LZI Ketamine Enzyme Immunoassay

For Beckman Coulter, Inc.

REF C68802 (100/37.5 mL R_1/R_2 Kit)

2-8°C

IVD For In Vitro Diagnostic Use Only

Lin-Zhi International, Inc.

For Sales Outside USA (OUS) Only

Intended Use

The LZI Ketamine Enzyme Immunoassay for Beckman Coulter, Inc. is intended for the qualitative and semi-quantitative determination of norketamine in human urine at the cutoff value of 50 ng/mL when calibrated against norketamine. The assay is designed for prescription use with a number of automated clinical chemistry analyzers. The semi-quantitative mode is for purposes of enabling laboratories to determine an appropriate dilution of the specimen for verification by a confirmatory method such as GC/MS or LC/MS, or permitting laboratories to establish quality control procedures.

The assay provides only a preliminary analytical result. A more specific alternative chemical confirmatory method (e.g., gas or liquid chromatography and mass spectrometry) must be used to obtain a confirmed analytical result (1, 2). Clinical consideration and professional judgment should be exercised with any drug of abuse test result, particularly when the preliminary test result is a preliminary positive.

Summary and Explanation of Test

Ketamine (2-[2-chlorophenyl]-2-[methylamino]-cyclohexanone) is a pharmaceutical derived from phencyclidine (PCP) and cyclohexamine. Mechanistically, it acts as a non-competitive N-methyl-D-aspartate (NMDA)-receptor antagonist. The NMDA-receptor is involved in sensory input at the spinal, thalamic, limbic and cortical levels (3, 4).

Ketamine has been shown to have a number of beneficial pharmacological properties. It is primarily considered an anaesthetic with a good safety profile. (5) Its major drawback, limiting its clinical use, is the occurrence of emergence reactions or dissociative effects (e.g., hallucinations, vivid dreams, floating sensations and delirium.) (3, 6). Recently, extensive research has been carried out on the antidepressant properties of ketamine (7-9).

The frequent use of ketamine can lead to addiction and dependence (10). Ketamine posseses narcotic effects similar to phencyclidine (PCP) and hallucinogenic effects similar to lysergic acid diethylamide (LSD) (11, 12). The recreational use of ketamine as a rave, party, and nightclub drug has increased over time, thus increasing public concerns about the potential hazards of this drug (13-15).

Ketamine undergoes rapid N-demethylation by liver microsomal cytochrome P450 enzymes CYP 3A4, CYP 2B6, and CYP 2C9 to form its primary metabolite, norketamine, which is pharmacologically active, and an inactive metabolite, 6-hydroxynorketamine (16, 17). A small percentage of unchanged ketamine (2.3 %), norketamine (1.6 %), and dehydronorketamine (16.2 %) are eliminated in urine, whereas 80 % is present as the glucuronide conjugates of hydroxylated metabolites of ketamine (18-21). While dehydronorketamine is present at higher levels and for a longer period of time than ketamine and norketamine in urine, dehydronorketamine has a lower stability, potentially limiting its utility in the detection of ketamine abuse (22).

Assay Principle

The LZI Ketamine Enzyme Immunoassay is a homogeneous enzyme immunoassay ready-to-use liquid reagent. 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 (23). The drug-labeled G6PDH conjugate is traceable to a commercially available ketamine standard and referred to as ketamine-labeled G6PDH conjugate. Enzyme activity decreases upon binding to the antibody, and the norketamine concentration in the sample is measured in terms of enzyme activity. In the absence of ketamine and/or norketamine in the sample, ketamine-labeled G6PDH conjugate is bound to antibody, and the enzyme activity is inhibited. On the other hand, when ketamine and/or norketamine is present in the sample, antibody would bind to free ketamine and/or norketamine; the unbound ketamine-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.

Reagents Provided

Antibody/Substrate Reagent (R_1): Contains a mouse monoclonal anti-ketamine antibody, glucose-6-phosphate (G6P), nicotinamide adenine dinucleotide (NAD), stabilizers, and sodium azide (0.09 %) as a preservative.

