DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

October 14, 2016

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

Re: K161714
Trade/Device Name: Immunalysis Barbiturates Urine Enzyme Immunoassay,
Immunalysis Multi-Drug Calibrators
Regulation Number: 21 CFR 862.3150
Regulation Name: Barbiturate test system
Regulatory Class: II
Product Code: DIS, DKB
Dated: September 1, 2016
Received: September 6, 2016

Dear Joseph 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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

# Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
*See PRA Statement below.*

510(k) Number *(if known)*
k161714

Device Name
Immunalysis Barbiturates Urine Enzyme Immunoassay
Immunalysis Multi-Drug Calibrators

Indications for Use *(Describe)*
Immunalysis Barbiturates Urine Enzyme Immunoassay

The Immunalysis Barbiturates Urine Enzyme Immunoassay 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 Barbiturates in human urine with automated clinical chemistry analyzers. This assay is calibrated against Secobarbital. This in vitro diagnostic device is for prescription use only.

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

The Immunalysis Barbiturates Urine Enzyme Immunoassay 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 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.

Immunalysis Multi-Drug Calibrators:

The Immunalysis Multi-Drug Calibrators are intended for in vitro diagnostic use for the calibration of assays for the following analytes: Benzoylecgonine, Methamphetamine, Morphine, PCP, Secobarbital 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

A. General Information

1. Applicant Name: Immunalysis Corporation
   829 Towne Center Drive
   Pomona, CA 91767
2. Company Contact: Joseph Ginete
   Regulatory Affairs Specialist II
   Phone: (909) 482-0840
   Email: jginete@immunalysis.com
3. Date prepared: October 13, 2016

B. Device Identification

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

C. Regulatory Information

1. Device Classification: II
2. Regulation Number: 21 CFR 862.3150 Barbiturate Test System
   21 CFR 862.3200 Calibrators, Drug Specific
3. Panel: Toxicology (91)
4. Product Code: DIS
   DKB
5. Predicate Device: DRI ® Barbiturates EIA Assay
6. Predicate Company: Diagnostic Reagents, Inc.
7. Predicate K Number: K955928

D. Device Description

The Immunalysis Barbiturates Urine Enzyme Immunoassay consists of antibody/ substrate reagent and enzyme conjugate reagent. The antibody/ substrate reagent includes a recombinant antibody to Secobarbital, a mouse monoclonal antibody to Secobarbital, glucose-6-phosphate (G6P) and nicotinamide adenine dinucleotide (NAD) in HEPES buffer with sodium azide as a preservative. The enzyme conjugate reagent includes Barbiturates labeled with glucose-6-phosphate dehydrogenase (G6PDH) in HEPES buffer with sodium azide as a preservative.

Immunalysis Multi-Drug Calibrators are included as part of the test system and provided separately. The calibrator kit includes four levels of drugs and a negative calibrator in a ready-to-use format. Automated clinical chemistry analyzers capable of maintaining a constant temperature, pipetting samples and reagents, mixing reagents, timing the reaction accurately and measuring enzymatic rates spectrophotometrically at 340nm can be used to perform the assay.

The Immunalysis Barbiturates Urine Enzyme Immunoassay uses barbiturates recombinant and monoclonal antibody. The assay is based on the competition of Barbiturates 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 and enzyme activity. The enzyme G6PDH activity is determined at 340 nm spectrophotometrically by the conversion of NAD to NADH.

E. Intended Use

1. The Immunalysis Barbiturates Urine Enzyme Immunoassay 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 Barbiturates in human urine with automated clinical chemistry analyzers. This assay is calibrated against Secobarbital. This *in vitro* diagnostic device is for prescription use only.

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

   The Immunalysis Barbiturates Urine Enzyme Immunoassay 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 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.

2. Immunalysis Multi-Drug Calibrators
   The Immunalysis Multi-Drug Calibrators are intended for *in vitro* diagnostic use for the calibration of assays for the following analytes: Benzoylecgonine, Methamphetamine, Morphine, PCP, Secobarbital and Oxazepam. The calibrators are designed for prescription use with immunoassays.

