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

A. 510(k) Number:

k143502

B. Purpose for Submission:

New device

C. Measurand:

Opiates

D. Type of Test:

Qualitative and semi-quantitative homogeneous enzyme immunoassay

E. Applicant:

Immunalysis Corporation

F. Proprietary and Established Names:

Immunalysis Opiates Enzyme Immunoassay
Immunalysis Opiates Urine Calibrators 300
Immunalysis Opiates Urine Calibrators 2000
Immunalysis Multi-Drug Controls

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DJG – Opiate Test System	II	862.3650	91 – Toxicology
DLJ– Clinical Toxicology Calibrator	II	862.3200	91 – Toxicology
DIF – Clinical Toxicology Control Material	I, reserved	862.3280	91 – Toxicology

H. Intended Use:

1. Intended use(s):

   See Indication(s) for use below.

2. Indication(s) for use:

The Immunalysis Opiates Urine Enzyme Immunoassay is a homogeneous enzyme immunoassay with a dual cutoff of 300ng/mL and 2000ng/mL. The assay is intended for use in laboratories for the qualitative and semi-quantitative analysis of opiates in human urine with automated clinical chemistry analyzers. This assay is calibrated against Morphine. 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 GC-MS or permitting laboratories to establish quality control procedures.

The Immunalysis Opiates 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. Gas Chromatography/Mass Spectrometry (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 Opiates Urine Calibrators 300 are intended for in vitro diagnostic use for the calibration of assays for the analytes currently listed in the package insert: Morphine. The Immunalysis Opiates Urine Calibrators 300 consists of 4 levels, with Level 1 containing 100ng/mL, Level 2 containing 300ng/mL, Level 3 containing 500ng/mL and Level 4 containing 1000ng/mL of morphine. The calibrators are designed for prescription use with homogenous enzyme immunoassays on automated clinical chemistry analyzers.

The Immunalysis Multi-Drug Controls are intended for in vitro diagnostic use to monitor the performance of assays for the analytes currently listed in the package insert: Benzoylecgonine, Methadone, Methamphetamine, Morphine, PCP, Secobarbital and Oxazepam for Immunalysis Multi-Drug Controls 1 and Benzoylecgonine, Methamphetamine and Morphine for Immunalysis Multi-Drug Controls 2. The controls are designed for prescription use with homogenous enzyme immunoassays on automated clinical chemistry analyzers.

The Immunalysis Opiates Urine Calibrators 2000 are intended for in vitro diagnostic use for the calibration of assays for the analytes currently listed in the package insert: Morphine. The Immunalysis Opiates Urine Calibrators 2000 consists of 4 levels, with Level 1 containing 1000ng/mL, Level 2 containing 2000ng/mL, Level 3 containing 4000ng/mL and Level 4 containing 6000ng/mL of morphine. The calibrators are designed for prescription use with homogenous enzyme immunoassays on automated clinical chemistry analyzers.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

Performance data was obtained using the Beckman AU400e clinical chemistry analyzer.

I. Device Description:

The Immunalysis Opiates Urine Enzyme Immunoassay Kit contains two reagents, which are provided as ready-to-use:

- Antibody/Substrate Reagent (RA) – This reagent contains monoclonal antibodies to morphine, glucose-6-phosphate (G6P) and nicotinamide adenine dinucleotide (NAD) in Tris buffer with Sodium Azide as a preservative.
- Enzyme Conjugate Reagent (RE) – This reagent contains glucose-6-phosphate dehydrogenase (G6PDH) labeled with morphine in Tris buffer with Sodium Azide as a preservative.

The Immunalysis Opiates Urine Calibrators 300, the Immunalysis Opiates Urine Calibrators 2000, and the Immunalysis Multi-Drug Controls are sold as individual bottles and are liquid and ready-to-use. The negative calibrator is a processed, drug-free synthetic urine matrix with sodium azide as a preservative. Each calibrator and control level contains a known concentration of a specific drug analyte spiked into the negative calibrator matrix (see tables below).

