510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K203527

B Applicant

Immunalysis Corporation

C Proprietary and Established Names

Immunalysis Tapentadol Urine HEIA™

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DJG	Class II	21 CFR 862.3650 - Opiate Test System	TX - Clinical Toxicology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Tapentadol

C Type of Test:

Qualitative and Semi-quantitative Enzyme Immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

For in vitro diagnostic use.

The Immunalysis Tapentadol Urine HEIA™ is a homogeneous enzyme immunoassay with a cutoff of 200 ng/mL. The assay is intended for use in laboratories for the qualitative and semi-quantitative analysis of tapentadol in human urine with automated clinical chemistry analyzers. This assay is calibrated against tapentadol. This in vitro diagnostic device is for prescription use only.

The Immunalysis Tapentadol Urine HEIA™ 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-Tandem Mass Spectrometry (LC-MS/MS) is the preferred confirmatory method.

Clinical consideration and professional judgment should be applied to any test result, particularly when preliminary positive results are used.

The semi-quantitative mode is for purposes of enabling laboratories to determine an appropriate dilution of the specimen for confirmation using a confirmatory method such as Gas Chromatography/ Mass Spectrometry (GC-MS) or Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS).

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Beckman Coulter AU 480 chemistry analyzer.

IV Device/System Characteristics:

A Device Description:

The Immunalysis Tapentadol Urine HEIA™ consists of ready to use reagents as follows:

- 1 bottle (25 mL, 60 mL, 100 mL, or 500 mL) of Antibody/Substrate Reagent (Reagent A) containing recombinant antibodies to Tapentadol, glucose-6-phosphate (G6P) and nicotinamide adenine dinucleotide (NAD) (<0.5%) in Tris buffer with Sodium Azide as a preservative.
- 1 bottle (25 mL, 60 mL, 100 mL, or 500 mL) of Enzyme Conjugate Reagent (Reagent E) containing glucose-6-phosphate dehydrogenase (G6PDH) labeled with tapentadol (<0.5%) in Tris buffer with Sodium Azide as a preservative.

B Principle of Operation:

The assay is based on the competition of tapentadol labeled enzyme glucose-6-phosphate dehydrogenase (G6PDH) and the free drug in the urine sample for the fixed amount of rabbit anti-tapentadol 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 and enzyme activity. The enzyme G6PDH activity is determined at 340 nm spectrophotometrically by the conversion of NAD to NADH.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Immunalysis Tramadol Urine Enzyme Immunoassay

B Predicate 510(k) Number(s):
K141803

C Comparison with Predicate(s):

Device & Predicate Device(s):	K203527	K141803
Device Trade Name	Immunalysis Tapentadol Urine HEIA™	Immunalysis Tramadol Enzyme Immunoassay
General Device Characteristic Similarities		
Intended Use	Same	For the qualitative and semi-quantitative analysis of an opioid in human urine with automated clinical chemistry analyzers.
Test Principle	Same	Homogeneous enzyme immunoassay
User Environment	Same	For use in laboratories
Sample Matrix	Same	Human urine
Mass Spectrometry Confirmation	Same	Required for preliminary positive analytical results
General Device Characteristic Differences		
Antibody	Recombinant FAB antibody to Tapentadol	Goat Polyclonal Antibody to Tramadol
Calibrator	Tapentadol	Tramadol

VI Standards/Guidance Documents Referenced:

- ISO 14971:2007 Medical Devices – Application of Risk Management to Medical Devices
- EN ISO 14971:2012 Medical Devices – Application of Risk Management to Medical Devices

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A precision study was performed over 20 days, two runs per day in duplicates (20 x 2 x 2 replicates per panel member) for a total of 80 replicates (N=80) per sample on 3 lots of reagent. Nine panel members were prepared using drug free negative urine as the base sample and 8 panel members were spiked to concentrations of assay cutoff and ±25%, ±50%, ±75%, ±100% of the cutoff (200 ng/mL). The concentrations used for spiking were confirmed by liquid chromatography tandem mass spectrometry (LC-MS/MS).

