences - Reagent</b>		
<b>Item</b>	Predicate Device Microgenics, Inc. DRI Methamphetamines Assay k093114	Candidate Device Immunoanalysis Methamphetamine Urine Enzyme Immunoassay
<b>Antibody</b>	Monoclonal antibodies to Methamphetamine and/or Amphetamine	Monoclonal antibody to Methamphetamine

<b>Similarities - Calibrators</b>		
<b>Item</b>	Predicate Device Lin-Zhi International Multi- Analyte Urine Drugs of Abuse Calibrators k051088	Candidate Device Immunoanalysis Multi-Drug Calibrators
<b>Matrix</b>	Urine	Same
<b>Calibrator Levels</b>	5 Levels	Same
<b>Storage</b>	2 – 8°C until expiration date	Same

<b>Differences - Calibrators</b>		
<b>Item</b>	<b>Predicate Device Lin-Zhi International Multi- Analyte Urine Drugs of Abuse Calibrators k051088</b>	<b>Candidate Device Immunoanalysis Multi-Drug Calibrators</b>
<b>Analytes</b>	benzoylecgonine, d- methamphetamine, methadone, morphine, oxazepam, secobarbital, phencyclidine, propoxyphene	benzoylecgonine, methamphetamine, morphine, PCP

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

CLSI EP07-A2: Interference Testing in Clinical Chemistry: Approved Guideline - Second Edition

**L. Test Principle:**

The assay is based on the competition of Methamphetamine labeled enzyme glucose-6-phosphate dehydrogenase (G6PDH) and the free drug in the urine sample for a fixed amount of antibody binding sites. In the absence of the free drug in the sample, the antibody binds the drug enzyme conjugate and enzyme activity is inhibited. This creates a dose response relationship between drug concentration in the urine sample and enzyme activity. The enzyme G6PDH activity is determined at 340 nm spectrophotometrically by the conversion of NAD to NADH.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

*a. Precision/Reproducibility:*

The sponsor performed precision studies in-house following the guidelines provided in CLSI EP5-A2. The study was performed using drug free urine samples spiked with methamphetamine and analyzed on a Beckman Coulter / Olympus AU400e Chemistry Analyzer. Samples were measured in duplicate in two runs per day for 20 days (n = 80). The data are summarized in the following tables:

Qualitative analysis (500 ng/mL cutoff)

Concentration (ng/mL)	% of cutoff	Result
0	-100	80 Neg / 0 Pos
125	-75	80 Neg / 0 Pos
250	-50	80 Neg / 0 Pos
375	-25	80 Neg / 0 Pos
500	Cutoff	41 Neg / 39 Pos
625	+25	80 Pos / 0 Neg
750	+50	80 Pos / 0 Neg
875	+75	80 Pos / 0 Neg
1000	+100	80 Pos / 0 Neg

Qualitative analysis (1000 ng/mL cutoff)

Concentration	% of cutoff	Result
0	-100	80 Neg / 0 Pos
250	-75	80 Neg / 0 Pos
500	-50	80 Neg / 0 Pos
750	-25	80 Neg / 0 Pos
1000	Cutoff	44 Neg / 36 Pos
1250	+25	80 Pos / 0 Neg
1500	+50	80 Pos / 0 Neg
1750	+75	80 Pos / 0 Neg
2000	+100	80 Pos / 0 Neg

Semi-quantitative analysis (500 ng/mL cutoff)

Concentration	% of cutoff	Result
0	-100	80 Neg / 0 Pos
125	-75	80 Neg / 0 Pos
250	-50	80 Neg / 0 Pos
375	-25	80 Neg / 0 Pos
500	Cutoff	35 Neg / 45 Pos
625	+25	80 Pos / 0 Neg
750	+50	80 Pos / 0 Neg
875	+75	80 Pos / 0 Neg
1000	+100	80 Pos / 0 Neg

Semi-quantitative analysis (1000 ng/mL cutoff)

