

**ARK™ Ketamine II Assay**

This ARK Diagnostics, Inc. package insert for the ARK Ketamine II Assay must be read prior to use. Package insert instructions must be followed accordingly. The assay provides a simple and rapid analytical screening procedure for detecting ketamine in urine. Reliability of the assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Report any serious incident that has occurred in relation to the device to the manufacturer and the appropriate competent authority as applicable.












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**Key to Symbols Used**

	Batch code	 YYYY-MM-DD	Use by/Expiration date
	Catalog Number		Manufacturer
	Authorized Representative		CE Mark with notified body number
	In Vitro Diagnostic Medical Device		Temperature limitation
	Consult Instructions for Use		Reagent 1/ Reagent 2
	For Prescription Use Only		

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Reagent Kit  5083-0001-00

Reagent Kit  5083-0001-01

Reagent Kit  5083-0001-02

Reagent Kit  5083-0001-03

## 1 Name

### **ARK Ketamine II Assay**

## 2 Intended Use

The ARK Ketamine II Assay is an immunoassay intended for the qualitative detection and/or semi-quantitative estimation of Ketamine in human urine at cutoffs of 50 ng/mL and 100 ng/mL.

The semi-quantitative mode is for the purpose of (1) 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 (2) permitting laboratories to establish quality control procedures.

The ARK Ketamine II Assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used in order to obtain a confirmed positive 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 exercised with any drug test result, particularly when the preliminary test result is positive.

## 3 Summary and Explanation of Test

Ketamine (*dl* 2-(2-chlorophenyl)-2(methylamino) cyclohexanone hydrochloride) is a synthetic, non-barbiturate and rapid-acting general anesthetic that is indicated for use in both human and veterinary surgical procedures.<sup>1,2</sup>

Ketamine is a Schedule III substance under the United States Controlled Substances Act for its potential for abuse and risk of dependence. Ketamine is structurally and pharmacologically similar to phencyclidine (PCP), but is less potent, has a faster onset and shorter duration of action relative to PCP. Ketamine produces a variety of symptoms including, but not limited to anxiety, dysphoria, disorientation, insomnia, flashbacks, hallucinations, and psychotic episodes.<sup>1,3</sup>

Following administration in humans, ketamine is *N*-demethylated by liver microsomal cytochrome P450 enzymes into norketamine, which is the major active metabolite that may contribute to the analgesic effect following ketamine administration. Norketamine is then dehydrogenated to produce dehydronorketamine. Urinary concentrations of ketamine, norketamine and dehydronorketamine have been detected in human urine specimens following ketamine use. Approximately 2% is excreted in urine as unchanged ketamine, 2% as norketamine, 16% as dehydronorketamine and the rest as conjugates of hydroxylated metabolites.<sup>4-11</sup>

## 4 Principles of the Procedure

The ARK Ketamine II Assay is a homogeneous enzyme immunoassay. The assay is based on competition between a drug labeled with recombinant glucose-6-phosphate dehydrogenase (rG6PDH) and free drug from the urine sample, for a

fixed amount of specific antibody binding sites. In the absence of free drug from the sample, rabbit monoclonal anti-Ketamine antibody binds to the drug labeled with rG6PDH and causes a decrease in enzyme activity. In the presence of Ketamine from the specimen, enzyme activity increases and is directly related to the Ketamine concentration. Endogenous G6PDH does not interfere because the coenzyme NAD functions only with the bacterial enzyme used in the assay. The enzyme activity is determined spectrophotometrically at 340 nm by measuring the conversion of nicotinamide adenine dinucleotide (NAD) to NADH.

## 5 Reagents

REF	Product Description	Quantity/Volume
5083-0001-00	<b>ARK Ketamine II Assay</b> <b>Reagent [R1] – Antibody/Substrate</b> Rabbit monoclonal antibodies to Ketamine, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, sodium azide, and stabilizers	1 X 28 mL
	<b>Reagent [R2] – Enzyme</b> Ketamine derivative labeled with recombinant glucose-6-phosphate dehydrogenase (rG6PDH), bovine serum albumin, buffer, sodium azide and stabilizers	1 X 14 mL

REF	Product Description	Quantity/Volume
5083-0001-01	<b>ARK Ketamine II Assay</b> <b>Reagent [R1] – Antibody/Substrate</b> Rabbit monoclonal antibodies to Ketamine, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, sodium azide, and stabilizers	1 X 115 mL
	<b>Reagent [R2] – Enzyme</b> Ketamine derivative labeled with recombinant glucose-6-phosphate dehydrogenase (rG6PDH), bovine serum albumin, buffer, sodium azide and stabilizers	1 X 58 mL