Summary of Precision – Qualitative

Concentration (ng/mL)	% of cutoff	# of determinations	Result
Lot# 1			
0	-100%	80	80 Negative
50	-75%	80	80 Negative
100	-50%	80	80 Negative
150	-25%	80	80 Negative
200	Cutoff	80	41 Neg / 39 Pos
250	+25%	80	80 Positive
300	+50%	80	80 Positive
350	+75%	80	80 Positive
400	+100%	80	80 Positive
Lot# 2			
0	-100%	80	80 Negative
50	-75%	80	80 Negative
100	-50%	80	80 Negative
150	-25%	80	80 Negative
200	Cutoff	80	35 Neg / 45 Pos
250	+25%	80	80 Positive
300	+50%	80	80 Positive
350	+75%	80	80 Positive
400	+100%	80	80 Positive

Concentration (ng/mL)	% of cutoff	# of determinations	Result
Lot# 3			
0	-100%	80	80 Negative
50	-75%	80	80 Negative
100	-50%	80	80 Negative
150	-25%	80	80 Negative
200	Cutoff	80	42 Neg / 38 Pos
250	+25%	80	80 Positive
300	+50%	80	80 Positive
350	+75%	80	80 Positive
400	+100%	80	80 Positive

Summary of Precision - Semi-Quantitative

Concentration (ng/mL)	% of cutoff	# of determinations	Mean Conc. (ng/mL)	Qualitative Interpretative Result	SD	CV (%)
Lot# 1						
0	-100%	80	-3	80 Negative	8.0	N/A
50	-75%	80	48	80 Negative	4.7	9.7
100	-50%	80	99	80 Negative	7.5	7.6
150	-25%	80	161	80 Negative	5.8	3.6
200	Cutoff	80	215	2 Neg / 78 Pos	8.6	4.0
250	+25%	80	268	80 Positive	10.0	3.7
300	+50%	80	304	80 Positive	17.6	5.8
350	+75%	80	372	80 Positive	25.4	6.8
400	+100%	80	431	80 Positive	25.2	5.9
Lot# 2						
0	-100%	80	-4	80 Negative	8.9	N/A
50	-75%	80	50	80 Negative	4.8	9.7
100	-50%	80	100	80 Negative	7.8	7.7
150	-25%	80	162	80 Negative	7.6	4.7
200	Cutoff	80	213	8 Neg / 72 Pos	10.6	5.0
250	+25%	80	263	80 Positive	12.3	4.7
300	+50%	80	298	80 Positive	17.6	5.9
350	+75%	80	359	80 Positive	20.2	5.6
400	+100%	80	417	80 Positive	21.7	5.2
Lot# 3						
0	-100%	80	-3	80 Negative	7.1	N/A
50	-75%	80	49	80 Negative	4.4	8.9
100	-50%	80	102	80 Negative	6.9	6.8

Concentration (ng/mL)	% of cutoff	# of determinations	Mean Conc. (ng/mL)	Qualitative Interpretative Result	SD	CV (%)
150	-25%	80	162	80 Negative	6.1	3.8
200	Cutoff	80	215	7 Neg / 73 Pos	9.7	4.5
250	+25%	80	266	80 Positive	9.9	3.7
300	+50%	80	303	80 Positive	16.0	5.3
350	+75%	80	369	80 Positive	20.7	5.6
400	+100%	80	422	80 Positive	20.6	4.9

2. Linearity:
A linearity study in the semi-quantitative mode was conducted by spiking a drug free urine pool with a high concentration of tapentadol above the highest calibrator. Additional linearity samples were made by serially diluting the high concentration specimen with drug free urine to achieve concentrations ranging from 100 to 1100 ng/mL. The 0 ng/mL specimen was made from drug free urine. Each pool was tested in triplicate to calculate the mean concentration values that were used to calculate drug recovery of tapentadol. The assay drug recovery percentage ranged from 95.8 to 110.4 %. Linearity test results in semi-quantitative mode are presented below.

