510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

k190397

B Applicant

Immunalysis Corporation

C Proprietary and Established Names

Immunalysis Carisoprodol Metabolite / Meprobamate Urine HEIA

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QBK	Class II	21 CFR 862.3590 - Meprobamate Test System	TX - Clinical Toxicology

II Submission/Device Overview:

A Purpose for Submission:

New device

B Measurand:

Carisoprodol metabolite (Meprobamate)

C Type of Test:

Qualitative Immunoassay

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The Immunalysis Carisoprodol Metabolite / Meprobamate Urine HEIA is a homogenous enzyme immunoassay for the qualitative analysis of carisoprodol metabolite, Meprobamate, at a cutoff of 280 ng/mL in human urine. The assay is intended for use in laboratories with automated clinical chemistry analyzers. This in vitro diagnostic device is for prescription use only.

The Immunalysis Carisoprodol Metabolite / Meprobamate 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 drug of abuse test result, particularly when preliminary positive results are used.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Assay performance was established using the Olympus AU400e analyzer.

IV Device/System Characteristics:

A Device Description:

The Immunalysis Carisoprodol Metabolite / Meprobamate Urine HEIA is based on the competition of carisoprodol labeled enzyme glucose-6-phosphate dehydrogenase (G6PDH) and the free Meprobamate in the urine sample for the fixed amount of sheep anti-carisoprodol antibody binding sites. In the absence of the free Meprobamate 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 nicotinamide adenine dinucleotide (NAD) to NADH.

B Principle of Operation:

The Immunalysis Carisoprodol Metabolite / Meprobamate Urine HEIA is based on the competition of carisoprodol labeled enzyme glucose-6-phosphate dehydrogenase (G6PDH) and the free drug in the urine sample for the fixed amount of sheep anti-carisoprodol 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 nicotinamide adenine dinucleotide (NAD) to NADH.

V Substantial Equivalence Information:

A Predicate Device Name(s):

LZI Carisoprodol Metabolite (Meprobamate) Enzyme Immunoassay

B Predicate 510(k) Number(s):

DEN170010

C Comparison with Predicate(s):

Device & Predicate Device(s):	k190397	DEN170010
Device Trade Name	Immunalysis Carisoprodol Metabolite / Meprobamate Urine HEIA	LZI Carisoprodol Metabolite (Meprobamate) Enzyme Immunoassay
General Device Characteristic Similarities		
Intended Use/Indications For Use	For the analysis of carisoprodol metabolite (meprobamate) in human urine.	Same
Test Principle	Homogeneous Enzyme Immunoassay	Same
User Environment	Laboratory Use	Same
Sample Matrix	Human Urine	Same
Mass spectrometry confirmation	Required to confirm preliminary positive analytical results	Same
General Device Characteristic Differences		
Calibrator material	Carisoprodol	Meprobamate
Antibody	Polyclonal sheep antibodies to carisoprodol	Monoclonal mouse antibodies to meprobamate

VI Standards/Guidance Documents Referenced:

The sponsor satisfied all special controls as outlined in 21 CFR 862.3590.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

The following laboratory performance studies were performed to determine substantial equivalence of the Immunalysis Carisoprodol Urine HEIA to the predicate device.

Precision/ Cutoff Characterization

A precision/Cutoff Characterization study for meprobamate was performed for ten days using three product lots with two runs per day in replicates of four on drug free urine (N=80) spiked with meprobamate to concentrations of the equivalent of the meprobamate cutoff and ±25%, ±50%, ±75%, and ±100% of the cutoff. The spiked concentrations were confirmed by Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS). The study verified that the cutoff serves as a boundary between a negative and positive interpretation of a qualitative result.

