May 9, 2022

Immunalysis Corporation
Elina Arroyo
Manager Regulatory Affairs
829 Towne Center Drive
Pomona, California 91767

Re: K203527
Trade/Device Name: Immunalysis Tapentadol Urine HEIA™
Regulation Number: 21 CFR 862.3650
Regulation Name: Opiate Test System
Regulatory Class: Class II
Product Code: DJG
Dated: February 10, 2022
Received: February 11, 2022

Dear Elina Arroyo:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. 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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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 https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Marianela Perez-Torres, Ph.D.
Deputy Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
k203527

Device Name
Immunalysis Tapentadol Urine HEIA™

Indications for Use *(Describe)*
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).

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

510(K) NUMBER: K203527

A. GENERAL INFORMATION

Applicant Name: Immunalysis Corporation
829 Towne Center Drive
Pomona, CA 91767
Establishment # 2020952

Company Contact: Elina Arroyo
Associate Director, Regulatory Affairs
1 312-208-1514
elina.arroyo@abbott.com

Date Prepared: February 10, 2022

B. DEVICE IDENTIFICATION

Trade or Proprietary Names: Immunalysis Tapentadol Urine HEIA™

Common Name: Tapentadol Urine Enzyme Immunoassay

C. REGULATORY INFORMATION

Device Classification Name: Enzyme Immunoassay, Opiates

Product Codes: DJG

Regulatory Class: Class II

Classification Regulation: 21 CFR 862.3650, Opiate Test System

Panel: Toxicology (91)

Predicate Device: Immunalysis Tramadol Enzyme Immunoassay [K141803]

D. DEVICE DESCRIPTION

The Immunalysis Tapentadol Urine HEIA™ is a homogeneous enzyme immunoassay 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).

Tapentadol is a centrally acting analgesic approved by the FDA in 2008 to treat moderate to severe pain in adults. It is a μ-opioid receptor agonist and is classified as a Schedule II controlled substance. The therapeutic doses of tapentadol are generally between 50 and 600 mg/ day (the range specified by the package insert)[1] with a median of 200 mg/day. About 99% of ingested tapentadol undergoes glucuronide conjugation (55%) and sulfate conjugation (15%) before excretion into the urine[2,3]. Wu et al[4]. described urine concentrations of tapentadol and its metabolites in 736 samples. The parent drug and all three metabolites were detected together in 79.9% of positive specimens (n = 586); the parent drug was detected together with glucuronide conjugate in 7.1% of positive samples. Parent drug was detected without metabolites in 49 samples. The median

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[1] Janssen Pharmaceuticals, Inc. https://www.nucynta.com/hcp/ir/individualized-dosing/

[2] Terlinden R, Ossig J, Fliegert F, Lange C, Goehler K. Absorption, metabolism, and excretion of 14C-labeled tapentadol HCl in healthy male subjects. Eur J Drug Metab Pharmacokinetics 2007; 32:163–169.

[3] DePriest AZ, Puet BL, Holt AC, Roberts A, Cone EJ. Metabolism and disposition of prescription opioids: A Review. Forensic Sci Rev. 2015 Jul;27(2):115-45. Review.

[4] Wu F, Slawson MH, Johnson-Davis KL. Metabolic patterns of fentanyl, meperidine, methylphenidate, tapentadol and tramadol observed in urine, serum or plasma. J Anal Toxicol. 2017;41(4):289-299

concentration observed for tapentadol was 3,104 ng/mL, and the concentrations of tapentadol exceeding 5,000 ng/mL were found in 37.5% of positive samples.

E. INTENDED 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).

F. COMPARISON WITH PREDICATE

Immunalysis Tramadol Enzyme Immunoassay was selected as the predicate because both Tapentadol and Tramadol are in the opioid family and share identical characteristics except for the analyte being detected. The following **Table 5-1** includes a summary of the technological characteristics.

