Revised 20 Jun 2008 **IVD**

For the rapid determination of methamphetamine and its metabolites in human urine

For *in vitro* diagnostic use only.

INTENDED USE

DRG International, Inc. Methamphetamine Screen Test Card and Test Strip devices are in vitro diagnostic (IVD), lateral flow, immunochromatographic, qualitative urinary assays for rapid detection of methamphetamine and its metabolites in human urine at the Substance Abuse Mental Health Services Administration (SAMHSA) cut-off level of 1000 ng/ml. The tests are designed to obtain a visual, qualitative result and are intended for professional use only. They are not intended for quantitative analysis, nor for over-the-counter sale.
The DRG Methamphetamine Screen Test provides only preliminary analytical data. A more specific, alternative method is required to obtain a confirmed analytical result. SAMHSA has established gas chromatography / mass spectrometry (GC/MS) as the preferred confirmatory method. Clinical considerations and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are indicated.

SUMMARY AND EXPLANATION OF TEST

Methamphetamine causes central nervous system stimulation, anxiety, paranoia, psychosis, hyperthermia, anorexia, hypertension, and cardiovascular damage. Some studies indicate that high dose abuse of methamphetamine may lead to tolerance, physiologic dependency and permanent damage to certain essential nerve structures in the brain. Methamphetamine is a sympathomimetic amine that is usually taken orally, intravenously or by inhalation. Methamphetamine is readily absorbed from the gastrointestinal tract and deactivated by the liver via deamination and hydroxylation. It is excreted, partly unchanged, in urine, with an elimination half-life of 10 hours for the d-isomer and 30 hours for the l-isomer. Weakly active metabolites (mainly d/l-norephedrines) are eliminated with a half-life between 8 and 16 hours after ingestion. About 40% of methamphetamine ingested is excreted unchanged. Thus, methamphetamine is the primary urinary marker for detecting methamphetamine use.
The DRG Methamphetamine Screen Test is a rapid, visual, lateral flow, competitive, immunochromatographic assay for the qualitative detection of methamphetamine its analogs, and its metabolites in human urine. These in vitro diagnostic screening tests are based on immunoassay principles and designed specifically for the assay and identification of methamphetamine and its metabolites at a cut-off level of 1000 ng/ml or higher, as set by SAMHSA.

PRINCIPLE OF THE PROCEDURE

The DRG Methamphetamine Screen Test is a competitive immunoassay in which chemically modified and bound methamphetamine conjugate competes with urinary methamphetamine and its metabolites for limited,

specific methamphetamine antibody binding sites. Each test device contains a sample reaction unit, a pink-colored, antibody-colloidal gold conjugate unit pre-labeled with specific antibody, and a chromatographic membrane pre-coated with drug conjugate in the device test region.
When free drug is absent from urine or at concentrations lower than the urinary detection cut-off level, the pink-colored, antibody-colloidal gold conjugate is free to bind to the immobilized drug conjugate pre-coated on the chromatographic membrane test region. Consequently, a pink-colored band will form in the test region indicating a negative result. When drug is present in urine at concentrations at or exceeding the detection cut-off level, it will bind to limited epitopes on the pink-colored, antibody-colloidal gold conjugate, completely competing with drug conjugate in the test region. In such cases, no band forms in the test region, indicating a positive result.
The DRG® Methamphetamine Screen Test also provides a built-in process control. A pink-colored band should always appear in the control region, regardless of the presence of any urinary methamphetamine and its metabolites. This pink-colored control band verifies that: 1) sufficient urine volume was added, and 2) proper flow was obtained. If the control band is missing, the test was not performed correctly or failed to function correctly. In summary, negative urine will produce two pink-colored bands, one in the control region and one in the test region. Positive urine will produce one pink-colored band in the control region only.

REAGENTS AND MATERIALS SUPPLIED

Test device with the following components: a sample reaction unit, a pink-colored, colloidal gold conjugate unit, and a chromatographic membrane unit.
A disposable sample pipette comes with the test card.
Test instructions

MATERIALS REQUIRED BUT NOT PROVIDED

- Urine sample collection containers
- Timer or clock

WARNINGS AND PRECAUTIONS

- **For *in vitro* diagnostic use.**
- Avoid cross contamination of urine samples by using a new sample collection container and pipette for each urine sample.
- Urine specimens may be potentially infectious. Avoid contact with skin by wearing gloves and proper laboratory attire. Properly handle and dispose of all used test devices in an approved biohazard container.
- Do not use a test device beyond the expiration date imprinted on the outside of the foil pouch.

