

ARK™ UR-144/JWH-018 Assay

This ARK Diagnostics, Inc. package insert for the ARK UR-144/JWH-018 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 UR-144, JWH-018 and their metabolites 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.

Customer Service












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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
	Consult Instructions for Use		Reagent 1 / Reagent 2
	Temperature limitation		In Vitro Diagnostic Medical Device
Rx Only	For Prescription Use Only		

1 Name

ARK™ UR-144/JWH-018 Assay

2 Intended Use

The ARK UR-144/JWH-018 Assay is an immunoassay intended for the qualitative determination of UR-144, JWH-018 and their metabolites in human urine at a cutoff concentration of 10 ng/mL. The assay is intended for use in laboratories with automated clinical chemistry analyzers. This *in vitro* diagnostic device is for prescription use only.

The ARK UR-144/JWH-018 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

Synthetic cannabinoids are part of a group of drugs called new psychoactive substances (NPS), which are designer drugs intended to mimic the effects of illicit drugs. These substances are called cannabinoids because they interact with the same CB₁ and CB₂ cannabinoid receptors as tetrahydrocannabinol (THC), the main psychoactive ingredient in marijuana. Although synthetic cannabinoids are functionally similar to THC, many of these substances are not structurally related to THC. Synthetic cannabinoids became popular under the brand names “Spice” and “K2”, in part due to their ability to escape detection by standard cannabinoid screening tests. Synthetic cannabinoids are marketed under a wide variety of specific brand names, including Joker, Black Mamba, Kush, and Kronik. Synthetic cannabinoids are used in a variety of ways, with the most common method being sprayed onto dried plant material and smoked. Potential adverse effects of synthetic cannabinoid use include anxiety, agitation, hallucinations, dizziness, seizures, rapid heart rate and vomiting.¹⁻⁹

4 Principles of the Procedure

The ARK UR-144/JWH-018 Assay is a homogeneous enzyme immunoassay method used for the analysis of drug in human urine. The assay is based on competition between drug in the specimen and drug labeled with recombinant glucose-6-phosphate dehydrogenase (rG6PDH) for antibody binding sites. As the latter binds antibody, enzyme activity decreases. In the presence of drug from the specimen, enzyme activity increases and is directly related to the drug concentration. Active enzyme converts nicotinamide adenine dinucleotide (NAD) to NADH in the presence of glucose-6-phosphate (G6P), resulting in an absorbance change that is measured spectrophotometrically. Endogenous G6PDH does not interfere because the coenzyme NAD functions only with the bacterial enzyme used in the assay.

5 Reagents

REF	Product Description	Quantity/Volume
5054-0001-00	ARK UR-144/JWH-018 Assay Reagent [R1] – Antibody/Substrate rabbit polyclonal antibodies to UR-144/JWH-018 metabolite, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, sodium azide, and stabilizers	1 X 28 mL
	Reagent [R2] – Enzyme UR-144/JWH-018 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
5054-0001-01	ARK UR-144/JWH-018 Assay Reagent [R1] – Antibody/Substrate rabbit polyclonal antibodies to UR-144/JWH-018 metabolite, glucose-6-phosphate, nicotinamide adenine dinucleotide, bovine serum albumin, sodium azide, and stabilizers	1 X 115 mL
	Reagent [R2] – Enzyme UR-144/JWH-018 derivative labeled with recombinant glucose-6-phosphate dehydrogenase (rG6PDH), bovine serum albumin, buffer, sodium azide and stabilizers	1 X 58 mL

Reagent Handling and Storage

ARK UR-144/JWH-018 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 UR-144/JWH-018 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. For prescription use only.
- 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.¹⁰
- 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 specimens 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 – 11.0.¹¹
- 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 UR-144/JWH-018 Assay – [REF] 5054-0001-00 or 5054-0001-01

Materials Required – Provided Separately

ARK UR-144/JWH-018 Negative Calibrator – [REF] 5054-0002-01

ARK UR-144/JWH-018 Cutoff Calibrator – [REF] 5054-0002-02

Quality Controls – ARK UR-144/JWH-018 Control – [REF] 5054-0003-00

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 UR-144/JWH-018 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 10 ng/mL Cutoff Calibrator to distinguish negative and positive samples. Run the Low and High Controls as Negative and Positive respectively. Report test results less than the response value for the Cutoff Calibrator as Negative. Report test results equal to or greater than the response value for the Cutoff Calibrator as Positive.

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
- A stored calibration curve was effective up to at least 25 days based on supporting data

Quality Control (QC) and Calibration

Laboratories should establish QC procedures for the ARK UR-144/JWH-018 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 UR-144/JWH-018 Control is intended for use in quality control of the ARK UR-144/JWH-018 Assay.

The Low Control should be Negative and the High Control should be Positive relative to the 10 ng/mL Cutoff Calibrator.

