



Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

January 5, 2016

IMMUNALYSIS CORPORATION
JOSEPH GINETE
REGULATORY AFFAIRS SPECIALIST II
829 TOWNE CENTER DR
POMONA CA 91767

Re: K151771

Trade/Device Name: Immunalysis Benzodiazepines Urine Enzyme Immunoassay,
Immunalysis Multi-drug Calibrators

Regulation Number: 21 CFR 862.3170

Regulation Name: Benzodiazepine test system

Regulatory Class: II

Product Code: JXM, DKB

Dated: December 24, 2015

Received: December 28, 2015

Dear Mr. Ginete:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>. Also, please note the regulation entitled, “Misbranding by reference to premarket notification” (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm> for the CDRH’s Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address <http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm>.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)

Device Name

Immunoanalysis Benzodiazepines Urine Enzyme Immunoassay
Immunoanalysis Multi-Drug Calibrators

Indications for Use (Describe)

The Immunoanalysis Benzodiazepines Urine Enzyme Immunoassay is a homogeneous enzyme immunoassay with a cutoff of 200ng/mL. The assay is intended for use in laboratories for the qualitative and semi-quantitative analysis of Benzodiazepines in human urine with automated clinical chemistry analyzers. This assay is calibrated against Oxazepam. This in-vitro 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 Immunoanalysis Benzodiazepines 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 Immunoanalysis Multi-Drug Calibrators are intended for in vitro diagnostic use for the calibration of assays for the analytes currently listed in the package insert: Benzoyllecgonine, Morphine and Oxazepam. The calibrators are designed for prescription use with immunoassays.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92(c).

A. Contact Information

1. Manufacturer: Immunalysis Corporation
2. Contact Name: Joseph Ginete
3. Contact Title: Regulatory Affairs Specialist II
4. Address: 829 Towne Center Drive Pomona, CA 91767
5. Phone: (909) 482-0840
6. Fax: (909) 482-0850
7. Email: jginete@immunalysis.com
8. Summary prepared on: December 24, 2015

B. Device Information

1. Trade Name: Immunalysis Benzodiazepine Urine Enzyme Immunoassay
Immunalysis Multi-Drug Calibrators
2. Common Name: Immunalysis Benzodiazepine Urine Enzyme Immunoassay
Immunalysis Multi-Drug Calibrators

C. Regulatory Information

1. Device Classification: II
2. Regulation Number: 21 CFR862.3170 Benzodiazepine Test System
21 CFR 862.3200 Clinical Toxicology Calibrator
3. Panel: Toxicology(91)
4. Product Code: JXM
DKB

D. Legally Marketed Device to Which We are Claiming Equivalence (807.92(A)(3))

1. Predicate Device: DRI® Benzodiazepines Assay
LZI Multiple Analyte Drugs of Abuse Calibrators
and Controls
2. Predicate Company: Microgenics
Lin-Zhi International, Inc.
3. Predicate K Number: K930529
K051088

E. Device Description

1. The assay consists of antibody/ substrate reagent and enzyme conjugate reagent. The antibody/ substrate reagent includes monoclonal antibodies to Benzodiazepine, glucose-6-phosphate (G6P) and nicotinamide adenine dinucleotide (NAD) in HEPES buffer with Sodium Azide as a preservative. The enzyme conjugate reagent includes Benzodiazepines derivative labeled with glucose-6-phosphate dehydrogenase (G6PDH) in HEPES buffer with Sodium Azide as a preservative.
2. 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:

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

F. Intended Use

1. Immunalysis Benzodiazepine Urine Enzyme Immunoassay

The Immunalysis Benzodiazepine Urine Enzyme Immunoassay is a homogeneous enzyme immunoassay with a cutoff of 200ng/mL. The assay is intended for use in laboratories for the qualitative and semi-quantitative analysis of Benzodiazepine in human urine with automated clinical chemistry analyzers. This assay is calibrated against Oxazepam. This in-vitro 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 Benzodiazepine 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.