REF	Product Description	Quantity/Volume
5083-0001-02	<b>ARK Ketamine II Assay</b> <b>Reagent [R1] – Antibody/Substrate</b> Rabbit monoclonal antibodies to Ketamine, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, sodium azide, and stabilizers	1 X 500 mL
	<b>Reagent [R2] – Enzyme</b> Ketamine derivative labeled with recombinant glucose-6-phosphate dehydrogenase (rG6PDH), bovine serum albumin, buffer, sodium azide and stabilizers	1 X 250 mL

REF	Product Description	Quantity/Volume
5083-0001-03	<b>ARK Ketamine II Assay</b> <b>Reagent [R1] – Antibody/Substrate</b> Rabbit monoclonal antibodies to Ketamine, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, sodium azide, and stabilizers	1 X 58 mL
	<b>Reagent [R2] – Enzyme</b> Ketamine derivative labeled with recombinant glucose-6-phosphate dehydrogenase (rG6PDH), bovine serum albumin, buffer, sodium azide and stabilizers	1 X 29 mL

## Reagent Handling and Storage

ARK Ketamine II Assay reagents are provided liquid, ready to use and may be used directly from the refrigerator. When not in use, reagents must be stored at 2–8°C (36–46°F), upright and with screw caps tightly closed. If stored as directed, reagents are stable until the expiration date printed on the label. Do not freeze reagents. Avoid prolonged exposure to temperatures above 32°C (90°F).

**Improper storage of reagents can affect assay performance.**

ARK Ketamine II products contain ≤0.09% sodium azide. As a precaution, affected plumbing including instrumentation should be flushed adequately with water to mitigate the potential accumulation of explosive metal azides. No special handling is required regarding other assay components.

## 6 Warnings and Precautions

- For *In Vitro* Diagnostic Use laboratory professional use only.
- For prescription use only. *Caution: US federal law restricts this device to sale by or on the order of a licensed practitioner.*
- Reagents **R1** and **R2** are provided as a matched set and should not be interchanged with reagents from different lot numbers.
- Do not use reagents after the expiration date.
- Reagents contain ≤0.09% sodium azide.

## 7 Specimen Collection and Preparation for Analysis

- Each laboratory is responsible for supplying a valid specimen for analysis according to their quality procedures.
- Human urine is required. Treat as potentially infectious material.
- Collect urine using standard sampling cups and procedures. Care should be taken to preserve the chemical and physical integrity of the urine sample from the time it is collected until the time it is assayed, including during transport. Fresh urine specimens are suggested.
- Cap the urine sample immediately after collection, store refrigerated at 2–8°C (36–46°F) and assay within 7 days after collection. If the assay cannot be performed within 7 days, store the urine sample frozen at -20°C for up to 2 months prior to analysis.<sup>12,13</sup>
- Do not induce foaming and avoid repeated freezing and thawing to preserve the integrity of the specimen from the time it is collected until the time it is assayed.
- The presence of bubbles or foam on the sample can lead to short sample delivery and erroneous results.
- Frozen specimens must be thawed and mixed thoroughly prior to analysis.
- Centrifuge specimens with high turbidity or visible particulate matter before testing.
- Each laboratory should consult available literature and internal data regarding specimen stability. The recommended pH range for urine specimens is 4.0 – 11.0.<sup>14</sup>

- Obtain another sample for testing if adulteration of the sample is suspected. Adulteration of urine specimens can affect the test result.

## 8 Procedure

### Materials Provided

ARK Ketamine II Assay – [REF](#) 5083-0001-00, 5083-0001-01, 5083-0001-02, or 5083-0001-03

### Materials Required – Provided Separately

ARK Ketamine II Calibrator (Set) – [REF](#) 5083-0002-00

ARK Ketamine II Calibrator A (Negative) – [REF](#) 5083-0002-01

ARK Ketamine II Calibrator B (50 ng/mL Cutoff) – [REF](#) 5083-0002-02

ARK Ketamine II Calibrator C (100 ng/mL Cutoff) – [REF](#) 5083-0002-03

ARK Ketamine II Control (25 ng/mL and 75 ng/mL) – [REF](#) 5083-0003-00

ARK Ketamine II Control (75 ng/mL and 125 ng/mL) – [REF](#) 5083-0003-01

### Instruments

Reagents R1 and R2 may need to be transferred to analyzer-specific reagent containers prior to use. Avoid cross-contamination of R1 and R2.

Many automated clinical chemistry analyzers with photometric rate determination at 340 nm are suitable. Consult the analyzer-specific application sheet for programming the ARK Ketamine II Assay, available from your distributor or ARK Customer Service. Application Protocol Sheets bearing the CE Mark have been verified by the manufacturer. It is the responsibility of the laboratory to perform all appropriate validation for use of the assay with other settings or analyzers. Refer to the instrument-specific operator's manual for daily maintenance.