Immunalysis Opiates Urine Calibrators 300				
Analyte	Level 1	Level 2	Level 3	Level 4
Morphine	100 ng/mL	300 ng/mL	500 ng/mL	1000 ng/mL
Immunalysis Opiates Urine Calibrators 2000				
Analyte	Level 1	Level 2	Level 3	Level 4
Morphine	1000 ng/mL	2000 ng/mL	4000 ng/mL	6000 ng/mL

Immunalysis Multi-Drug Controls 1		
Analyte	LOW Control 1	HIGH Control 1
Benzoylecgonine	112.5 ng/mL	187.5 ng/mL
Methadone	225 ng/mL	375 ng/mL
Methamphetamine	375 ng/mL	625 ng/mL
Morphine	225 ng/mL	375 ng/mL
PCP	19 ng/mL	31 ng/mL
Secobarbital	150 ng/mL	250 ng/mL
Oxazepam	150 ng/mL	250 ng/mL

Immunalysis Multi-Drug Controls 2		
Analyte	LOW Control 2	HIGH Control 2
Benzoylecgonine	225 ng/mL	375 ng/mL
Methamphetamine	750 ng/mL	1250 ng/mL
Morphine	1500 ng/mL	2500 ng/mL

J. Substantial Equivalence Information:

1. Predicate device name(s):

   DRI DAU Opiate Assay
   LZI Multiple Analyte Urine Drugs of Abuse Calibrators and Controls

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

   k011150
   k051088

3. Comparison with predicate:

Opiates Assay		
Item	Immunalysis Opiates Urine EIA	DAU Opiate Assay k011150
Intended Use	For the qualitative and semi-quantitative determination of the presence of opiates in human urine at a cutoff of 300 ng/mL and 2000 ng/mL	Same
Type of Product	Analytical Reagents	Same
Measured Analytes	Opiates	Same
Test Matrix	Urine	Same
Cutoff Levels	300 ng/mL and 2000 ng/mL of Morphine	Same
Test System	Homogeneous Enzyme Immunoassay (EIA)	Same
Materials	Antibody/Substrate Reagents and Enzyme Labeled Conjugate	Same
Mass Spectroscopy Confirmation	Required for preliminary positive analytical results	Same
Antibody	Monoclonal antibody to Opiates	Same
Storage	2-8°C until expiration date	Same

Calibrators		
Item	Immunalysis Opiates Urine Calibrators 300 and 2000	LZI Multiple Analytes Calibrators and Controls k051088
Analytes	Morphine	Benzoylecgonine, d-methamphetamine, methadone, morphine, oxazepam, secobarbital, phencyclidine, propxyphene
Matrix	Processed, drug-free synthetic urine	Same
Calibrator Levels	5 levels (Negative, Level 1-4)	5 levels (Negative, Low, Cutoff, Intermediate, High)
Storage	2-8°C until expiration date	Same

Multi-Drug Controls		
Item	Immunalysis Multi-Drug Controls	LZI Multiple Analytes Calibrators and Controls k051088
Analytes	Benzoylecgonine, methadone, methamphetamine, morphine, PCP, secobarbital, oxazepam	Benzoylecgonine, d-methamphetamine, methadone, morphine, oxazepam, secobarbital, phencyclidine, propxyphene
Matrix	Processed, drug-free synthetic urine	Same
Control Levels	4 levels (LOW Control 1+2, HIGH Control 1+2)	2 levels (Control Level 1+2)
Storage	2-8°C until expiration date	Same

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

CLSI EP5-A2, "Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline—Second Edition"

CLSI EP7-A2, "Interference Testing in Clinical Chemistry; Approved Guideline—Second Edition"

L. Test Principle:

The assay is based on the competition of opiates labeled enzyme glucose-6-phosphate dehydrogenase (G6PDH) and the free drug in the urine sample for the 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 340nm spectrophotometrically by the conversion of NAD to NADH.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

A precision/cutoff characterization study was performed by an in-house technician for 20 days, 2 runs per day in duplicate (N=80) on drug-free negative urine samples spiked with morphine to concentrations of ±0%, ±25%, ±50%, ±75%, and ±100% of each cutoff. The morphine concentrations in spiked samples were confirmed by mass spectrometry.

