



November 21, 2019

Lin-Zhi International, Inc.
Bernice Lin
VP of Operations
2945 Oakmead Village Court
Santa Clara, CA 95051

Re: k192299

Trade/Device Name: LZI Cotinine II Enzyme Immunoassay
Regulation Number: 21 CFR 862.3220
Regulation Name: Carbon monoxide test system
Regulatory Class: Class I, reserved
Product Code: MKU
Dated: August 19, 2019
Received: August 23, 2019

Dear Bernice Lin:

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 -S

Marianela Perez-Torres, Ph.D.
Deputy Director (Acting)
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)
k192299

Device Name

LZI Cotinine II Enzyme Immunoassay

Indications for Use (Describe)

The LZI Cotinine II Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of cotinine in human urine at the cutoff value of 200 ng/mL when calibrated against cotinine. The assay is intended as an aid in the detection of cotinine after use or exposure to tobacco products. The assay is designed for prescription use with a number of automated clinical chemistry analyzers.

The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) or (2) permitting laboratories to establish quality control procedures.

The assay provides only a preliminary analytical result. A more specific alternative chemical method (e.g., gas or liquid chromatography and mass spectrometry) must be used in order to obtain a confirmed analytical result. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.

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) Number: k192299

510(k) Summary of Safety and Effectiveness

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

Submitted On

August 21, 2019

Last Updated On

November 20, 2019

Introduction

According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitter Name, Address, and Contact:

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2945 Oakmead Village Court
Santa Clara, CA 95051
Phone: (408) 970-8811
Fax: (408) 970-9030
e-mail: bclin@lin-zhi.com

Contact: Bernice Lin, Ph.D.
VP Operations

Device Name and Classification

Classification Name: Enzyme Immunoassay, Nicotine and Nicotine Metabolites
Class II, MKU (91 Toxicology),
21 CFR 862.3220

Common Name: Homogeneous Cotinine Enzyme Immunoassay

Proprietary Name: LZI Cotinine II Enzyme Immunoassay

Legally Marketed Predicate Device(s)

The LZI Cotinine II Enzyme Immunoassay is substantially equivalent to the NicCheckI Test Strips (k963733) manufactured by Dynagen, Inc. The LZI Cotinine II Enzyme Immunoassay is identical or similar to its predicate in terms of intended use, method principle, device components, and clinical performance.

Device Description

The LZI Cotinine II Enzyme Immunoassay is a homogeneous enzyme immunoassay with ready-to-use liquid reagents. The assay is based on competition between drug in the sample and drug labeled with the enzyme glucose-6-phosphate dehydrogenase (G6PDH) for a fixed amount of antibody in the reagent. Enzyme activity decreases upon binding to the antibody, and the drug concentration in the sample is measured in terms of enzyme activity. In the absence of drug in the sample, cotinine-labeled G6PDH conjugate is bound to antibody, and the enzyme activity is inhibited. On the other hand, when free drug is present in the sample, antibody would bind to free drug; the unbound cotinine-labeled G6PDH then exhibits its maximal enzyme activity. Active enzyme converts nicotinamide adenine dinucleotide (NAD) to NADH, resulting in an absorbance change that can be measured spectrophotometrically at 340 nm.

The LZI Cotinine II Enzyme Immunoassay is a kit comprised of two reagents, an R₁ and R₂, which are bottled separately but sold together within the kit.

The R₁ solution contains mouse monoclonal anti-cotinine antibody, glucose-6-phosphate (G6P) nicotinamide adenine dinucleotide (NAD), stabilizers, and sodium azide (0.09 %) as a preservative. The R₂ solution contains glucose-6-phosphate dehydrogenase (G6PDH) labeled with cotinine in buffer with sodium azide (0.09 %) as a preservative.

Intended Use

The LZI Cotinine II Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of cotinine in human urine at the cutoff value of 200 ng/mL when calibrated against cotinine. The assay is intended as an aid in the detection of cotinine after use or exposure to tobacco products. The assay is designed for prescription use with a number of automated clinical chemistry analyzers.