F. Comparison With Predicate

| Attribute | **Predicate Device DRI Barbiturates Assay** | **Candidate Device Immunalysis Barbiturates Urine EIA** |
|---|---|---|
| **Similarities** | | |
| **Intended Use** | For the qualitative and semi-quantitative determination of the presence of Barbiturates in human urine at a cutoff of 200 ng/mL | Same |
| **User Environment** | For use in laboratories | Same |
| **Measured Analytes** | Barbiturate | Same |
| **Test System** | Enzyme immunoassay | Same |
| **Materials** | Antibody/substrate reagents and enzyme labeled conjugate | Same |
| **Sample Matrix** | Urine | Same |
| **Cutoff Levels** | 200 ng/mL of Barbiturates | Same |
| **Mass Spectrometry Confirmation** | Required for preliminary positive analytical results | Same |
| **Storage** | 2 – 8° C until expiration date | Same |
| **Calibrator Form** | Liquid | Same |
| **Control Levels** | Two levels (150 ng/mL and 250 ng/mL) | Same |
| **Calibrator Levels** | One negative and four levels (100, 200, 500 and 1000 ng/mL) | Same |
| **Differences** | | |
| **Antibody** | Monoclonal antibody to Barbiturates | Recombinant and monoclonal antibodies to Barbiturates |

G. Performance Characteristics:
The following laboratory performance studies were performed to determine substantial equivalence of the Immunalysis Barbiturates Urine Enzyme Immunoassay to the predicate. All studies utilized the Beckman Coulter AU 400e instrument.

1. Precision/ Cutoff Characterization – Study was performed for 20 days, 2 runs per day in replicates of 2 on drug free urine (N=80) spiked with secobarbital to concentrations of ±25%, ±50%, ±75%, and ±100% of the cutoff (200 ng/mL). 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 following is a summary table of the qualitative analysis for the 200 ng/mL cutoff test data results.

| Table 1 - Qualitative Analysis | | | |
|---|---|---|---|
| Concentration (ng/mL) | % of cutoff | # of determinations | Total Result |
| 0 | -100% | 80 | 80 Negative |
| 50 | -75% | 80 | 80 Negative |
| 100 | -50% | 80 | 80 Negative |
| 150 | -25% | 80 | 80 Negative |
| 200 | Cutoff | 80 | 33 Neg/47 Pos |
| 250 | +25% | 80 | 80 Positive |
| 300 | +50% | 80 | 80 Positive |
| 350 | +75% | 80 | 80 Positive |
| 400 | +100% | 80 | 80 Positive |

The following is a summary table of the semi-quantitative analysis for the 200 ng/mL cutoff test data results.

| Table 2 - Semi-Quantitative Analysis | | | |
|---|---|---|---|
| Concentration (ng/mL) | % of cutoff | # of determinations | Total Result |
| 0 | -100% | 80 | 80 Negative |
| 50 | -75% | 80 | 80 Negative |
| 100 | -50% | 80 | 80 Negative |
| 150 | -25% | 80 | 80 Negative |
| 200 | Cutoff | 80 | 23 Neg/ 57 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 – 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 following is a summary table of qualitative results:

| Table 3 - Structurally Related Compounds – Qualitative | | | |
|---|---|---|---|
| Compound | Concentration Tested (ng/mL) | Result | Cross-Reactivity (%) |
| Secobarbital | 200 | Positive | 100 |
| Allobarbital | 690 | Positive | 29.0 |
| Alphenal | 190 | Positive | 105.3 |
| Amobarbital | 200 | Positive | 100.0 |
| Aprobarbital | 700 | Positive | 28.6 |
| Barbital | 9,000 | Positive | 2.2 |
| Butabarbital | 510 | Positive | 39.2 |
| Butalbital | 290 | Positive | 69.0 |
| Butobarbital | 190 | Positive | 105.3 |
| Cyclopentobarbital | 200 | Positive | 100.0 |
| Hexobarbital | 70,000 | Positive | 0.3 |
| Mephobarbital | 65,000 | Positive | 0.3 |

| Table 3 - Structurally Related Compounds – Qualitative | | | |
|---|---|---|---|
| Compound | Concentration Tested (ng/mL) | Result | Cross-Reactivity (%) |
| Pentobarbital | 420 | Positive | 47.6 |
| Phenobarbital | 460 | Positive | 43.5 |
| Phenytoin | 100,000 | Negative | <0.2 |
| Talbutal | 220 | Positive | 90.9 |
| Thiopental | 3,700 | Positive | 5.4 |

The following is a summary table of semi-quantitative results:

| Table 4 - Structurally Related Compounds – Semi-Quantitative | | | |
|---|---|---|---|
| Compound | Concentration Tested (ng/mL) | Result | Cross-Reactivity (%) |
| Secobarbital | 200 | Positive | 100 |
| Allobarbital | 690 | Positive | 29.0 |
| Alphenal | 190 | Positive | 105.3 |
| Amobarbital | 200 | Positive | 100.0 |
| Aprobarbital | 700 | Positive | 28.6 |
| Barbital | 9,000 | Positive | 2.2 |
| Butabarbital | 510 | Positive | 39.2 |
| Butalbital | 290 | Positive | 69.0 |
| Butobarbital | 190 | Positive | 105.3 |
| Cyclopentobarbital | 200 | Positive | 100.0 |
| Hexobarbital | 70,000 | Positive | 0.3 |
| Mephobarbital | 65,000 | Positive | 0.3 |
| Pentobarbital | 420 | Positive | 47.6 |
| Phenobarbital | 460 | Positive | 43.5 |
| Phenytoin | 100,000 | Negative | <0.2 |
| Talbutal | 220 | Positive | 90.9 |
| Thiopental | 3,700 | Positive | 5.4 |

3. Interference – Structurally unrelated compounds were evaluated in qualitative and semi-quantitative modes by spiking the potential interferent into drug free urine containing secobarbital at ±25% of the cutoff. All potential interferents analyzed verified that assay performance is unaffected by externally ingested compounds. The results of this study are indicated in the table below.

| Table 5 - Structurally Unrelated Compounds | | | | | |
|---|---|---|---|---|---|
| Compound | Concentration Tested (ng/mL) | -25% Cutoff (150 ng/mL) | | +25% Cutoff (250 ng/mL) | |
| | | Qualitative | Semi-Quantitative | Qualitative | Semi-Quantitative |
| 4-Bromo-2,5,Dimethoxyphenethylamine | 100,000 | Negative | Negative | Positive | Positive |
| Acetaminophen | 500,000 | Negative | Negative | Positive | Positive |
| Acetylsalicyclic Acid | 100,000 | Negative | Negative | Positive | Positive |

| Table 5 - Structurally Unrelated Compounds | | | | | |
|---|---|---|---|---|---|
| Compound | Concentration Tested (ng/mL) | -25% Cutoff (150 ng/mL) | | +25% Cutoff (250 ng/mL) | |
| | | Qualitative | Semi-Quantitative | Qualitative | Semi-Quantitative |
| 6-Acetylcodeine | 100,000 | Negative | Negative | Positive | Positive |
| 6-Acetylmorphine | 100,000 | Negative | Negative | Positive | Positive |
| Alprazolam | 100,000 | Negative | Negative | Positive | Positive |
| 7-Aminoclonazepam | 100,000 | Negative | Negative | Positive | Positive |
| 7-Aminoflunitrazepam | 100,000 | Negative | Negative | Positive | Positive |
| 7-Aminonitrazepam | 100,000 | Negative | Negative | Positive | Positive |
| Amitriptyline | 100,000 | Negative | Negative | Positive | Positive |
| S-(+) Amphetamine | 100,000 | Negative | Negative | Positive | Positive |
| Benzylpiperazine | 100,000 | Negative | Negative | Positive | Positive |
| Bromazepam | 100,000 | Negative | Negative | Positive | Positive |
| Buprenorphrine | 100,000 | Negative | Negative | Positive | Positive |
| Bupropion | 100,000 | Negative | Negative | Positive | Positive |
| Caffeine | 500,000 | Negative | Negative | Positive | Positive |
| Cannabidiol | 100,000 | Negative | Negative | Positive | Positive |
| Cannabinol | 100,000 | Negative | Negative | Positive | Positive |
| Carbamazepine | 100,000 | Negative | Negative | Positive | Positive |
| Carisoprodol | 100,000 | Negative | Negative | Positive | Positive |
| Chlordiazepoxide | 100,000 | Negative | Negative | Positive | Positive |
| Chlorpromazine | 100,000 | Negative | Negative | Positive | Positive |
| cis-Tramadol | 100,000 | Negative | Negative | Positive | Positive |
| Clobazam | 100,000 | Negative | Negative | Positive | Positive |
| Clomipramine | 100,000 | Negative | Negative | Positive | Positive |
| Clonazepam | 100,000 | Negative | Negative | Positive | Positive |
| Clozapine | 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 |
| Demoxepam | 100,000 | Negative | Negative | Positive | Positive |
| Desalkyflurazepam | 100,000 | Negative | Negative | Positive | Positive |
| Desipramine | 100,000 | Negative | Negative | Positive | Positive |
| Dextromethorphan | 100,000 | Negative | Negative | Positive | Positive |
| Diazepam | 100,000 | Negative | Negative | Positive | Positive |
| Digoxin | 100,000 | Negative | Negative | Positive | Positive |
| Dihydrocodeine | 100,000 | Negative | Negative | Positive | Positive |
| Diphenhydramine | 500,000 | Negative | Negative | Positive | Positive |
| Dehydronorketamine | 25,000 | Negative | Negative | Positive | Positive |
| Delta-9-THC | 100,000 | Negative | Negative | Positive | Positive |
| Doxepin | 100,000 | Negative | Negative | Positive | Positive |
| EDDP | 100,000 | Negative | Negative | Positive | Positive |
| EMDP | 100,000 | Negative | Negative | Positive | Positive |
| 1R,2S(-)-Ephedrine | 100,000 | Negative | Negative | Positive | Positive |
| 1S,2R(+)-Ephedrine | 100,000 | Negative | Negative | Positive | Positive |
| Ethyl glucuronide | 100,000 | Negative | Negative | Positive | Positive |

| Table 5 - Structurally Unrelated Compounds | | | | | |
|---|---|---|---|---|---|
| Compound | Concentration Tested (ng/mL) | -25% Cutoff (150 ng/mL) | | +25% Cutoff (250 ng/mL) | |
| | | Qualitative | Semi-Quantitative | Qualitative | Semi-Quantitative |
| Ethylmorphine | 100,000 | Negative | Negative | Positive | Positive |
| Fenfluramine | 100,000 | Negative | Negative | Positive | Positive |
| Fentanyl | 100,000 | Negative | Negative | Positive | Positive |
| Flunitrazepam | 100,000 | Negative | Negative | Positive | Positive |
| Fluoxetine | 100,000 | Negative | Negative | Positive | Positive |
| Flurazepam | 100,000 | Negative | Negative | Positive | Positive |
| Haloperidol | 100,000 | Negative | Negative | Positive | Positive |
| Heroin | 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 | 500,000 | Negative | Negative | Positive | Positive |
| Imipramine | 100,000 | Negative | Negative | Positive | Positive |
| Ketamine | 100,000 | Negative | Negative | Positive | Positive |
| Lamotrignine | 100,000 | Negative | Negative | Positive | Positive |
| Levorphanol tartrate | 100,000 | Negative | Negative | Positive | Positive |
| Lidocaine | 100,000 | Negative | Negative | Positive | Positive |
| Lorazepam | 100,000 | Negative | Negative | Positive | Positive |
| Lorazepam Glucuronide | 50,000 | Negative | Negative | Positive | Positive |
| Lormetazepam | 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 |
| S(+)-Methamphetamine | 100,000 | Negative | Negative | Positive | Positive |
| Methadone | 500,000 | Negative | Negative | Positive | Positive |
| Methaquolone | 100,000 | Negative | Negative | Positive | Positive |
| Methoxetamine | 100,000 | Negative | Negative | Positive | Positive |
| Methylone | 100,000 | Negative | Negative | Positive | Positive |
| Methylphenidate | 100,000 | Negative | Negative | Positive | Positive |
| Midazolam | 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 | 50,000 | Negative | Negative | Positive | Positive |
| N-desmethyltapentadol | 100,000 | Negative | Negative | Positive | Positive |
| Nalorphine | 100,000 | Negative | Negative | Positive | Positive |

