

D. Interference

The following compounds were evaluated for potential positive and/or negative interference with the DrugCheck Dip Drug Test. All compounds were dissolved in the drug control solutions with 50% below and 50% above cutoff concentration and tested with DrugCheck Dip Drug Test. 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	Dopamine	Penicillin-G
Acetone	(+/-)-Epinephrine	Pheniramine
Acetylsalicylic acid	Erythromycin	Phenothiazine
Albumin	Ethanol	l-Phenylephrine
Ampicillin	Furosemide	*-Phenylethylamine
Ascorbic Acid	Glucose	Procaine
Aspartame	Guaiaccol Glyceryl Ether	Pseudoephedrine
Aspirin	Hemoglobin	Quinidine
Atropine	Ibuprofen	Ranitidine
Benzocaine	(+/-)-Isoproterenol	Riboflavin
Bilirubin	Ketamine	Sodium Chloride
Caffeine	Levorphanol	Sulindac
Chloroquine	Lidocaine	Theophylline
(+)-Chlorpheniramine	Myoglobin	Tyramine
(+/-)-Chlorpheniramine	(+)-Naproxen	4-Dimethylaminoantipyrine
Creatine	Niacinamide	(1R,2S)-(-)-N-Methyl-Ephedrine
Dexbrompheniramine	Nicotine	
Dextromethorphan	(+/-)-Norephedrine	
Diphenhydramine	Oxalic Acid	

E. Effect of Specimen pH

Drug sample solutions with 50% below and 50% above cutoff concentrations were adjusted to pH 4-9 and tested using DrugCheck Dip Drug Test. 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.

F. 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 DrugCheck Dip Drug Test. 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.

BIBLIOGRAPHY OF SUGGESTED READING

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DRUGCHECK® Dip Drug Test

FOR IN VITRO DIAGNOSTIC USE

The DrugCheck® Dip Drug Test 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)
AMIP	d-Amphetamine	1000
BAR	Secobarbital	300
BUP	Buprenorphine	10
BZO	Oxazepam	300
COC150	Benzoylcegonine	150
COC	Benzoylcegonine	300
MDMA	3,4-methylenedioxyamphet- phetamine	500
MET500	d-Methamphetamine	500
MET	d-Methamphetamine	1000
MTD	Methadone	300
OPI300	Morphine	300
OPI	Morphine	2000
OXY	Oxycodone	100
PCP	Phencyclidine	25
PPX	Propoxyphene	300
TCA	Nortriptyline	1000
THC	11-nor- Δ^9 -THC-9-COOH	50

The configurations of the DrugCheck Dip Drug Test consist of any combination of the drugs listed above. The DrugCheck Dip Drug Test 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) and Liquid Chromatography/Mass Spectrometry (LC/MS) are the preferred confirmation method.

SUMMARY AND EXPLANATION

Amphetamine/Methamphetamine and metabolites are potent central nervous system stimulants. Acute doses induce euphoria, alertness, and sense of increased energy and power. Responses from chronic use can include anxiety, paranoia, psychotic behavior, and cardiac dysrhythmias. Methamphetamine and amphetamine are excreted in urine as unchanged drug along with deaminated or hydroxylated derivatives. Methamphetamine also metabolizes to amphetamine in the body. As a result, urine specimens from most methamphetamine users contain both unchanged parent drug and the amphetamine metabolite.

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, tolerance, physical dependence and psychological dependence on barbiturates can occur. Barbiturates are taken orally, or by intravenous and intramuscular injections. Members of the barbiturate drug class typically excrete in urine as parent compound and 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. Most benzodiazepines are excreted in the urine as conjugates and metabolites.

Buprenorphine is a synthetic thebaine derivative that has both analgesic and opioid antagonist properties. As an analgesic, it is about 25 to 40 times more potent than morphine. Symptoms of overdose include confusion, dizziness, pinpoint pupils, hallucinations, hypotension, respiratory difficulty, seizures and coma. Buprenorphine is metabolized in man primarily by N-dealkylation and conjugation to form norbuprenorphine, (which is pharmacologically active), and conjugates of Buprenorphine and norbuprenorphine. Within 144 hours of a single intramuscular dose of drug, 95% is eliminated as unchanged drug and the various conjugates and metabolites, with 68% in the feces and 27% 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 (MDMA) 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 heat stroke. 3,4-methylenedioxyamphetamine is taken orally in tablets or capsules and is excreted in urine as parent compound and metabolites including methylenedioxyamphetamine (MDA).

Methadone is a synthetic analgesic drug originally used for the treatment of narcotic addiction and pain management. The psychological effects induced by using methadone are analgesia, sedation, and respiratory depression. Overdose of methadone may cause coma or even death. Methadone is taken orally or intravenously, 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 6-acetylmorphine (6-AM), morphine, and morphine glucuronide. Codeine also partially metabolizes to morphine and morphine glucuronide. Thus, the presence of morphine or morphine glucuronide in the urine can indicate 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. 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).

Propoxyphene is a mildly effective narcotic analgesic that has been in clinical use since the 1950's. It is less potent than codeine and bears a close structural relationship to methadone. Propoxyphene is available in oral formulations either as the hydrochloride or as the napsylate salt, and is often dosed in combination with aspirin or acetaminophen. Overdosage of propoxyphene can result in stupor, coma, convulsions, respiratory depression, cardiac arrhythmias, hypotension, pulmonary edema and circulatory collapse. Propoxyphene is metabolized primarily via N-demethylation to norpropoxyphene. The amounts of metabolites excreted in the 20 hour urine following a 130 mg single oral dose of propoxyphene hydrochloride were: 1.1% propoxyphene, 13.2% norpropoxyphene and 0.7% dinorpropoxyphene.

Tetrahydrocannabinol (THC) 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 extensively metabolized by the liver; the primary metabolite of marijuana excreted in the urine is 11-nor- Δ^9 -tetrahydrocannabinol-9-carboxylic acid. The elimination of THC and metabolites in urine is highly dependent on frequency of drug use and the physiology of the user.

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

TEST PRINCIPLE

The DrugCheck Dip Drug 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 in the test region and a pad containing colored antibody-colloidal gold conjugate. During the test, the urine sample is allowed to migrate upward and re-hydrate the antibody-colloidal gold conjugate. The mixture then migrates along the membrane chromatographically by the capillary action to the immobilized drug-protein band on the test region. When drug is absent in the urine, the colored antibody-colloidal gold conjugate and immobilized drug-protein 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-colloidal gold conjugate to the drug-protein 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 both test line and control line, and a positive urine sample will generate only 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 and rabbit antibody. It also contains a membrane coated with drug-protein conjugate in the test band and goat anti-rabbit antibody in the control band.

- * One instruction sheet
- * Security seals (if applicable)

MATERIAL REQUIRED BUT NOT PROVIDED

- * Timer
- * Specimen collection container
- * External positive and negative controls

WARNINGS AND PRECAUTIONS

- * For professional in vitro diagnostic use only
- * Urine specimens and used devices 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.
- * A positive test result does not always mean an individual has taken the drug illegally as the drug can be administered legally.
- * Do not store and/or expose reagent kits at temperature greater than 30°C. Do not freeze.

STORAGE

The DrugCheck Dip Drug Test should be stored at 2-30°C (36-86°F) in the original sealed pouch. Do not freeze. Do not store and/or expose reagent kits to a temperature greater than 30°C.

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.

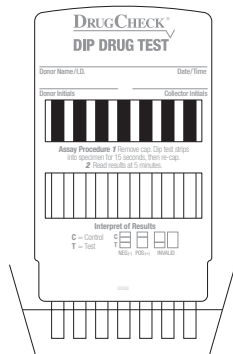
ASSAY PROCEDURE FOR DRUG TEST

Preparation

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

Testing

1. Remove the card test device from the sealed pouch write the donor name or ID in the section provided, and then remove the cap to expose the sampling tips.
2. 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.
3. Read results of drugs of abuse tests in 5 minutes. Do not interpret result after 10 minutes. Refer to interpretation of results section.

