

ProScreen™ Drugs of Abuse Test

FOR IN VITRO DIAGNOSTIC USE

INTENDED USE

The ProScreen Drugs of Abuse Test is a one-step immunoassay for the qualitative detection of multiple drugs and drug metabolites in human urine.

Test	Drug Analytes	Cutoff (ng/ml)
Amphetamine (AMP)	d-Amphetamine	1000
Cocaine metabolite (COC)	Benzoylcegonine	300
Methamphetamine (MET500)	d-Methamphetamine	500
Methamphetamine (MET1000)	d-Methamphetamine	1000
Opiates (OPI300)	Morphine	300
Opiates (OPI2000)	Morphine	2000
Phencyclidine (PCP)	Phencyclidine	25
Tetrahydrocannabinol (THC)	11-nor- Δ^9 -THC-9-COOH	50

The Configurations of the ProScreen Drugs of Abuse Test can consist of any combination of the drugs listed above. This assay is used to obtain a visual, qualitative result and is intended for professional use.

This assay provides only a preliminary result. Clinical consideration and professional judgment must be applied to any drug of abuse test result, particularly in evaluating a preliminary positive result. In order to obtain a confirmed analytical result, a more specific alternate chemical method is needed. Gas Chromatography/Mass Spectroscopy (GC/MS) is the preferred confirmation method.

SUMMARY AND EXPLANATION

Cocaine is a potent central nervous system stimulant and a local anesthetic found in the leaves of the coca plant. The psychological effects induced by using cocaine are euphoria, confidence and sense of increased energy. These psychological effects are accompanied by increased heart rate, dilation of the pupils, fever, tremors and sweating. Cocaine is excreted in the urine primarily as benzoylecgonine in a short period of time. Benzoylecgonine has a biological half-life of 5 to 8 hours, which is much longer than that of cocaine (0.5 to 1.5 hour), and can be generally detected for 24 to 60 hours after cocaine use or exposure.

Amphetamine/Methamphetamine, amphetamine, and metabolites are potent central nervous system stimulants. Acute higher doses induce euphoria, alertness, and sense of increased energy and power. More acute responses produce anxiety, paranoia, psychotic behavior, and cardiac dysrhythmias. Methamphetamine is excreted in urine as amphetamine and oxidized as deaminated and hydroxylated derivatives. However, methamphetamine is also excreted to some extent unchanged. Thus the presence of the parent compound in the urine indicates methamphetamine use.

Opiates, such as heroin, morphine, and codeine, are central nervous system (CNS) depressants. The use of opiates at high doses produces euphoria and release from anxiety. Physical dependence is apparent in users and leads to depressed coordination, disrupted decision making, decreased respiration, hypothermia and coma. Heroin is quickly metabolized to morphine, morphine glucuronide and 6-acetylmorphine. Thus, the presence of morphine (or the metabolite, morphine glucuronide) in the urine indicates heroin, morphine, and/or codeine use.

Phencyclidine, commonly known as "angel dust" and "crystal cyclone", is an arylcyclohexylamine that is originally used as an anesthetic agent and a veterinary tranquilizer. The drug is abused by oral or nasal ingestion, smoking, or intravenous injection. It produces hallucinations, lethargy, disorientation, loss of coordination, trance-like ecstatic states, a sense of euphoria and visual distortions. It is well absorbed following all routes of administration. Unchanged PCP is excreted in urine in moderate amounts (10% of the dose).

Tetrahydrocannabinol is generally accepted to be the principle active component in marijuana. When ingested or smoked, it produces euphoric effects. Abusers exhibit central nervous system effects, altered mood and sensory perceptions, loss of coordination, impaired short term memory, anxiety, paranoia, depression, confusion, hallucinations and increased heart rate. When marijuana is ingested, the drug is metabolized by the liver, the primary metabolite of marijuana excreted in the urine is 11-nor- Δ^9 -tetrahydrocannabinol-9-carboxylic acid. Therefore, the presence of detected cannabinoids, including the primary carboxyl metabolite, in the urine indicate marijuana/cannabis use.

The length of time following drug use of which a positive result may occur is dependent upon several factors, including the frequency and amount of drug, metabolic rate, excretion rate, drug half-life, and the drug user's age, weight, activity and diet.

One-step immunoassays are widely used for the analysis of specific substances in biological fluids. The sensitivity and speed of one-step immunoassay have made them the widely accepted method of preliminary screening for drugs of abuse. The ProScreen Drugs of Abuse Test is a simple, fast, and visually read one-step immunoassay for the qualitative detection of cocaine metabolite, methamphetamine, opiates, phencyclidine, and THC in human urine.

TEST PRINCIPLE

The ProScreen Drugs of Abuse Test is based on the principle of competitive immunochemical reaction between a chemically labeled drug (drug-protein conjugate) and the drug or drug metabolites which may be present in the urine sample for the limited antibody binding sites. The test contains a nitrocellulose membrane strip pre-coated with drug-protein conjugate (or antibody) in the test region and a pad containing colored antibody (or drug-protein)-colloidal gold conjugate. During the test, the urine sample is allowed to migrate upward and dehydrate the antibody (or drug-protein)-colloidal gold conjugate. The mixture then migrates along the membrane chromatographically by the capillary action to the immobilized drug-protein (or antibody) band on the test region. When drug is absent in the urine, the colored antibody (or drug-protein)-colloidal gold conjugate and immobilized drug-protein (or antibody) bind specifically to form a visible line in the test region as the antibody complexes with the drug-protein. When drug is present in the urine, it will compete with drug-protein for the limited antibody sites. The line on the test region will become less intense with increasing drug concentration. When a sufficient concentration of drug is present in the urine, it will fill the limited antibody binding sites. This will prevent attachment of the colored antibody (or drug-protein)-colloidal gold conjugate to the drug-protein (or antibody) on the test region. Therefore, the presence of the line on the test region indicates a **negative** result for the drug and the absence of the test line on the test region indicates a **positive** result for the drug.

A visible line generated by a different antigen/antibody reaction is also present at the control region of the test strip. This line should always appear, regardless of the presence of drugs or metabolites in the urine sample. This means that a **negative** urine sample will produce **two** lines (test line and control line), and a **positive** urine sample will generate only **one** line (control line). The presence of control line serves as a built-in control, which demonstrates that the test is performed properly.

REAGENTS & MATERIALS SUPPLIED

- 25 individually wrapped test devices. Each device contains a colloidal gold pad coated with antibody (or drug-protein) and rabbit antibody. It also contains a membrane coated with drug-bovine protein conjugate (or antibody) in the test band and goat anti-rabbit antibody in the control band.
- One instruction sheet

MATERIAL REQUIRED BUT NOT PROVIDED

- Timer

WARNINGS AND PRECAUTIONS

- For professional *in vitro* diagnostic use only.
- Urine specimens may be potentially infectious. Proper handling and disposal methods should be established.
- Avoid cross-contamination of urine samples by using a new specimen collection container for each urine sample.
- Test device should remain sealed until ready for use.
- Do not use the test kit after the expiration date.

STORAGE

The ProScreen Drugs of Abuse Test should be stored at 2-30°C (36-86°F) in the original sealed pouch. Do not freeze.

SPECIMEN COLLECTION AND HANDLING

Fresh urine does not require any special handling or pretreatment. A fresh urine sample should be collected in the container provided. Alternately, a clean, dry plastic or glass container may be used for specimen collection. If the specimen will not be tested after the specimen collection, the specimen may be refrigerated at 2-8°C up to 2 days or frozen at -20°C for longer period of time. Specimens that have been refrigerated must be equilibrated to room temperature prior to testing. Specimens previously frozen must be thawed and mixed thoroughly prior to testing.

Note: Urine specimens and all materials coming in contact with them should be handled and disposed as if capable of transmitting infection. Avoid contact with skin by wearing gloves and proper laboratory attire.

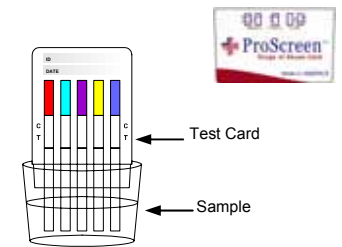
ASSAY PROCEDURE

Preparation

- If specimen, control, or test devices have been stored at refrigerated temperatures, allow them to warm to room temperature before testing.
- Do not open test device pouch until ready to perform the test.

Testing

- Remove the test device from the sealed pouch, and remove the cap to expose the sampling tips.
- Immerse the sampling tips into the urine specimen for about 15 seconds, and then place the test device on a flat surface with the cap on.
- Wait 5 minutes to read Positive results. Do not interpret result after 10 minutes.

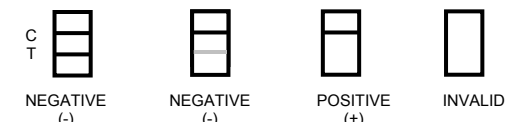


INTERPRETATION OF RESULTS

Negative (-): **Two** colored lines should be observed in the viewing window. The line in the test region is the drug probe line. The line in the control region is the control line, which is used to indicate proper performance of the device. The test line may have varying intensity either weaker or stronger in color than that of the control line.

Positive (+): Only **one** colored line appears in the control region. The complete absence of a test line with a clear white background indicates a positive result.

Invalid: No colored line appears in the control region. If the control line does not form, the test result is inconclusive and should be repeated.



QUALITY CONTROL

The ProScreen Drugs of Abuse Cassette contains a built-in control feature that verifies the proper sample volume has been used and that the reagents are migrating properly. A line must form in the Control band region regardless of the presence or absence of drugs or metabolites. If the line in the Control region does not form, the test is invalid.

Obtaining a valid test result does not necessarily ensure that your patient result is correct, because the built-in control feature does not monitor the performance of the entire assay. To ensure proper assay performance, it is recommended that the cassettes be tested once a week with external positive and negative controls. The external controls should be targeted to +/-50% of the stated assay cutoff level and are available from commercial sources. External controls should be tested using the same procedure as a donor specimen. It is important to make sure that the control values yield expected results. If the controls do not perform as expected, review the instructions for use and repeat the test. If unexpected results continue to occur, contact U.S. Diagnostics for technical assistance before testing patient specimens. Additional controls may be tested according to guidelines or requirements of local, state, and/or federal regulations or accrediting organizations.

LIMITATIONS OF PROCEDURE

- The assay is designed for use with human urine only.
- A positive result with any of the tests indicates only the presence of a drug/metabolite and does not indicate or measure intoxication.
- There is a possibility that technical or procedural errors as well other substances as factors not listed may interfere with the test and cause false results. See SPECIFICITY for lists of substances that will produce positive results, or that do not interfere with test performance.
- If adulteration is suspected, the test should be repeated with new sample.

PERFORMANCE CHARACTERISTICS

A. Accuracy

The accuracy of the ProScreen Drugs of Abuse Test was evaluated in comparison to commercially available immunoassays. Over one hundred negative urine samples obtained from a clinical laboratory were tested by both ProScreen Drugs of Abuse Test and commercially available immunoassays. Of these negative urine samples tested, all were found negatives by

both methods (100% agreement on negative samples). In a separate study, positive urine samples, obtained from clinical laboratories where the drug concentrations were determined by GC/MS, were tested by ProScreen Drugs of Abuse Test and commercial immunoassays.

The results are presented below:

Analyte	GC/MS (ng/ml)	ProScreen (+/-)	Commercial Kit (+/-)
Amphetamine	<628	0/19	0/19
	678-934	2/3	3/2
	1043-1287	9/0	9/0
	≥1366	59/0	59/0
Cocaine metabolite	<150	0/15	0/15
	210-279	3/5	2/6
	327-423	7/0	7/0
	443-10,000	71/0	71/0
Methamphetamine 1000	<376	0/17	0/17
	519-912	1/6	1/6
	1,017-1,473	6/0	6/0
	1,587-291,000	58/0	58/0
Opiates 300	<50	0/15	0/15
	150-280	1/5	2/4
	337-450	6/0	6/0
	502-230,140	78/0	78/0
Opiates 2000	<1,197	0/18	0/18
	1,460-1,969	4/2	2/4
	2,073-2,585	5/0	5/0
	2,629-230,140	49/0	49/0
PCP	<5.0	0/15	0/15
	14-24.5	1/3	2/2
	28-33	5/0	5/0
	38-36,210	57/0	57/0
THC	<15	0/15	0/15
	35-50	2/7	3/6
	51-66	20/0	20/0
	70-507	36/0	36/0

C. Precision

The precision of the ProScreen Drugs of Abuse Test was evaluated by testing three lots of the test devices at four study sites with spiked drug sample solutions on three consecutive days. Sample concentrations were confirmed by GC/MS.