The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) or (2) permitting laboratories to establish quality control procedures.

The assay provides only a preliminary analytical result. A more specific alternative chemical method (e.g., gas or liquid chromatography and mass spectrometry) must be used in order to obtain a confirmed analytical result. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.

Comparison to Predicate Device

The LZI Cotinine II Enzyme Immunoassay is substantially equivalent to the NicCheckI Test Strips manufactured by Dynagen, Inc. which was cleared by the FDA under the premarket notification k963733 for its stated intended use.

The following table compares the LZI Cotinine II Enzyme Immunoassay with the predicate device.

Device Characteristics	Subject Device (k192299) LZI Cotinine II Enzyme Immunoassay	Predicate Device (k963733) NicCheckI Test Strips
Intended Use	The LZI Cotinine II Enzyme Immunoassay is intended for the qualitative and semi-quantitative determination of cotinine in human urine at the cutoff value of 200 ng/mL when calibrated against cotinine. The assay is intended as an aid in the detection of cotinine after use or exposure to tobacco products. The assay is designed for prescription use with a number of automated clinical chemistry analyzers. The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of the specimen for confirmation by a confirmatory method such as gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) or (2) permitting laboratories to establish quality control procedures. <i>This assay provides a rapid screening procedure for determining the presence of cotinine in urine. The assay provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is positive.</i>	NicCheck I Test Strips may be used to detect nicotine and/or its metabolites in urine as an aid in indicating the smoking status of the individual and in planning appropriate treatment. The test will also aid in the identification of a smoker as a low or high nicotine consumer. The NicCheck I test is for professional use only. Individuals, such as physicians, nurses, pharmacists, medical technologists, and paramedical personnel may perform the test.
Analyte	cotinine	cotinine
Cutoff	200 ng/mL	200 ng/mL
Matrix	urine	urine
Calibrators Level	0, 100, 200, 400, and 1000 ng/mL	N/A
Controls Level	150 ng/mL and 250 ng/mL	N/A
Storage	2-8°C until expiration date.	2-8°C until 2 years from date of manufacture. Test strips are susceptible to conditions of high humidity, the canister must be kept tightly closed after removal of the required number of strips.

Performance Characteristics Summary:

Beckman Coulter® AU480 Analyzer

Precision: 200 ng/mL Cutoff

The assay was tested in qualitative (ΔOD , mAU) and semi-quantitative (ng/mL) mode using a modified NCCLS-EP5 protocol. Cotinine sample concentrations were prepared by spiking a cotinine standard into a pool of negative human urine at concentrations $\pm 25\%$, $\pm 50\%$, $\pm 75\%$, and $\pm 100\%$ of cutoff concentration.

Results shown below were obtained by testing all samples in replicate of two, two runs a day (one in the morning and one in the afternoon) for 22 days on one AU480 automatic clinical analyzer for a total of 88 runs. Samples were evaluated against the assay's calibration curve in both qualitative and semi-quantitative modes. One single lot of reagents, calibrators, and controls were used and stored at 2-8°C when not in use.

Semi-Quantitative Precision Analysis Summary: Qualitative Results

Cotinine Concentration	Within Run (N=22)	Total Precision (N=88)
	Qualitative Response	Qualitative Response
0 ng/mL	-	-
50 ng/mL	-	-
100 ng/mL	-	-
150 ng/mL	-	-
200 ng/mL	-	-
250 ng/mL	+	+
300 ng/mL	+	+
350 ng/mL	+	+
400 ng/mL	+	+

Semi-Quantitative Positive/Negative Results:

200 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Cotinine Concentration	% of Cutoff	# of Determination	EIA Result	# of Determination	EIA Result
0 ng/mL	0.0 %	22	22 Negative	88	88 Negative
50 ng/mL	25.0 %	22	22 Negative	88	88 Negative
100 ng/mL	50.0 %	22	22 Negative	88	88 Negative
150 ng/mL	75.0 %	22	22 Negative	88	88 Negative
200 ng/mL	100.0 %	22	14 Neg/8 Pos	88	55 Neg/33 Pos
250 ng/mL	125.0 %	22	22 Positive	88	88 Positive
300 ng/mL	150.0 %	22	22 Positive	88	88 Positive
350 ng/mL	175.0 %	22	22 Positive	88	88 Positive
400 ng/mL	200.0 %	22	22 Positive	88	88 Positive

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Qualitative Positive/Negative Results:

200 ng/mL Cutoff Result:		Within Run (N=22)		Total Precision (N=88)	
Cotinine Concentration	% of Cutoff	# of Determination	EIA Result	# of Determination	EIA Result
0 ng/mL	0.0 %	22	22 Negative	88	88 Negative
50 ng/mL	25.0 %	22	22 Negative	88	88 Negative
100 ng/mL	50.0 %	22	22 Negative	88	88 Negative
150 ng/mL	75.0 %	22	22 Negative	88	88 Negative
200 ng/mL	100.0 %	22	10 Neg/12 Pos	88	51 Neg/37 Pos
250 ng/mL	125.0 %	22	22 Positive	88	88 Positive
300 ng/mL	150.0 %	22	22 Positive	88	88 Positive
350 ng/mL	175.0 %	22	22 Positive	88	88 Positive
400 ng/mL	200.0 %	22	22 Positive	88	88 Positive

Linearity:

To demonstrate linearity of the entire assay range, a drug free–urine pool spiked with cotinine at 1000 ng/mL was serially diluted. Each sample was run in 10 replicates and the average was used to determine percent recovery compared to the expected target value.

Observed values were obtained and acceptable if measurements were $\pm 15\%$ of the expected values. Recovery values (Expected Value divided by the Observed Value) were considered acceptable between 85 – 115%.

Samples from the linear range of the assay (100 ng/mL to 1000 ng/mL) were tested with recovery ranging from 97.9% to 110.8%.

Target Concentration (ng/mL)	Determined (ng/mL)	% Recovery
1000	978.9	97.9%
900	919.6	102.2%
800	851.7	106.5%
700	766.0	109.4%
600	664.8	110.8%
500	539.1	107.8%
400	395.0	98.8%
300	302.4	100.8%
200	199.9	100.0%
100	109.0	109.0%
20	33.5	167.5%
0	19.3	N/A

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Method Comparison - Clinical Samples:

A total of one-hundred and four (104) unaltered clinical samples were tested with the LZI Cotinine II Enzyme Immunoassay on the Beckman Coulter® AU480 automated clinical analyzer. Samples were evaluated against the assay's calibration curve in both qualitative and semi-quantitative modes. All samples were tested in singlet.

All samples were confirmed with LC/MS for cotinine concentrations. Samples were collected by *Lin-Zhi International, Inc.* (LZI).

Semi-Quantitative Accuracy Study:

Discrepant samples determined as compared to cotinine concentration from LC/MS.

Candidate Device Results	Negative	<50 % of Cutoff	Near Cutoff Negative (between -50 % of cutoff to the cutoff)	Near Cutoff Positive (between cutoff and +50 % of cutoff)	High Positive (>50 % above cutoff)	% Agreement
Positive	0	0	1*	11	16	96.4 %
Negative	20	32	23	1**	0	98.7 %

Sample #	LC/MS Methadone (ng/mL)	Pos/Neg Result	AU480 EIA Pos/Neg Result
57*	128.6	+	+
78**	204.2	+	-

* Discrepant between 50% below cutoff and cutoff concentration (100 – 199.9 ng/mL)

** Discrepant between cutoff and 50% above cutoff concentration (200 – 299.9 ng/mL)

Qualitative Accuracy Study:

Discrepant samples determined as compared to cotinine concentration from LC/MS.