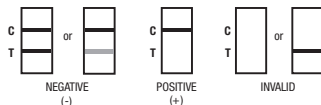


INTERPRETATION OF RESULTS

Negative (-): A colored line appears at the control region (C) and a colored line appears at a specific drug test region (T1, T2 for 2-drug strip and T for 1-drug strip). The appearance of a control line and test line indicates a negative test result for that particular test. The test lines may have varying intensity either weaker or stronger in color than that of the control line.

Positive (+): A colored line appears in the control region and no colored line appears at a specific drug test region. The complete absence of a test line indicates a preliminary positive result for that particular drug. A preliminary positive result for a drug indicates that the concentration of that drug in urine is at or above the cutoff level.

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 sufficient 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 and must be repeated.

To ensure proper kit performance, it is recommended that the DrugCheck Dip Drug Test devices be tested using external controls with each new lot of product and each new shipment. External controls are available from commercial sources. Additional testing may be necessary to comply with the requirements accrediting organizations and/or local, state, and/or federal regulators.

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, and those 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 DrugCheck Dip Drug Test was evaluated in comparison to commercially available drug screen tests and GC/MS. Sixty (60) negative urine samples collected from presumed non-user volunteers were tested by both DrugCheck Dip Drug Test and commercially available drug screen tests. Of these negative urine samples tested, all were correctly identified as negative by both methods. In a separate study, positive urine samples, obtained from clinical laboratories where the drug concentrations were determined by GC/MS (HPLC for TCA), were tested by DrugCheck Dip Drug Test 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	0	10	55	98.5
	(-)	15	9	1	0	100
BAR	(+)	0	1	5	83	97.8
	(-)	15	7	2	0	95.7
BUP	(+)	0	0	8	35	97.7
	(-)	18	6	1	0	100
BZO	(+)	0	2	13	37	100
	(-)	18	18	0	0	94.7
COCC150	(+)	0	1	7	60	100
	(-)	15	10	0	0	96.2
COCC300	(+)	0	0	8	71	98.8
	(-)	15	8	1	0	100
MDMA	(+)	0	1	6	37	100
	(-)	24	6	0	0	96.8
MET500	(+)	0	2	8	64	100
	(-)	15	4	0	0	90.5
MET1000	(+)	0	0	5	58	98.4
	(-)	20	8	1	0	100
MTD	(+)	0	0	6	65	98.6
	(-)	15	5	1	0	100
OPI300	(+)	0	1	6	77	100
	(-)	16	6	0	0	95.7
OPI2000	(+)	0	2	9	45	100
	(-)	15	6	0	0	91.3
OXY	(+)	0	2	6	47	100
	(-)	15	6	0	0	91.3
PPX	(+)	0	0	6	64	98.6
	(-)	10	7	1	0	100
PCP	(+)	0	0	4	56	96.8
	(-)	15	4	2	0	100
TCA	(+)	0	1	12	9	100
	(-)	23	11	0	0	97.1
THC	(+)	0	1	24	32	100
	(-)	15	12	0	0	96.4

B. Precision

A study was conducted at three physician offices and Ameditech in an effort to determine the precision of the DrugCheck Dip Drug Test across three (3) consecutive days. Testing was conducted on the Amphetamine, Barbiturates, Benzodiazepines, Buprenorphine, Cocaine (300 and 150 assays), Marijuana, Methamphetamine (1000 and 500 assays), Methylenedioxymethamphetamine, Methadone, Opiates (2000 and 300 assays), Oxycodone, Phencyclidine, Propoxyphene, and Tricyclic Antidepressants assays using three different lots of product to demonstrate the within-run, between-run and between-operator precision. An identical panel of coded samples, containing drugs at specific concentrations around each assay cutoff was blinded and tested at each site. The correlation with expected results for the solutions targeted to +/-50% of the cutoff was >99% across all lots, all sites and all operators.

C. Specificity

The specificity for the DrugCheck Dip Drug 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 following compounds produce positive results when tested at levels greater than the concentrations listed below.

Compound	Conc. (ng/ml)	Compound	Conc. (ng/ml)
Amphetamine			
d-Amphetamine	1000	d-Methamphetamine	50,000
l-Amphetamine	2500	(+/-)3,4-MDMA	50,000
(+/-)3,4-MDA	1250		
Barbiturates			
Secobarbital	300	Butabarbital	400
Allobarbital	600	Butalbital	300
Alphenal	200	Butethal	450
Amobarbital	1500	Pentobarbital	400
Acrobarbital	300	Phenobarbital	450
Barbital	1500		
Benzodiazepines			
Oxazepam	300	Flunitrazepam	300
Alprazolam	400	Flurazepam	300
Bromazepam	250	Lorazepam	500
Chlordiazepoxide	300	Medazepam	300
Clobazam	1000	Nitrazepam	250
Clonazepam	500	Nordiazepam	150
Clorazepate	150	Przepam	500
Desalkylflurazepam	200	Temazepam	200
Diazepam	450	Triazolam	450
Estazolam	300		
Buprenorphine			
Buprenorphine	10	Buprenorphine-3-beta-D-glucuronide	7.5
Norbuprenorphine	2500		
Codeine	>100,000	Norbuprenorphine-3-beta-D-glucuronide	150
Morphine	>100,000		
Nalorphine	10,000		
Cocaine Metabolite (150)			
Benzoylcegonine	150	Cocaeethylene	>100,000
Cocaine	5000	Ecgonine methyl esters	>100,000
Ecgonine	>100,000		
Cocaine Metabolite (300)			
Benzoylcegonine	300	Cocaine	300
Methamphetamine (500)			
d-Methamphetamine	500	(+/-)3,4-MDMA	2000
l-Amphetamine	50,000	l-Methamphetamine	10,000
l-Amphetamine	>100,000	Ephedrine	50,000
(+/-)3,4-MDEA	50,000	Mephentermine	50,000
(+/-)3,4-MDA	100,000		
Methamphetamine (1000)			
d-Methamphetamine	1000	(+/-)3,4-MDMA	3000
l-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	4000
(+/-)3,4-MDEA	450		
Methadone			
(+/-) Methadone	300	Methadol	1500
Opiates (300)			
Morphine	300	Hydrocodone	500
Codeine	250	Hydromorphone	500
Ethylmorphine	300	Morphine-3-glucuronide	300
Heroin(diacetylmorphine)	750	Nalorphine	5000
Opiates (2000)			
Morphine	2000	Hydrocodone	4000
Codeine	2000	Hydromorphone	5000
Ethylmorphine	1000	Morphine-3-glucuronide	2500
Heroin(diacetylmorphine)	5000	Nalorphine	5000
Oxycodone			
Oxycodone	100	Morphine	>100,000
Hydrocodone	5000	Codeine	50,000
Hydromorphone	50,000	Heroin	5000
PCP			
Phencyclidine	25	Tenocyclidine	2000
PPX			
d-Propoxyphene	300	d-Norpropoxyphene	300
THC			
T11-nor-Δ ⁹ -THC-9-COOH	50	Δ ⁹ -tetrahydrocannabinol	5000
T11-hydroxy-Δ ⁹ -THC	1000	Cannabidiol	10,000
Δ ⁹ -tetrahydrocannabinol	5000	Cannabidiol	>100,000
Tricyclic Antidepressant			
Nortriptyline	1000	Promazine	1500
Nordoxepin	2000	Desipramine	400
Trimipramine	2000	Doxepin	3000
Amitriptyline	1500	Maprotiline	2000