2. Immunalysis Multi-Drug Calibrators

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: Benzoyllecgonine, Morphine, PCP and Oxazepam. The calibrators are designed for prescription use with immunoassays.

G. Comparison of the new device with the predicate device

Item	Benzodiazepines Assay K930529	Immunalysis Benzodiazepines Urine EIA
Intended Use	For the qualitative and semi-quantitative determination of the presence of Benzodiazepines in human urine at a cutoff of 200ng/mL	For the qualitative and semi-quantitative determination of the presence of Benzodiazepines in human urine at a cutoff of 200ng/mL
Type of Product	Analytical Reagents	Analytical Reagents
Measured Analytes	Benzodiazepine	Benzodiazepine
Test Matrix	Urine	Urine
Cutoff Levels	200ng/mL of Oxazepam	200ng/mL of Oxazepam
Test System	Homogeneous Enzyme Immunoassay	Homogeneous Enzyme Immunoassay
Materials	Liquid Ready-to-Use Two Reagent Assay (R1 and R2)	Antibody/Substrate Reagents and Enzyme Labeled Conjugate
Mass Spectroscopy Confirmation	Required for preliminary positive analytical results	Required for preliminary positive analytical results
Antibody	Sheep Polyclonal to Benzodiazepine	Monoclonal antibody to Benzodiazepines
Storage	2 – 8°C until expiration date	2 – 8°C until expiration date

Item	LZI Multiple Analyte K051088	Immunalysis Multi-Drug Calibrator
Analyte	benzoyllecgonine, d-methamphetamine, methadone, morphine, oxazepam, secobarbital, phencyclidine, propoxyphene	benzoyllecgonine, morphine, PCP, oxazepam
Matrix	Urine	Urine
Calibrator Levels	5 Levels – See Table 2 Below	5 Levels (Negative and Level 1, 2, 3 and 4) - See Device Description Table 1
Storage	2 – 8°C until expiration date	2 – 8°C until expiration date

Analyte	Multiple Analyte Calibrators			
	Low	Cutoff	Intermediate	High
d-Methamphetamine	250ng/mL	500ng/mL	750ng/mL	1000ng/mL
Morphine	1000ng/mL	2000ng/mL	4000ng/mL	6000ng/mL
Phencyclidine	12.5ng/mL	25ng/mL	50ng/mL	100ng/mL
Benzoyllecgonine	75ng/mL	150ng/mL	300ng/mL	1000ng/mL
Oxazepam	100ng/mL	200ng/mL	500ng/mL	1000ng/mL
Secobarbital	100ng/mL	200ng/mL	500ng/mL	1000ng/mL
Propoxyphene	150ng/mL	300ng/mL	600ng/mL	1000ng/mL
Methadone	150ng/mL	300ng/mL	600ng/mL	1000ng/mL

H. The following laboratory performance studies were performed to determine substantial equivalence of the Immunalysis Benzodiazepines Urine Enzyme Immunoassay to the predicate

1. Precision/ Cutoff Characterization/ Reproducibility - Precision/Cutoff Characterization – Study was performed for 20 days, 2 runs per day in duplicate on drug free urine (N=80) spiked with oxazepam to concentration of $\pm 25\%$, $\pm 50\%$, $\pm 75\%$, and $\pm 100\%$ of the cutoff. The spiked concentrations were confirmed by mass spectrometry (MS). The study verified that the cutoff serves as a boundary between a negative and positive interpretation of a qualitative result. The instruments used for this was Beckman Coulter AU 400e.

- a. The following is a summary table of the Qualitative Analysis for the 200ng/mL cutoff test data results.

Concentration (ng/mL)	% of cutoff	# of determinations	Result
0	-100%	80	80 Negative
50	-75%	80	80 Negative
100	-50%	80	80 Negative
150	-25%	80	80 Negative
200	Cutoff	80	37 Neg / 43 Pos
250	+25%	80	80 Positive
300	+50%	80	80 Positive
350	+75%	80	80 Positive
400	+100%	80	80 Positive

b. The following is a summary table of the Semi-Quantitative Analysis for the 200ng/mL cutoff test data results.