### Assay Sequence

To run or calibrate the assay, see the instrument-specific operator's manual.

### Qualitative Results

Use the 50 ng/mL Calibrator B as a Cutoff Calibrator to distinguish negative and positive samples. Run the Low (25ng/mL) and High (75 ng/mL) Controls as Negative and Positive respectively. Report test results less than the rate (mA/min) value for the Cutoff Calibrator B (50 ng/mL) as Negative. Report results equal to or greater than the rate (mA/min) value for the Cutoff Calibrator as Positive.

Use the 100 ng/mL Calibrator C as a Cutoff Calibrator to distinguish negative and positive samples. Run the Low (75ng/mL) and High (125 ng/mL) Controls as Negative and Positive respectively. Report test results less than the rate (mA/min) value for the Cutoff Calibrator C (100 ng/mL) as Negative. Report results equal to or greater than the rate (mA/min) value for the Cutoff Calibrator as Positive.

### Semi-quantitative Results

Perform a 5-point calibration procedure; run calibrators in duplicate. Verify the calibration curve with the ARK Ketamine II Assay Low and High quality controls according to the established laboratory quality assurance plan. Specimens with

sample results above the highest ARK Ketamine II calibrator level (500 ng/mL) may be diluted in ARK Ketamine II Calibrator A (Negative urine) and retested.

#### **When to Re-Calibrate**

- Whenever a new lot number of reagents is used
- Whenever indicated by quality control results
- Whenever required by standard laboratory protocols

#### **Quality Control (QC) and Calibration**

Laboratories should establish QC procedures for the ARK Ketamine II Assay. All quality control requirements and testing should be performed in conformance with local, state and/or federal regulations or accreditation requirements.

Each laboratory should establish its own ranges for each new lot of controls. Control results should fall within established ranges as determined by laboratory procedures and guidelines. The ARK Ketamine II Control is intended for use in quality control of the ARK Ketamine II Assay.

In Qualitative Mode, the Low Control (25 ng/mL) should be Negative and the High Control (75 ng/mL) should be Positive relative to the 50 ng/mL Cutoff Calibrator. Also, the Low Control (75 ng/mL) should be Negative and the High Control (125 ng/mL) should be Positive relative to the 100 ng/mL Cutoff Calibrator.

## **9 Results and Expected Values**

A more specific confirmatory method, such as LC-MS/MS or GC-MS, is required in order to obtain a confirmed positive result.

#### **Qualitative Analysis – Negative Results**

A specimen that gives a rate (mA/min) value less than the ARK Ketamine II Calibrator B or C Cutoff rate (mA/min) values is interpreted as negative to the relative cutoff level; either the specimen does not contain Ketamine or Ketamine is present in a concentration below the relative cutoff levels of this assay.

#### **Qualitative Analysis – Positive Results**

A specimen that gives a rate (mA/min) value equal to or greater than the ARK Ketamine II Calibrator B or C Cutoff rate (mA/min) values is interpreted as positive to the relative cutoff level, indicating that Ketamine is present.

Results of this test should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

#### **Semi-quantitative Analysis**

The actual Ketamine concentration cannot be determined with this assay. Semi-quantitative results for positive specimens enable the laboratory to determine an appropriate dilution of the specimen for the confirmatory method. Semi-quantitative results also permit the laboratory to establish quality control procedures and assess reproducibility. Specimens with sample results above the highest ARK Ketamine II calibrator level (500 ng/mL) may be diluted in ARK Ketamine II Calibrator A (Negative urine) and retested.

Results of this test should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings, particularly when the preliminary result is positive.

## 10 Limitations

- The assay is designated for use with human urine only.
- ARK Ketamine II Assay reagents, ARK Ketamine II calibrators and ARK Ketamine II controls were developed as companion products. Performance with substituted products cannot be assured.
- A positive result using the ARK Ketamine II Assay indicates only the presence of Ketamine and does not necessarily correlate with the extent of physiological and psychological effects.
- **Do not use Boric Acid as a preservative.**
- Interpretation of results must take into account that urine concentrations can vary extensively with fluid intake and other biological variables.
- It is possible that substances other than those tested in the specificity study may interfere with the test and cause false results.

## 11 Specific Performance Characteristics

The following performance characteristics were collected on the Beckman Coulter AU680<sup>®</sup> automated clinical chemistry analyzer using the ARK Ketamine II Assay.

### Precision

Drug-free, negative human urine was supplemented with Ketamine (0 to 100 ng/mL for 50 ng/mL Cutoff, and 0.0 to 200 ng/mL for 100 ng/mL Cutoff). Each level was assayed in quadruplicate twice a day for 20 days (N=160) and evaluated qualitatively and semi-quantitatively. Results are summarized in the tables below.

#### Qualitative Precision

##### 50 ng/mL Cutoff

Ketamine (ng/mL)	Relative % Cutoff	# of Results	Results
0.0	-100	160	160 Negative
12.5	-75	160	160 Negative
25.0	-50	160	160 Negative
37.5	-25	160	160 Negative
50.0	Cutoff	160	30 Negative/ 130 Positive
62.5	+25	160	160 Positive
75.0	+50	160	160 Positive
87.5	+75	160	160 Positive
100.0	+100	160	160 Positive

100 ng/mL Cutoff

<b>Ketamine (ng/mL)</b>	<b>Relative % Cutoff</b>	<b># of Results</b>	<b>Results</b>
0.0	-100	160	160 Negative
25.0	-75	160	160 Negative
50.0	-50	160	160 Negative
75.0	-25	160	160 Negative
100.0	Cutoff	160	69 Negative/ 91 Positive
125.0	+25	160	160 Positive
150.0	+50	160	160 Positive
175.0	+75	160	160 Positive
200.0	+100	160	160 Positive

Semi-quantitative Precision

50 ng/mL Cutoff

<b>Ketamine (ng/mL)</b>	<b>Relative % Cutoff</b>	<b># of Results</b>	<b>Mean (ng/mL)</b>	<b>Results</b>
0.0	-100	160	1.04	160 Negative
12.5	-75	160	13.05	160 Negative
25.0	-50	160	26.09	160 Negative
37.5	-25	160	38.87	160 Negative
50.0	Cutoff	160	52.02	39 Negative / 121 Positive
62.5	+25	160	64.53	160 Positive
75.0	+50	160	76.96	160 Positive
87.5	+75	160	89.14	160 Positive
100.0	+100	160	103.06	160 Positive

100 ng/mL Cutoff

<b>Ketamine (ng/mL)</b>	<b>Relative % Cutoff</b>	<b># of Results</b>	<b>Mean (ng/mL)</b>	<b>Results</b>
0.0	-100	160	1.04	160 Negative
25.0	-75	160	26.09	160 Negative
50.0	-50	160	52.02	160 Negative
75.0	-25	160	76.96	160 Negative
100.0	Cutoff	160	103.06	52 Negative / 108 Positive
125.0	+25	160	128.59	160 Positive
150.0	+50	160	152.84	160 Positive
175.0	+75	160	178.96	160 Positive
200.0	+100	160	202.30	160 Positive

### Analytical Recovery

Drug-free, negative human urine was spiked with Ketamine across the assay range of the semi-quantitative calibration curve. Each sample was run in replicates of 6 over two calibrated curves in semi-quantitative mode and the average was used to determine percent recovery compared to the expected value.

Expected Value (ng/mL)	Observed Value (ng/mL)	Recovery (%)
20.0	21.22	106.1
50.0	52.07	104.1
100.0	103.65	103.7
200.0	209.13	104.6
300.0	312.43	104.1
400.0	421.67	105.4
500.0	526.90	105.4

### Analytical Specificity

All compounds tested were added to drug-free, negative human urine and tested with the ARK Ketamine II Assay in both qualitative and semi-quantitative modes.

The following structurally related compounds were added to drug-free, negative human urine and tested with the ARK Ketamine II Assay to determine the approximate equivalence to the 50 and 100 ng/mL Ketamine cutoff. These concentrations were used to determine the percent cross-reactivity according to the formula:

$\% \text{ Cross-reactivity} = (\text{Cutoff concentration} / \text{Concentration approximately equivalent to the 50 or 100 ng/mL cutoff}) \times 100$

For compounds that did not produce a positive result, the highest concentration tested was used to calculate percent cross-reactivity.