Concentration	% of cutoff	Result
0	-100	80 Neg / 0 Pos
250	-75	80 Neg / 0 Pos
500	-50	80 Neg / 0 Pos
750	-25	80 Neg / 0 Pos
1000	Cutoff	37 Neg / 43 Pos
1250	+25	80 Pos / 0 Neg
1500	+50	80 Pos / 0 Neg
1750	+75	80 Pos / 0 Neg
2000	+100	80 Pos / 0 Neg

b. *Linearity/assay reportable range:*

A drug free urine pool was spiked with a high concentration of Methamphetamine (at a level above the highest calibrator) and was used as the high value specimen. Additional pools were made by serially diluting the high value specimen with drug free urine in increments of about 10%. Aliquots from each pool were analyzed in triplicate in the semi-quantitative mode.. For each known concentration, drug recovery was calculated using the mean concentration of the replicates. The results of the study are summarized below:

Expected Concentration (ng/mL)	Mean Concentration (ng/mL)	Recovery (%)
200	272.7	136.4
400	436.8	109.2
600	674.6	112.4
800	830.0	103.8
1000	1107.6	110.8
1200	1247.0	103.9
1400	1481.2	105.8
1600	1711.5	107.0
1800	1917.4	106.5
2000	2080.7	104.0
2200	2226.4	101.2

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

The analytes in the calibrators have been traced to a commercially available standard solution. The standard is certified material with the concentration verified by GC-MS or LC/MS-MS. This standard is diluted with calibrator buffer to make the calibrators in the desired concentrations. The concentrations are confirmed by Gas Chromatography and Mass Spectrometry Analysis (GC-MS) and/or Liquid Chromatography/ Tandem Mass Spectrometry (LC/MS-MS).

Stability protocols and acceptance criteria for the calibrators were reviewed and found to be acceptable. The sponsor claims that when stored at 2 – 8° C calibrators and controls are stable for one year. The sponsor claims that once opened, the calibrators and controls are stable for 60 days when stored at 2 – 8° C.

The Negative Calibrator is a processed, drug free urine matrix. The standard is compared to a reference negative standard to ensure that it is free of analyte. Value is assigned when the test is within the acceptable range.

Values are assigned to the controls and calibrators once the GC/MS or LC/MS/MS results are within the acceptable ranges. The negative standard is prepared with BSA Buffer. The standard is compared to a reference negative standard to ensure that it is free of analyte. The value is assigned when the test is within the acceptable range.

*d. Detection limit:*

Not applicable.

*e. Analytical specificity:*

Potential interference from non-structurally related compounds and endogenous compounds was evaluated in both the qualitative and semi-quantitative modes by following CLSI EP 7-A2: Interference Testing in Clinical Chemistry. Potential interferents were spiked into drug free urine containing Methamphetamine at  $\pm 25\%$  of the cutoff (375 ng/mL and 625 ng/mL for the 500 ng/mL cutoff or 750 ng/mL and 1,250 ng/mL for the 1,000 ng/mL cutoff). The following compounds at 100,000 ng/mL were found not to interfere with the assay at either cutoff in qualitative or semi-quantitative mode.

4-Bromo-2,5-Dimethoxy phenethylamine	Ethylmorphine	Norbuprenorphine
6-Acetylmorphine	Fentanyl	Norcodeine
7-Aminoclonazepam	Flunitrazepam	Nordiazepam
Alprazolam	Fluoxetine	Normorphine
Amitriptyline	Flurazepam	Norpropoxyphene
Amobarbital	Heroin	Nortriptyline
Benzylpiperazine	Hexobarbital	Oxazepam
Bromazepam	Hydrocodone	Oxycodone
Buprenorphine	Hydromorphone	Oxymorphone
Bupropion	11-hydroxy- $\Delta$ -9-THC	Phencyclidine
Butobarbital	Ibuprofen	Pentazocine
Carbamazepine	Imipramine	Pentobarbital
Chlordiazepoxide	Ketamine	Phenobarbital
Chlorpromazine	Levorphanol Tartrate	Phentermine
cis-Tramadol	Lidocaine	Phenytoin
Clobazam	Lorazepam	Prazepam
Clomipramine	LSD	Propranolol
Clonazepam	Maprotiline	Protriptyline
Cocaine	Meperidine	Ranitidine
Codeine	Meprobamate	Ritalinic Acid
Cyclobenzaprine	Methadone	Secobarbital
N-Desmethylpentadol	Methaqualone	Sufentanil Citrate
Delta-9-THC	Methylphenidate	Temazepam