Table 5-1 Comparison to Predicate Device

Attribute	Candidate Device Immunalysis Tapentadol Urine HEIA™	Predicate Device Immunalysis Tramadol Enzyme Immunoassay [K141803]
Similarities		
Intended Use	Identical	For the qualitative and semi-quantitative analysis of an opioid in human urine with automated clinical chemistry analyzers.
Test Principle	Identical	Homogeneous enzyme immunoassay
User Environment	Identical	For use in laboratories
Sample Matrix	Identical	Human urine
Mass Spectrometry Confirmation	Identical	Required for preliminary positive analytical results
Reagent Storage	Identical	2-8°C until expiration date
Assay Materials	Identical	Two analytical reagents: antibody/substrate reagent and enzyme labeled conjugate reagent
Assay Cutoff Level	Identical	200 ng/mL
Instrumentation	Identical	Automated Clinical chemistry analyzer
Differences		
Antibody	Recombinant FAB antibody to Tapentadol	Goat Polyclonal Antibody to Tramadol
Calibrator	Tapentadol	Tramadol

G. PERFORMANCE CHARACTERISTICS

The following laboratory performance studies were performed to determine substantial equivalence of the Immunalysis Tapentadol Urine HEIA™ to the predicate device. Assay performance was established using the Beckman Coulter AU480 chemistry analyzer.

1. Precision

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) on 3 lots of reagent. Nine panel members were made 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 mass spectrometry (LC-MS/MS). The data demonstrates all sample concentration ranging from -100% to -25% of the cutoff were negative and all sample concentrations ranging from +25% to +100% of cutoff were positive for both qualitative and semi-quantitative interpretations. The %CV of the semi-quantitative results ranged from 3.6 to 9.7 for all lots tested. The study established the repeatability of the assay. Test results in qualitative and semi-quantitative modes for a representative lot are presented in **Tables 2** to **7**.

Table 2. Precision – Qualitative Lot#1

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	41 Neg / 39 Pos
250	+25%	80	80 Positive
300	+50%	80	80 Positive
350	+75%	80	80 Positive
400	+100%	80	80 Positive

Table 3. Precision – Qualitative Lot#2

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	35 Neg / 45 Pos
250	+25%	80	80 Positive
300	+50%	80	80 Positive
350	+75%	80	80 Positive
400	+100%	80	80 Positive

Table 4. Precision – Qualitative Lot#3

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	42 Neg / 38 Pos
250	+25%	80	80 Positive
300	+50%	80	80 Positive
350	+75%	80	80 Positive
400	+100%	80	80 Positive

Table 5. Precision - Semi-Quantitative Lot#1

Concentration (ng/mL)	% of Cutoff	# of Determinations	Mean Conc. (ng/mL)	Result
0	-100%	80	-3	80 Negative
50	-75%	80	48	80 Negative
100	-50%	80	99	80 Negative
150	-25%	80	161	80 Negative
200	Cutoff	80	215	2 Neg / 78 Pos
250	+25%	80	268	80 Positive
300	+50%	80	304	80 Positive
350	+75%	80	372	80 Positive
400	+100%	80	431	80 Positive

Table 6. Precision - Semi-Quantitative Lot#2

Concentration (ng/mL)	% of Cutoff	# of Determinations	Mean Conc. (ng/mL)	Result
0	-100%	80	-4	80 Negative
50	-75%	80	50	80 Negative
100	-50%	80	100	80 Negative
150	-25%	80	162	80 Negative
200	Cutoff	80	213	8 Neg / 72 Pos
250	+25%	80	263	80 Positive
300	+50%	80	298	80 Positive
350	+75%	80	359	80 Positive
400	+100%	80	417	80 Positive

Table 7. Precision - Semi-Quantitative Lot#3

Concentration (ng/mL)	% of Cutoff	# of Determinations	Mean Conc. (ng/mL)	Result
0	-100%	80	-3	80 Negative
50	-75%	80	49	80 Negative
100	-50%	80	102	80 Negative
150	-25%	80	162	80 Negative
200	Cutoff	80	215	7 Neg / 73 Pos
250	+25%	80	266	80 Positive
300	+50%	80	303	80 Positive
350	+75%	80	369	80 Positive
400	+100%	80	422	80 Positive

2. Specificity and 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 are presented in **Table 8**. Cross-reactivity test results in semi-quantitative mode are presented in **Table 9**.