Candidate Device Results	Negative	<50 % of Cutoff	Near Cutoff Negative (between -50 % of cutoff to the cutoff)	Near Cutoff Positive (between cutoff and +50 % of cutoff)	High Positive (>50 % above cutoff)	% Agreement
Positive	0	0	1*	11	16	96.4 %
Negative	20	32	23	1**	0	98.7 %

Sample #	LC/MS Methadone (ng/mL)	Pos/Neg Result	AU680 EIA Qualitative Result (mAU)	Pos/Neg Result	Qualitative Cutoff Rate (mAU)
57*	128.6	+	146.6	+	126.4
78**	204.2	+	93.8	-	126.4

* Discrepant between 50% below cutoff and cutoff concentration (100 – 199.9 ng/mL)

** Discrepant between cutoff and 50% above cutoff concentration (200 – 299.9 ng/mL)

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Cross-reactivity

The Cross-reactivity of various potentially interfering drugs were tested by spiking various concentrations of each substance into a pool of negative human urine and then evaluated against the assay's calibration curve in both qualitative and semi-quantitative modes. All samples were tested in replicates.

The table below lists the concentration of each test compound that gave a response approximately equivalent to that of the cutoff calibrator (as positive) or the maximal concentration of the compound tested that gave a response below the response of the cutoff calibrator (as negative). Compounds tested at high concentration with results below the cutoff value were listed as Not Detected (ND).

Cotinine:

Compound	Target Concentration (ng/mL)	% Cross-reactivity
(-)-Cotinine	200	100.00%

Cotinine Metabolites:

Compound	Target Concentration (ng/mL)	% Cross-reactivity
(+)-Anabasine	250,000	0.08%
S(-)-Nicotine	25,000	0.80%
Nicotinic Acid (Niacin)	100,000	0.20%
(-) Norcotinine	1000	20.00%
(+) Norcotinine	100,000	0.20%
(R, S)-Norcotinine	850	23.53%
(±)-Nornicotine	250,000	0.08%
trans-3'-hydroxycotinine	10,000	2.00%

Structurally unrelated compounds were additionally spiked into pooled negative human urine to desired concentrations (as described above). These solutions were then split into three portions; one without cotinine, and the remaining two that were further spiked with cotinine standards to a final cotinine concentration of 150 ng/mL or 250 ng/mL (as negative or positive controls, $\pm 25\%$ cutoff concentration, respectively). Samples were then evaluated against the assay's calibration curve in both qualitative and semi-quantitative modes. All samples were tested in replicates.

Structurally Unrelated Pharmacological Compounds:

Cross-reactant	Spiked [] (ng/mL)	Spiked Cotinine Concentration		
		0 ng/mL	150 ng/mL Control	250 ng/mL Control
Acetaminophen	100,000	ND	Neg	Pos
6-Acetylmorphine	100,000	ND	Neg	Pos
Acetylsalicylic Acid	100,000	ND	Neg	Pos

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Structurally Unrelated Pharmacological Compounds, continued:

Cross-reactant	Spiked [] (ng/mL)	Spiked Cotine Concentration		
		0 ng/mL	150 ng/mL Control	250 ng/mL Control
Amitriptyline	100,000	ND	Neg	Pos
Amlodipine Besylate	100,000	ND	Neg	Pos
Amoxicillin	100,000	ND	Neg	Pos
Azelastine	100,000	ND	Neg	Pos
<i>d</i> -Amphetamine	100,000	ND	Neg	Pos
Atorvastatin	20,000	ND	Neg	Pos
Benzoyllecgonine	100,000	ND	Neg	Pos
Brompheniramine	100,000	ND	Neg	Pos
Buprenorphine	15,000	ND	Neg	Pos
Bupropion	100,000	ND	Neg	Pos
Caffeine	100,000	ND	Neg	Pos
Carbamazepine	100,000	ND	Neg	Pos
Carbinoaxmine	100,000	ND	Neg	Pos
Cetirizine	100,000	ND	Neg	Pos
Chlorpheniramine	100,000	ND	Neg	Pos
Chlorpromazine	100,000	ND	Neg	Pos
Clemastine	100,000	ND	Neg	Pos
Clomipramine	100,000	ND	Neg	Pos
Codeine	100,000	ND	Neg	Pos
Cyproheptadine	100,000	ND	Neg	Pos
Desipramine	100,000	ND	Neg	Pos
Desloratadine	100,000	ND	Neg	Pos
Dexchlorpheniramine	100,000	ND	Neg	Pos
Diphenhydramine	100,000	ND	Neg	Pos
Doxylamine	100,000	ND	Neg	Pos
Duloxetine	100,000	ND	Neg	Pos
Emedastine	100,000	ND	Neg	Pos
Fentanyl (citrate)	10,000	ND	Neg	Pos
Fexofenadine	100,000	ND	Neg	Pos
Fluoxetine	100,000	ND	Neg	Pos
Fluphenazine	100,000	ND	Neg	Pos
Gabapentin	100,000	ND	Neg	Pos
Hydrocodone	100,000	ND	Neg	Pos
Hydromorphone	100,000	ND	Neg	Pos
Hydroxyzine	100,000	ND	Neg	Pos
Ibuprofen	100,000	ND	Neg	Pos
Imipramine	100,000	ND	Neg	Pos
Lisinopril	100,000	ND	Neg	Pos
Levocabastine	100,000	ND	Neg	Pos
Losartan	10,000	ND	Neg	Pos

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Structurally Unrelated Pharmacological Compounds, continued:

Cross-reactant	Spiked [] (ng/mL)	Spiked Cotinine Concentration		
		0 ng/mL	150 ng/mL Control	250 ng/mL Control
Loratidine	100,000	ND	Neg	Pos
MDA (3,4-methylenedioxyamphetamine)	100,000	ND	Neg	Pos
MDEA	100,000	ND	Neg	Pos
MDMA (3,4-methylenedioxymethamphetamine)	100,000	ND	Neg	Pos
Meperidine	100,000	ND	Neg	Pos
Metformin	100,000	ND	Neg	Pos
Methapyrilene	100,000	ND	Neg	Pos
Metoprolol	100,000	ND	Neg	Pos
Methadone	100,000	ND	Neg	Pos
<i>d</i> -Methamphetamine	100,000	ND	Neg	Pos
Morphine	100,000	ND	Neg	Pos
Nortriptyline	100,000	ND	Neg	Pos
Omeprazole	100,000	ND	Neg	Pos
Oxazepam	100,000	ND	Neg	Pos
Oxycodone	100,000	ND	Neg	Pos
Oxymorphone	100,000	ND	Neg	Pos
Phenobarbital	100,000	ND	Neg	Pos
Promethazine	100,000	ND	Neg	Pos
(1S,2S)-(+)-Pseudoephedrine	100,000	ND	Neg	Pos
Quetiapine	100,000	ND	Neg	Pos
Ranitidine	100,000	ND	Neg	Pos
Salbutamol (Albuterol)	100,000	ND	Neg	Pos
Sertraline	100,000	ND	Neg	Pos
Terfenadine	100,000	ND	Neg	Pos
THC-COOH (11-Nor-Delta-9-THC-9-carboxylic acid)	1,000	ND	Neg	Pos
<i>l</i> -Thyroxine	10,000	ND	Neg	Pos
Tramadol	100,000	ND	Neg	Pos
Tripolidine	100,000	ND	Neg	Pos
Zolpidem	10,000	ND	Neg	Pos

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Endogenous compounds were spiked into pooled negative human urine to desired concentrations. These solutions were then split into three portions; one without cotinine, and the remaining two that were further spiked with cotinine standards to a final cotinine concentration of 150 ng/mL or 250 ng/mL (as negative or positive controls, $\pm 25\%$ cutoff concentration, respectively). Samples were then evaluated against the assay's calibration curve in both qualitative and semi-quantitative modes. All samples were tested in replicates.