Desipramine	Morphine	11-nor-9 carboxy THC
Dextromethorphan	Morphine-3 $\beta$ -glucuronide	Thioridazine
Diazepam	Morphine-6 $\beta$ -glucuronide	Triazolam
Dihydrocodeine	Nalorphine	Trifluoromethyl phenyl-piperazine
Doxepin	Naloxone	Trimipramine
EDDP	Naltrexone	Venlafaxine
Ethyl $\beta$ -D-glucuronide	Nitrazepam	

In addition, Acetaminophen, Acetylsalicylic Acid, Benzoyllecgonine, and Caffeine were found not to interfere at a concentration of 500,000 ng/mL.

The following endogenous substances at the concentrations listed below did not interfere with the assay at either cutoff in qualitative or semi-quantitative mode:

Compound	Concentration Tested
Acetone	1.0 g/dL
Ascorbic Acid	1.5 g/dL
Bilirubin	0.002 g/dL
Creatinine	0.5 g/dL
Ethanol	1.0 g/dL
Galactose	0.01 g / dL
$\gamma$ -Globulin	0.5 g/dL
Glucose	2.0 g/dL
Hemoglobin	0.150 g/dL
Human Serum Albumin	0.5 g/dL
Oxalic Acid	0.1 g/dL
Riboflavin	0.0075 g/dL
Sodium Azide	1% w/v
Sodium Chloride	6.0 g/dL
Sodium Fluoride	1% w/v
Urea	6.0 g/dL

Boric acid at a concentration of 1% w/v was found to cause false negative results at +25% and +50% of the cutoff for both qualitative and semi-quantitative modes. The labeling recommends that Boric Acid not be used as a preservative for urine samples.

Effect of pH: The sponsor evaluated the effect of pH on the test results using both qualitative and semi-quantitative modes. Drug free urine containing Methamphetamine at  $\pm$  25% of the cutoff (375 ng/mL and 625 ng/mL for the 500 ng/mL cutoff and 750 ng/mL and 1250 ng/mL for the 1000 ng/mL cutoff) were pH adjusted using hydrochloric acid or sodium hydroxide. pH values of 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 9.0, 10.0 and 11.0 did not interfere with the test result at either cutoff in qualitative or semi-quantitative mode.

Effect of specific gravity: The sponsor evaluated the effect of specific gravity on the test results using both qualitative and semi-quantitative modes. Drug free urine containing Methamphetamine at  $\pm 25\%$  of the cutoff (375 ng/mL and 625 ng/mL for the 500 ng/mL cutoff and 750 ng/mL and 1250 ng/mL for the 1000 ng/mL cutoff) were adjusted using salt or albumin. Specific Gravity values of 1.000, 1.002, 1.005, 1.010, 1.015, 1.020, 1.025 and 1.030 did not interfere with the test result at either cutoff in qualitative or semi-quantitative mode.

Cross reactivity from structurally related compounds was evaluated in the qualitative and semi-quantitative modes by spiking into drug-free urine. Each potential cross-reacting compound was spiked and evaluated independently, and each spiked sample was tested in singlicate. No differences were observed between the qualitative and semi-quantitative modes. The compounds tested and the concentration approximately equivalent to the 500 and 1000 ng/mL cutoffs are listed below:

500 ng/mL cutoff		
Compound	Concentration Tested (ng/mL)	Cross-Reactivity (%)
(+) Methamphetamine	500	100.00
(-) Methamphetamine	90,000	0.56
(+) Amphetamine	20,000	2.50
(-) Amphetamine	900,000	0.06
Methylenedioxyamphetamine (MDA)	18,000	2.78
Methoxyamphetamine (PMA)	15,000	3.33
Methylenedioxymethamphetamine (MDMA)	800	62.50
MDEA	3,000	16.67
Fenfluramine	7,000	7.14
(+) Pseudoephedrine	75,000	0.67
(-) Pseudoephedrine	300,000	0.17
(-) Ephedrine	65,000	0.77
(+) Ephedrine	1,000,000	<0.05
Phentermine	500,000	0.10
Tyramine	850,000	0.06
Phenylephrine	800,000	0.06
Diphenhydramine	1,000,000	<0.050
Phenylpropanolamine	1,000,000	< 0.0005

1000 ng/mL cutoff		
Compound	Concentration Tested (ng/mL)	Cross-Reactivity (%)
(+) Methamphetamine	1,000	100.00
(-) Methamphetamine	200,000	0.44
(+) Amphetamine	60,000	2.50
(-) Amphetamine	1,000,000	<0.10
Methylenedioxyamphetamine (MDA)	40,000	2.50
Methoxyamphetamine (PMA)	40,000	3.33
Methylenedioxymethamphetamine (MDMA)	1,000	71.43
MDEA	5,000	14.29
Fenfluramine	10,000	6.06
(+) Pseudoephedrine	200,000	0.67
(-) Pseudoephedrine	1,000,000	0.13
(-) Ephedrine	200,000	0.57
(+) Ephedrine	1,000,000	<0.10
Phentermine	1,000,000	<0.10
Tyramine	1,000,000	<0.10
Phenylephrine	1,000,000	<0.10
Diphenhydramine	1,000,000	<0.10
Phenylpropanolamine	1,000,000	<0.10

*f. Assay cut-off:*

Analytical performance of the device around the claimed cutoff is described in the precision section M.1.a. above.

2. Comparison studies:

*a. Method comparison with predicate device:*

The method comparison study was performed in-house using unaltered, clinical urine samples obtained from clinical testing laboratories. A total of 80 samples were analyzed using both the 500 ng/mL and 1000 ng/mL cutoffs. Each sample was run in singlicate on a Beckman Coulter AU400e Chemistry Analyzer and the result was compared to that obtained by liquid chromatography/mass spectroscopy (LC/MS). The results of the assay performance compared to LC/MS are summarized below:

500 ng/mL cutoff (n = 80)

Candidate Device Result	Methamphetamine Concentration by LC/MS (ng/mL)			
	< 250	250 – 499	500 – 750	> 750
Qualitative / POS	0	0	4	36
Qualitative / NEG	36	4	0	0
Semi-quant / POS	0	1*	4	36
Semi-quant / NEG	36	3	0	0

Qualitative agreement among positives = 40 / 40 (100%)

Qualitative agreement among negatives = 40 / 40 (100%)

Semi-quant agreement among positives = 40 / 40 (100%)

Semi-quant agreement among negatives = 39 / 40 (98%)

\*Discordant sample – 500 ng/mL cutoff

Candidate Device Result				LC/MS result (ng/mL)
Sample ID	Qualitative result	Semi-quantitative		
		Conc (ng/mL)	Result	
358433ZA	POS	544.9	POS	494

1000 ng/mL cutoff (n = 80)

Candidate Device Result	Methamphetamine Concentration by LC/MS (ng/mL)			
	< 500	500 – 999	1000 – 1500	> 1500
Qualitative / POS	0	0	16	24
Qualitative / NEG	36	4	0	0
Semi-quant / POS	0	0	3	36
Semi-quant / NEG	36	4	1*	0

Qualitative agreement among positives = 40 / 40 (100%)

Qualitative agreement among negatives = 40 / 40 (100%)

Semi-quant agreement among positives = 39 / 40 (98%)

Semi-quant agreement among negatives = 40 / 40 (100%)

\*Discordant sample – 1000 ng/mL cutoff

Candidate Device Result				LC/MS result (ng/mL)
Sample ID	Qualitative result	Semi-quantitative		
		Conc (ng/mL)	Result	
358429ZA	POS	998.5	NEG	1017

b. *Matrix comparison:*

Not applicable. This device is intended to be used with urine samples 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):

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.