

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 |
| Rx Only | 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.^{1,2}

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.^{1,3}

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.⁴⁻¹¹

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 | ARK Ketamine II Assay Reagent [R1] – Antibody/Substrate Rabbit monoclonal antibodies to Ketamine, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, sodium azide, and stabilizers | 1 X 28 mL |
| | Reagent [R2] – Enzyme 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 | ARK Ketamine II Assay Reagent [R1] – Antibody/Substrate Rabbit monoclonal antibodies to Ketamine, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, sodium azide, and stabilizers | 1 X 115 mL |
| | Reagent [R2] – Enzyme 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 | ARK Ketamine II Assay Reagent [R1] – Antibody/Substrate Rabbit monoclonal antibodies to Ketamine, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, sodium azide, and stabilizers | 1 X 500 mL |
| | Reagent [R2] – Enzyme 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 | ARK Ketamine II Assay Reagent [R1] – Antibody/Substrate Rabbit monoclonal antibodies to Ketamine, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, sodium azide, and stabilizers | 1 X 58 mL |
| | Reagent [R2] – Enzyme 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.^{12,13}
- 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 – 11.0.¹⁴

- 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[®] 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

| Ketamine (ng/mL) | Relative % Cutoff | # of Results | Results |
|-------------------------|--------------------------|---------------------|-----------------------------|
| 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

| Ketamine (ng/mL) | Relative % Cutoff | # of Results | Mean (ng/mL) | Results |
|-------------------------|--------------------------|---------------------|---------------------|-------------------------------|
| 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

| Ketamine (ng/mL) | Relative % Cutoff | # of Results | Mean (ng/mL) | Results |
|-------------------------|--------------------------|---------------------|---------------------|-------------------------------|
| 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 |
| Mirtazepine (Remeron) | 100,000 | NEG | 100,000 | NEG |
| Montelukast (Singulair) | 100,000 | NEG | 100,000 | NEG |
| Morphine | 100,000 | NEG | 100,000 | NEG |
| Morphine-3 β -D-glucuronide | 100,000 | NEG | 100,000 | NEG |
| Morphine-6 β -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 |
| Phenylephedrine | 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

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

100ng/mL Cutoff

Qualitative 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 |

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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