AMP (ng/ml)	0	500	750	1000	1250	1500	2000
Result (+/-)	0/135	0/135	34/101	75/60	110/25	135/0	135/0
COC (ng/ml)	0	150	225	300	375	450	600
Result (+/-)	0/135	0/135	30/105	65/70	96/36	135/0	135/0
MET 1000 (ng/ml)	0	500	750	1000	1250	1500	2000
Result (+/-)	0/135	0/135	31/104	77/58	98/37	135/0	135/0
OPI 300 (ng/ml)	0	150	225	300	375	450	600
Result (+/-)	0/135	0/135	33/102	70/65	95/40	135/0	135/0
OPI 2000 (ng/ml)	0	1000	1500	2000	2500	3000	4000
Result (+/-)	0/135	0/135	37/98	76/59	104/31	135/0	135/0
PCP (ng/ml)	0	12.5	18.75	25	31.25	37.5	50
Result (+/-)	0/135	0/135	26/109	62/73	99/36	135/0	135/0
THC (ng/ml)	0	25	37.5	50	62.5	75	100
Result (+/-)	0/135	0/135	27/108	58/77	91/44	135/0	135/0

D. Specificity

The specificity for the ProScreen Drugs of Abuse Test was determined by testing various drugs, drug metabolites, and other compounds that are likely to be present in urine. All compounds were prepared in drug-free normal human urine. The effect of specimen pH (4.5-8.5) and

specific gravity (1.0-1.040) on the ProScreen Drugs of Abuse Test was also evaluated and found not to interfere with ProScreen Drugs of Abuse Test.

The following compounds produce positive results when tested at levels greater than the concentrations listed below.

Compound	Concentration (ng/ml)
Amphetamine	
d-Amphetamine	1,000
dl-Amphetamine	2,500
Aspirin	1,250
3,4-methylenedioxyamphetamine (MDA)	50,000
d-Methamphetamine	50,000
3,4-methylenedioxymethamphetamine (MDMA)	
Cocaine Metabolite	
Benzoyllecgonine	300
Cocaine	300
Methamphetamine	
d-Methamphetamine	1000
d-Amphetamine	50,000
l-Amphetamine	>100,000
(+/-)3,4-methylenedioxyethylamphetamine(MDEA)	50,000
(+/-)3,4-methylenedioxyamphetamine (MDA)	100,000
3,4 methylenedioxymethamphetamine (MDMA)	3,000
l-Methamphetamine	10,000
Ephedrine	>100,000
Mephentermine	75,000
Opiates 300ng/ml	
Morphine	300
Codeine	300
Ethylmorphine	300
Heroin (diacetylmorphine)	750
Hydrocodone	500
Hydromorphone	500
6-Monoacetylmorphine (6-MAM)	350
Morphine-3-glucuronide	300
Nalorphine	5,000
Opiates 2000ng/ml	
Morphine	2,000
Codeine	2,000
Ethylmorphine	1,000
Heroin (diacetylmorphine)	5,000
Hydrocodone	40,000
Hydromorphone	50,000
6-Monoacetylmorphine (6-MAM)	3,000
Morphine-3-glucuronide	2,500
Nalorphine	5,000
PCP	
Phencyclidine	25
Tenocyclidine	2,000
THC	
11-nor- Δ^9 -THC-9-carboxylic acid	50
11-hydroxy- Δ^9 -tetrahydrocannabinol	1,000
Δ^9 -tetrahydrocannabinol	5,000
Δ^9 -tetrahydrocannabinol	5,000
Cannabinol	10,000
Cannabidiol	>100,000

The following compounds were found not to cross-react when tested at concentrations up to 100 µg/ml.

Acetaminophen	Dopamine	(+/-)-Norephedrine
Acetone	(+/-)-Epinephrine	Oxalic Acid
Albumin	Erythromycin	Penicillin-G
Amitriptyline	Ethanol	Pheniramine
Ampicillin	Furosemide	Phenothiazine
Ascorbic Acid	Glucose	l-Phenylephrine
Aspartame	Guaiacol Glyceryl Ether	β -Phenylethylamine
Aspirin	Hemoglobin	Procaine
Atropine	Ibuprofen	Quinidine
Benzocaine	Imipramine	Ranitidine
Bilirubin	(+/-)-	Riboflavin
Caffeine	Isoproterenol	Sodium Chloride
Chloroquine	Ketamine	Sulindac
(+)-Chlorpheniramine	Levorphanol	Theophylline
(+/-)-Chlorpheniramine	Lidocaine	Trimipramine
Creatine	Maprotiline	Tyramine
Dexbrompheniramine	(+)-Naproxen	4-Dimethylaminoantipyrine
Dextromethorphan	Niacinamide	(1R,2S)-(-)-N-Methyl-Ephedrine
Diphenhydramine	Nicotine	

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