Qualitative Analysis (for 300ng/mL cutoff)			
Concentration (ng/mL)	% of cutoff	# of determinations	Result
0	-100%	80	80 Negative
75	-75%	80	80 Negative
150	-50%	80	80 Negative
225	-25%	80	80 Negative
300	Cutoff	80	37 Negative/43 Positive
375	+25%	80	80 Positive
450	+50%	80	80 Positive
525	+75%	80	80 Positive
600	+100%	80	80 Positive

Qualitative Analysis (for 2000ng/mL cutoff)			
Concentration (ng/mL)	% of cutoff	# of determinations	Result
0	-100%	80	80 Negative
500	-75%	80	80 Negative
1000	-50%	80	80 Negative
1500	-25%	80	80 Negative
2000	Cutoff	80	42 Negative/38 Positive
2500	+25%	80	80 Positive
3000	+50%	80	80 Positive
3500	+75%	80	80 Positive
4000	+100%	80	80 Positive

Semi-Quantitative Analysis (for 300ng/mL cutoff)			
Concentration (ng/mL)	% of cutoff	# of determinations	Result
0	-100%	80	80 Negative
75	-75%	80	80 Negative
150	-50%	80	80 Negative
225	-25%	80	80 Negative
300	Cutoff	80	20 Negative/60 Positive
375	+25%	80	80 Positive
450	+50%	80	80 Positive
525	+75%	80	80 Positive
600	+100%	80	80 Positive

Semi-Quantitative Analysis (for 2000ng/mL cutoff)			
Concentration (ng/mL)	% of cutoff	# of determinations	Result
0	-100%	80	80 Negative
500	-75%	80	80 Negative
1000	-50%	80	80 Negative
1500	-25%	80	80 Negative
2000	Cutoff	80	41 Negative/39 Positive
2500	+25%	80	80 Positive
3000	+50%	80	80 Positive
3500	+75%	80	80 Positive
4000	+100%	80	80 Positive

b. Linearity/assay reportable range:

A linearity study in the semi-quantitative mode was conducted by spiking a drug-free urine pool with a high concentration of morphine and generating serial dilutions in increments of 10% to achieve concentrations ranging from 100ng/mL to 1100ng/mL for the 300 ng/mL cutoff, and 600 ng/mL to 6600 ng/mL for the 2000 ng/mL cutoff. Each concentration was tested in triplicate and drug recovery calculated using the mean concentration of the replicates. The results are summarized below:

Linearity/ Recovery – 300ng/mL		
Expected Concentration (ng/mL)	Mean Concentration (ng/mL)	Recovery (%)
100	91.6	91.6
200	203.7	101.8

300	292.8	97.6
400	410.1	102.5
500	488.1	97.6
600	651.1	108.5
700	759.4	108.5
800	840.6	105.1
900	906.5	100.7
1000	1024.1	102.4
1100	1069.9	97.3

Linearity/ Recovery – 2000ng/mL		
Expected Concentration (ng/mL)	Mean Concentration (ng/mL)	Recovery (%)
600	635.0	105.8
1200	1295.2	107.9
1800	1750.9	97.3
2000	2079.0	104.0

2400	2231.1	93.0
3000	3142.9	104.8
3600	3852.7	107.0
4200	4465.4	106.3
4800	5101.8	106.3
5400	5789.0	107.2
6000	5972.3	99.5
6600	6637.7	100.6

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

Traceability

Calibrators and controls are prepared from a commercially available, certified standard solution. This standard solution is diluted with the negative calibrator matrix to make the calibrator and control materials in the desired concentrations. The concentrations are confirmed by GC/MS or LC/MS-MS. The negative calibrator is a processed, drug-free urine matrix.

Value Assignment/Expected Values

A commercially available standard solution is added to the negative calibrator matrix to make the calibrator and control materials in the desired concentrations. Concentrations are confirmed by GC/MS or LC/MS-MS. If any of the analytes are below the acceptable range, the calibrator or control is adjusted and re-tested. Values are assigned once the GC/MS or LC/MS-MS results are within the acceptable range. The negative calibrator 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.

Stability

A closed-vial accelerated stability study and an onboard, open vial stability study were conducted on one lot each of calibrators, and controls. Real-time stability studies are ongoing. All stability protocols were reviewed and found acceptable. These studies support the one year stability claim for closed vials and 28 days stability claim for open vials of calibrators, and controls when stored at 2-8°C.

d. *Detection limit:*
Not applicable.

e. *Analytical specificity:*

An analytical specificity study to evaluate possible interference from non-structurally and structurally related compounds was performed in the qualitative and semi-quantitative mode for each cutoff concentration.

Structurally related compounds

To evaluate potential cross-reactants for the Immunalysis Opiates Urine Enzyme Immunoassay kit, morphine and other opiates were spiked into drug free urine at concentrations that will yield a result that is equivalent to the 300ng/mL or 2000ng/mL Opiates cutoff. The results were the same for the qualitative and semi-quantitative modes.

Structurally Related Compounds (for 300ng/mL cutoff)				
Compound	Concentration Tested (ng/mL)	Result	Morphine Equivalents (ng/mL)	Cross-Reactivity (%)
6-Acetylmorphine	150	POS	300	200.0
Codeine	200	POS	300	150.0
Dihydrocodeine	150	POS	300	200.0
Ethylmorphine	300	POS	300	100.0
Heroin	300	POS	300	100.0
Hydrocodone	400	POS	300	75.0
Levorphanol	8,000	POS	300	3.8
Morphine-3-Glucuronide	200	POS	300	150.0
Morphine-6-Glucuronide	100	POS	300	300.0
Hydromorphone	700	POS	300	42.9
Nalorphine	2,000	POS	300	15.0
Naloxone	60,000	POS	300	0.5
Norcodeine	25,000	POS	300	1.2
Normorphine	25,000	POS	300	1.2
Oxycodone	10,000	POS	300	3.0

Oxymorphone	20,000	POS	300	1.5

Structurally Related Compounds (for 2000ng/mL cutoff)				
Compound	Concentration Tested (ng/mL)	Result	Morphine Equivalents(ng/mL)	Cross-Reactivity (%)
6-Acetylmorphine	2,000	POS	2,000	100.0
Codeine	2,000	POS	2,000	100.0
Dihydrocodeine	600	POS	2,000	333.3
Ethylmorphine	2,000	POS	2,000	100.0
Heroin	4,000	POS	2,000	50.0
Hydrocodone	4,000	POS	2,000	50.0
Levorphanol	100,000	POS	2,000	2.0
Morphine-3-Glucuronide	2,000	POS	2,000	100.0
Morphine-6-Glucuronide	600	POS	2,000	333.3
Hydromorphone	8,000	POS	2,000	25.0
Nalorphine	28,000	POS	2,000	7.1
Naloxone	500,000	POS	2,000	0.4
Norcodeine	300,000	POS	2,000	0.7
Normorphine	300,000	POS	2,000	0.7
Oxycodone	100,000	POS	2,000	2.0
Oxymorphone	200,000	NEG	2,000	1.0

Non-structurally related compounds

Potential interference from non-structurally related drugs and metabolites was evaluated in the qualitative and semi-quantitative modes by spiking these compounds into drug free urine containing morphine at ±25% of the 300 cutoff (225 ng/mL and 375ng/mL) and ±25% of the 2000ng/mL cutoff (1500ng/mL and 2500ng/mL). The results were the same for the qualitative and semi-quantitative modes.

