

One Step Multi-Drug, Multi-Line Screen Test Device

Package Insert for 2, 3, 4, 5 & 6 Drug Screen Device

Instruction Sheet for testing of any combination of the following drugs:
COC, AMP, mAMP, THC, OPI, PCP

A rapid, one step screening test for the simultaneous, qualitative detection of multiple drugs and drug metabolites in human urine.

For healthcare professionals including professionals at point of care sites use only.

For in vitro diagnostic use only.

INTENDED USE

The One Step Multi-Drug Multi-line Screen Test Device is a lateral flow chromatographic immunoassay for the qualitative detection of multiple drugs and drug metabolites in urine at the following cut-off concentrations: 300 ng/mL Benzoylcegonine (Cocaine metabolite), 1,000 ng/mL Amphetamine, 1,000 ng/mL Methamphetamine, 50 ng/mL 11-nor- Δ^9 -THC-9-COOH (THC), 2,000 ng/mL Opiate, 25 ng/mL Phencyclidine, in urine.

This assay provides only a preliminary analytical test result. A more specific alternate chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography/mass spectrometry (GC/MS) is the preferred confirmatory method. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.

SUMMARY

COCAINE (COC)

Cocaine is a potent central nervous system (CNS) stimulant and a local anesthetic. Initially, it brings about extreme energy and restlessness while gradually resulting in tremors, oversensitivity and spasms. In large amounts, cocaine causes fever, unresponsiveness, and difficulty in breathing and unconsciousness.

Cocaine is often self-administered by nasal inhalation, intravenous injection and free-base smoking. It is excreted in the urine in a short time primarily as Benzoylcegonine^{1,2}. Benzoylcegonine, a major metabolite of cocaine, has a longer biological half-life (5-8 hours) than cocaine (0.5-1.5 hours), and can generally be detected for 24-48 hours after cocaine exposure².

AMPHETAMINE (AMP)

Amphetamine is a Schedule II controlled substance available by prescription (Dexedrine®) and is also available on the illicit market. Amphetamines are a class of potent sympathomimetic agents with therapeutic applications. They are chemically related to the human body's natural catecholamines: epinephrine and norepinephrine. Acute higher doses lead to enhanced stimulation of the central nervous system and induce euphoria, alertness, reduced appetite, and a sense of increased energy and power. Cardiovascular responses to Amphetamines include increased blood pressure and cardiac arrhythmias. More acute responses produce anxiety, paranoia, hallucinations, and psychotic behavior. The effects of

Amphetamines generally last 2-4 hours following use, and the drug has a half-life of 4-24 hours in the body. About 30% of Amphetamines are excreted in the urine in unchanged form, with the remainder as hydroxylated and deaminated derivatives.

METHAMPHETAMINE (mAMP)

Methamphetamine is an addictive stimulant drug that strongly activates certain systems in the brain. Methamphetamine is closely related chemically to amphetamine, but the central nervous system effects of Methamphetamine are greater. Methamphetamine is made in illegal laboratories and has a high potential for abuse and dependence. The drug can be taken orally, injected, or inhaled. Acute higher doses lead to enhanced stimulation of the central nervous system and induce euphoria, alertness, reduced appetite, and a sense of increased energy and power. Cardiovascular responses to Methamphetamine include increased blood pressure and cardiac arrhythmias. More acute responses produce anxiety, paranoia, hallucinations, psychotic behavior, and eventually, depression and exhaustion.

The effects of Methamphetamine generally last 2-4 hours and the drug has a half-life of 9-24 hours in the body. Methamphetamine is excreted in the urine primarily as an unchanged drug, with about 4-10% eliminated as amphetamine. Thus, the presence of the parent compound in the urine indicates Methamphetamine use. A dose of Methamphetamine is generally detectable in the urine for 3-5 days, depending on urine pH level.

MARIJUANA (THC)

THC (Δ^9 -tetrahydrocannabinol) is the primary active ingredient in cannabinoids (marijuana). When smoked or orally administered, it produces euphoric effects. Users have impaired short term memory and slowed learning. They may also experience transient episodes of confusion and anxiety. Long term relatively heavy use may be associated with behavioral disorders. The peak effect of smoking marijuana occurs in 20-30 minutes and the duration is 90-120 minutes after one cigarette. Elevated levels of urinary metabolites are found within hours of exposure and remain detectable for 3-10 days after smoking. The main metabolite excreted in the urine is 11-nor- Δ^9 -tetrahydrocannabinol-9-carboxylic acid (Δ^9 -THC-COOH)³.