Enzyme-drug Conjugate Reagent (R_2): Contains glucose-6-phosphate dehydrogenase (G6PDH) labeled with ketamine in buffer with sodium azide (0.09 %) as a preservative.

Calibrators and Controls*

**Calibrators and Controls are sold separately or as a semi-quantitative set and contain negative human urine with sodium azide as a preservative.*

Qualitative Calibration	REF
LZI Norketamine Qualitative Calibrator NKET Cutoff Calibrator (50 ng/mL)	C68804

Semi-Quantitative Calibration	REF
LZI Universal Negative Calibrator	C68807
LZI Norketamine Semi-Quantitative Calibrator Set NKET Low Calibrator (25 ng/mL) NKET Cutoff Calibrator (50 ng/mL) NKET Intermediate #1 Calibrator (100 ng/mL) NKET Intermediate #2 Calibrator (250 ng/mL) NKET High Calibrator (500 ng/mL)	C68803

Controls	REF
LZI Norketamine Level 1 Control NKET Level 1Control (37.5 ng/mL)	C68805
LZI Norketamine Level 2 Control NKET Level 2 Control (62.5 ng/mL)	C68806

Others

Wedge	REF
OSR Bottle kit, 20 x 60 mL	63093
OSR Bottle kit, 20 x 30 mL	63094

Precautions and Warning

- *This test is for in vitro diagnostic use only. Harmful if swallowed.*
- *Reagent contains sodium azide as a preservative, which may form explosive compounds in metal drain lines. When disposing such reagents or wastes, always flush with a large volume of water to prevent azide build-up. See National Institute for Occupational Safety and Health Bulletin: Explosive Azide Hazards (24).*
- *Do not use the reagents beyond their expiration dates.*

Reagent Preparation and Storage

The reagents are ready to use. No reagent preparation is required. All assay components should be refrigerated at 2-8ºC when not in use.

Specimen Collection and Handling

Use fresh urine specimens for the test. If the sample cannot be analyzed immediately, it may be refrigerated at 2-8ºC for seven days. For longer storage, keep sample frozen at -20ºC and then thaw before use (22). Adulteration may cause erroneous results. If sample adulteration is suspected, obtain a new sample and both samples should be forwarded to a laboratory for testing.

Handle all urine specimens as if they are potentially infectious.

Instrument

Clinical chemistry analyzers capable of maintaining a constant temperature, pipetting sample, mixing reagents, measuring enzyme rates at 340 nm and timing the reaction accurately can be used to perform this homogeneous immunoassay.

Performance characteristics presented in this package insert have been validated on the Beckman Coulter AU480 automated clinical analyzer.

Assay Procedure

Analyzers with the specifications indicated above are suitable for performing this homogeneous enzyme immunoassay. Refer to the specific parameters used for each analyzer before performing the assay.

For qualitative analysis, use the 50 ng/mL as the cutoff calibrator. The cutoff is normalized to 100. Positive samples are ≥ 100 and are flagged with a (P).

For semi-quantitative analysis, use all six calibrators including the universal negative calibrator. Recalibration should be performed after reagent bottle change or a change in calibrators or reagent lot. Two levels of controls are available for monitoring of each cutoff level. Use the 37.5 ng/mL and 62.5 ng/mL controls for the 50 ng/mL cutoff level.

Calibration and Quality Control

Good laboratory practices recommend the use of at least two levels of control specimens (one positive and one negative control near the cutoff) to ensure proper assay performance. Controls should be run with each new calibration and after specific maintenance or troubleshooting procedures as detailed in the instrument system manual. Each laboratory should establish its own control frequency. If any trends or sudden change in control value are observed, review all operating parameters, or contact your local Beckman Coulter Representative for further assistance. Laboratories should comply with all federal, state, and local laws, as well as all guidelines and regulations.

Results

Note: A positive test result does not necessarily mean a person took a specific drug and a negative test result does not necessarily mean a person did not take a specific drug. There are a number of factors that influence the reliability of drug tests.

Qualitative: The cutoff calibrator, which contains 50 ng/mL of norketamine, is used as a reference for distinguishing positive from negative samples. A sample with a change in absorbance (ΔmAU) equal to or greater than that obtained with the cutoff calibrator is considered positive. A sample with a change in absorbance (ΔmAU) lower than that obtained with the cutoff calibrator is considered negative.