Concentration (ng/mL)	% of cutoff	# of determinations	Result
0	-100%	80	80 Negative
50	-75%	80	80 Negative
100	-50%	80	80 Negative
150	-25%	80	80 Negative
200	Cutoff	80	34 Neg / 46 Pos
250	+25%	80	80 Positive
300	+50%	80	80 Positive
350	+75%	80	80 Positive
400	+100%	80	80 Positive

2. Specificity and Cross-Reactivity – Various Benzodiazepines or structurally similar compounds were spiked into drug free urine at levels that will yield a result that is equivalent to the cutoff. The study verified assay performance relative to the ability of the device to exclusively determine certain drugs, in both the qualitative and semi-quantitative modes. The instrument used for this test was a Beckman Coulter AU 400e.

a. The qualitative result summary table for the 200ng/mL cutoff is outlined below:

Compound	Concentration Tested (ng/mL)	Result	Cross-Reactivity (%)
Oxazepam	200	POS	100.0
Alpha-hydroxyalprazolam	110	POS	181.8
Alprazolam	120	POS	166.7
7-Aminoclonazepam	100,000	NEG	< 0.002
7-Aminoflunitrazepam	3,500	POS	5.7
7-Aminonitrazepam	35,000	POS	0.6
Bromazepam	750	POS	26.7
Chlordiazepoxide	1,600	POS	12.5
Clorazepate	200	POS	100.0
Clobazam	650	POS	30.8
Clonazepam	180	POS	111.1
Demoxepam	5,500	POS	3.6
Desalkylflurazepam	75	POS	266.7
Diazepam	100	POS	200.0
Estazolam	225	POS	88.9
Flunitrazepam	125	POS	160.0
Flurazepam	110	POS	181.8
Lorazepam	60	POS	333.3
Lorazepam glucuronide	180	POS	111.1
Lormetazepam	50	POS	400.0

Table 5 - Structurally Related Compounds (for 200 ng/mL cutoff) - Qualitative

Compound	Concentration Tested (ng/mL)	Result	Cross-Reactivity (%)
Medazepam	500	POS	40.0
Midazolam	40	POS	500.0
Nitrazepam	700	POS	28.6
Norchlordiazepoxide	2,200	POS	9.1
Nordiazepam	180	POS	111.1
Oxazepam glucuronide	1,300	POS	15.4
Prazepam	95	POS	210.5
Temazepam	110	POS	181.8
Temazepam glucuronide	700	POS	28.6
Triazolam	50	POS	400.0

b. The semi-quantitative result summary table for the 200ng/mL cutoff is outlined below:

Table 6 - Structurally Related Compounds (for 200ng/mL cutoff) – Semi-Quantitative

Compound	Concentration Tested (ng/mL)	Result	Cross-Reactivity (%)
Oxazepam	200	POS	100.0
Alpha-hydroxyalprazolam	110	POS	181.8
Alprazolam	120	POS	166.7
7-Aminoclonazepam	100,000	NEG	< 0.002
7-Aminoflunitrazepam	3,500	POS	5.7
7-Aminonitrazepam	35,000	POS	0.6
Bromazepam	750	POS	26.7
Chlordiazepoxide	1,600	POS	12.5
Clorazepate	200	POS	100.0
Clobazam	650	POS	30.8
Clonazepam	180	POS	111.1
Demoxepam	5,500	POS	3.6
Desalkylflurazepam	75	POS	266.7
Diazepam	100	POS	200.0
Estazolam	225	POS	88.9
Flunitrazepam	125	POS	160.0
Flurazepam	110	POS	181.8
Lorazepam	60	POS	333.3
Lorazepam glucuronide	180	POS	111.1
Lormetazepam	50	POS	400.0
Medazepam	500	POS	40.0
Midazolam	40	POS	500.0
Nitrazepam	700	POS	28.6
Norchlordiazepoxide	2,200	POS	9.1
Nordiazepam	180	POS	111.1
Oxazepam glucuronide	1,300	POS	15.4
Prazepam	95	POS	210.5
Temazepam	110	POS	181.8
Temazepam glucuronide	700	POS	28.6
Triazolam	50	POS	400.0

3. Interference - Structurally unrelated compounds were evaluated in qualitative and semi-quantitative modes by spiking the potential interferent into drug free urine containing oxazepam at $\pm 25\%$ of the cutoff. All potential interferents analyzed verified that assay performance is unaffected by externally ingested compounds. The instrument used for this test was a Beckman Coulter AU 400e.

a. The following is a table of the structurally non-similar compounds for the 200ng/mL cutoff:

Table 7 - Structurally Unrelated Compounds (for 200ng/mL cutoff)

Compound	Concentration Tested (ng/mL)	-25% Cutoff (150ng/mL)		+25% Cutoff (250ng/mL)	
		Qualitative	Semi-Quantitative	Qualitative	Semi-Quantitative
4-Bromo-2,5-Dimethoxyphenethylamine	100,000	Negative	Negative	Positive	Positive
6-Acetylcodeine	100,000	Negative	Negative	Positive	Positive
6-Acetylmorphine	100,000	Negative	Negative	Positive	Positive
Acetaminophen	500,000	Negative	Negative	Positive	Positive
Acetylsalicylic Acid	500,000	Negative	Negative	Positive	Positive
Amitriptyline	100,000	Negative	Negative	Positive	Positive
Amobarbital	100,000	Negative	Negative	Positive	Positive
S-(+) Amphetamine	100,000	Negative	Negative	Positive	Positive
Benzoylcegonine	500,000	Negative	Negative	Positive	Positive
Benzylpiperazine	100,000	Negative	Negative	Positive	Positive
Buprenorphine	100,000	Negative	Negative	Positive	Positive
Bupropion	100,000	Negative	Negative	Positive	Positive
Butabarbital	100,000	Negative	Negative	Positive	Positive
Caffeine	500,000	Negative	Negative	Positive	Positive
Carbamazepine	100,000	Negative	Negative	Positive	Positive
Chlorpromazine	100,000	Negative	Negative	Positive	Positive
cis-Tramadol	100,000	Negative	Negative	Positive	Positive
Clomipramine	100,000	Negative	Negative	Positive	Positive
Cannabidiol	100,000	Negative	Negative	Positive	Positive
Cannabinol	100,000	Negative	Negative	Positive	Positive
Carisoprodol	100,000	Negative	Negative	Positive	Positive
Cocaine	100,000	Negative	Negative	Positive	Positive
Codeine	100,000	Negative	Negative	Positive	Positive
Cotinine	100,000	Negative	Negative	Positive	Positive
Cyclobenzaprine	100,000	Negative	Negative	Positive	Positive
Delta-9-THC	100,000	Negative	Negative	Positive	Positive
Desipramine	100,000	Negative	Negative	Positive	Positive
N-desmethyltapentadol	100,000	Negative	Negative	Positive	Positive
Dextromethorphan	100,000	Negative	Negative	Positive	Positive
Dihydrocodeine	100,000	Negative	Negative	Positive	Positive
Diphenhydramine	500,000	Negative	Negative	Positive	Positive
Doxepin	100,000	Negative	Negative	Positive	Positive
Ecgonine	100,000	Negative	Negative	Positive	Positive
Ecgonine methyl ester	100,000	Negative	Negative	Positive	Positive
EDDP	100,000	Negative	Negative	Positive	Positive

Table 7 - Structurally Unrelated Compounds (for 200ng/mL cutoff)

Compound	Concentration Tested (ng/mL)	-25% Cutoff (150ng/mL)		+25% Cutoff (250ng/mL)	
		Qualitative	Semi-Quantitative	Qualitative	Semi-Quantitative
1R,2S(-)-Ephedrine	100,000	Negative	Negative	Positive	Positive
1S,2R(+)-Ephedrine	100,000	Negative	Negative	Positive	Positive
Ethyl β-D-glucuronide	100,000	Negative	Negative	Positive	Positive
Ethylmorphine	100,000	Negative	Negative	Positive	Positive
Fenfluramine	100,000	Negative	Negative	Positive	Positive
Fentanyl	100,000	Negative	Negative	Positive	Positive
Fluoxetine	100,000	Negative	Negative	Positive	Positive
Heroin	100,000	Negative	Negative	Positive	Positive
Hexobarbital	100,000	Negative	Negative	Positive	Positive
Hydrocodone	100,000	Negative	Negative	Positive	Positive
Hydromorphone	100,000	Negative	Negative	Positive	Positive
11-hydroxy-delta-9-THC	100,000	Negative	Negative	Positive	Positive
Ibuprofen	100,000	Negative	Negative	Positive	Positive
Imipramine	100,000	Negative	Negative	Positive	Positive
Ketamine	100,000	Negative	Negative	Positive	Positive
Lamotrigine	100,000	Negative	Negative	Positive	Positive
Levorphanol Tartrate	100,000	Negative	Negative	Positive	Positive
Lidocaine	100,000	Negative	Negative	Positive	Positive
LSD	100,000	Negative	Negative	Positive	Positive
Maprotiline	100,000	Negative	Negative	Positive	Positive
(+)-MDA	100,000	Negative	Negative	Positive	Positive
MDEA	100,000	Negative	Negative	Positive	Positive
MDMA	100,000	Negative	Negative	Positive	Positive
Meperidine	100,000	Negative	Negative	Positive	Positive
Meprobamate	100,000	Negative	Negative	Positive	Positive
Methadone	500,000	Negative	Negative	Positive	Positive
S(+)-Methamphetamine	100,000	Negative	Negative	Positive	Positive
Methaqualone	100,000	Negative	Negative	Positive	Positive
Methylphenidate	100,000	Negative	Negative	Positive	Positive
Morphine	100,000	Negative	Negative	Positive	Positive
Morphine-3 -glucuronide	100,000	Negative	Negative	Positive	Positive
Morphine-6 -glucuronide	100,000	Negative	Negative	Positive	Positive
Nalorphine	100,000	Negative	Negative	Positive	Positive
Naloxone	100,000	Negative	Negative	Positive	Positive
Naltrexone	100,000	Negative	Negative	Positive	Positive
Norbuprenorphine	100,000	Negative	Negative	Positive	Positive
Norcodeine	100,000	Negative	Negative	Positive	Positive
Normorphine	100,000	Negative	Negative	Positive	Positive
Norpropoxyphene	100,000	Negative	Negative	Positive	Positive
Norpseudoephedrine	100,000	Negative	Negative	Positive	Positive
Nortriptyline	100,000	Negative	Negative	Positive	Positive
Oxycodone	100,000	Negative	Negative	Positive	Positive
Oxymorphone	100,000	Negative	Negative	Positive	Positive

Table 7 - Structurally Unrelated Compounds (for 200ng/mL cutoff)

Compound	Concentration Tested (ng/mL)	-25% Cutoff (150ng/mL)		+25% Cutoff (250ng/mL)	
		Qualitative	Semi-Quantitative	Qualitative	Semi-Quantitative
PCP	100,000	Negative	Negative	Positive	Positive
Pentazocine	100,000	Negative	Negative	Positive	Positive
Pentobarbital	100,000	Negative	Negative	Positive	Positive
Phentermine	100,000	Negative	Negative	Positive	Positive
Phenobarbital	100,000	Negative	Negative	Positive	Positive
Phenylephedrine	100,000	Negative	Negative	Positive	Positive
Phenylpropanolamine	100,000	Negative	Negative	Positive	Positive
Phenytoin	100,000	Negative	Negative	Positive	Positive
PMA	100,000	Negative	Negative	Positive	Positive
Propoxyphene	100,000	Negative	Negative	Positive	Positive
Propranolol	100,000	Negative	Negative	Positive	Positive
Protriptyline	100,000	Negative	Negative	Positive	Positive
R,R(-)-Pseudoephedrine	100,000	Negative	Negative	Positive	Positive
S,S(+)-Pseudoephedrine	100,000	Negative	Negative	Positive	Positive
Ranitidine	100,000	Negative	Negative	Positive	Positive
Ritalinic Acid	100,000	Negative	Negative	Positive	Positive
Salicylic Acid	100,000	Negative	Negative	Positive	Positive
Secobarbital	100,000	Negative	Negative	Positive	Positive
Sertraline	100,000	Negative	Negative	Positive	Positive
Sufentanil Citrate	100,000	Negative	Negative	Positive	Positive
11-nor-9 carboxy THC	100,000	Negative	Negative	Positive	Positive
Theophylline	100,000	Negative	Negative	Positive	Positive
Thioridazine	100,000	Negative	Negative	Positive	Positive
Trifluoromethylphenyl-piperazine	100,000	Negative	Negative	Positive	Positive
Trimipramine	100,000	Negative	Negative	Positive	Positive
Trazodone	100,000	Negative	Negative	Positive	Positive
Venlafaxine	100,000	Negative	Negative	Positive	Positive
Zolpidem Tartrate	100,000	Negative	Negative	Positive	Positive

b. Endogenous compounds interference was evaluated in qualitative and semi-quantitative modes by spiking the potential interferent into drug free urine containing oxazepam at $\pm 25\%$ of the cutoff. All potential interferents analyzed verified that assay performance is unaffected by internally existing physiological conditions. The instrument used for this test was a Beckman Coulter AU 400e. The following is a summary table of the endogenous compounds results for the 200ng/mL cutoff:

Table 8 - Endogenous Compounds (for 200ng/mL cutoff)

Compound	Concentration Tested (ng/mL)	-25% Cutoff (150ng/mL)		+25% Cutoff (250ng/mL)	
		Qualitative	Semi-Quantitative	Qualitative	Semi-Quantitative
Acetone	1.0 g/dL	Negative	Negative	Positive	Positive
Ascorbic Acid	1.5 g/dL	Negative	Negative	Positive	Positive
Bilirubin	0.002 g/dL	Negative	Negative	Positive	Positive

Table 8 - Endogenous Compounds (for 200ng/mL cutoff)

Compound	Concentration Tested (ng/mL)	-25% Cutoff (150ng/mL)		+25% Cutoff (250ng/mL)	
		Qualitative	Semi-Quantitative	Qualitative	Semi-Quantitative
Creatinine	0.5 g/dL	Negative	Negative	Positive	Positive
Ethanol	1.0 g/dL	Negative	Negative	Positive	Positive
Galactose	0.01 g/dL	Negative	Negative	Positive	Positive
γ-Globulin	0.5 g/dL	Negative	Negative	Positive	Positive
Glucose	2.0 g/dL	Negative	Negative	Positive	Positive
Hemoglobin	0.115 g/dL	Negative	Negative	Positive	Positive
Human Serum Albumin	0.5 g/dL	Negative	Negative	Positive	Positive
Oxalic Acid	0.1 g/dL	Negative	Negative	Positive	Positive
Riboflavin	0.0075 g/dL	Negative	Negative	Positive	Positive
Sodium Azide	1% w/v	Negative	Negative	Positive	Positive
Sodium Chloride	6.0 g/dL	Negative	Negative	Positive	Positive
Sodium Fluoride	1% w/v	Negative	Negative	Positive	Positive
Urea	6.0 g/dL	Negative	Negative	Positive	Positive

- c. Boric Acid interference was also evaluated at a concentration of 1% w/v, at $\pm 25\%$ and $\pm 50\%$ of the cutoff, in both the qualitative and semi-quantitative modes. The following is a summary table of the test results at $\pm 25\%$ of the assay cutoff of 200ng/mL:

Table 9 – Boric Acid (for 200ng/mL cutoff)

Compound	Concentration Tested (ng/mL)	-25% Cutoff (150ng/mL)		+25% Cutoff (250ng/mL)	
		Qualitative	Semi-Quantitative	Qualitative	Semi-Quantitative
Boric Acid	1% w/v	Negative	Negative	Negative	Negative

- d. The following is a summary table of the test results at $\pm 50\%$ of the assay cutoff of 200ng/mL:

Table 10 – Boric Acid (for 200ng/mL cutoff)

Compound	Concentration Tested (ng/mL)	-50% Cutoff (100ng/mL)		+50% Cutoff (300ng/mL)	
		Qualitative	Semi-Quantitative	Qualitative	Semi-Quantitative
Boric Acid	1% w/v	Negative	Negative	Negative	Negative

- e. Boric Acid at a concentration of 1% w/v was found to cause false negative results at $\pm 25\%$ and $\pm 50\%$ ng/mL of the cutoff in both the qualitative and semi-quantitative modes. The following statement is provided in the Limitations section of the labeling: *Boric Acid at 1%w/v may cause false negative results. Boric Acid is not recommended as a preservative for urine.*
- f. To evaluate 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 oxazepam at $\pm 25\%$ of the 200ng/mL cutoff. No positive or negative interference was observed at urine pH values ranging from 3.0 to 11.0 for

each test mode. The following is a summary table of the effect of pH results for the 200ng/mL cutoff:

Table 11 - Effect of pH (for 200ng/mL cutoff)					
Test Parameter	Value	-25% Cutoff (150ng/mL)		+25% Cutoff (250ng/mL)	
		Qualitative	Semi-Quantitative	Qualitative	Semi-Quantitative
pH	3.0	NEG	NEG	POS	POS
pH	4.0	NEG	NEG	POS	POS
pH	5.0	NEG	NEG	POS	POS
pH	6.0	NEG	NEG	POS	POS
pH	7.0	NEG	NEG	POS	POS
pH	8.0	NEG	NEG	POS	POS
pH	9.0	NEG	NEG	POS	POS
pH	10.0	NEG	NEG	POS	POS
pH	11.0	NEG	NEG	POS	POS

- g. To evaluate potential interference from the specific gravity of urine, device performance in the qualitative and semi-quantitative modes was tested using a range of physiologically relevant 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 oxazepam at $\pm 25\%$ of the 200ng/mL cutoff. No positive or negative interference was observed at urine specific gravity values ranging from 1.000 to 1.030 for each test mode. The following is a summary table of the effect of specific gravity results for the 200ng/mL cutoff:

Table 12 - Effect of Specific Gravity (for 200ng/mL cutoff)					
Test Parameter	Value	-25% Cutoff (150ng/mL)		+25% Cutoff (250ng/mL)	
		Qualitative	Semi-Quantitative	Qualitative	Semi-Quantitative
Specific Gravity	1.000	NEG	NEG	POS	POS
Specific Gravity	1.002	NEG	NEG	POS	POS
Specific Gravity	1.005	NEG	NEG	POS	POS
Specific Gravity	1.010	NEG	NEG	POS	POS
Specific Gravity	1.015	NEG	NEG	POS	POS
Specific Gravity	1.020	NEG	NEG	POS	POS
Specific Gravity	1.025	NEG	NEG	POS	POS
Specific Gravity	1.030	NEG	NEG	POS	POS

4. Linearity/ Recovery - A linearity study in the semi-quantitative mode was conducted by spiking a drug free urine pool with a high concentration of oxazepam as a high value specimen. Additional pools were made by serially diluting the high value specimen with drug free urine to achieve concentrations ranging from 100ng/mL to 1100ng/mL. Each pool was tested in triplicate to calculate the mean concentration values that were used to calculate drug recovery. The instrument used for this test was a Beckman Coulter AU 400e.