Precision test results in qualitative mode are presented in the table below:

Meprobamate Concentration (ng/mL)	% of Cutoff	Sample Size	Result		
			Lot 1	Lot 2	Lot 3
0	-100%	80	80 Negative	80 Negative	80 Negative
70	-75%	80	80 Negative	80 Negative	80 Negative
140	-50%	80	80 Negative	80 Negative	80 Negative
210	-25%	80	80 Negative	80 Negative	80 Negative
280	Cutoff	80	40 Neg/40 Pos	38 Neg/42 Pos	39 Neg/41 Pos
350	+25%	80	80 Positive	80 Positive	80 Positive
420	+50%	80	80 Positive	80 Positive	80 Positive
490	+75%	80	80 Positive	80 Positive	80 Positive
560	+100%	80	80 Positive	80 Positive	80 Positive

2. Analytical Specificity/Interference:

Specificity and Cross-Reactivity

Compounds that were determined by the sponsor to be structurally and functionally similar to meprobamate were spiked into drug-free urine at levels that will yield a result that is equivalent to the cutoff and were evaluated as potential cross-reactant in the test device. Each compound was evaluated in replicates of four. Each compound was an independent spike and no drug mixes were used.

Compound	Compound Conc. (ng/mL)	Result	Cross-Reactivity (%)
Meprobamate	280	POS	100
Carisoprodol	100	POS	280
Buprenorphine	100,000	NEG	<0.1%
Codeine	100,000	NEG	<0.1%
Darunavir	200,000	NEG	N/D
Dihydrocodeine	100,000	NEG	<0.1%
Efavirenz	200,000	NEG	N/D
Felbamate	120,000	POS	0.2
Hydrocodone	100,000	NEG	<0.1%
Hydromorphone	100,000	NEG	<0.1%
Meperidine	100,000	NEG	<0.1%
Methocarbamol	200,000	NEG	N/D
Mitomycin C	200,000	NEG	N/D
Morphine	100,000	NEG	<0.1%
Morphine-3-glucuronide	100,000	NEG	<0.1%
Morphine-6-glucuronide	100,000	NEG	<0.1%
Naloxone	100,000	NEG	<0.1%
Naltrexone	100,000	NEG	<0.1%
Neostigmine	200,000	NEG	N/D
Norbuprenorphine	100,000	NEG	<0.1%
Norcodeine	100,000	NEG	<0.1%
Normorphine	100,000	NEG	<0.1%
Oxycodone	100,000	NEG	<0.1%
Oxymorphone	100,000	NEG	<0.1%
Propoxyphene	100,000	NEG	<0.1%
Retigabine	200,000	NEG	N/D
Ritonavir	200,000	NEG	N/D
Rivastigmine	200,000	NEG	N/D
Tramadol	100,000	NEG	<0.1%
Trazadone	100,000	NEG	<0.1%
Venlafaxine	100,000	NEG	<0.1%
Zafirlukast	200,000	NEG	N/D

Interference – Structurally Unrelated Compounds

Structurally unrelated compounds were evaluated by spiking the potential interferent at concentrations of at least 50 µg/mL into drug free urine containing analyte at ±25% of the cutoff. The levels of structurally unrelated compounds that did not interfere in the assay are presented in the table below.

Compounds for which interference with the assay was not detected		
4-Bromo-2,5,Dimethoxyphenethylamine	Dehydronorketamine	Naproxen
Acetaminophen	Delta-9-THC	Nitrazepam
Acetylsalicylic Acid	Doxepin	11-nor-9 carboxy THC
6-Acetylcodeine	Doxylamine	Nordiazepam
Alphenal	Ecgonine	Norketamine
6-Acetylmorphine	Ecgonine methyl ester	Norpropoxyphene
Alprazolam	EDDP	Norpseudoephedrine
7-Aminoclonazepam	EMDP	Nortriptyline
7-Aminoflunitrazepam	1R,2S(-)-Ephedrine	O-desmethyl tramadol
7-Aminonitrazepam	1S,2R(+)-Ephedrine	O-desmethyl venlafaxine
Amitriptyline	Ethyl glucuronide	Olanzapine
Amobarbital	Ethylmorphine	Oxazepam
S-(+) Amphetamine	Fenfluramine	PCP
Aprobarbital	Fentanyl	Pentobarbital
Barbital	Flunitrazepam	Pentazocine
Benzoylecgonine	Fluoxetine	Phenazepam
Benzylpiperazine	Flurazepam	Phenobarbital
Bromazepam	Haloperidol	Phentermine
Bupropion	Heroin	Phenylephedrine
Butabarbital	Hexobarbital	Phenytoin
Butalbital	11-hydroxy-delta-9-THC	Phenylpropanolamine
Caffeine	Ibuprofen	PMA
Cannabidiol	Imipramine	Prazepam
Cannabinol	Ketamine	Propranolol
Carbamazepine	Labetalol	Protriptyline
Chlordiazepoxide	Lamotrigine	R,R(-)-Pseudoephedrine
Chlorpromazine	Levorphanol tartrate	S,S(+)-Pseudoephedrine
cis-Tramadol	Lidocaine	Ritalinic Acid
Clobazam	Lorazepam	Salicylic Acid
Clomipramine	Lorazepam Glucuronide	Secobarbital
Clonazepam	Lormetazepam	Sertraline
Clozapine	LSD	Sufentanil Citrate
Cocaine	Maprotiline	Talbutal
Cotinine	MDA	Tapentadol
Cyclobenzaprine	MDEA	Temazepam
Cyclopentobarbital	MDMA	Theophylline
Demoxepam	S(+)-Methamphetamine	Thiopental
Desakylflurazepam	Methadone	Thioridazine
Desipramine	Methaqualone	Triazolam
Dextromethorphan	Methoxetamine	Trifluoromethylphenyl-piperazine
Diazepam	Methylone	Trimipramine