Table 8. 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

Compound	Compound Conc. (ng/mL)	Tapentadol Equivalent Conc. (ng/mL)	Result	Cross-Reactivity (%)
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

Table 9. 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
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

3. 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 in **Table 10**.

Table 10. 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
Amobarbital	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
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

Compound	Conc. Tested (ng/mL)
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
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

Compound	Conc. Tested (ng/mL)
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
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

Compound	Conc. Tested (ng/mL)
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
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

Compound	Conc. Tested (ng/mL)
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

4. 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 in **Tables 11 and 12**. Boric acid interference test results at ±50% of the cutoff in qualitative and semi-quantitative modes are presented in **Table 13.**

Table 11. 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

Table 12. Non-interfering Urine Preservative

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

Table 13. 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

5. 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.

6. Interference - Specific Gravity

To evaluate potential interference from the specific gravity of urine on the assay's ability to detect tapentadol, 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 tapentadol 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.

7. Linearity/Recovery

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 pools were made by serially diluting the high concentration specimen with drug free urine to achieve concentrations ranging from 1100 to 100 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 study confirmed the linear range to be 100-1100 ng/mL. The assay drug recovery percentage ranged from 95.8 to 110.4 %. Linearity test results in semi-quantitative mode are presented in **Tables 14**.

Table 14. 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

8. Calibration Duration

Drug free negative urine spiked with tapentadol at ±25% of the cutoff were tested in qualitative and semi-quantitative mode at time points up to 14 days. At the initial time point, a two-point calibration curve was established in qualitative mode and a multi-point calibration curve was established in semi-quantitative mode. This calibration was used through the duration of this study. The test results met acceptance criteria at each time point. The recommended frequency of calibration is 14 days.

9. Tapentadol Stability in Urine

Urine samples were collected from 4 participants who reported taking tapentadol in the last 24 hours. These samples were tested within 4 hours of sample collection. Test results indicated that urine samples containing tapentadol are stable for up to 14 days stored at 2°C - 8°C.

10. Method Comparison

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™ in both qualitative and semi-quantitative modes and Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS). The instruments used were the Beckman Coulter AU480 chemistry analyzer and an Agilent 6430 Liquid Chromatography-Tandem Mass Spectrometry. The method comparison study demonstrates that the Immunalysis Tapentadol Urine HEIA™ is an accurate test method in comparison to LC-MS/MS with a positive percent agreement (PPA) and negative percent agreement (NPA) of 100% and 100%, respectively. The results are presented from **Tables 15** and **16**.

Table 15. Method Comparison Results by Concentration Range

Immunalysis Tapentadol Urine HEIA™ Result		LC-MS/MS Tapentadol Concentration				Agreement (%)
		< 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)	
Qual.	Positive	0	0	14	81	**100% (95/95)**
	Negative	46	19	0	0	**100% (65/65)**
Semi-Quant.	Positive	0	0	14	81	**100% (95/95)**
	Negative	46	19	0	0	**100% (65/65)**

Table 16. Method Comparison Results Compared to LC-MS/MS

Immunalysis Tapentadol Urine HEIA™		LC-MS/MS	
		(+)	(-)
Qualitative	**(+)**	95	0
	(-)	0	65
Semi-Quantitative	**(+)**	95	0
	(-)	0	65

H. CONCLUSION

The information provided in this pre-market notification demonstrates that the Immunalysis Tapentadol Urine HEIA™ is substantially equivalent to the legally marketed predicate device.