Linearity/Recovery – Tapentadol

Expected Concentration (ng/mL)	Mean Concentration (ng/mL)	Recovery (%)
0	3.0	N/A
100	110.4	110.4
200	211.6	105.8
300	298.2	99.4
400	417.3	104.3
500	531.2	106.2
600	614.1	102.4
700	721.7	103.1
800	827.3	103.4
900	907.8	100.9
1000	980.1	98.0
1100	1054.3	95.8

3. Analytical Specificity/Interference:

Cross Reactivity

Structurally and functionally similar compounds were spiked into drug free urine at levels that will yield a result that is equivalent to the cutoff. The data demonstrates all sample compounds tested were negative by both the qualitative and semi-quantitative interpretations except for N-desmethyl tapentadol and tapentadol glucuronide. The % of cross- reactivity of the semi-quantitative results was < 0.2 % for all compounds tested except for N-desmethyl tapentadol with 15.7% and tapentadol glucuronide with 0.5% of cross- reactivity. Cross-reactivity test results in qualitative mode and semi-quantitative mode are presented in below.

Cross-Reactivity – Qualitative

Compound	Compound Conc. ng/mL)	Tapentadol Equivalent Conc. (ng/mL)	Result	Cross-Reactivity (%)
Chlorpromazine	100,000	< 200	NEG	<0.2
Clomipramine	100,000	<200	NEG	<0.2
Cyclobenzaprine	100,000	<200	NEG	<0.2
Doxepin	100,000	<200	NEG	<0.2
Imipramine	100,000	<200	NEG	<0.2
O-desmethyl tramadol	100,000	<200	NEG	<0.2
O-desmethyl venlafaxine	100,000	<200	NEG	<0.2
N-desmethyl tapentadol	1,275	200	POS	15.7
N-desmethyl tramadol	100,000	<200	NEG	<0.2
N-desmethyl venlafaxine	100,000	<200	NEG	<0.2
Tapentadol glucuronide	43,000	200	POS	0.5
Tramadol	100,000	<200	NEG	<0.2
Trimipramine	100,000	<200	NEG	<0.2
Venlafaxine	100,000	<200	NEG	<0.2

Cross-Reactivity – Semi-Quantitative

Compound	Compound Conc. (ng/mL)	Tapentadol Equivalent Conc. (ng/mL)	Mean Value (ng/mL)	Result	Cross-Reactivity (%)
Chlorpromazine	100,000	< 200	47.3	NEG	<0.2
Clomipramine	100,000	<200	47.6	NEG	<0.2
Cyclobenzaprine	100,000	<200	1.0	NEG	<0.2
Doxepin	100,000	<200	0.9	NEG	<0.2
Imipramine	100,000	<200	69.7	NEG	<0.2

Compound	Compound Conc. (ng/mL)	Tapentadol Equivalent Conc. (ng/mL)	Mean Value (ng/mL)	Result	Cross-Reactivity (%)
O-desmethyl tramadol	100,000	<200	101.0	NEG	<0.2
O-desmethyl venlafaxine	100,000	<200	1.8	NEG	<0.2
N-desmethyl tapentadol	1,275	200	214.3	POS	15.7
N-desmethyl tramadol	100,000	<200	6.0	NEG	<0.2
N-desmethyl venlafaxine	100,000	<200	1.9	NEG	<0.2
Tapentadol glucuronide	43,000	200	211.7	POS	0.5
Tramadol	100,000	<200	2.5	NEG	<0.2
Trimipramine	100,000	<200	10.8	NEG	<0.2
Venlafaxine	100,000	<200	-1.6	NEG	<0.2

Interference – Structurally Unrelated Compounds

Structurally unrelated compounds were evaluated in qualitative and semi-quantitative modes by spiking the potential interferent into drug free urine containing tapentadol at ±25% of the cutoff. The levels of structurally unrelated compounds that did not interfere in the assay are presented below.

