

ProScreen™ Drug Screen Cassette

FOR IN VITRO DIAGNOSTIC USE

INTENDED USE

The ProScreen™ Drug Screen Cassette is a one-step immunoassay for the qualitative detection of multiple drugs and drug metabolites in human urine at the following cutoff concentrations:

Test	Calibrator	Cut-off (ng/ml)
AMP	Amphetamine	300
BAR	Secobarbital	300
BZO	Oxazepam	200
COC	Benzoylcegonine	300
MDMA	3,4-methylenedioxyamphetamine	500
MET 300	Methamphetamine	300
MET 1000	Methamphetamine	1000
MTD	Methodone	300
OPI 300	Morphine	300
OPI 2000	Morphine	2000
OXY	Oxycodone	100
PCP	Phencyclidine	25
TCA	Nortriptyline	1000
THC	11-nor- ⁹ -THC-9-COOH	50

The configurations of this assay consist of any combination of the tests listed above. This assay is used to obtain a visual, qualitative result and is intended for professional use only.

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

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.

Barbiturates are classified as central nervous system depressants. These products produce a state of intoxication that is similar to alcohol intoxication. Symptoms include slurred speech, loss of motor coordination and impaired judgment. Depending on the dose, frequency, and duration of use, one can rapidly develop tolerance, physical dependence and psychological dependence on barbiturates. Barbiturates are taken orally, or by intravenous and intramuscular injections. They are excreted in urine as parent compound as well as metabolites.

Benzodiazepines are central nervous system (CNS) depressants commonly prescribed for the short-term treatment of anxiety and insomnia. In general, benzodiazepines act as hypnotics in high doses, as anxiolytics in moderate doses and as sedatives in low doses. The use of benzodiazepines can result in drowsiness and confusion. Psychological and physical dependence on benzodiazepines can develop if high doses of the drug are given over a prolonged period. Benzodiazepines are taken orally or by intramuscular or intravenous injection, and are extensively oxidized in the liver to metabolites. Parent compounds, as well as metabolites are excreted in the urine.

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.

3,4-methylenedioxyamphetamine is classified as both a stimulant and a hallucinogen. Like methamphetamine, adverse effects of 3,4-methylenedioxyamphetamine use include jaw clenching, teeth grinding, dilated pupils, perspiring, anxiety, blurred vision, vomiting, and increased blood pressure and heart rate. Overdose of 3,4-methylenedioxyamphetamine may cause heart failure or extreme heart stroke. 3,4-methylenedioxyamphetamine is taken orally in tablets or capsules and excreted in urine as parent compound as well as metabolic.

Methodone is a synthetic analgesic drug originally used for the treatment of narcotic addiction. The psychological effects induced by using methodone are analgesia, sedation, and respiratory depression. Overdose of methodone may cause coma or even death. Methodone is taken orally or intravenously and is metabolized in the liver and has a biological half-life of 15-60 hours.

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.

Oxycodone is a semi-synthetic opioid with a structural similarity to codeine. It produces potent euphoria, analgesic and sedative effects, and has a dependence liability similar to morphine. Oxycodone is most often administered orally and is metabolized by demethylation to noroxycodone and oxymorphone followed by glucuronidation and excreted in urine. The window of detection for oxycodone in urine is expected to be similar to that of other opioids such as morphine.

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.

Tricyclic antidepressants (TCAs) have been prescribed for depression and compulsive disorders. Because of the possibility of causing serious cardiac complications, TCAs can be lethal if misused at high doses. TCAs are taken orally or sometimes by injection. TCAs are metabolized in the liver. Both TCAs and their metabolites are excreted in urine mostly in the form of metabolites for up to ten days.

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.

TEST PRINCIPLE

The ProScreen™ Drug Screen Cassette 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 consists of different test strips in a plastic test strip holder. The test strip 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. A pipette is also enclosed.

- 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™ Drug Screen Cassette 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.

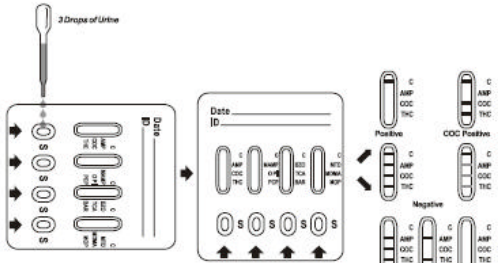
ASSAY PROCEDURE

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 cassette test device from the sealed pouch.
- Place the test on a clean level surface. Hold the dropper vertically and transfer 3 full drops of urine (approximately 100 ul total volume) to the specimen well (S) of the test device, and then start the timer.
- Read result in 5 minutes. Do not interpret result after 10 minutes.

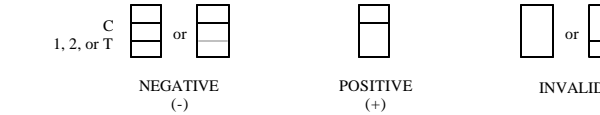


INTERPRETATION OF RESULTS

Negative (-): Colored lines appear in both Control Region (C) and Test Region (1, 2, or T). The line in the control region is the control line, which is used to indicate proper performance of the device. The line in the test region is the drug probe line. The test line may have varying intensity either weaker or stronger in color than that of the control line.

Positive (+): One colored line appears in the control region. No line appears in the test region. The complete absence of a test line indicates a positive result for that drug.

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

An internal procedural control is included in the test device. A line must form in the Control band region regardless of the presence or absence of drugs or metabolites. The presence of the line in the Control region indicates that the proper sample volume has been used and that the reagents are migrating properly. If the line in the Control region does not form, the test is considered invalid.

To ensure proper kit performance, it is recommended that the test devices be tested once a week with external controls. External controls are available from commercial sources. It is important to make sure that the control values are within established limits. If the values of external control do not fall within established limits, the test results are invalid. 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 error 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

Accuracy

The accuracy of the ProScreen™ Drug Screen Cassette was evaluated in comparison to commercially available drug screen tests. Sixty (60) negative urine samples collected from presumed non-user volunteers were tested by both ProScreen™ Drug Screen Cassette I and commercially available drug screen tests. Of these negative urine samples tested, all were found negatives by both methods. In a separate study, positive urine samples, obtained from clinical laboratories where the drug concentrations were determined by GC/MS (TCA concentrations were determined by HPLC), were tested by ProScreen™ Drug Screen Cassette I and commercial drug screen tests. The results of accuracy study are presented below:

Drug Test	GC/MS (<-50% C/O)	GC/MS (-50% C/O to C/O)	GC/MS (C/O to +50% C/O)	GC/MS (>+50% C/O)	% Agreement with GC/MS
AMP	(+) 0 (-) 15	1 6	8 0	62 0	100 95.5
BAR	(+) 0 (-) 15	1 7	4 3	83 0	96.7 95.7
BZO	(+) 0 (-) 15	2 10	10 1	49 0	98.3 92.6
COC	(+) 0 (-) 15	2 6	8 0	70 0	100 91.3
MDMA	(+) 0 (-) 24	1 6	6 0	37 0	100 96.8
MET 300	(+) 0 (-) 15	1 5	6 0	68 0	100 95.2
MET1000	(+) 0 (-) 20	1 7	6 0	58 0	100 96.4
MTD	(+) 0 (-) 15	0 5	6 1	65 0	98.6 100
OPI300	(+) 0 (-) 16	1 6	6 0	77 0	100 95.7
OPI 2000	(+) 0 (-) 15	2 6	9 0	45 0	100 91.3
OXY	(+) 0 (-) 15	1 7	6 0	47 0	100 95.7
PCP	(+) 0 (-) 15	1 3	5 0	36 0	100 94.7
TCA	(+) 0 (-) 23	1 11	12 0	9 0	100 97.1
THC	(+) 0 (-) 15	4 5	24 0	32 0	100 83.3

Precision

The precision of the ProScreen™ Drug Screen Card II 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	150	225	300	375	450
(+/-)	0/135	0/135	32/103	72/63	103/32	135/0
BAR (ng/ml)	0	150	225	300	375	450
(+/-)	0/135	0/135	30/105	70/65	99/36	135/0
BZO (ng/ml)	0	100	150	200	250	300
(+/-)	0/135	0/135	31/104	74/61	100/35	135/0
COC (ng/ml)	0	150	225	300	375	450
(+/-)	0/135	0/135	35/100	72/63	102/33	135/0
MDMA (ng/ml)	0	250	375	500	625	750
(+/-)	0/135	0/135	29/106	74/61	103/32	135/0
MET300 (ng/ml)	0	150	225	300	375	450
(+/-)	0/135	0/135	32/103	77/58	99/36	135/0
MET1000 (ng/ml)	0	500	750	1000	1250	1500
(+/-)	0/135	0/135	30/105	74/61	96/39	135/0
MTD (ng/ml)	0	150	225	300	375	450
(+/-)	0/135	0/135	32/103	73/62	102/33	135/0
OPI300 (ng/ml)	0	150	225	300	375	450
(+/-)	0/135	0/135	33/102	70/65	95/40	135/0
OPI2000 (ng/ml)	0	1000	1500	2000	2500	3000
(+/-)	0/135	0/135	34/101	72/63	100/35	135/0
OXY (ng/ml)	0	50	75	100	125	150
(+/-)	0/135	0/135	29/106	71/64	99/36	135/0
PCP (ng/ml)	0	12.5	18.75	25	31.25	37.5
(+/-)	0/135	0/135	31/104	73/62	99/36	135/0
TCA (ng/ml)	0	500	750	1000	1250	1500
(+/-)	0/135	0/135	24/111	60/75	99/36	135/0
THC (ng/ml)	0	25	37.5	50	62.5	75
(+/-)	0/135	0/135	33/102	67/68	99/36	135/0

Specificity

The specificity for the ProScreen™ Drug Screen Cassette 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 following compounds produce positive results when tested at levels greater than the concentrations listed below.

Compound	Conc. (ng/ml)	Compound	Conc. (ng/ml)
Amphetamines			
d-Amphetamine	300	d-Methamphetamine	20,000
dl-Amphetamine	750	(+/-)3,4-MDMA	20,000
(+/-)3,4-MDA	400		
Barbiturates			
Secobarbital	300	Butabarbital	400
Allobarbital	600	Butalbital	300
Alphenal	200	Butethal	450
Amobarbital	1500	Pentobarbital	400
Aprobarbital	300	Phenobarbital	450
Barbital	1500		
Benzodiazepines			
Oxazepam	200	Flunitrazepam	200
Alprazolam	250	Flurazepam	200
Bromazepam	150	Lorazepam	300
Chlordiazepoxide	250	Medazepam	250
Clobazam	700	Nitrazepam	150
Clonazepam	350	Nordiazepam	100
Clorazepate	100	Prazepam	350
Desalkylflurazepam	150	Temazepam	150
Diazepam	300	Triazolam	300
Estazolam	200		
Cocaine			
Benzoylcegonine	300	Cocaine	300
Methamphetamine (300)			
d-Methamphetamine	300	(+/-)3,4-MDMA	1,200
d-Amphetamine	30,000	l-Methamphetamine	6,000
l-Amphetamine	60,000	Ephedrine	100,000
(+/-)3,4-MDEA	30,000	Mephentermine	25,000
(+/-)3,4-MDA	50,000		
Methamphetamine (1000)			
d-Methamphetamine	1000	(+/-)3,4-MDMA	3,000
d-Amphetamine	50,000	l-Methamphetamine	10,000
l-Amphetamine	>100,000	Ephedrine	>100,000
(+/-)3,4-MDEA	50,000	Mephentermine	75,000
(+/-)3,4-MDA	100,000		
MDMA			
(+/-)3,4-MDMA	500	(+/-)3,4-MDA	4,000
(+/-)3,4-MDEA	450		
Methadone			
(+/-) Methadone	300	Methadol	1,500
Opiates (300)			
Morphine	300	Hydrocodone	500
Codeine	300	Hydromorphone	500
Ethylmorphine	300	Morphine-3-glucuronide	300
Heroin	750	Nalorphine	5,000
Opiates (2000)			
Morphine	2,000	Hydrocodone	4,000
Codeine	2,000	Hydromorphone	5,000
Ethylmorphine	1,000	Morphine-3-glucuronide	2,500
Heroin	5,000	Nalorphine	5,000
Oxycodone			
Oxycodone	100	Morphine	>100,000
Hydrocodone	5000	Codeine	50,000
Hydromorphone	50,000	Heroin	>100,000
PCP			
Phencyclidine	25	Tenocyclidine	2,000

THC

11-nor- Δ^9 -THC-9-COOH	50	Δ^9 -tetrahydrocannabinol	5,000
11-hydroxy- Δ^9 -THC	1,000	Cannabinol	10,000
Δ^8 -tetrahydrocannabinol	5,000	Cannabidiol	>100,000

Tricyclic Antidepressant

Nortriptyline	1,000	Promazine	1,500
Nordoxepin	2,000	Desipramine	400
Trimipramine	2,000	Doxepin	3,000
Amitriptyline	1,500	Maprotiline	2,000

Interference

Two pools of drug-free urine were spiked with drug standards to 50% below and 50% above cutoff concentrations. The drug concentrations were confirmed by GC/MS. The following compounds were evaluated for potential positive and/or negative interference with the ProScreen™ Drug Screen Cassette. All compounds were dissolved in the spiked sample solutions and tested with ProScreen™ Drug Screen Cassette. An unaltered sample was used as a control.

No positive interference or negative interference was found for the following compounds when tested at concentrations up to 100 µg/ml.

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

Effect of Specimen pH

Drug sample solutions with 50% below and 50% above cutoff concentrations were adjusted to pH 4-9 and tested using ProScreen™ Drug Screen Cassette. An unaltered sample was used as a control. The results demonstrate that varying ranges of specimen pH do not interfere with the performance of the test.

Effect of Specimen Specific Gravity

Drug sample solutions with 50% below and 50% above cutoff concentrations were adjusted to specific gravity 1.003-1.04 and tested using ProScreen™ Drug Screen Cassette. An unaltered sample was used as a control. The results demonstrate that varying ranges of specimen specific gravity do not interfere with the performance of the test.

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