9 Results and Expected Values

The actual concentration of drug and its metabolites cannot be determined. A confirmatory method is required.

Qualitative Analysis – Negative Results

A specimen that gives a response value less than the ARK UR-144/JWH-018 Cutoff Calibrator response value is interpreted as negative.

Qualitative Analysis – Positive Results

A specimen that gives a response value equal to or greater than the ARK UR-144/JWH-018 Cutoff Calibrator response value is interpreted as positive.

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

10 Limitations

- The assay is designated for use with human urine only.
- ARK UR-144/JWH-018 Assay reagents, calibrators and controls were developed as companion products. Performance with substituted products cannot be assured.

- A positive result using the ARK UR-144/JWH-018 Assay indicates only the presence of drug and its metabolites and does not necessarily correlate with the extent of physiological and psychological effects.
- 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 UR-144/JWH-018 Assay.

Precision

Drug-free, negative human urine was supplemented with UR-144 Pentanoic Acid (calibrator analyte) ranging from 0.0 to 20.0 ng/mL. Each level was assayed in quadruplicate twice a day for 20 days (N=160). Results are summarized in the table below.

Human Urine (ng/mL)	Relative % Cutoff	# of Results	Qualitative Precision Results
0.0	-100	160	160 Negative
2.5	-75	160	160 Negative
5.0	-50	160	160 Negative
7.5	-25	160	160 Negative
10.0	Cutoff	160	88 Negative; 72 Positive
12.5	+25	160	160 Positive
15.0	+50	160	160 Positive
17.5	+75	160	160 Positive
20.0	+100	160	160 Positive

Analytical Specificity

UR-144 and JWH-018 Metabolites and Structurally Related Compounds

Synthetic cannabinoids are extensively metabolized, with little to no unchanged parent drug found in human urine. The active metabolites of synthetic cannabinoids may prolong the parent drug's psychotropic effects and contribute to its toxicological profile.¹²⁻²²

All compounds tested were added to drug-free, negative human urine.

The cross-reactivity of the following UR-144 and JWH-018 metabolites and structurally related compounds was evaluated by spiking these compounds into drug-free, negative human urine to determine the minimum concentration that would give a positive result approximately equivalent to the 10 ng/mL cutoff. These concentrations were used to determine the percent cross-reactivity according to the formula:

% Cross-reactivity = (Cutoff concentration / Lowest concentration of cross-reactant causing a positive result) X 100

Compound	Concentration (ng/mL)	Percent Cross-reactivity (%)
UR-144 pentanoic acid	10.0	100.00
JWH-018 pentanoic acid	8.3	120.48
JWH-018 N-(5-hydroxypentyl)	19.5	51.28
JWH-018 4-hydroxyindole	187.0	5.35
JWH-018 5-hydroxyindole	95.0	10.53
AM-2201 N-(4-hydroxypentyl)	14.6	68.49
AM-2201 6-hydroxyindole	8.0	125.00
JWH-073 N-(4-hydroxybutyl)	13.8	72.46
JWH-073 6-hydroxyindole	27.1	36.90
JWH-073 N-butanoic acid	8.5	117.65
JWH-018	20.6	48.54
AM-2201	39.0	25.64
JWH-073	15.3	65.36
JWH-019	37.0	27.03
JWH-022	32.0	31.25
JWH-200	15.2	65.79
JWH-007	510.0	1.96
JWH-122	528.0	1.89
JWH-015	494.0	2.02
JWH-398	500.0	2.00
3-(1-naphthoyl)-1H-indole	150.0	6.67
JWH-122 N-(5-hydroxypentyl)	75.0	13.33
JWH-122 N-(4-hydroxypentyl)	50.0	20.00
JWH-122 pentanoic acid	50.0	20.00
JWH-250 N-pentanoic acid	3,000	0.33
MAM2201 N-4-hydroxypentyl	92.0	10.87
JWH-210 5-hydroxypentyl	3,400	0.29
JWH-073 N-(3-hydroxybutyl)	15.6	64.10
JWH-203	5,000	0.20
UR-144	19.0	52.63
UR-144 N-heptyl	18.4	54.35
UR-144 N-(5-bromopentyl)	31.0	32.26
UR-144 N-(5-chloropentyl)	17.5	57.14
UR-144 N-(5-hydroxypentyl) metabolite	15.4	64.94
UR-144 N-(5-hydroxypentyl)- β -D-glucuronide	15.9	62.89
A-796260	17.2	58.14
A-834735	13.2	75.76
AB-005	25.0	40.00

Compound	Concentration (ng/mL)	Percent Cross-reactivity (%)
AM-2233	950.0	1.05
RCS-4 2-methoxy isomer	1,750	0.57
XLR-11	20.0	50.00
XLR-11 N-(4-hydroxypentyl) metabolite	15.9	62.89
XLR-11 N-(4-pentenyl)	29.0	34.48
UR-144 4-Hydroxypentyl metabolite	18.9	52.91
UR-144 N-(4-chloropentyl) metabolite	70.0	14.29
RCS-4	100,000	<0.01
RCS-8	65,000	0.02
JWH-081	16,000	0.06
5F-PB-22	30,000	0.03
AM-694	500.0	2.00
CP47497-C8	100,000	<0.01
Delta-9-THC	50,000	<0.02
CP47497	50,000	<0.02
AM 2232	45.0	22.22
BB-22	50,000	<0.02
BB-22 3-carboxyindole	50,000	<0.02
JWH-018 N-(5-hydroxypentyl)-B-D-Glucuronide	10.0	100.00
JWH-201	100,000	<0.01
JWH-210	6,500	0.15
JWH-250	20,000	0.05
JWH-250 5-hydroxyindole	50,000	<0.02
PB-22	100,000	<0.01
PB-22 N-pentanoic acid	4,000	0.25
PB-22 N-(5-hydroxypentyl)	4,500	0.22

High concentrations of the following structurally related compounds were added to drug-free, negative human urine and tested with the ARK UR-144/JWH-018 Assay. The compounds at the concentrations listed below were negative when tested with the ARK UR-144/JWH-018 Assay.

Compound	Concentration Tested (ng/mL)
AB-PINACA N-(4-hydroxypentyl)	80,000
AB-PINACA N-(5-hydroxypentyl)	80,000
5-fluoro AB PINACA N-(4-hydroxypentyl)	100,000
ADB-PINACA pentanoic acid	100,000
ADB-PINACA N-(4-hydroxypentyl)	100,000
ADBICA N-pentanoic acid	100,000
ADBICA N-(4-hydroxypentyl)	100,000
ADBICA N-(5-hydroxypentyl)	100,000

Structurally Unrelated Compounds

The following structurally unrelated compounds were added to drug-free, negative human urine and tested with the ARK UR-144/JWH-018 Assay. The compounds at the concentrations listed below were negative when tested with the ARK UR-144/JWH-018 Assay.

Compound	Concentration Tested (ng/mL)
4-bromo-2,5-dimethoxyphenethylamine	100,000
6-Acetylcodeine	100,000
6-Acetylmorphine	100,000
7-Aminoclonazepam	100,000
7-Aminoflunitrazepam	100,000
7-Aminonitrazepam	100,000
11-nor-9-carboxy- Δ 9-THC	100,000
Acetaminophen	500,000
Acetylsalicylic Acid	500,000
Alprazolam	100,000
Amitriptyline	100,000
Amobarbital	100,000
S-(+)-Amphetamine	100,000
Benzoylcegonine	500,000
Benzylpiperazine	100,000
Bromazepam	100,000
Buprenorphine	100,000
Bupropion	100,000
Butabarbital	100,000
Butalbital	100,000
Caffeine	500,000
Cannabidiol	100,000
Cannabinol	100,000
Carbamazepine	100,000
Carisoprodol	100,000
Chlordiazepoxide	100,000
Chlorpromazine	100,000
cis-Tramadol	100,000
Clobazam	100,000
Clomipramine	100,000
Clonazepam	100,000
Cocaine	100,000
Codeine	100,000
Cotinine	100,000
Cyclobenzaprine	100,000
Desalkylflurazepam	100,000
Demoxepam	100,000
Desipramine	100,000
Dextromethorphan	100,000
Diazepam	100,000
Dihydrocodeine	100,000
Δ 9-THC	100,000
Diphenhydramine	500,000
Doxepin	100,000
Ecgonine	100,000

Compound	Concentration Tested (ng/mL)
Ecgonine Methyl Ester	100,000
EDDP	100,000
1R,2S (-) Ephedrine	100,000
1S,2R (+) Ephedrine	100,000
Ethyl-β-D-Glucuronide	100,000
Ethylmorphine	100,000
Fenfluramine (+)	100,000
Fenfluramine (-)	100,000
Fentanyl	100,000
Flunitrazepam	100,000
Fluoxetine	100,000
Flurazepam	100,000
Heroin	100,000
Hexobarbital	100,000
Hydrocodone	100,000
Hydromorphone	100,000
11-hydroxy-Δ9-THC	100,000
Ibuprofen	500,000
Imipramine	100,000
Ketamine	100,000
Lamotrigine	100,000
Levorphanol Tartrate	100,000
Lidocaine	100,000
Lorazepam	100,000
Lorazepam Glucuronide	50,000
Lormetazepam	100,000
LSD	100,000
Maprotiline	100,000
(+)-MDA	100,000
MDEA	100,000
MDMA	100,000
Meperidine	100,000
Meprobamate	100,000
Methadone	500,000
S(+)-Methamphetamine	100,000
Methaqualone	100,000
Methylphenidate	100,000
Midazolam	100,000
Morphine	100,000
Morphine-3β-D-Glucuronide	50,000
Morphine-6β-D-Glucuronide	50,000
N-Desmethyltapentadol	100,000
Nalorphine	100,000
Naloxone	100,000
Naltrexone	100,000
Naproxen	100,000
Nitrazepam	100,000
Norbuprenorphine	50,000
Norcodeine	100,000
Nordiazepam	100,000
Normorphine	100,000
Norpropoxyphene	100,000
Norpseudoephedrine	100,000

Compound	Concentration Tested (ng/mL)
Nortriptyline	100,000
Oxazepam	100,000
Oxazepam Glucuronide	50,000
Oxycodone	100,000
Oxymorphone	100,000
PCP	100,000
Pentazocine	100,000
Phentermine	100,000
Pentobarbital	100,000
Phenobarbital	100,000
Phenylephedrine	100,000
Phenylpropanolamine	100,000
Phenytoin	100,000
PMA	100,000
Prazepam	100,000
Propoxyphene	100,000
Propranolol	100,000
Protriptyline	100,000
R,R (+)- Pseudoephedrine	100,000
S,S (-)- Pseudoephedrine	100,000
Ranitidine	100,000
Ritalinic Acid	100,000
Salicylic Acid	100,000
Secobarbital	100,000
Sertraline	100,000
Sufentanil Citrate	50,000
Temazepam	100,000
Theophylline	100,000
Thioridazine	100,000
Triazolam	100,000
Trifluoromethylphenylpiperazine	100,000
Trimipramine	100,000
Trazodone	100,000
Venlafaxine	100,000
Zolpidem Tartrate	100,000

Interference – Endogenous Substances

High concentrations of the following endogenous substances were added to urine spiked with UR-144 Pentanoic Acid at \pm 50% of the cutoff concentration. No interference was observed when tested with the ARK UR-144/JWH-018 Assay.

Compound	Concentration Tested	5 ng/mL (-50% Cutoff)	15 ng/mL (+50% Cutoff)
Acetone	1000 mg/dL	Negative	Positive
Ascorbic Acid	1500 mg/dL	Negative	Positive
Bilirubin – Conjugated	2 mg/dL	Negative	Positive
Bilirubin – Unconjugated	2 mg/dL	Negative	Positive
Boric Acid	1% w/v	Negative	Positive
Creatinine	500 mg/dL	Negative	Positive
Ethanol	1000 mg/dL	Negative	Positive
Galactose	10 mg/dL	Negative	Positive
Glucose	2000 mg/dL	Negative	Positive
Hemoglobin	300 mg/dL	Negative	Positive
Human Albumin	500 mg/dL	Negative	Positive
Human Gamma Globulin	500 mg/dL	Negative	Positive
Oxalic Acid	100 mg/dL	Negative	Positive
Riboflavin	7.5 mg/dL	Negative	Positive
Sodium Azide	1% w/v	Negative	Positive
Sodium Chloride	6000 mg/dL	Negative	Positive
Sodium Fluoride	1% w/v	Negative	Positive
Urea	6000 mg/dL	Negative	Positive

Interference – Specific Gravity and pH

Urine samples with specific gravity values ranging from 1.002 to 1.030 and pH values ranging from 3.0 to 11.0 were tested in the presence of the two levels of UR-144 Pentanoic Acid at \pm 50% of the cutoff concentration. No interference was observed when tested with the ARK UR-144/JWH-018 Assay.

Method Comparison

A total of fifty-one (51) unaltered clinical human urine specimens that are not individually identifiable were tested with the ARK UR-144/JWH-018 Assay in qualitative mode and the results were compared to LC-MS/MS. Results are summarized in the table below.

		LC-MS/MS	
ARK UR-144/JWH-018 Assay (10 ng/mL Cutoff)		(+)	(-)
	(+)	23	3*
	(-)	0	25

*Three (3) samples had LC-MS/MS values between the low control (5 ng/mL) and the assay cutoff (10 ng/mL).

An additional seven (7) unaltered clinical human urine specimens that are not individually identifiable were tested with the ARK UR-144/JWH-018 Assay in qualitative mode and the results were compared to another commercially available immunoassay screening method as a reference. Results are summarized in the table below.

Sample ID #	ARK UR-144/JWH-018 Assay (10 ng/mL Cutoff)	Comparative Screening Method
1	Negative	Negative
2	Negative	Negative
3	Positive*	Positive
4	Positive*	Negative
5	Negative	Negative
6	Positive*	Negative
7	Negative	Negative

*These three (3) samples were confirmed to be positive by LC-MS/MS.

12 References

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