### *Cross-reactivity of Ketamine and its metabolites*

Compound	Concentration Approximately Equivalent to the Cutoff (50 ng/mL)	Concentration Approximately Equivalent to the Cutoff (100 ng/mL)	Cross-reactivity (%)	
			50 ng/mL Cutoff	100 ng/mL Cutoff
NorKetamine	109.8	211.7	45.5	47.2
Dehydronorketamine	410.8	664.6	12.2	15.0
(S)-Ketamine	2,000.0	4,000.0	2.5	2.5

**Cross-reactivity of structurally related compounds**

Compound	Concentration Approximately Equivalent to the Cutoff (50 ng/mL)	Concentration Approximately Equivalent to the Cutoff (100 ng/mL)	Cross-reactivity (%)	
			50 ng/mL Cutoff	100 ng/mL Cutoff
Methoxetamine	50,000	100,000	0.1	0.1
Normethoxetamine	>100,000	>100,000	0.0	0.0
desmethylnormethoxetamine (hydroxetamine)	17,000	32,500	0.3	0.3
Deoxymethoxetamine	50,000	100,000	0.1	0.1
Tilidine	>100,000	>100,000	0.0	0.0
Nortilidine	>100,000	>100,000	0.0	0.0
Venlafaxine	>100,000	>100,000	0.0	0.0

**Structurally unrelated compounds**

Compound	50 ng/mL Cutoff		100 ng/mL Cutoff	
	Concentration Tested (ng/mL)	POS/NEG	Concentration Tested (ng/mL)	POS/NEG
(+)-MDA	100,000	NEG	100,000	NEG
11-hydroxy-delta-9-THC	100,000	NEG	100,000	NEG
11-nor-9-carboxy-THC	500,000	NEG	500,000	NEG
1R,2S (-)-Ephedrine	100,000	NEG	100,000	NEG
1S,2R (+)-Ephedrine	100,000	NEG	100,000	NEG
4-Bromo-2,5-Dimethoxyphenethylamine	100,000	NEG	100,000	NEG
6-Acetylcodeine	100,000	NEG	100,000	NEG
6-Acetylmorphine	100,000	NEG	100,000	NEG
6β-Naltrexol	100,000	NEG	100,000	NEG
7-Aminoclonazepam	100,000	NEG	100,000	NEG
7-Aminoflunitrazepam	100,000	NEG	100,000	NEG
7-Aminonitrazepam	100,000	NEG	100,000	NEG
Acetaminophen	500,000	NEG	500,000	NEG
Acetylsalicylic Acid	100,000	NEG	100,000	NEG
Albuterol or Salbutamol (Ventolin)	100,000	NEG	100,000	NEG
Alprazolam	100,000	NEG	100,000	NEG
Amitriptyline	100,000	NEG	100,000	NEG
Amobarbital	100,000	NEG	100,000	NEG
Aripiprazole (Abilify)	100,000	NEG	100,000	NEG
Atenolol (Tenormin)	100,000	NEG	100,000	NEG
Atorvastatin (Lipitor)	100,000	NEG	100,000	NEG
Benzoyllecgonine	100,000	NEG	100,000	NEG
Benzylpiperazine	100,000	NEG	100,000	NEG
Bromazepam	100,000	NEG	100,000	NEG

Budesonide (Pulmicort)	90,000	NEG	100,000	NEG
Buprenorphine	100,000	NEG	100,000	NEG
Bupropion	100,000	NEG	100,000	NEG
Buspirone (Buspar)	100,000	NEG	100,000	NEG
Butabarbital	100,000	NEG	100,000	NEG
Butalbital	500,000	NEG	500,000	NEG
Caffeine	500,000	NEG	500,000	NEG
Cannabidiol	100,000	NEG	100,000	NEG
Cannabinol	100,000	NEG	100,000	NEG
Carbamazepine	100,000	NEG	100,000	NEG
Carbamazepine-10,11-epoxide	100,000	NEG	100,000	NEG
Carisoprodol	100,000	NEG	100,000	NEG
Chlordiazepoxide	100,000	NEG	100,000	NEG
Chlorpromazine	100,000	NEG	100,000	NEG
Ciprofloxacin	100,000	NEG	100,000	NEG
cis-Tramadol	100,000	NEG	100,000	NEG
Clobazam	100,000	NEG	100,000	NEG
Clomipramine	100,000	NEG	100,000	NEG
Clonazepam	100,000	NEG	100,000	NEG
Cocaine	100,000	NEG	100,000	NEG
Codeine	100,000	NEG	100,000	NEG
Cotinine	100,000	NEG	100,000	NEG
Cyanocobalamin (Vitamin B12)	100,000	NEG	100,000	NEG
Cyclobenzaprine	100,000	NEG	100,000	NEG
Delta-9-THC	100,000	NEG	100,000	NEG
Demoxepam	100,000	NEG	100,000	NEG
Desalkylflurazepam	100,000	NEG	100,000	NEG
Desipramine	100,000	NEG	100,000	NEG
Desmethyl Ofloxacin	100,000	NEG	100,000	NEG
Dextromethorphan	100,000	NEG	100,000	NEG
Diazepam	100,000	NEG	100,000	NEG
Diclofenac (Voltaren)	100,000	NEG	100,000	NEG
Digoxin	100,000	NEG	100,000	NEG
Dihydrocodeine	100,000	NEG	100,000	NEG
Diphenhydramine	500,000	NEG	500,000	NEG
Doxepin	100,000	NEG	100,000	NEG
Doxylamine	100,000	NEG	100,000	NEG
Duloxetine (Cymbalta)	100,000	NEG	100,000	NEG
Ecgonine	100,000	NEG	100,000	NEG
Ecgonine Methyl Ester	100,000	NEG	100,000	NEG
EDDP	100,000	NEG	100,000	NEG
Ethylmorphine	100,000	NEG	100,000	NEG
Ethyl-β-D-glucuronide	100,000	NEG	100,000	NEG
Famotidine (Pepcid)	100,000	NEG	100,000	NEG
Fenfluramine (-)	100,000	NEG	100,000	NEG
Fenfluramine (+)	100,000	NEG	100,000	NEG
Fentanyl	100,000	NEG	100,000	NEG