| Table 5 - Structurally Unrelated Compounds | | | | | |
|---|---|---|---|---|---|
| Compound | Concentration Tested (ng/mL) | -25% Cutoff (150 ng/mL) | | +25% Cutoff (250 ng/mL) | |
| | | Qualitative | Semi-Quantitative | Qualitative | Semi-Quantitative |
| Naloxone | 100,000 | Negative | Negative | Positive | Positive |
| Naltrexone | 100,000 | Negative | Negative | Positive | Positive |
| Naproxen | 100,000 | Negative | Negative | Positive | Positive |
| Nitrazepam | 100,000 | Negative | Negative | Positive | Positive |
| 11-nor-9 carboxy THC | 100,000 | Negative | Negative | Positive | Positive |
| Norbuprenorphine | 50,000 | Negative | Negative | Positive | Positive |
| Norcodeine | 100,000 | Negative | Negative | Positive | Positive |
| Nordiazepam | 100,000 | Negative | Negative | Positive | Positive |
| Norketamine | 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 |
| Olanzapine | 100,000 | Negative | Negative | Positive | Positive |
| Oxazepam | 100,000 | Negative | Negative | Positive | Positive |
| Oxycodone | 100,000 | Negative | Negative | Positive | Positive |
| Oxymorphone | 100,000 | Negative | Negative | Positive | Positive |
| PCP | 100,000 | Negative | Negative | Positive | Positive |
| Pentazocine | 100,000 | Negative | Negative | Positive | Positive |
| Phentermine | 100,000 | Negative | Negative | Positive | Positive |
| Phenylephedrine | 100,000 | Negative | Negative | Positive | Positive |
| Phenylpropanolamine | 100,000 | Negative | Negative | Positive | Positive |
| PMA | 100,000 | Negative | Negative | Positive | Positive |
| Prazepam | 100,000 | Negative | Negative | Positive | Positive |
| Proproxyphene | 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 | 500,000 | Negative | Negative | Positive | Positive |
| Sertraline | 100,000 | Negative | Negative | Positive | Positive |
| Sufentanil Citrate | 50,000 | Negative | Negative | Positive | Positive |
| Tapentadol | 100,000 | Negative | Negative | Positive | Positive |
| Temazepam | 100,000 | Negative | Negative | Positive | Positive |
| Theophylline | 100,000 | Negative | Negative | Positive | Positive |
| Thioridazine | 100,000 | Negative | Negative | Positive | Positive |
| Triazolam | 100,000 | Negative | Negative | Positive | Positive |
| Trifluoromethylphenyl-piperazine | 100,000 | Negative | Negative | Positive | Positive |

| Table 5 - Structurally Unrelated Compounds | | | | | |
|---|---|---|---|---|---|
| Compound | Concentration Tested (ng/mL) | -25% Cutoff (150 ng/mL) | | +25% Cutoff (250 ng/mL) | |
| | | Qualitative | Semi-Quantitative | Qualitative | Semi-Quantitative |
| Trimipramine | 100,000 | Negative | Negative | Positive | Positive |
| Trazodone | 100,000 | Negative | Negative | Positive | Positive |
| Venlafaxine | 100,000 | Negative | Negative | Positive | Positive |
| Verapamil | 100,000 | Negative | Negative | Positive | Positive |
| Zolpidem Tartrate | 100,000 | Negative | Negative | Positive | Positive |

4. Interference – Endogenous compounds were evaluated in qualitative and semi-quantitative modes by spiking the potential interferent into drug free urine containing secobarbital at ±25% of the cutoff. All potential interferents analyzed verified that assay performance is unaffected by internally existing physiological conditions. The results of this study are indicated in the table below:

| Table 6 - Endogenous Compounds | | | | | |
|---|---|---|---|---|---|
| Compound | Concentration Tested | -25% Cutoff (150 ng/mL) | | +25% Cutoff (250 ng/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 |
| 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 | 0.300 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 |

5. Boric Acid Interference – Boric acid at a concentration of 1% w/v was evaluated in qualitative and semi-quantitative modes by spiking the potential interferent into drug free urine containing secobarbital at ±25% of the cutoff. The results of this study are indicated in the table below. Due to the interference observed at ±25% of the cutoff, potential interference was also evaluated at ±50% of the cutoff. The results of this study are indicated in the table below.

| **Table 7 – Boric Acid** | | | | | |
|---|---|---|---|---|---|
| Compound | Concentration Tested | **-25% Cutoff (150 ng/mL)** | | **+25% Cutoff (250 ng/mL)** | |
| | | Qualitative | Semi-Quantitative | Qualitative | Semi-Quantitative |
| Boric Acid | 1% w/v | Negative | Negative | **Negative** | **Negative** |

| **Table 8 – Boric Acid** | | | | | |
|---|---|---|---|---|---|
| Compound | Concentration Tested | **-50% Cutoff (100 ng/mL)** | | **+50% Cutoff (300 ng/mL)** | |
| | | Qualitative | Semi-Quantitative | Qualitative | Semi-Quantitative |
| Boric Acid | 1% w/v | Negative | Negative | **Negative** | **Negative** |

6. pH Interference – To evaluate potential interference from the effect of urine pH, 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 secobarbital 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. The results of this study are indicated in the table below.