Semi-Quantitative: The semi-quantitative mode is for purposes of (1) enabling laboratories to determine an appropriate dilution of the specimen for verification by a confirmatory method such as GC/MS, LC/MS or (2) permitting laboratories to establish quality control procedures. When an approximation of concentration is required, a calibration curve can be established with six calibrators. The concentration of norketamine in the sample may then be estimated from the calibration curve.

Limitations

1. *A preliminary positive result from this assay indicates only the presence of norketamine. The test is not intended for quantifying this single analyte in samples.*
2. *A preliminary positive result does not necessarily indicate drug abuse.*
3. *A negative result does not necessarily mean a person did not take illegal drugs.*
4. *Care should be taken when reporting results, as numerous factors (e.g., fluid intake, endogenous or exogenous interferants) may influence the urine test result.*
5. *Preliminary positive results must be confirmed by other affirmative, analytical methods (e.g., chromatography), preferably GC/MS or LC/MS.*
6. *The test is designed for use with human urine only.*
7. *This test should not be used for therapeutic drug monitoring.*

Typical Performance Characteristics

The results shown below were performed with a single Beckman Coulter AU480 automated chemistry analyzer.

Precision:

Semi-quantitative analysis: The following concentrations were determined with reference curves from five calibrators. Typical results (ng/mL) are as follows:

50 ng/mL Cutoff		Within Run (N = 22)		Run-to-Run (N = 88)	
Norketamine Concentration	**% of Cutoff**	**# Samples**	**EIA Result**	**# Samples**	**EIA Result**
0 ng/mL	0 %	22	22 Neg	88	88 Neg
12.5 ng/mL	25 %	22	22 Neg	88	88 Neg
25 ng/mL	50 %	22	22 Neg	88	88 Neg
37.5 ng/mL	75 %	22	22 Neg	88	88 Neg
50 ng/mL	100 %	22	3 Neg/ 19 Pos	88	15 Neg/ 73 Pos
62.5 ng/mL	125 %	22	22 Pos	88	88 Pos
75 ng/mL	150 %	22	22 Pos	88	88 Pos
87.5 ng/mL	175 %	22	22 Pos	88	88 Pos
100 ng/mL	200 %	22	22 Pos	88	88 Pos

Qualitative analysis: The following concentrations were evaluated. Typical qualitative results (measured by ΔOD, mAU) are as follows:

50 ng/mL Cutoff		Within Run (N = 22)		Run-to-Run (N = 88)	
Norketamine Concentration	**% of Cutoff**	**# Samples**	**EIA Result**	**# Samples**	**EIA Result**
0 ng/mL	0 %	22	22 Neg	88	88 Neg
12.5 ng/mL	25 %	22	22 Neg	88	88 Neg
25 ng/mL	50 %	22	22 Neg	88	88 Neg
37.5 ng/mL	75 %	22	22 Neg	88	88 Neg
50 ng/mL	100 %	22	1 Neg/ 21 Pos	88	8 Neg/ 80 Pos
62.5 ng/mL	125 %	22	22 Pos	88	88 Pos
75 ng/mL	150 %	22	22 Pos	88	88 Pos
87.5 ng/mL	175 %	22	22 Pos	88	88 Pos
100 ng/mL	200 %	22	22 Pos	88	88 Pos

Accuracy: One hundred eleven (111) unaltered clinical urine specimens and pooled urine samples spiked with norketamine were tested with the LZI Ketamine Enzyme Immunoassay and confirmed with LC/MS. Specimens with a combined norketamine and ketamine concentration greater than or equal to 50 ng/mL by LC/MS are defined as positive, and specimens with a combined norketamine and ketamine concentration below 50 ng/mL by LC/MS are defined as negative in the table below. Near cutoff samples are defined as ± 50 % of the cutoff value. The correlation results are summarized as follows:

Semi-Quantitative Accuracy Study:

50 ng/mL Cutoff	Neg	< 50 % of the cutoff	Near Cutoff Neg	Near Cutoff Pos	High Pos	% Agree-ment
Positive	0	2*	2**	6	62	100.0 %
Negative	20	4	15	0	0	90.7 %

The following table summarizes the results for the semi-quantitative discordant samples:

Sample #	NKET LC/MS (ng/mL)	KET LC/MS (ng/mL)	Total NKET + KET LC/MS (ng/mL)	Pos/ Neg Result	AU480 EIA Semi-Quantitative Result (ng/mL)	Pos/ Neg Result
24*	17.0	0.0	17.0	-	227.9	+
26*	19.6	0.0	19.6	-	228.2	+
31**	14.3	12.8	27.1	-	133.2	+
34**	0.0	32.3	32.3	-	58.3	+

Qualitative Accuracy Study:

50 ng/mL Cutoff	Neg	< 50 % of the cutoff	Near Cutoff Neg	Near Cutoff Pos	High Pos	% Agree-ment
Positive	0	2*	2**	6	62	100.0 %
Negative	20	4	15	0	0	90.7 %

The following table summarizes the results for the qualitative discordant samples:

Sample #	NKET LC/MS (ng/mL)	KET LC/MS (ng/mL)	Total NKET + KET LC/MS (ng/mL)	Pos/ Neg Result	AU480 EIA Qualitative Result (mAU)	Pos/ Neg Result
24*	17.0	0.0	17.0	-	308.2	+
26*	19.6	0.0	19.6	-	312.1	+
31**	14.3	12.8	27.1	-	190.8	+
34**	0.0	32.3	32.3	-	90.9	+

Calibration Cutoff Average = 69.3 mAU

** Discordant between negative and <50 % cutoff concentration (0.1 – 24.9 ng/mL)*

*** Discordant between 50 % of cutoff and cutoff concentration (25 – 49.9 ng/mL)*

Analytical Recovery: To demonstrate recovery for purposes of sample dilution and quality control of the entire assay range, a drug free–urine pool spiked with norketamine at 500 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.

Target Concentration (ng/mL)	Determined Concentration Range (ng/mL)	Determined Concentration Average (ng/mL)	Average % Recovery
500	494.5 – 523.6	506.9	101.4 %
450	470.1 – 492.2	480.8	106.8 %
400	436.7 – 469.2	449.7	112.4 %
350	380.8 – 399.0	390.8	111.7 %
300	318.1 – 345.4	330.3	110.1 %
250	240.5 – 256.8	247.4	99.0 %
200	206.9 – 212.7	210.1	105.0 %
150	157.0 – 162.0	159.9	106.6 %
100	96.4 – 102.0	98.3	98.3 %
50	47.3 – 54.3	48.9	97.8 %
7.5	6.4 – 9.1	8.2	108.9 %
0	0.4 – 3.9	2.2	N/A

Specificity: Various potentially interfering substances were tested for cross-reactivity with the assay. Test compounds were spiked into a drug free–urine pool to various concentrations and evaluated with the assay's calibration curve in both qualitative and semi-quantitative modes.

The following table 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 (100,000 ng/mL) with results below the cutoff value were listed as Not Detected (ND). Compounds tested below the high concentration (100,000 ng/mL) that gave a result below the cutoff value were given a "< %" value.

Ketamine and Metabolites:

Cross-reactant	Concentration (ng/mL)	% Cross-reactivity
Norketamine	50	100.00 %
Ketamine	25	200.00 %
Dehydronorketamine	2,000	2.50 %
Hydronorketamine	100,000	ND

Structurally Related Compounds:

Cross-reactant	Concentration (ng/mL)	% Cross-reactivity
Deschloroketamine	1,600	3.13 %
Methoxetamine	100,000	0.05 %
Phencyclidine	100,000	0.05 %

Structurally Unrelated Compounds:

Cross-reactant	Spiked [ ] (ng/mL)	Spiked Norketamine Concentration		
		0 ng/mL	37.5 ng/mL Control	62.5 ng/mL Control
6-Acetylmorphine	100,000	ND	Neg	Pos
Acetaminophen	100,000	ND	Neg	Pos
Acetylsalicylic Acid	100,000	ND	Neg	Pos
Amitriptyline	50,000	<0.10 %	Neg	Pos
Amlodipine Besylate	100,000	ND	Neg	Pos
Amoxicillin	100,000	ND	Neg	Pos
d-Amphetamine	100,000	ND	Neg	Pos
Atorvastatin	100,000	ND	Neg	Pos
Benzoylecgonine	100,000	ND	Neg	Pos
Buprenorphine	50,000	<0.10 %	Neg	Pos
Bupropion	100,000	ND	Neg	Pos
Caffeine	100,000	ND	Neg	Pos
Carbamazepine	10,000	<0.50 %	Neg	Pos
Carbamazepine-10,11-epoxide	10,000	<0.50 %	Neg	Pos
Cetirizine	100,000	ND	Neg	Pos
Chlorpheniramine	100,000	ND	Neg	Pos
Chlorpromazine	10,000	<0.50 %	Neg	Pos
Clomipramine	100,000	ND	Neg	Pos
Codeine	100,000	ND	Neg	Pos
Desipramine	100,000	ND	Pos	Pos
(±)-10,11-Dihydro-10-Hydroxycarbamazepine	10,000	<0.50 %	Neg	Pos
Diphenhydramine	100,000	ND	Neg	Pos
Duloxetine	100,000	ND	Neg	Pos
Fentanyl (citrate)	10,000	<0.50 %	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
Ibuprofen	100,000	ND	Neg	Pos
Imipramine	60,000	<0.08 %	Pos	Pos

Structurally Unrelated Compounds, continued:

Cross-reactant	Spiked [ ] (ng/mL)	Spiked Norketamine Concentration		
		0 ng/mL	37.5 ng/mL Control	62.5 ng/mL Control
Lisinopril	100,000	ND	Neg	Pos
Losartan	100,000	ND	Neg	Pos
Loratadine	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	Pos	Pos
Metformin	100,000	ND	Neg	Pos
Metoprolol	100,000	ND	Neg	Pos
Methadone	100,000	ND	Neg	Pos
d-Methamphetamine	100,000	ND	Neg	Pos
Morphine	100,000	ND	Neg	Pos
Nalmefene	100,000	ND	Neg	Pos
Nicotine	100,000	ND	Neg	Pos
Norfentanyl	10,000	<0.50 %	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	15,000	<0.33 %	Pos	Pos
(1S,2S)-(+)Pseudoephedrine	100,000	ND	Neg	Pos
Quetiapine	50,000	<0.10 %	Neg	Pos
Ranitidine	100,000	ND	Neg	Pos
Salbutamol (Albuterol)	100,000	ND	Neg	Pos
Sertraline	100,000	ND	Neg	Pos
THC-COOH (11-Nor-Δ-9-THC-9-carboxylic acid)	100,000	ND	Neg	Pos
l-Thyroxine	100,000	ND	Neg	Pos
Tramadol	100,000	ND	Neg	Pos
Zolpidem	10,000	<0.50 %	Neg	Pos

It is possible that other substances and/or factors not listed above may interfere with the test and cause false positive results.

The following compounds which showed interference at ±25 % of cutoff concentrations were then spiked into negative urine and at ±50 % of cutoff concentrations (25 ng/mL and 75 ng/mL) for the assay. Results are summarized in the following table:

Cross-reactant	Spiked [ ] (ng/mL)	Spiked Norketamine Concentration		
		0 ng/mL	25 ng/mL	75 ng/mL
Desipramine	100,000	ND	Neg	Pos
Imipramine	60,000	<0.08 %	Neg	Pos
Meperidine	100,000	ND	Neg	Pos
Quetiapine	50,000	<0.10 %	Neg	Pos
Promethazine	15,000	<0.33 %	Neg	Pos
Carbamazepine	10,000	<0.50 %	Neg	Pos

Endogenous and Preservatives Compound Interference Study:

Various potentially interfering endogenous and preservative substances were tested for interference with the assay. Test compounds were split into three portions each and either left un-spiked or spiked to a norketamine concentration of either 37.5 or 62.5 ng/mL (the negative and positive control concentrations, respectively). These samples were then evaluated in semi-quantitative and qualitative modes. Only the preservative Boric Acid (1 % w/v) was found to cause interference with the assay.