Flunitrazepam	100,000	NEG	100,000	NEG
Fluoxetine	100,000	NEG	100,000	NEG
Flurazepam	100,000	NEG	100,000	NEG
Fluticasone Furoate (Trelegy Ellipta)	17,000	NEG	50,000	NEG
Formoterol (Foradil)	100,000	NEG	100,000	NEG
Gabapentin (Neurontin)	100,000	NEG	100,000	NEG
Haloperidol	100,000	NEG	100,000	NEG
Heroin	100,000	NEG	100,000	NEG
Hexobarbital	100,000	NEG	100,000	NEG
Hydrocodone	100,000	NEG	100,000	NEG
Hydromorphone	100,000	NEG	100,000	NEG
Ibuprofen	500,000	NEG	500,000	NEG
Imipramine	100,000	NEG	100,000	NEG
Ipratropium (Atrovent)	100,000	NEG	100,000	NEG
Lamotrigine	100,000	NEG	100,000	NEG
Levorphanol	100,000	NEG	100,000	NEG
Lidocaine	100,000	NEG	100,000	NEG
Loratadine (Claritin)	100,000	NEG	100,000	NEG
Lorazepam	100,000	NEG	100,000	NEG
Lorazepam Glucuronide	100,000	NEG	100,000	NEG
Lormetazepam	100,000	NEG	100,000	NEG
Losartan (Cozaar)	100,000	NEG	100,000	NEG
LSD	100,000	NEG	100,000	NEG
L-Thyroxine (Synthroid)	100,000	NEG	100,000	NEG
Lurasidone (Latuda)	100,000	NEG	100,000	NEG
Maprotiline	100,000	NEG	100,000	NEG
MDEA	100,000	NEG	100,000	NEG
MDMA	100,000	NEG	100,000	NEG
Meperidine	100,000	NEG	100,000	NEG
Meprobamate	100,000	NEG	100,000	NEG
Metformin (Glucophage)	100,000	NEG	100,000	NEG
Methadone	100,000	NEG	100,000	NEG
Methaqualone	100,000	NEG	100,000	NEG
Methoxisopropamine	100,000	NEG	100,000	NEG
Methylphenidate	100,000	NEG	100,000	NEG
Methylphenidate Metabolite (Ritalinic Acid)	100,000	NEG	100,000	NEG
Midazolam	100,000	NEG	100,000	NEG
Mirtazapine (Remeron)	100,000	NEG	100,000	NEG
Montelukast (Singulair)	100,000	NEG	100,000	NEG
Morphine	100,000	NEG	100,000	NEG
Morphine-3 $\beta$ -D-glucuronide	100,000	NEG	100,000	NEG
Morphine-6 $\beta$ -D-glucuronide	100,000	NEG	100,000	NEG
Nalorphine	100,000	NEG	100,000	NEG
Naloxone	100,000	NEG	100,000	NEG
Naltrexone	100,000	NEG	100,000	NEG