| **Table 9 - Effect of pH** | | | | |
|---|---|---|---|---|
| pH Value | **-25% Cutoff (150 ng/mL)** | | **+25% Cutoff (250 ng/mL)** | |
| | Qualitative | Semi-Quantitative | Qualitative | Semi-Quantitative |
| 3.0 | Negative | Negative | Positive | Positive |
| 4.0 | Negative | Negative | Positive | Positive |
| 5.0 | Negative | Negative | Positive | Positive |
| 6.0 | Negative | Negative | Positive | Positive |
| 7.0 | Negative | Negative | Positive | Positive |
| 8.0 | Negative | Negative | Positive | Positive |
| 9.0 | Negative | Negative | Positive | Positive |
| 10.0 | Negative | Negative | Positive | Positive |
| 11.0 | Negative | Negative | Positive | Positive |

7. Specific Gravity Interference - 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 secobarbital at ±25% of the 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 results of this study are indicated in the table below.

| Table 10 - Effect of Specific Gravity | | | | |
|---|---|---|---|---|
| Specific Gravity Value | -25% Cutoff (150 ng/mL) | | +25% Cutoff (250 ng/mL) | |
| | Qualitative | Semi-Quantitative | Qualitative | Semi-Quantitative |
| 1.000 | Negative | Negative | Positive | Positive |
| 1.002 | Negative | Negative | Positive | Positive |
| 1.005 | Negative | Negative | Positive | Positive |
| 1.010 | Negative | Negative | Positive | Positive |
| 1.015 | Negative | Negative | Positive | Positive |
| 1.020 | Negative | Negative | Positive | Positive |
| 1.025 | Negative | Negative | Positive | Positive |
| 1.030 | Negative | Negative | Positive | Positive |

8. Linearity/ Recovery - A linearity study in the semi-quantitative mode was conducted by spiking a drug free urine pool with a high concentration of secobarbital above the highest calibrator. Additional pools were made by serially diluting the high concentration specimen with drug free urine to achieve concentrations ranging from 100 ng/mL 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. The results of this study are indicated in the table below.

| Table 11 - Linearity/ Recovery | | |
|---|---|---|
| Expected Concentration (ng/mL) | Mean Concentration (ng/mL) | Recovery (%) |
| 0 | -0.6 | N/A |
| 100 | 93.2 | 93.2 |
| 200 | 196.0 | 98.0 |
| 300 | 314.7 | 104.9 |
| 400 | 418.1 | 104.5 |
| 500 | 487.9 | 97.6 |
| 600 | 604.1 | 100.7 |
| 700 | 724.2 | 103.5 |
| 800 | 819.3 | 102.4 |
| 900 | 891.2 | 99.0 |
| 1000 | 968.7 | 96.9 |
| 1100 | 981.8 | 89.3 |

9. Method Comparison – Ninety-six deidentified, unaltered leftover clinical urine samples obtained from clinical testing laboratories were analyzed for barbiturates at an assay cutoff of 200 ng/mL with the Immunalysis Barbiturates Urine Enzyme Immunoassay in both qualitative and semi-quantitative modes and compared to results by mass spectrometry (LC/MS-MS). The instruments used were a Beckman Coulter AU 400e and an Agilent 6430 Liquid Chromatography Tandem Mass Spectrometer.

The following is a summary table of qualitative assay results:

| Table 12 – Qualitative Assay Performance verified by LC/MS-MS | | | | | |
|---|---|---|---|---|---|
| Type | Barbiturates Concentration | | | | Agreement (%) |
| | < 100 ng/mL | 100 ~ 199 ng/mL | 200 ~ 300 ng/mL | > 300 ng/mL | |
| Qualitative/ Positive | 0 | 0 | 8 | 44 | 100 |
| Qualitative/ Negative | 36 | 8 | 0 | 0 | 100 |

The following is a summary table of semi-quantitative assay results:

| Table 13 – Semi-Quantitative Assay Performance verified by LC/MS-MS | | | | | |
|---|---|---|---|---|---|
| Type | Barbiturates Concentration | | | | Agreement (%) |
| | < 100 ng/mL | 100 ~ 199 ng/mL | 200 ~ 300 ng/mL | > 300 ng/mL | |
| Semi-Quantitative/ Positive | 0 | 0 | 8 | 44 | 100 |
| Semi-Quantitative / Negative | 36 | 8 | 0 | 0 | 100 |

10. Immunalysis Multi-Drug Calibrators
    a. Traceability – all components of the calibrators have been traced to a commercially available secobarbital solution.
    b. Value Assignment – Calibrators are manufactured and tested by mass spectrometry. The negative calibrator is a processed, drug free urine matrix. The negative calibrator 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 secobarbital in the negative calibrator matrix. If any of the analytes are not within 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.

H. Conclusion

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