OPIATE (OPI)

Opiate refers to any drug that is derived from the opium poppy, including the natural products, morphine and codeine, and the semi-synthetic drugs such as heroin. Opioid is more general, referring to any drug that acts on the opioid receptor.

Opioid analgesics comprise a large group of substances which control pain by depressing the central nervous system. Large doses of morphine can produce higher tolerance levels, physiological dependency in users, and may lead to substance abuse. Morphine is excreted unmetabolized, and is also the major metabolic product of codeine and heroin. Morphine is detectable in the urine for several days after an opiate dose.⁴

PHENCYCLIDINE (PCP)

Phencyclidine, also known as PCP or Angel Dust, is a hallucinogen that was first marketed as a surgical anesthetic in the 1950's. It was removed from the market because patients receiving it became delirious and experienced hallucinations.

Phencyclidine is used in powder, capsule, and tablet form. The powder is either snorted or smoked after mixing it with marijuana or vegetable matter. Phencyclidine is most commonly administered by inhalation but can be used intravenously, intra-nasally, and orally. After low doses, the user thinks and acts swiftly and experiences mood swings from euphoria to depression. Self-injurious behavior is one of the devastating effects of Phencyclidine.

PCP can be found in urine within 4 to 6 hours after use and will remain in urine for 7 to 14

days, depending on factors such as metabolic rate, user's age, weight, activity, and diet.⁵ Phencyclidine is excreted in the urine as an unchanged drug (4% to 19%) and conjugated metabolites (25% to 30%).⁶

PRINCIPLE

The One Step Multi-Drug Screen Test Device is an immunoassay based on the principle of competitive binding. Drugs which may be present in the urine specimen compete against their respective drug conjugate for binding sites on their specific antibody.

During testing, a urine specimen migrates upward by capillary action. A drug, if present in the urine specimen below its cut-off concentration, will not saturate the binding sites of its specific antibody. The antibody will then react with the drug-protein conjugate and a visible colored line will show up in the test line region of the specific drug strip. The presence of drug above the cut-off concentration will saturate all the binding sites of the antibody. Therefore, the colored line will not form in the test line region.

A drug-positive urine specimen will not generate a colored line in the specific test line region of the strip because of drug competition, while a drug-negative urine specimen will generate a line in the test line region because of the absence of drug competition.

To serve as a procedural control, a colored line will always appear at the control line region, indicating that proper volume of specimen has been added and membrane wicking has occurred.

REAGENTS

Each test line contains anti-drug mouse monoclonal antibody and corresponding drug-protein conjugates. Control line contains goat anti-rabbit IgG polyclonal antibodies and rabbit IgG.

PRECAUTIONS

- For healthcare professionals including professionals at point of care sites.
- For *in vitro* diagnostic use only.
- Do not use after the expiration date.
- The test device should remain in the sealed pouch until use.
- All specimens should be considered potentially hazardous and handled in the same manner as an infectious agent.
- The used test device should be discarded according to federal, state and local regulations.

STORAGE AND STABILITY

Store as packaged in the sealed pouch at 2-30°C. The test device is stable through the expiration date printed on the sealed pouch. The test device must remain in the sealed pouch until use. **DO NOT FREEZE.** Do not use beyond the expiration date.

SPECIMEN COLLECTION AND PREPARATION

Urine Assay

The urine specimen must be collected in a clean and dry container. Urine collected at any time of the day may be used. Urine specimens exhibiting visible precipitates should be centrifuged, filtered, or allowed to settle to obtain a clear supernatant for testing.

Specimen Storage

Urine specimens may be stored at 2-8°C for up to 48 hours prior to testing. For prolonged storage, specimens may be frozen and stored below -20°C. Frozen specimens should be thawed and mixed well before testing.