a. The following is a summary table of the linearity/recovery:

Table 13 - Linearity/ Recovery		
Expected Concentration (ng/mL)	Mean Concentration (ng/mL)	Recovery (%)
100	94.2	94.2
200	213.7	106.8
300	313.9	104.6
400	389.7	97.4
500	511.6	102.3
600	637.2	106.2
700	693.2	99.0
800	820.7	102.6
900	907.6	100.8
1000	1025.3	102.5
1100	1061.1	96.5

5. Method Comparison – Eighty unaltered, anonymous and discarded clinical urine samples obtained from clinical testing laboratories were analyzed for benzodiazepines with the candidates on a Beckman Coulter AU 400e clinical chemistry analyzer and with LC/MS. Results were obtained in both qualitative and semi-quantitative modes.

a. The following is a comparison table of qualitative assay performance for the 200ng/mL cutoff:

Table 14 - Method Comparison (for 200ng/mL cutoff) – Qualitative

		LC/MS Confirmation	
		(+)	(-)
Test Device	(+)	42	0
	(-)	1	43

b. The following is a summary table of qualitative assay performance for the 200ng/mL cutoff:

Table 15 - Assay Performance verified by LC/MS – 200ng/mL Cutoff					
Type	Benzodiazepines Concentration				Agreement (%)
	< 100ng/mL	100 ~ 199 ng/mL	200 ~ 300 ng/mL	> 300 ng/mL	
Qualitative/ Positive	0	0	4	38	100
Qualitative/ Negative	36	7	1	0	98

c. The following is a comparison table of semi-quantitative assay performance for the 200ng/mL cutoff:

Table 16 - Method Comparison (for 200ng/mL cutoff) – Semi-Quantitative

		LC/MS Confirmation	
		(+)	(-)
Test Device	(+)	42	0
	(-)	1	43



d. The following is a summary table of semi-quantitative assay performance for the 200ng/mL cutoff:

Table 17 - Assay Performance verified by LC/MS – 200ng/mL Cutoff					
Type	Benzodiazepines Concentration				Agreement (%)
	< 100ng/mL	100 ~ 199 ng/mL	200 ~ 300 ng/mL	> 300 ng/mL	
Semi-Quantitative/ Positive	0	0	4	38	100
Semi-Quantitative / Negative	36	7	1	0	98

6. Immunalysis Multi-Drug Calibrators Analytical Performance

- a. Traceability – all components of the calibrators have been traced to a commercially available oxazepam solution.
- b. Closed Vial Stability (Accelerated) – A closed vial stability study was performed at 25°C to establish the initial vial expiration dating. All calibrator levels (1, 2, 3, and 4) were within specifications for Day 0, 8, 16, 24, 32, and 40. This accelerated stability study was performed to establish initial expiration dating. The stability study supported an initial expiration date of 12 months after testing on LC/MS. Real time stability studies are ongoing.
- c. Open Vial Stability – An open vial stability study was performed at 5°C to establish the initial open vial expiration dating on LC/MS. All calibrator levels (1, 2, 3, and 4) were within specifications for Day 0, 19, 26, 33, 41, and 60. This stability study supported an initial open vial expiration date of 60 days.
- d. Value Assignment – Calibrators are manufactured and are tested by mass spectrometry. 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. The non-zero calibrators are prepared by spiking a known concentration of oxazepam in the negative calibrator matrix. If any of the analytes are not of the acceptable range, then the calibrator is adjusted and re-tested. Values are assigned to the calibrators once the mass spectrometry results are within the acceptable ranges.

I. Proposed Labeling

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10

J. Conclusion

The information provided in this pre-market notification demonstrates that the Immunalysis Benzodiazepines Urine Enzyme Immunoassay is substantially equivalent to the legally marketed predicate device for its general intended use.