STORAGE AND STABILITY

The test devices supplied can be stored at room temperature or refrigerated (2-28°C) and will remain stable until the expiration date. **Do Not Freeze.**

SAMPLE COLLECTION AND PREPARATION

The fresh urine samples should be collected in a clean, dry container such that same-day testing may be performed. Urine specimens may be refrigerated at 2-8°C for 48hours, or frozen at -20°C for assaying at a later date. Specimens that have been refrigerated or frozen must be equilibrated to room temperature before testing. Urine samples exhibiting visible precipitates should be filtered, centrifuged or allowed to settle so that clear aliquots can be obtained for testing.

ASSAY PROCEDURE

Do not open foil pouch until ready to begin testing. Refrigerated test device should be allowed to equilibrate to room temperature (15-28°C) before pouch is opened.
Remove the test device from the sealed foil pouch by tearing along the notch.

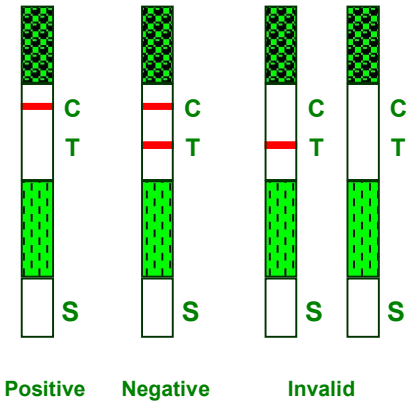
FOR TEST STRIP: Immerse the strips in urine with the arrow end pointing towards the urine. Do not introduce urine above the maximum level, as indicated by the arrows.
FOR TEST CARD: Draw the urine sample into the pipette and dispense four drops (approximately 0.2ml) into the sample well of test device.
Read the test result at five minutes.

IMPORTANT: In order to prevent an incorrect reading, do not read the test results after more than 10 minutes. After 10 minutes, the intensity of the colored lines may change or a new line may appear. To avoid confusion, discard the test device after interpreting the result.

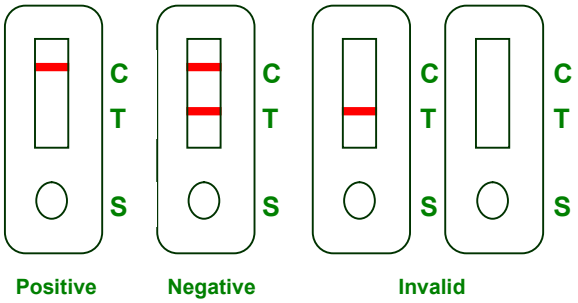
INTERPRETATION OF RESULTS

Negative: Two pink-colored bands appear, one in the control region and one in the test region. A negative result indicates free drug is absent from urine or at concentrations lower than the detection cut-off level of the test.
Positive: One pink-colored band appears in the control region with no apparent band appearing in the test region. A positive result indicates free drug is present in urine at concentrations at or exceeding the detection cut-off level of the test.
Invalid: No band appears in the control region, or a pink-colored band appears in the test region only. An invalid test result may be due to improper assay procedures or damage to the device. With an invalid result, the assay is inconclusive and the specimen should be re-tested using a new test device.
Note: The test band intensity may be weaker or stronger than that of the control band.

TEST STRIPS



TEST CARDS



PROCESS AND QUALITY CONTROL

Good laboratory practice requires use of control materials that ensure proper test device performance and reliability. Quality control standards are available for the validation of device functionality from commercial sources such as BioRad, Alltech and Biopool. To test the quality of control standards, use the assay procedure for testing urine samples. The SAMHSA recommended guidelines for drugs of abuse screening test devices indicate that controls should contain the drug of abuse analyte at levels at least 25% above cut-off values.

AFTER TESTING

Urine specimens may be potentially infectious. Avoid contact with skin by wearing gloves and proper laboratory attire. Properly handle and dispose of all used test devices in an approved biohazard container.

Residual urine should be disposed of in a medically approved manner after the completion of all testing, including the confirmatory assay.

PERFORMANCE CHARACTERISTICS

SENSITIVITY

The DRG Methamphetamine Screen Tests have been designed for detection of methamphetamine and its metabolites in urine at the detection sensitivity of 1000 ng/ml as suggested for immunoassay methods by SAMHSA. In sensitivity studies performed, concentrations of methamphetamine equal to or higher than 1000 ng/ml were identified as positive for all samples. Thus, the cut-off level of the DRG® Methamphetamine Screen Test was determined to be 1000 ng/ml for both the Test Card and Test Strip devices.

PRECISION

In order to determine the precision of both the DRG® Methamphetamine Screen Test Card and Test Strip devices, both within-lot and inter-lot reproducibility analytical studies were performed. Results of within-lot reproducibility analytical studies clearly showed excellent repeatability for all positive and negative urine samples using one lot of the DRG® Methamphetamine Screen Test Card devices and one of Test Strip devices. The results of inter-lot reproducibility studies clearly demonstrated that there was no appreciable inter-lot variation when testing both positive and negative samples across three different lots of DRG® