The Multi-Drug of Abuse Urine Cup Test is a rapid, qualitative immunosay assay for screening potential abuse of one or more drugs. This device detects any combination of up to twelve drugs or drug metabolites at or above the specified cutoff levels. This device is for health care professional use only.

### INTENDED USE

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### INSTRUCTIONS FOR USE

**One Step Assay**

**Rapid Visual Results** For sale in the European Union only

**For sale in the European Union only**

**undenied**

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

### SUMMARY

**Amphetamine (AMP, AMP300, AMP500)**

The detection of amphetamines in human urine has been widely used to assess abuse. Amphetamines are central nervous system stimulating drugs. They may induce alertness, wakefulness, increased energy, reduced hunger and an overall feeling of well-being. Overdose and extended usage of amphetamines may lead to substance abuse, which may cause severe and/or permanent damage to the human nervous system. Amphetamines appear in the urine within three hours after administration (any route), and remain present for approximately 24-48 hours after the last dose.

**Barbiturates (BAR)**

Barbiturates are central nervous system depressants and are used as hypnotic sedatives. Overdose and extended usage of barbiturates may lead to severe and/or permanent damage to the human nervous system. Barbiturates are classified as (1) ultra-short, (2) short-intermediate, and (3) long-acting. The duration range of ultra-short-acting compounds (secobarbital, pentobarbital, etc.) is from fifteen (15) minutes to six (6) hours. The duration range of intermediate-acting compounds (amobarbital, etc.) is from three (3) to twenty-four (24) hours. The duration range of long-acting compounds (phenobarbital, etc.) is from fifteen (15) to forty-eight (48) hours.

The most commonly abused barbiturates are short- and intermediate-acting agents. The long-acting agents are rarely subject to abuse. Barbiturate derivatives are excreted into urine in varying amounts of unchanged drug and metabolites. Long-acting barbiturates are excreted with a higher percentage of unchanged drug in the urine, while shorter-acting barbiturates are extensively metabolized and excreted in the urine with a smaller percentage of unchanged drug.

**Buprenorphine (BUP)**

Buprenorphine is a narcotic drug, and is also used in heroin substitution and detoxification treatment. Due to increased medical use of buprenorphine and its metabolites, buprenorphine and norbuprenorphine are also glucuronidated to the clinically inactive conjugates buprenorphine-3β-d-glucuronide and norbuprenorphine-3β-d-glucuronide. Buprenorphine and its metabolites are eliminated mainly in the feces (68%), with a smaller proportion excreted in urine (27%) over the course of several days. It has been reported that in suspected abusers, the concentration range for unconjugated buprenorphine was 2.3 - 796 ng/mL, and 5 - 2,580 ng/mL for unconjugated norbuprenorphine. It was also found that the concentration of free buprenorphine and norbuprenorphine in urine may be relatively small (< 0.4 ng/mL) if taken in clinically administered doses, but can reach up to 20 ng/mL if abused.

**Benzodiazepines (BZD)**

Benzodiazepines, including alprazolam, diazepam, lorazepam, triazolam, chloridiazepoxide, flurazepam and temazepam are sedative, hypnotic and anti-anxiety drugs commonly used as tranquilizers. Most benzodiazepines are extensively metabolized in the liver and excreted in the urine as metabolites. Benzodiazepines have a low potential for physical or psychological dependence. However, as with other central nervous system-stimulating drugs, they may induce drowsiness and muscle relaxation. Chronic abuse of benzodiazepines may result in intoxication, similar to drunken behavior. Overdose and extended usage of benzodiazepines may lead to coma and death. Benzodiazepines may remain detectable for 4-8 hours. The members of the benzodiazepine family are absorbed at different rates and their effects may vary with the absorption rate. They are excreted in the urine primarily as their parent compounds or as inactive metabolites only (e.g. oxazepam glucuronide) that are only detectable for one (1) to two (2) days. Oxazepam, a common metabolite of many benzodiazepines that is also a marketed drug (Serax), may remain detectable in urine for up to one week, making it a useful marker for benzodiazepine abuse.

**Cocaine (COC and COC150)**

Cocaine is a nervous system stimulant that can be addictive. Cocaine may appear in urine for only a few hours after use, whereas benzoylecgonine, a hydrolytic degradation product of cocaine, may be detectable in urine for over 2 days after cocaine use. Therefore the detection of benzoylecgonine in human urine is widely used to evaluate cocaine usage.

**Methamphetamine (MET, MET500, MET300)**

Methamphetamine overdose causes restlessness, confusion, anxiety, hallucinations, cardiac arrhythmias, hypertension, hyperthermia, circulatory collapse, convulsions and coma. Methamphetamine has been implicated in fatal poisonings following intravenous and oral administration. Chronic abusers may develop paranoid psychosis. d-Methamphetamine (d-desoxyephedrine, Desoxyn, Methedrine) is the N-methyl derivative of amphetamine, utilized in the treatment of obesity. Methamphetamine is administered by oral or nasal insufflation or intravenous injection, with a duration of 2-4 hours. Methamphetamine undergoes some N-demethylation to amphetamine, its major active metabolite. In normal conditions, up to 43% of a dose is eliminated, with about 4-7% as amphetamine. In acidic urine, up to 7% of the dose is excreted as amphetamine. The ratio of amphetamine to methamphetamine in alkaline urine the corresponding values are 2% and less than 0.1%. Methamphetamine urine concentrations of 0.5-4.0 mg/L are commonly observed during the first 24 hours after ingestion of 10 mg. Methamphetamine concentrations of 24-533 mg/L (mean value 142) have been observed in the urine of methamphetamine abusers.

**Morphine/Opiates (MOR/OP2000, MOR/OP300)**

Morphine is a popular marketed drug for treatment of moderate to severe pain. It is also a common metabolite of opiates [morphine, codeine (methyl-morphine), and heroin (a semi-synthetic derivative of morphine)]. Opiates are administered by smoking, intravenous injection, intramuscular injection or oral ingestion. Adverse or toxic effects of opiates usage include pupillary constriction, constipation, urinary retention, nausea, vomiting, hyperthermia, drowsiness, dizziness, apathy, confusion, respiratory depression, hypotension, cold and clammy skin, coma and pulmonary edema. Death may occur following an overdose.

The duration of effect of morphine is 3-6 hours. Morphine is metabolized extensively, with only 2-3% of the drug escaping the body. The active metabolite that is metabolized to morphine in the body; the pattern of urinary excretion of heroin is similar to that of morphine. Codeine is also extensively metabolized, with 10-15% of the dose demethylated to form morphine and norcodeine. It has been reported that unchanged morphine may remain detectable in urine for up to one week, which makes morphine a useful marker of opiate abuse.

**Methadone (MDT)**

Methadone, also marketed as Dolophine, Methadose and Amidone, possesses many of the pharmacologic properties of morphine and is approximately equipotent as an analgesic when administered parenterally. Unlike morphine, however, methadone produces marked sedative effects with repeated administration as a result of drug accumulation. Methadone has been used as a major substitute for opiates such as heroin, morphine, and codeine in drug maintenance treatment clinics. It is administered either orally or by intravenous or intra-muscular injection. The duration
of effect of methadone is 12-24 hours. Its major urinary excretion products are methadone, EDDP (2-ethylidene-1,3,5-trimethylcyclohexanol), and EMDP. Individual variations in the percentage of unchanged methadone excreted in urine have been observed due to urine pH, urine volume, dose and rate of metabolism. Methadone has been found in urine at levels higher than 1,000 ng/mL 24 hours after an overdose. Therefore the concentration of methadone in human urine has been used as a marker of methadone abuse.

**Oxycodone (OXY)**

Oxycodone is a semi-synthetic opioid with a structure similar to codeine. It is prescribed for the relief of moderate to severe pain. Like all opiate agonists, oxycodone provides pain relief by acting on opioid receptors in the spinal cord, brain, and possibly directly on the affected tissues. Oxycodone is a central nervous system depressant that may cause drowsiness, lethargy, weakness, and confusion. Toxicity in an overdose of oxycodone can lead to stupor, coma, muscle flaccidity, severe respiratory depression, hypotension and respiratory arrest.

Oxycodone is metabolized by demethylation into oxymorphone and noroxycodone. After a single 5 mg oral dose, 13-19% of oxycodone is excreted unchanged in a 24-hour urine collection. The time window for detection of oxycodone in urine is expected to be similar to that of other opioids such as morphine.

**Propoxyphene (PPX)**

Propoxyphene is a prescription drug for the relief of pain. Propoxyphene hydrochloride (Darvon, Dolene) is available in 32mg and 65mg capsules; propoxyphene napsylate (Darvon-N) is available in 100mg tablets or as a suspension. Propoxyphene is structurally related to methadone. As with many opioids, overdose can affect the brain region and cause respiratory depression. The progressive symptomatology of propoxyphene includes analgesia, stupor, respiratory depression and coma. The half-life of propoxyphene is 8-24 hours. Following oral administration, propoxyphene reaches its peak in 1 to 2 hours. There is great variability between subjects in the rate of clearance. The percentage of excreted unchanged propoxyphene in urine is less than 1%. The major metabolite of propoxyphene is norpropoxyphene. Therefore, the detection of norpropoxyphene is widely used for the testing of propoxyphene abuse. The half-life of norpropoxyphene is about 30 hours, and its accumulation with repeated doses may be responsible for some of the toxicity observed.

**Tricyclic Antidepressants (TCA)**

Tricyclic antidepressants (TCA) are antidepressant drugs that contain three fused aromatic rings in their chemical structure. TCA can be taken orally or intramuscularly. The progressive symptomatology of TCA includes agitation, confusion, hallucinations, hypotension, seizures, and EKG changes. The half-life of TCA varies from a few hours to a few days. Commonly used tricyclic antidepressants are excreted with a half-life of about 30-50% over 72 hours. Only 2% is excreted in feces. On average, 77% of an intravenous dose is excreted in urine and feces over 10 days. Therefore, PCP in human urine has been used as a marker for PCP abuse.

Concentrations of unchanged drug in the urine of ambulatory PCP users are usually between 0.04 and 3.4 mg/L.

**Propoxyphene**

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**MDMA**

MDMA is the most active principal detection of TCA or its metabolites in human urine has been used to screen for PCP abuse. The half-life of norpropoxyphene is 8-24 hours. Following oral administration, propoxyphene reaches its peak in 1 to 2 hours. Its duration of effect is 2-4 hours, and psychosis may last for weeks. PCP has three major metabolites; however, the percentage excreted unchanged in urine after an intravenous dose is 30-50% over 72 hours. Only 2% is excreted in feces. On average, 77% of an intravenous dose is excreted in urine and feces over 10 days. Therefore, PCP in human urine has been used as a marker for PCP abuse.

Concentrations of unchanged drug in the urine of ambulatory PCP users are usually between 0.04 and 3.4 mg/L.

**Phencyclidine (PCP)**

Phencyclidine (PCP), also called Angel Dust, Hog and Killer Weed, is a popular drug of abuse, as well as a legitimate veterinary tranquillizer. It is self-administered by smoking, nasal insufflation, intravenous injection or oral ingestion. Its duration of effect is 2-4 hours, and psychosis may last for weeks. PCP has three major metabolites; however, the percentage excreted unchanged in urine after an intravenous dose is 30-50% over 72 hours. Only 2% is excreted in feces. On average, 77% of an intravenous dose is excreted in urine and feces over 10 days. Therefore, PCP in human urine has been used as a marker for PCP abuse.

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**Tricyclic Antidepressants (TCA)**

Tricyclic antidepressants (TCA) are antidepressant drugs that contain three fused aromatic rings in their chemical structure. TCA can be taken orally or intramuscularly. The progressive symptomatology of TCA includes agitation, confusion, hallucinations, hypotension, seizures, and EKG changes. The half-life of TCA varies from a few hours to a few days. Commonly used tricyclic antidepressants are excreted with a half-life of about 30-50% over 72 hours. Only 2% is excreted in feces. On average, 77% of an intravenous dose is excreted in urine and feces over 10 days. Therefore, PCP in human urine has been used as a marker for PCP abuse.

Concentrations of unchanged drug in the urine of ambulatory PCP users are usually between 0.04 and 3.4 mg/L.

**Multiple Drug of Abuse Urine Cup Test**

4. Read the test results on all strips between 4 and 7 minutes.

3. Start the timer immediately.

2. Push the white knob all the way into the cup. Make sure the urine flows into the bottom chamber of the cup.

1. Confirm that the level of the urine sample in the cup is between the Min and Max marks.

**PRINCIPLE OF THE PROCEDURE**

The Multi-Drug of Abuse Urine Cup Test consists of any combination of between one (1) to twelve (12) individual test strip(s) for the drug(s) being tested. The assay is a one-step lateral flow chromatographic immunoassay based on the principle of competition for limited antibody binding sites between a drug or drug metabolite(s) in the sample and a drug-protein conjugate immobilized on a porous membrane support.

During testing, urine migrates to the test area of the membrane by capillary action, mobilizing the colored antibody conjugates. The antibody conjugates then move along the membrane to the test area. In the absence of drug or if the drug concentration is below the cutoff limit in the sample, the colored conjugates attach to the respective drug antigen immobilized in the test line region, forming a colored band (T line). If drug is present in the sample, the drug or drug metabolite(s) compete for the limited antibody binding sites. If the drug concentration is at or above the cutoff limit, the drug will saturate all the binding sites of the antibody, preventing the attachment of the colored conjugates to the antigen in the test line area of the membrane. Therefore no colored line will form.

The control line (C line) serves as an internal quality control of the system. It should always appear as a colored band regardless of the presence of the drug.

**REAGENTS AND MATERIALS SUPPLIED**

- 25 cups with built-in test strips & desiccants; each cup sealed in a foil pouch
- 1 package insert (instructions for use)

**MATERIALS REQUIRED BUT NOT PROVIDED**

- Timer
- External positive and negative controls

**PRECAUTIONS**

- The instructions must be followed exactly to obtain accurate results.
- Do not open the sealed pouch until ready to conduct the assay.
- Do not use expired devices.
- Dispose of all specimens and used assay materials as potentially biohazardous.
- Do not use the device if you are colorblind.

**STORAGE AND STABILITY**

- Store the product at room temperature 15-30°C (59-86°F). Each device may be used until the expiration date printed on the label if it remains sealed in its foil pouch.
- Do not freeze and/or expose this kit to temperatures over 30°C.

**SPECIMEN COLLECTION**

**IMPORTANT:** Do not open the pouch until ready to perform the test.

1. Remove the test cup from the pouch.
2. Label the cup with patient or control number identification and the date.
3. Have the patient remove the lid and urinate directly into the cup to at least the Min (minimum) level marked on the cup, up to the Max (maximum) level. Do not over fill. Put the lid back onto the cup. Wipe any splashes or spills that may be on the outside of the cup.
4. Immediately check the temperature strip on the cup. The temperature should be between 32-38°C (90-100°F). If the temperature is not in this range, the sample may be altered and another sample should be collected.
5. Make sure the cup is closed tightly with the lid.
6. Specimens may be kept at 15-30°C (59-86°F) for 8 hours or at 2-8°C for up to 3 days.
Do not freeze the cup.

**ASSAY PROCEDURE**

**Important:** Refrigerated specimens and other test materials, including cups, must be equilibrated to room temperature before testing.

1. Confirm that the level of the urine sample in the cup is between the Min and Max marks.
2. Push the white knob all the way into the cup. Make sure the urine flows into the bottom chamber of the cup.
3. Start the timer immediately.
4. Read the test results on all strips between 4 and 7 minutes.
INTERPRETATION OF RESULTS

Each test strip is labeled with an abbreviation for its target drug. For example, "COC" indicates a cocaine test. A complete list of abbreviations can be found in the Intended Use section on Page 1.

IMPORTANT:
- Read each test independently.
- Do not compare the color intensity of one test to another.
- Do not compare the color intensity of the T line to the C line.
- Do not interpret results after 7 minutes.

Preliminary Positive:
If the C line appears and there is no T line, the result is a preliminary positive for that drug. More than one test may be preliminary positive.

Note: Preliminary positive results should be confirmed with a more specific method. GC/MS or HPLC are the preferred confirmatory methods.

1 2 3 4 5 6
C T C
Preliminary positive for test 2 and test 3

Negative:
If both the C and T lines appear for a test, the result is negative for that drug. If both the C and T lines appear for all tests, the urine specimen is negative for all the drugs tested.

1 2 3 4 5 6
C T C
Note: Even a very faint T line is negative.

Invalid:
If no C line develops within 4 minutes on any test strip, the result is invalid. In this case, do not report test results. Repeat the assay with a new device. If the result is still invalid, stop using the device and contact the manufacturer.

1 2 3 4 5 6
C T C
Invalid for test 4 and test 5

QUALITY CONTROL

Built-in Control Features:
Each test contains a built-in control feature, the C line. The presence of the C line indicates that an adequate sample volume was used and that the reagents migrated properly. If a C line does not form, the result is invalid. Review the procedure and repeat with a new device.

External Quality Control:
Users should follow local guidelines concerning the running of external quality controls. SAMHSA recommends that the concentration of drug(s) in positive and negative controls be approximately 25% above and below the cutoff concentration of the assay.

LIMITATIONS
1. This kit is for professional in vitro diagnostic use only.
2. This device provides only preliminary qualitative analytical test results. A more specific alternate method must be used to obtain a confirmed analytical result.
3. This product is designed for testing human urine only.
4. Adulterants such as bleach or other strong oxidizing agents may produce erroneous test results. If adulteration is suspected, collect a fresh specimen and repeat the procedure with a new device.
5. Samples in which bacterial contamination is suspected should not be used. These contaminants may interfere with the test and cause false results.

EXPECTED VALUES
This device is capable of detecting specific drugs and/or drug metabolites in human urine at or above the cutoff concentrations in the Intended Use section on page 1.

PERFORMANCE CHARACTERISTICS

Accuracy
A comparison study was performed at two physician’s office laboratories (POL) and a reference laboratory. Samples were blind labeled and tested for each analyte (drug or drug metabolite). Each sample was tested at each site with the Multi-Drug of Abuse Urine Cup Test and the results were compared to GC/MS or HPLC/MS results. The test results were grouped into drug free, below 75% cutoff (negative), above 125% cutoff (positive), between 75% cutoff and between cutoff and 125% cutoff according to the analyte concentrations from GC/MS for all analytes except BUP and TCA, which were tested with HPLC/MS. Overall, this test exhibited more than 90% agreement with the selected analytical method for each analyte. The test results are tabulated below.

<table>
<thead>
<tr>
<th>Method</th>
<th>Multi-Drug of Abuse Urine Cup Test</th>
<th>Drug</th>
<th>Drug Cutoff (ng/mL)</th>
<th>GC/MS</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMP</td>
<td>1000</td>
<td>Positive</td>
<td>&gt;1000</td>
<td>Negative</td>
<td>100%</td>
</tr>
<tr>
<td>AMP300</td>
<td>300</td>
<td>Positive</td>
<td>&gt;1000</td>
<td>Negative</td>
<td>100%</td>
</tr>
<tr>
<td>AMP500</td>
<td>500</td>
<td>Positive</td>
<td>&gt;1000</td>
<td>Negative</td>
<td>100%</td>
</tr>
<tr>
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<td>200</td>
<td>Positive</td>
<td>&gt;1000</td>
<td>Negative</td>
<td>100%</td>
</tr>
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<td>BZD</td>
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<td>&gt;1000</td>
<td>Negative</td>
<td>100%</td>
</tr>
<tr>
<td>CEC</td>
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<td>Positive</td>
<td>&gt;1000</td>
<td>Negative</td>
<td>100%</td>
</tr>
<tr>
<td>CCO150</td>
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<td>Positive</td>
<td>&gt;1000</td>
<td>Negative</td>
<td>100%</td>
</tr>
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<td>Positive</td>
<td>&gt;1000</td>
<td>Negative</td>
<td>100%</td>
</tr>
<tr>
<td>MET500</td>
<td>500</td>
<td>Positive</td>
<td>&gt;1000</td>
<td>Negative</td>
<td>100%</td>
</tr>
<tr>
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</tr>
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<td>&gt;1000</td>
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<td>100%</td>
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<td>Negative</td>
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</tr>
<tr>
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<td>100%</td>
</tr>
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<td>Negative</td>
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</tr>
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</tr>
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<td>&gt;1000</td>
<td>Negative</td>
<td>100%</td>
</tr>
<tr>
<td>XTC</td>
<td>500</td>
<td>Positive</td>
<td>&gt;1000</td>
<td>Negative</td>
<td>100%</td>
</tr>
</tbody>
</table>
structurally related compounds. Compounds producing positive responses are listed below.

Reproducibility

The reproducibility of each test was determined by replicate assays of three different production lots with four levels of sample s: Drug-free, 75% cutoff, 125% cutoff and Positive to cutoff level of each analyte.

The common substances listed in this table were found not to interfere with test results at a concentration of 100 µg/mL.

REFERENCES


Drug-free and spiked urine pools were tested with the Multi-Drug of Abuse Urine Cup Test at various pH levels and specific gravities. pH ranges from pH 5 to pH 9 and specific gravity ranges from 1.002 – 1.035 g/mL did not affect the expected results in the study.

There is a possibility that other substances and/or factors not listed above (e.g., technical or procedural errors) may interfere with the test and cause false results.

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