Structurally Non-Similar Compounds (for 300ng/mL cutoff)			
Compound	Concentration Tested (ng/mL)	-25% Cutoff	+25% Cutoff
		Result	Result
4-Bromo-2,5,Dimethoxy-phenethylamine	100,000	Negative	Positive
Acetaminophen	500,000	Negative	Positive
Acetylsalicylic Acid	500,000	Negative	Positive
Alprazolam	100,000	Negative	Positive
(+) Amphetamine	500,000	Negative	Positive
Amitriptyline	100,000	Negative	Positive
Amobarbital	100,000	Negative	Positive

Benzoylecgonine	500,000	Negative	Positive
Benzylpiperazine	100,000	Negative	Positive
Bromazepam	100,000	Negative	Positive
Buprenorphine	100,000	Negative	Positive
Buprion	100,000	Negative	Positive
Butabarbital	100,000	Negative	Positive
Caffeine	500,000	Negative	Positive
Carbamazepine	100,000	Negative	Positive
Cocaine	100,000	Negative	Positive
Clomipramine	100,000	Negative	Positive
Clonazepam	100,000	Negative	Positive
Chloropromazine	100,000	Negative	Positive
Cyclobenzaprine	100,000	Negative	Positive
N-Desmethyltapentadol	100,000	Negative	Positive
Desipramine	100,000	Negative	Positive
Dextromethorphan	100,000	Negative	Positive
Diazepam	100,000	Negative	Positive
Diphenhydramine	500,000	Negative	Positive
Doxepin	100,000	Negative	Positive
Ephedrine	100,000	Negative	Positive
EDDP	100,000	Negative	Positive
Ethyl-glucuronide	100,000	Negative	Positive
Fenfluramine	100,000	Negative	Positive
Fluoxetine	100,000	Negative	Positive
Flurazepam	100,000	Negative	Positive
Hexobarbital	100,000	Negative	Positive
Ibuprofen	100,000	Negative	Positive
Imipramine	100,000	Negative	Positive
Ketamine	100,000	Negative	Positive
Lidocaine	100,000	Negative	Positive
LSD	100,000	Negative	Positive
Lorazepam	100,000	Negative	Positive
Maprotiline	100,000	Negative	Positive
MDEA	100,000	Negative	Positive
MDA	100,000	Negative	Positive
MDMA	100,000	Negative	Positive
Meperidine	50,000	Negative	Positive
Methadone	500,000	Negative	Positive
Methaqualone	100,000	Negative	Positive
(+) Methamphetamine	500,000	Negative	Positive
Meprobamate	100,000	Negative	Positive
Naltrexone	100,000	Negative	Positive
Nitrazepam	100,000	Negative	Positive
Norbuprenorphine	100,000	Negative	Positive
Nordiazepam	100,000	Negative	Positive
Nortryptyline	100,000	Negative	Positive

Norpropoxyphene	100,000	Negative	Positive
Oxazepam	100,000	Negative	Positive
Pentobarbital	100,000	Negative	Positive
Phenobarbital	100,000	Negative	Positive
Pentazocine	100,000	Negative	Positive
Phencyclidine	100,000	Negative	Positive
Phentermine	100,000	Negative	Positive
Phenylpropanolamine	500,000	Negative	Positive
PMA	100,000	Negative	Positive
(-)Pseudoephedrine	100,000	Negative	Positive
(+)Pseudoephedrine	100,000	Negative	Positive
Phenytoin	100,000	Negative	Positive
Protryptyline	100,000	Negative	Positive
Ranitidine	100,000	Negative	Positive
Ritalinic Acid	100,000	Negative	Positive
Secobarbital	100,000	Negative	Positive
Sufentanil	100,000	Negative	Positive
Temazepam	100,000	Negative	Positive
11-nor-9 carboxy THC	100,000	Negative	Positive
Tramadol	100,000	Negative	Positive
Trimipramine	100,000	Negative	Positive
Venlafaxine	100,000	Negative	Positive