Non-Interfering Structurally Unrelated Compounds

Compound	Conc. Tested (ng/mL)
4-Bromo-2,5,Dimethoxyphenethylamine	100,000
6-Acetylcodeine	100,000
6-Acetylmorphine	100,000
Alprazolam	100,000
7-Aminoclonazepam	100,000
7-Aminoflunitrazepam	100,000
7-Aminonitrazepam	100,000
Amitriptyline	100,000
d-Amphetamine	100,000
lAmobarbital	100,000
Atomoxetine	100,000
Benzoylecgonine	100,000
Benzylpiperazine	100,000
Bromazepam	100,000
Brompheniramine	100,000
Buprenorphine	100,000
Bupropion	100,000
Butabarbital	100,000
Butalbital	100,000

Compound	Conc. Tested (ng/mL)
Cannabidiol	100,000
Cannabinol	100,000
Carbamazepine	100,000
Cetirizine	100,000
Chlordiazepoxide	100,000
1-(3-Chlorophenylpiperazine) mCPP	100,000
Chlorpheniramine	100,000
Cimetidine	100,000
Citalopram	100,000
Clobazam	100,000
Clonazepam	100,000
Clozapine	100,000
Cocaine	100,000
Codeine	100,000
Cotinine	100,000
Dehydronorketamine	50,000
Demoxepam	100,000
Desakylflurazepam	100,000
Desipramine	100,000
Dextromethorphan	100,000
Dihydrohydroxcarbamazepine	100,000
Diazepam	100,000
Digoxin	100,000
Dihydrocodeine	100,000
Doxylamine	100,000
Duloxetine	100,000
Ecgonine	100,000
Ecgonine Methyl Ester	100,000
EDDP	100,000
EMDP	100,000
1S,2R (+)-Ephedrine	100,000
Ethylmorphine	100,000
Ethyl-β-D-Glucuronide	100,000
Fentanyl	100,000
Fenfluramine	100,000
Flunitrazepam	100,000
Fluoxetine	100,000
Flurazepam	100,000
Haloperidol	100,000
Heroin	100,000

Compound	Conc. Tested (ng/mL)
Hexobarbital	100,000
Hydrocodone	100,000
Hydromorphone	100,000
Ketamine	100,000
Lamotrigine	100,000
Levorphanol	100,000
Lidocaine	100,000
Lorazepam	100,000
Lorazepam Glucuronide	50,000
Lormetazepam	100,000
LSD	100,000
Maprotiline	100,000
MDA	100,000
MDEA	100,000
MDMA	100,000
Meperidine	100,000
Meprobamate	100,000
d-Methamphetamine	100,000
Methaquolone	100,000
Methoxetamine	100,000
Methylone	100,000
Methylphenidate	100,000
Midazolam	100,000
Morphine	100,000
Morphine-3-Glucuronide	100,000
Morphine-6-Glucuronide	100,000
Nalorphine	100,000
Naloxone	100,000
Naltrexone	100,000
Naproxen	100,000
Nitrazepam	100,000
Norbuprenorphine	100,000
Norcodeine	100,000
Nordiazepam	100,000
Norketamine	100,000
Normorphine	100,000
Noroxycodone	100,000
Norpropoxyphene	100,000
Norpseudoephedrine	100,000
Nortriptyline	100,000

Compound	Conc. Tested (ng/mL)
Olanzapine	100,000
Oxazepam	100,000
Oxazepam glucuronide	50,000
Oxycodone	100,000
Oxymorphone	100,000
Delta-9-THC	100,000
11-hydroxy-delta-9-THC	100,000
11-nor-9 carboxy THC	100,000
PCP	100,000
Pentazocine	100,000
Pentobarbital	100,000
Phenobarbital	100,000
Phentermine	100,000
R(-)-Phenylephrine	100,000
Phenylpropanolamine (PPA)	100,000
Phenytoin	100,000
PMA	100,000
PMMA	100,000
Prazepam	100,000
Propoxyphene	100,000
Propranolol	100,000
Protriptyline	100,000
R,R (-)-Pseudoephedrine	100,000
S,S (+)-Pseudoephedrine	100,000
Risperidone	100,000
Ritalinic Acid	100,000
Salicylic Acid	100,000
Secobarbital	100,000
Sertraline	100,000
Sufentanil	50,000
Temazepam	100,000
Theophylline	100,000
Thioridazine	100,000
Trazadone	100,000
Triazolam	100,000
3-Trifluoromethylphenyl-piperazine	100,000
Tyramine	100,000
Verapamil	100,000
Zolpidem	100,000
Carisoprodol	100,000