Compounds for which interference with the assay was not detected		
Digoxin	Methylphenidate	Verapamil
Diphenhydramine	Midazolam	Zolpidem Tartrate

Interference – Endogenous Compounds

Endogenous compounds and urine preservatives were evaluated by spiking the potential interferent into drug free urine containing meprobamate 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. Other than boric acid, assay performance was not affected by all the other internally existing physiological conditions tested. Endogenous compounds tested that did not interfere in the assay are presented in the table below.

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
Hemoglobulin	0.300 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 interference test results are presented in the table below.

Interferent	**-50% Cutoff (50 ng/mL) Result**	**+50% Cutoff (150 ng/mL) Result**
Boric Acid (1%w/v)	Negative	Negative

Boric Acid at 1% w/v may cause false negative results. The assay should not be used to test samples which contain boric acid.

3. Assay Reportable Range:

Not applicable. This device is intended for qualitative use only.

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

The device is traceable to a commercially available, certified, standard material for which the concentration is verified by GC-MS or LC-MS/ MS.

Accelerated stability and real time studies have been conducted for the device. Protocols and acceptance criteria were described and found to be acceptable. The manufacturer claims that when stored un-opened at 2-8 º C, the device is stable for 12 months.

5. Detection Limit:

See Precision/Reproducibility section in XII.A.1, above.

6. Assay Cut-Off:

Characterization of how the device performs analytically around the claimed cut-off concentration appears in the precision section, VII.A.1, above.

B Comparison Studies:

1. Method Comparison with Predicate Device:

One hundred and sixty-seven (167) de-identified, unaltered leftover clinical urine samples obtained from clinical testing laboratories were analyzed for total carisoprodol at an assay cutoff of 280 ng/mL with the Immunalysis Carisoprodol Urine HEIA on the Olympus AU400e compared to results by Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS). Method comparison results are presented in the tables below.

Immunalysis Meprobamate Urine HEIA Result	**LC-MS/MS Total Meprobamate Concentration**				**Agreement (%)**
	< 140 ng/mL (less than -50% cutoff)	**140-279 ng/mL (between -50% cutoff and cutoff)**	**280-420 ng/mL (between cutoff and +50% cutoff)**	**> 420 ng/mL (greater than +50% cutoff)**	
Positive	3	2	3	104	100% (107/107)
Negative	51	4	0	0	92% (55/60)

Results from this testing included three false positive samples with meprobamate concentrations less than 50% of the cutoff. It was determined in LC-MS/MS testing that each of these samples included carisoprodol, as described in the table below, which caused the positive device results.

Sample ID	**Qualitative Result**	**Carisoprodol (ng/mL)**
17990	POS	147
17977	POS	148

18077	POS	750

2. Matrix Comparison:

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

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):

To support their proposed cutoff of 280 ng/mL for detection of the carisoprodol metabolite meprobamate, the sponsor provided protocols for and results from a pharmacokinetic study. Urine samples in this study were evaluated both by the sponsor's device as well as confirmatory LC-MS/MS testing. After review, it was determined that the sponsor's proposed cutoff was clinically valid for the intended use of the device.

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.