Structurally Non-Similar Compounds (for 2000ng/mL cutoff)			
Compound	Concentration Tested (ng/mL)	**-25% Cutoff**	**+25% Cutoff**
		Result	Result
4-Bromo-2,5,Dimethoxy-phenethylamine	100,000	Negative	Positive
Acetaminophen	500,000	Negative	Positive
Acetylsalicylic Ac	500,000	Negative	Positive
Alprazolam	100,000	Negative	Positive
(+) Amphetamine	500,000	Negative	Positive
Amitriptyline	100,000	Negative	Positive
Amobarbital	100,000	Negative	Positive
Benzoylecgonine	500,000	Negative	Positive
Benzylpiperazine	100,000	Negative	Positive
Bromazepam	100,000	Negative	Positive
Buprenorphine	100,000	Negative	Positive
Buprion	100,000	Negative	Positive
Butabarbital	100,000	Negative	Positive
Caffeine	500,000	Negative	Positive
Carbamazepine	100,000	Negative	Positive
Cocaine	100,000	Negative	Positive
Clomipramine	100,000	Negative	Positive
Clonazepam	100,000	Negative	Positive

Chloropromazine	100,000	Negative	Positive
Cyclobenzaprine	100,000	Negative	Positive
N-Desmethyltapentadol	100,000	Negative	Positive
Desipramine	100,000	Negative	Positive
Dextromethorphan	100,000	Negative	Positive
Diazepam	100,000	Negative	Positive
Diphenhydramine	500,000	Negative	Positive
Doxepin	100,000	Negative	Positive
Ephedrine	100,000	Negative	Positive
EDDP	100,000	Negative	Positive
Ethyl-glucuronide	100,000	Negative	Positive
Fenfluramine	100,000	Negative	Positive
Fluoxetine	100,000	Negative	Positive
Flurazepam	100,000	Negative	Positive
Hexobarbital	100,000	Negative	Positive
Ibuprofen	100,000	Negative	Positive
Imipramine	100,000	Negative	Positive
Ketamine	100,000	Negative	Positive
Lidocaine	100,000	Negative	Positive
LSD	100,000	Negative	Positive
Lorazepam	100,000	Negative	Positive
Maprotiline	100,000	Negative	Positive
MDEA	100,000	Negative	Positive
MDA	100,000	Negative	Positive
MDMA	100,000	Negative	Positive
Meperidine	100,000	Negative	Positive
Methadone	500,000	Negative	Positive
Methaqualone	100,000	Negative	Positive
(+) Methamphetamine	500,000	Negative	Positive
Meprobamate	100,000	Negative	Positive
Naltrexone	100,000	Negative	Positive
Nitrazepam	100,000	Negative	Positive
Norbuprenorphine	100,000	Negative	Positive
Nordiazepam	100,000	Negative	Positive
Nortryptyline	100,000	Negative	Positive
Norpropoxyphene	100,000	Negative	Positive
Oxazepam	100,000	Negative	Positive
Pentobarbital	100,000	Negative	Positive
Phenobarbital	100,000	Negative	Positive
Pentazocine	100,000	Negative	Positive
Phencyclidine	100,000	Negative	Positive
Phentermine	100,000	Negative	Positive
Phenylpropanolamine	500,000	Negative	Positive
PMA	100,000	Negative	Positive
(-)Pseudoephedrine	100,000	Negative	Positive
(+)Pseudoephedrine	100,000	Negative	Positive