Naproxen	100,000	NEG	100,000	NEG
N-desmethyiltapentadol	100,000	NEG	100,000	NEG
Nicotine	100,000	NEG	100,000	NEG
Nitrazepam	100,000	NEG	100,000	NEG
Norbuprenorphine	100,000	NEG	100,000	NEG
Norcodeine	100,000	NEG	100,000	NEG
Nordiazepam	100,000	NEG	100,000	NEG
Normorphine	100,000	NEG	100,000	NEG
Norpropoxyphene	100,000	NEG	100,000	NEG
Norpseudoephedrine	100,000	NEG	100,000	NEG
Norsertaline	100,000	NEG	100,000	NEG
Nortriptyline	100,000	NEG	100,000	NEG
Ofloxacin	100,000	NEG	100,000	NEG
Olodaterol (Striverdi Respimat)	100,000	NEG	100,000	NEG
Omeprazole (Prilosec and Losec)	100,000	NEG	100,000	NEG
Oxazepam	100,000	NEG	100,000	NEG
Oxcarbazepine (Trileptal)	100,000	NEG	100,000	NEG
Oxycodone	100,000	NEG	100,000	NEG
Oxymorphone	100,000	NEG	100,000	NEG
Paliperidone (Invega)	100,000	NEG	100,000	NEG
Paraxanthine	100,000	NEG	100,000	NEG
PCP	100,000	NEG	100,000	NEG
Pentazocine	100,000	NEG	100,000	NEG
Pentobarbital	100,000	NEG	100,000	NEG
Phenobarbital	100,000	NEG	100,000	NEG
Phentermine	100,000	NEG	100,000	NEG
Phenylephrine	100,000	NEG	100,000	NEG
Phenylpropanolamine	100,000	NEG	100,000	NEG
Phenytoin	100,000	NEG	100,000	NEG
PMA	100,000	NEG	100,000	NEG
Prazepam	100,000	NEG	100,000	NEG
Prazosin (Minipress)	100,000	NEG	100,000	NEG
Propoxyphene	100,000	NEG	100,000	NEG
Propranolol	100,000	NEG	100,000	NEG
Protriptyline	100,000	NEG	100,000	NEG
Quetiapine (Seroquel)	100,000	NEG	100,000	NEG
(R)-10-monohydroxy carbamazepine	100,000	NEG	100,000	NEG
R,R (-)-Pseudoephedrine	100,000	NEG	100,000	NEG
trans-10,11-Dihydro-10,11- dihydroxy Carbamazepine	100,000	NEG	100,000	NEG
Ranitidine	100,000	NEG	100,000	NEG
(S)-10-monohydroxy carbamazepine	100,000	NEG	100,000	NEG
S-(+)-Amphetamine	500,000	NEG	500,000	NEG
S(+)-Methamphetamine	500,000	NEG	500,000	NEG

S,S (+)-Pseudoephedrine	100,000	NEG	100,000	NEG
Salicylic Acid	100,000	NEG	100,000	NEG
Secobarbital	100,000	NEG	100,000	NEG
Sertraline	100,000	NEG	100,000	NEG
Sufentanil Citrate	100,000	NEG	100,000	NEG
Temazepam	100,000	NEG	100,000	NEG
Testosterone	100,000	NEG	100,000	NEG
Theophylline	100,000	NEG	100,000	NEG
Thioridazine	100,000	NEG	100,000	NEG
Tianeptine (Stablon, Tatinol, and Coaxil)	100,000	NEG	100,000	NEG
Tiotropium (Spiriva)	100,000	NEG	100,000	NEG
Trazodone	100,000	NEG	100,000	NEG
Triazolam	100,000	NEG	100,000	NEG
Trifluoromethylphenylpiperazine	100,000	NEG	100,000	NEG
Trimipramine	100,000	NEG	100,000	NEG
Valacyclovir (Valtrex)	100,000	NEG	100,000	NEG
Verapamil	100,000	NEG	100,000	NEG
Xylazine	100,000	NEG	100,000	NEG
Zolpidem Tartrate	100,000	NEG	100,000	NEG

### Interference – Endogenous Substances

High concentrations of the following endogenous substances were added into Ketamine -spiked urine ( $\pm$  25% of the cutoff concentration). No interference was observed when tested with the ARK Ketamine II Assay.

Compound	Concentration Tested	Cutoff 50 ng/mL		Cutoff 100 ng/mL	
		25 ng/mL (-50% Cutoff)	75 ng/mL (+50% Cutoff)	75 ng/mL (-25% Cutoff)	125 ng/mL (+25% Cutoff)
Acetone	1000 mg/dL	NEG	POS	NEG	POS
Ascorbic Acid	1000 mg/dL	NEG	POS	NEG	POS
Bilirubin – Conjugated	2 mg/dL	NEG	POS	NEG	POS
Bilirubin – Unconjugated	2 mg/dL	NEG	POS	NEG	POS
Creatinine	500 mg/dL	NEG	POS	NEG	POS
Ethanol	1000 mg/dL	NEG	POS	NEG	POS
Galactose	10 mg/dL	NEG	POS	NEG	POS
Gamma Globulin	500 mg/dL	NEG	POS	NEG	POS
Glucose	2000 mg/dL	NEG	POS	NEG	POS
Hemoglobin	300 mg/dL	NEG	POS	NEG	POS
Human Albumin	500 mg/dL	NEG	POS	NEG	POS
Oxalic Acid	100 mg/dL	NEG	POS	NEG	POS
Riboflavin	7.5 mg/dL	NEG	POS	NEG	POS
Sodium Azide	1% w/v	NEG	POS	NEG	POS