MATERIALS

Materials Provided

- Test devices
- Package insert

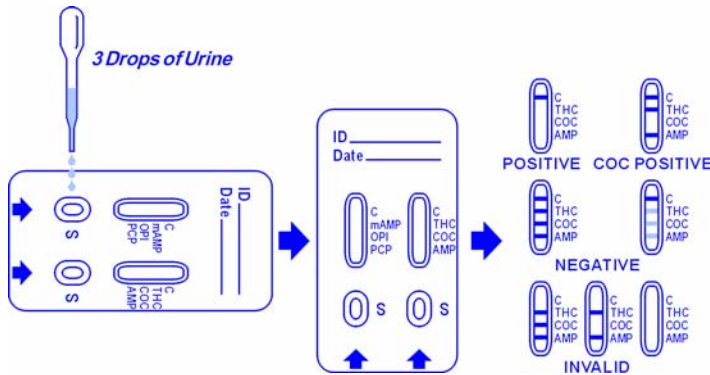
Materials Required But Not Provided

- Specimen collection container
- External controls
- Timer

DIRECTIONS FOR USE

Allow the test device, urine specimen, and/or controls to equilibrate to room temperature (15-30°C) prior to testing.

1. Bring the pouch to room temperature before opening it. Remove the test device from the sealed pouch and use it as soon as possible.
2. Place the test device on a clean and level surface. Hold the dropper vertically and transfer 3 full drops of urine (approx. 100 ul total volume) to the specimen well (S) of the test device, and then start the timer. Avoid trapping air bubbles in the specimen well (S). See the illustration below.
3. Wait for the colored lines(s) to appear. The results should be read at 5 minutes. Do not interpret results after 10 minutes.



(Please refer to the illustration above)

POSITIVE: No line appears in the Test region (T) for a specific drug tested. One reddish line appears in the control region (C). The positive result indicates that the drug concentration in the urine sample exceeds the designated cut-off for a specific drug.

NEGATIVE: * The appearance of a colored line in C region and a colored line in the T region for a specific drug indicate a negative test result. Up to four colored lines may appear: one line in the C region, and up to three lines in the T region. This negative result indicates that the drug concentrations in the urine sample are below the designated cut-off levels for a particular drug tested.

***NOTE:** The shade of reddish color in the test region (T) may vary, but it should be considered negative whenever there is even a faint color line.

INVALID: Control line fails to appear. Insufficient specimen volume or incorrect procedural techniques are the most likely reasons for control line failure. Review the procedure and repeat the test with a new test strip. If the problem persists, discontinue using the device and contact your local distributor.

QUALITY CONTROL

A procedural control is included in the test. A red line appearing in the control region (C) is considered an internal procedural control. It confirms sufficient specimen volume, adequate membrane wicking and correct procedural technique.

Control standards are not supplied with this kit. However, it is recommended that positive and negative controls be tested as good laboratory practice to confirm the test procedure and to verify proper test performance.

LIMITATIONS

1. The One Step Multi-Drug Screen Test Device provides only a qualitative, preliminary analytical result. A secondary analytical method must be used to obtain a confirmed result. Gas chromatography/mass spectrometry (GC/MS) is the preferred confirmatory method.^{3,4,7}
2. There is a possibility that technical or procedural errors, as well as other interfering substances in the urine specimen may cause erroneous results.
3. Adulterants, such as bleach and/or alum, in urine specimens may produce erroneous results regardless of the analytical method used. If adulteration is suspected, the test should be repeated with another urine specimen.
4. A Positive result does not indicate level or intoxication, administration route or concentration in urine.
5. A Negative result may not necessarily indicate drug-free urine. Negative results can be obtained when drug is present but below the cut-off level of the test.
6. Test does not distinguish between drugs of abuse and certain medications.

PERFORMANCE CHARACTERISTICS

Accuracy

A side-by-side comparison was conducted using the One Step Multi-Drug Screen Test Device and commercially available drug rapid tests. Testing was performed on approximately 1,000 specimens previously collected from subjects presenting for Drug Screen Testing. Presumptive positive results were confirmed by GC/MS. Negative urine samples were screened initially by Predicate test, 10% negative samples were confirmed by GC/MS. The following compounds were quantified by GC/MS and contributed to the total amount of drugs found in presumptive positive urine samples tested in the following clinical studies:

Test	Compounds Contributed to the Totals of GC/MS
AMP	Amphetamine
COC	Benzoylcegonine
mAMP	Methamphetamine
OPI	Morphine, Codeine
PCP	Phencyclidine
THC	11-nor 9-carboxy-delta-9-tetrahydrocannabinol

The following results were tabulated:

Method	Multi-Drug Multi-Line	GC/MS					% agreement with GC/MS
		Neg.*	Neg. (< -25% cutoff)	Near cutoff neg. (-25% cutoff to cutoff)	Near cutoff pos. (cutoff to +25% cutoff)	Pos. (> +25% cutoff)	
AMP	Positive	0	0	1	14	114	94%
	Negative	150	2	12	8	0	99%
COC	Positive	0	0	1	13	99	95%
	Negative	150	8	22	4	2	99%
mAMP	Positive	0	0	0	4	116	90%
	Negative	150	0	12	6	8	>99%
OPI	Positive	0	0	2	19	111	98%
	Negative	150	0	14	1	1	99%
THC	Positive	0	5	3	12	114	95%
	Negative	150	14	6	2	4	95%
PCP	Positive	0	0	2	6	64	90%
	Negative	150	0	2	3	5	99%

*Negative urine samples were screened initially by Predicate test, 10% negative samples were confirmed by GC/MS

Method	Predicate Test Results		% Agreement with Predicate Test	
	Positive	Negative		
AMP	Positive	129	0	>99%
	Negative	0	172	>99%
COC	Positive	112	1	>99%
	Negative	0	186	99%
mAMP	Positive	121	0	>99%
	Negative	0	175	>99%
OPI	Positive	132	0	99%
	Negative	1	164	>99%
THC	Positive	124	0	>99%
	Negative	0	176	>99%
PCP	Positive	72	0	>99%
	Negative	0	160	>99%

Analytical Sensitivity

A drug-free urine pool was spiked with drugs to the concentrations at $\pm 50\%$ cut-off and $\pm 25\%$ cut-off. The results are summarized below.

Drug conc. (Cut-off range)	n	COC		AMP		mAMP	
		-	+	-	+	-	+
0% Cut-off	30	30	0	30	0	30	0
-50% Cut-off	30	30	0	30	0	30	0
-25% Cut-off	30	25	5	26	4	25	5
Cut-off	30	20	10	23	7	23	7
+25% Cut-off	30	5	25	7	23	6	24
+50% Cut-off	30	0	30	0	30	0	30

Drug conc. (Cut-off range)	n	THC		OPI		PCP	
		-	+	-	+	-	+
0% Cut-off	30	30	0	30	0	30	0
-50% Cut-off	30	30	0	30	0	30	0
-25% Cut-off	30	24	6	26	4	26	4
Cut-off	30	15	15	11	19	19	11
+25% Cut-off	30	6	24	5	25	5	25
+50% Cut-off	30	0	30	0	30	0	30

Eighty (80) drops of these samples for each drug test were also run using ACON's multi-drug test device by an untrained operator at a physician's office. Based on GC/MS data, the operator obtained a statistically similar positive agreement, negative agreement and overall agreement rate as the laboratory personnel.

Analytical Specificity

The following table lists the concentration of compounds (ng/mL) that are detected positive in urine by the One Step Multi-Drug Screen Test Device at 5 minutes.

COCAINE	
Benzoylcegonine	300
Cocaine HCl	780
Cocaethylene	12,500
Ecgonine HCl	32,000
AMPHETAMINE	
D-Amphetamine	1,000
D,L-Amphetamine sulfate	3,000
L-Amphetamine	50,000
(±)3,4-Methylenedioxyamphetamine	2,000
Phentermine	3,000
METHAMPHETAMINE	
D-Methamphetamine	1,000
p-Hydroxymethamphetamine	30,000
L-Methamphetamine	8,000
(±)-3,4-Methylenedioxymethamphetamine	2,000
Mephentermine	50,000
MARIJUANA (THC)	
11-nor- Δ^9 -THC-9 COOH	50
Cannabinol	20,000
11-nor- Δ^8 -THC-9 COOH	30
Δ^8 -THC	15,000
Δ^9 -THC	15,000
OPIATES	
Morphine	2,000
Codeine	2,000
Ethylmorphine	5,000
Hydrocodone	12,500
Hydromorphone	5,000
Levophanol	75,000
6-Monoacetylmorphine	5,000
Morphine 3- β -D-glucuronide	2,000
Norcodeine	12,500
Normorphine	50,000
Oxycodone	25,000
Oxymorphone	25,000
Procaine	150,000
Thebaine	100,000
PCP	
Phencyclidine	25
4-Hydroxyphencyclidine	12,500

Precision

A study was conducted at three physician offices by untrained operators using three different lots of product to demonstrate the within run, between run and between operator precision. An identical panel of coded specimens, containing drugs at the concentration of $\pm 50\%$ and $\pm 25\%$ cut-off level, was labeled as a blind and tested at each site. The results are given below:

Drug conc. (ng/mL)	n per site	Site A		Site B		Site C	
		-	+	-	+	-	+
0	90	90	0	90	0	90	0
-50% Cutoff	90	90	0	88	2	89	1
-25% Cutoff	90	80	10	70	20	70	20
+25% Cutoff	90	34	56	13	77	12	78
+50% Cutoff	90	5	85	5	85	3	87

Effect of Urinary Specific Gravity

Fifteen (15) urine samples of normal, high, and low specific gravity ranges (1.000-1.037) were spiked with drugs at 50% below and 50% above cut-off levels respectively. The Multi-Drug Screen Test was tested in duplicate using fifteen drug-free urine and spiked urine samples. The results demonstrate that varying ranges of urinary specific gravity does not affect the test results.

Effect of the Urinary pH

The pH of an aliquoted negative urine pool was adjusted to a pH range of 5 to 9 in 1 pH unit increments and spiked with drugs at 50% below and 50% above cut-off levels. The spiked, pH-adjusted urine was tested with the One Step Multi-Drug Screen Test Device. The results demonstrate that varying ranges of pH does not interfere with the performance of the test.

Cross-Reactivity

A study was conducted to determine the cross-reactivity of the test with compounds in either drug-free urine or Cocaine, Amphetamine, Methamphetamine, Marijuana, Opiate or Phencyclidine positive urine. The following compounds show no cross-reactivity when tested with the One Step Multi-Drug Screen Test Device at a concentration of 100 μ g/mL.

Non Cross-Reacting Compounds

Acetaminophen	β-Estradiol	Penicillin-G
Acetophenetidin	Estrone-3-sulfate	Perphenazine
N-Acetylprocainamide	Ethyl-p-aminobenzoate	Phenelzine
Acetylsalicylic acid	Fenoprofen	Trans-2-phenylcyclo-propylamine hydrochloride
Aminopyrine	Furosemide	L-Phenylephrine
Amitriptyline	Gentisic acid	β-Phenylethylamine
Amoxicillin	Hemoglobin	Phenylpropanolamine
Ampicillin	Hydralazine	Prednisolone
L-Ascorbic acid	Hydrochlorothiazide	Prednisone
Apomorphine	Hydrocortisone	Promazine
Aspartame	O-Hydroxyhippuric acid	Promethazine
Atropine	p-Hydroxyamphetamine	DL-Propranolol
Benzilic acid	3-Hydroxytyramine	D-Propoxyphene
Benzoic acid	Ibuprofen	D-Pseudoephedrine
Benzphetamine	Imipramine	Quinacrine
Bilirubin	Iproniazid	Quinidine
(±) - Brompheniramine	(±) - Isoproterenol	Quinine
Caffeine	Isoxsuprine	Ranitidine
Cannabidiol	Ketamine	Salicylic acid
Chloralhydrate	Ketoprofen	Serotonin
Chloramphenicol	Labetalol	Sulfamethazine
Chlorothiazide	Loperamide	Sulindac
(±) - Chlorpheniramine	Maprotiline	Temazepam
Chlorpromazine	MDE	Tetracycline
Chlorquine	Meperidine	Tetrahydrocortisone, 3-acetate
Cholesterol	Meprobamate	Tetrahydrocortisone3-(β-D-glucuronide)
Clomipramine	Methadone	Tetrahydrozoline
Clonidine	Methoxyphenamine	Thiamine
Cortisone	Nalidixic acid	Thioridazine
(-) Cotinine	Naloxone	DL-Tyrosine
Creatinine	Naltrexone	Tolbutamide
Deoxycorticosterone	Naproxen	Triamterene
Dextromethorphan	Niacinamide	Trifluoperazine
Diazepam	Nifedipine	Trimethoprim
Diclofenac	Norethindrone	Trimipramine
Diflunisal	D-Norpropoxyphene	Tryptamine
Digoxin	Noscapine	DL-Tryptophan
Diphenhydramine	DL-Octopamine	Tyramine
Doxylamine	Oxalic acid	Uric acid
(-) -Ψ-Ephedrine	Oxazepam	Verapamil
[1R,2S](-)Ephedrine	Oxolinic acid	Zomepirac
(L) - Epinephrine	Oxymetazoline	
Erythromycin	Papaverine	

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