Endogenous or Preservative Substance	Spiked [ ] (mg/dL)	Spiked Norketamine Concentration		
		0 ng/mL	37.5 ng/mL Control	62.5 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 (CaCl2)	300	Neg	Neg	Pos
Citric Acid (pH 3)	800	Neg	Neg	Pos
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
Human Serum Albumin	500	Neg	Neg	Pos
Oxalic Acid	100	Neg	Neg	Pos
Potassium Chloride	3000	Neg	Neg	Pos
Riboflavin	7.5	Neg	Neg	Pos
Sodium Azide	1000	Neg	Neg	Pos

Endogenous and Preservatives Compound Interference Study, continued:

Endogenous or Preservative Substance	Spiked [ ] (mg/dL)	Spiked Norketamine Concentration		
		0 ng/mL	37.5 ng/mL Control	62.5 ng/mL Control
Sodium Chloride	3000	Neg	Neg	Pos
Sodium Fluoride	1000	Neg	Neg	Pos
Sodium Phosphate	300	Neg	Neg	Pos
Urea	6000	Neg	Neg	Pos
Uric Acid	10	Neg	Neg	Pos

The following compound which showed interference at ±25 % of cutoff concentrations were then spiked into negative urine and at ±50 % of cutoff concentrations (25 ng/mL and 75 ng/mL) for the assay. Interference was still observed with Boric Acid. Results are summarized in the following table:

Endogenous or Preservative Substance	Spiked [ ] (mg/dL)	Spiked Norketamine Concentration		
		0 ng/mL	25 ng/mL	75 ng/mL
Boric Acid	1000	Neg	Neg	Neg

pH Interference Study: pH 3 to pH 11 was tested for interference with the assay. Each pH level was split into three portions each and either left un-spiked or spiked to a norketamine concentration of either 37.5 ng/mL or 62.5 ng/mL (the negative and positive control concentrations, respectively). These samples were then evaluated in semi-quantitative and qualitative modes. No pH interference was observed.

pH	Spiked Norketamine Concentration		
	0 ng/mL	37.5 ng/mL Control	62.5 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

Specific Gravity: Samples ranging in specific gravity from 1.000 to 1.025 were split into three portions each and either left un-spiked or spiked to a norketamine concentration of either 37.5 or 62.5 ng/mL (the negative and positive control concentrations, respectively). These samples were then evaluated in semi-quantitative and qualitative modes. No interference was observed.

Specific Gravity	Spiked Norketamine Concentration		
	0 ng/mL	37.5 ng/mL Control	62.5 ng/mL Control
1.0030	Neg	Neg	Pos
1.0050	Neg	Neg	Pos
1.0080	Neg	Neg	Pos
1.0100	Neg	Neg	Pos
1.0150	Neg	Neg	Pos
1.0180	Neg	Neg	Pos
1.0200	Neg	Neg	Pos
1.0220	Neg	Neg	Pos
1.0250	Neg	Neg	Pos

Symbols Used

EC REP	Authorized Representative	LOT	Lot Number
	Biological Risks		Manufacturer
CE	CE Mark	REAGENT 1	R_1, Antibody/ Substrate Reagent
	Consult Instructions for Use	REAGENT 2	R_2, Enzyme-Drug Conjugate Reagent
CONTENTS	Contents	REF	Reference Number
COO	Country of Origin	SDS	Safety Data Sheet
	Date of Manufacture		Temperature Limits
GTIN	Global Trade Item Number		Use-by Date
IVD	*In Vitro* Diagnostic medical device		

Additional Information

For more detailed information on AU 8 series and DxC AU Systems, refer to the appropriate system manual.

Since Beckman Coulter does not manufacture the reagent or perform quality control or other tests on individual lots, Beckman Coulter cannot be responsible for the quality of the data obtained which is caused by performance of the reagent, any variation between lots of reagent, or protocol changes by the manufacturer.

Shipping Damage

Please notify your Beckman Coulter Clinical Support Center if this product is received damaged.

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