Compound	Conc. Tested (ng/mL)
1R,2S (-)-Ephedrine	100,000
Acetaminophen	500,000
Acetylsalicyclic Acid	500,000
α-hydroxyalprazolam	100,000
Barbital	100,000
Caffeine	500,000
Cyclopentobarbital	100,000
Diphenhydramine	300,000
Ibuprofen	500,000
LAAM	100,000
Labetalol	100,000
Loratadine	100,000
Mephenytoin	100,000
Methadone	500,000
Methylphenylsuccinimide (mCPP)	100,000
Mirtazapine	100,000
n-desmethylcitalopram	100,000
Nor-LAAM	100,000
Noroxymorphone	100,000
Normesuximide	100,000
PEMA	100,000
Phenazepam	100,000
Procaine	100,000

Interference – Endogenous Compounds and Urine Preservatives

Endogenous compounds and urine preservatives were evaluated in qualitative and semi-quantitative modes by spiking the potential interferent into drug free urine containing tapentadol at ±25% of the cutoff. Due to the interference of boric acid observed at ±25% of the cutoff, potential interference was also evaluated at ±50% of the cutoff. Endogenous compounds and urine preservative tested that did not interfere in the assay are presented below.

Non-interfering Endogenous Compounds

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
γ-Globulin	0.5 g/dL
Glucose	2.0 g/dL
Hemoglobin	0.3 g/dL
Human Serum Albumin	0.5 g/dL
Oxalic Acid	0.1 g/dL
Riboflavin	0.0075 g/dL
Sodium Chloride	6.0 g/dL
Urea	6.0 g/dL

Non-interfering Urine Preservative

Compound	Concentration Tested
Sodium Azide	1% w/v
Sodium Fluoride	1% w/v

Boric acid interference test results at ±50% of the cutoff in qualitative and semi-quantitative modes are presented in below.

Interference at ±50% of the Cutoff

Compound	Concentration Tested	-50% Cutoff (50 ng/mL)		+50% Cutoff (150 ng/mL)	
		Qualitative Result	Semi-Quantitative Result	Qualitative Result	Semi-Quantitative Result
Boric Acid	1% w/v	Negative	Negative	**Negative**	**Negative**

The sponsor includes the following limitation in the labeling: “Boric Acid at 1% w/v may cause false negative results. The assay should not be used to test samples which contain boric acid.”

Interference – pH

To evaluate potential interference from the effect of urine pH on the assay's ability to detect tapentadol, 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 tapentadol at ±25% of the cutoff. No positive or negative interference was observed at urine pH values ranging from 3.0 to 11.0 for each test mode.

4. Assay Reportable Range:

   Not applicable

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   The assay calibrators are traceable to a commercially-available, certified, standard material with the concentration verified by GC-MS or LC-MS/MS.

6. Detection Limit:

   Not applicable

7. Assay Cut-Off:
   The assay cut-off is 200ng/mL of tapentadol in urine.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   A method comparison study was performed using 160 deidentified remnant unaltered clinical urine samples obtained from clinical testing laboratories. The urine samples were analyzed for tapentadol using the Immunalysis Tapentadol Urine HEIA on the Beckman Coulter AU480 chemistry analyzer in both qualitative and semi-quantitative modes and LC-MS/MS (Agilent 6430 Liquid Chromatography-Tandem Mass Spectrometry). The method results of the comparison study showed a positive percent agreement (PPA) and negative percent agreement (NPA) of 100% and 100%, respectively. The results are presented below.

Method Comparison Results by Concentration Range

Immunalysis Tapentadol Urine HEIA Result		LC-MS/MS Tapentadol Concentration			
		< 100 ng/mL (less than -50% cutoff)	100 – 199 ng/mL (between -50% cutoff and cutoff)	200 - 300 ng/mL (between cutoff and +50% cutoff)	> 300 ng/mL (greater than +50% cutoff)
Qualitative	Positive	0	0	14	81
	Negative	46	19	0	0
Semi-Quantitative	Positive	0	0	14	81
	Negative	46	19	0	0

2. Matrix Comparison:

Not applicable. The assay is intended for use only with urine samples.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable

2. Clinical Specificity:

Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Not applicable

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.