Compound	Concentration Tested	Cutoff 50 ng/mL		Cutoff 100 ng/mL	
		25 ng/mL (-50% Cutoff)	75 ng/mL (+50% Cutoff)	75 ng/mL (-25% Cutoff)	125 ng/mL (+25% Cutoff)
Sodium Chloride	6000 mg/dL	NEG	POS	NEG	POS
Sodium Fluoride	1% w/v	NEG	POS	NEG	POS
Urea	6000 mg/dL	NEG	POS	NEG	POS
Uric Acid	10 mg/dL	NEG	POS	NEG	POS

#### Interference – Boric Acid

One percent (1%) w/v of boric acid was added into Ketamine -spiked urine ( $\pm 50\%$  of the 50ng/mL cutoff concentration, and  $\pm 25\%$  of the 100ng/mL cutoff concentration). Results are provided in the table below.

Compound	Concentration Tested	Cutoff 50 ng/mL		Cutoff 100 ng/mL	
		25 ng/mL (-50% Cutoff)	75 ng/mL (+50% Cutoff)	75 ng/mL (-25% Cutoff)	125 ng/mL (+25% Cutoff)
Boric Acid	1% w/v	NEG	NEG	NEG	NEG

#### Interference – Specific Gravity and pH

Urine samples with specific gravity values from 1.000 to 1.030 and pH values ranging from 3.0 to 11.0 were tested in the presence of the two levels of Ketamine at  $\pm 50\%$  of the 50 ng/mL cutoff concentration, and two levels of Ketamine at  $\pm 25\%$  of the 100 ng/mL cutoff concentration. No interference was observed when tested with the ARK Ketamine II Assay.

#### Method Comparison

A total of two hundred seventy-three (273) unaltered clinical human urine specimens that are not individually identifiable were analyzed for ketamine with the ARK Ketamine II Assay in both qualitative and semiquantitative modes. Based on LC-MS/MS results, there were five (5) samples with concentrations between the 50 ng/mL and the 100 ng/mL cutoffs. The data obtained with the ARK Ketamine II Assay were compared to LC-MS/MS. Results are summarized in the table below.

### 50ng/mL Cutoff

Qualitative method comparison with LC-MS/MS as reference method

<b>ARK Ketamine II Assay Results</b>	<b>&lt;50% of cutoff concentration by LC-MS/MS (&lt;25 ng/mL)</b>	<b>Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration by LC-MS/MS) (25-49 ng/mL)</b>	<b>Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration by LC-MS/MS) (50-75 ng/mL)</b>	<b>High Positive (Greater than 50% above the cutoff concentration by LC-MS/MS) (&gt;75 ng/mL)</b>
<b>Positive</b>	0	0	4	46
<b>Negative</b>	223	0	0	0

Semi-quantitative method comparison with LC-MS/MS as reference method

<b>ARK Ketamine II Assay Results</b>	<b>&lt;50% of cutoff concentration by LC-MS/MS (&lt;25 ng/mL)</b>	<b>Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration by LC-MS/MS) (25-49 ng/mL)</b>	<b>Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration by LC-MS/MS) (50-75 ng/mL)</b>	<b>High Positive (Greater than 50% above the cutoff concentration by LC-MS/MS) (&gt;75 ng/mL)</b>
<b>Positive</b>	0	0	4	46
<b>Negative</b>	223	0	0	0

### 100ng/mL Cutoff

Qualitative method comparison with LC-MS/MS as reference method

<b>ARK Ketamine II Assay Results</b>	<b>&lt;50% of cutoff concentration by LC-MS/MS (&lt;50 ng/mL)</b>	<b>Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration by LC-MS/MS) (50-99 ng/mL)</b>	<b>Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration by LC-MS/MS) (100-150 ng/mL)</b>	<b>High Positive (Greater than 50% above the cutoff concentration by LC-MS/MS) (&gt;150 ng/mL)</b>
<b>Positive</b>	0	0	5	40
<b>Negative</b>	223	5	0	0

### Semi-quantitative method comparison with LC-MS/MS as reference method

ARK Ketamine II Assay Results	<50% of cutoff concentration by LC-MS/MS (<50 ng/mL)	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration by LC-MS/MS) (50-99 ng/mL)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration by LC-MS/MS) (100-150 ng/mL)	High Positive (Greater than 50% above the cutoff concentration by LC-MS/MS) (>150 ng/mL)
Positive	0	0	5	40
Negative	223	5	0	0

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## 13 Trademarks

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