Phenytoin	100,000	Negative	Positive
Protryptyline	100,000	Negative	Positive
Ranitidine	100,000	Negative	Positive
Ritalinic Acid	100,000	Negative	Positive
Secobarbital	100,000	Negative	Positive
Sufentanil	100,000	Negative	Positive
Temazepam	100,000	Negative	Positive
11-nor-9 carboxy THC	100,000	Negative	Positive
Tramadol	100,000	Negative	Positive
Trimipramine	100,000	Negative	Positive
Venlafaxine	100,000	Negative	Positive

Endogenous compounds

Potential interference from endogenous compounds was evaluated in the qualitative and semi-quantitative modes, by spiking these compounds into drug free urine containing morphine at ±25% of the 300ng/mL cutoff (225ng/mL and 375ng/mL) and 2000ng/mL cutoff (1500ng/mL cutoff and 2500ng/mL). The results were the same for the qualitative and semi-quantitative modes.

Endogenous Compounds (for 300ng/mL cutoff)			
Compound	Concentration Tested	**-25% Cutoff**	**+25% Cutoff**
Acetone	1.0 g/dL	Negative	Positive
Ascorbic Acid	1.5 g/dL	Negative	Positive
Bilirubin	0.002 g/dL	Negative	Positive
Boric Acid	**1 % w/v**	**Negative**	**Negative**
Creatinine	0.5 g/dL	Negative	Positive
Ethanol	1.0 g/dL	Negative	Positive
Galactose	0.01 g/dL	Negative	Positive
γ-Globulin	0.5 g/dL	Negative	Positive
Glucose	2.0 g/dL	Negative	Positive
Hemoglobin	0.300 g/dL	Negative	Positive
Human Serum Albumin	0.5 g/dL	Negative	Positive
Oxalic Acid	0.1 g/dL	Negative	Positive
Riboflavin	**0.0075 g/dL**	**Negative**	**Negative**
Sodium Azide	1% w/v	Negative	Positive
Sodium Chloride	6.0 g/dL	Negative	Positive
Sodium Fluoride	1% w/v	Negative	Positive
Urea	6.0 g/dL	Negative	Positive

Endogenous Compounds (for 2000ng/mL cutoff)			
Compound	Concentration Tested	**-25% Cutoff**	**+25% Cutoff**
Acetone	1.0 g/dL	Negative	Positive
Ascorbic Acid	1.5 g/dL	Negative	Positive
Bilirubin	0.002 g/dL	Negative	Positive
Boric Acid	**1% w/v**	**Negative**	**Negative**
Creatinine	0.5 g/dL	Negative	Positive
Ethanol	1.0 g/dL	Negative	Positive
Galactose	0.01 g/dL	Negative	Positive
γ-Globulin	0.5 g/dL	Negative	Positive
Glucose	2.0 g/dL	Negative	Positive
Hemoglobin	0.300 g/dL	Negative	Positive
Human Serum Albumin	0.5 g/dL	Negative	Positive
Oxalic Acid	0.1 g/dL	Negative	Positive
Riboflavin	0.0075 g/dL	Negative	Positive
Sodium Azide	1% w/v	Negative	Positive
Sodium Chloride	6.0 g/dL	Negative	Positive
Sodium Fluoride	1% w/v	Negative	Positive
Urea	6.0 g/dL	Negative	Positive

Compounds that showed interference were further evaluated by spiking them into drug free urine containing morphine at ±50% of the cutoff. Riboflavin at 0.0075 g/dL caused a false negative response for morphine at ±25% but not at ±50% of the 300 ng/mL cutoff. Boric Acid at 1% w/v caused a false negative response for morphine at ±25% and ±50% of the 300 ng/mL cutoff, and caused a false negative response for morphine at ±25% but not at ±50% of the 2000 ng/mL cutoff. The results were the same for the qualitative and semi-quantitative modes.