Endogenous Substance	Concentration Tested (ng/mL)	Spiked Cotinine Concentration		
		0 ng/mL	150 ng/mL Control	250 ng/mL Control
Acetone	1000	Neg	Neg	Pos
Ascorbic Acid	1500	Neg	Neg	Pos
Bilirubin	2	Neg	Neg	Pos
Boric Acid	1000	Neg	Neg	Neg
Calcium Chloride (CaCl ₂)	300	Neg	Neg	Pos
Citric Acid (pH 3)	800	Neg	Neg	Neg
Creatinine	500	Neg	Neg	Pos
Ethanol	1000	Neg	Neg	Pos
Galactose	10	Neg	Neg	Pos
γ -Globulin	500	Neg	Neg	Pos
Glucose	3000	Neg	Neg	Pos
Hemoglobin	300	Neg	Neg	Pos
β -hydroxybutyric Acid	100	Neg	Neg	Pos
HAS	500	Neg	Neg	Pos
Oxalic Acid	100	Neg	Neg	Pos
Potassium Chloride	6000	Neg	Neg	Pos
Riboflavin	0.3	Neg	Neg	Pos
Urea	6000	Neg	Neg	Pos
Uric Acid	10	Neg	Neg	Pos
Sodium Azide	1000	Neg	Neg	Pos
Sodium Chloride	6000	Neg	Neg	Pos
Sodium Fluoride	1000	Neg	Neg	Pos
Sodium Phosphate	300	Neg	Neg	Pos

The following endogenous compounds which showed interference at $\pm 25\%$ of cutoff concentrations were then spiked into negative urine and at $\pm 50\%$ of cutoff concentrations (100 ng/mL and 300 ng/mL) for the assay.

Interference was observed with Boric Acid at 1 % w/v and Citric Acid. No other significant undesired cross-reactants or endogenous substance interference was observed.

Endogenous Substance	Concentration Tested (ng/mL)	Spiked Cotinine Concentration		
		0 ng/mL	100 ng/mL Control	300 ng/mL Control
Boric Acid	1000	Neg	Neg	Neg
Citric Acid (pH 3)	800	Neg	Neg	Neg

Performance Characteristics Summary, continued:

Beckman Coulter® AU480 Analyzer

Specific Gravity:

Samples ranging in specific gravity from 1.005 to 1.028 were split into three portions each and either left un-spiked or further spiked to a final methadone concentration of either 150 ng/mL or 250 ng/mL (as negative or positive controls, $\pm 25\%$ cutoff concentration, respectively). These samples were then evaluated in qualitative mode. No interference was observed.

pH Interference Study:

Negative urine and urine spiked with cotinine to the final cotinine concentration of either 150 ng/mL or 250 ng/mL (as negative or positive controls, $\pm 25\%$ cutoff concentration, respectively) were adjusted to the following pH levels and tested by the assay. The pH adjusted solutions were evaluated against the cutoff calibrator.

No major interference between pH 3 to pH 11. Results are summarized in the following table:

pH	Spiked Cotinine Concentration		
	0 ng/mL	150 ng/mL Control	250 ng/mL Control
pH 3	Neg	Neg	Pos
pH 4	Neg	Neg	Pos
pH 5	Neg	Neg	Pos
pH 6	Neg	Neg	Pos
pH 7	Neg	Neg	Pos
pH 8	Neg	Neg	Pos
pH 9	Neg	Neg	Pos
pH 10	Neg	Neg	Pos
pH 11	Neg	Neg	Pos

Summary:

The information provided in this pre-market notification demonstrates that the LZI Cotinine II Enzyme Immunoassay is substantially equivalent to the legally marketed predicate device for its general intended use. Substantial equivalence was demonstrated through comparison of intended use and physical properties to the commercially available predicate device as confirmed by chromatography/mass spectrometry (GC/MS or LC/MS), an independent analytical method. The information supplied in this pre-market notification provides reasonable assurance that the LZI Cotinine II Enzyme Immunoassay is safe and effective for its stated intended use.