The following statement is provided in the limitations section of the labeling: *"Boric Acid is not recommended as a preservative for urine. Boric Acid and Riboflavin can cause a falsely low test result."*

pH and Specific Gravity

For potential interference from the pH of urine, device performance in the qualitative and semi-quantitative modes was tested using a range of urine pH values (3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 9.0, 10.0 and 11.0). All test samples were prepared in drug free urine containing morphine at ± 25 of the 300ng/mL cutoff (225ng/mL and 375ng/mL) and 2000ng/mL cutoff (1500ng/mL and 2500ng/mL). No positive or negative interference was observed at urine pH values ranging from 3.0 to 11.0 for each test mode.

For potential interference from the specific gravity of urine, device performance in the qualitative and semi-quantitative modes was tested using a range of urine specific gravity values (1.000, 1.002, 1.005, 1.010, 1.015, 1.020, 1.025 and 1.030). All test samples were prepared in drug free urine containing morphine at ± 25% of the 300ng/mL cutoff (225ng/mL and 375ng/mL) and 2000ng/mL cutoff (1500ng/mL and 2500ng/mL). No positive or negative interference was observed at urine specific gravity values ranging

from 1.000 to 1.030 for each test mode.

f. Assay cut-off:

Characterization of how the device performs analytically around the claimed cutoff concentrations of 300 ng/mL and 2000 ng/mL is described in the precision section, M.1.a. above.

2. Comparison studies:

a. Method comparison with predicate device:

80 unaltered urine samples from clinical testing laboratories were analyzed by the candidate device in the qualitative and semi-quantitative modes on the Beckman Coulter AU400e clinical chemistry analyzer and the comparative mass spectrometry based quantitative method (LC/MS) for morphine and other opiates. The results from the study are summarized below:

Assay Performance verified by LC/MS (300ng/mL Cutoff – Qualitative)				
Candidate Device Results	Total Opiate Concentration			
	< 150ng/mL (<50% cutoff)	150 ~ 299 ng/mL (-50% to cutoff)	300 ~ 450 ng/mL (cutoff to +50%)	> 450 ng/mL (>50% cutoff)
Positive	0	1	5	35
Negative	36	3	0	0

Discordant Result Summary (300ng/mL Cutoff – Qualitative)		
Qualitative Results	LC/MS Confirmation	
Test Device	Qualitative	Total Opiate Concentration (ng/mL)
Positive	Negative	200

% Agreement among positives is 98%.

% Agreement among negatives is 100%.

Assay Performance verified by LC/MS (2000ng/mL Cutoff – Qualitative)				
Candidate Device Results	Total Opiate Concentration			
	< 1000ng/mL (<50% cutoff)	1000~1999 ng/mL (-50% to cutoff)	2000~3000 ng/mL (cutoff to +50%)	> 3000 ng/mL (>50% cutoff)
Positive	0	0	5	35
Negative	36	4	0	0

% Agreement among positives is 100%.

% Agreement among negatives is 100%.

Assay Performance verified by LC/MS (300ng/mL Cutoff – Semi-quantitative)				
Candidate Device Results	Total Opiate Concentration			
	< 150ng/mL (<50% cutoff)	150 ~ 299 ng/mL (-50% to cutoff)	300 ~ 450 ng/mL (cutoff to +50%)	> 450 ng/mL (>50% cutoff)
Positive	0	0	5	35
Negative	36	4	0	0

% Agreement among positives is 100%.

% Agreement among negatives is 100%.

Assay Performance verified by LC/MS (2000ng/mL Cutoff – Semi-quantitative)				
Candidate Device Results	Total Opiate Concentration			
	< 1000ng/mL (<50% cutoff)	1000~1999 ng/mL (-50% to cutoff)	2000~3000 ng/mL (cutoff to +50%)	> 3000 ng/mL (>50% cutoff)
Positive	0	0	5	35
Negative	36	4	0	0

% Agreement among positives is 100%.

% Agreement among negatives is 100%.

b. Matrix comparison:

Not applicable. Urine is the only claimed matrix for the candidate device.

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.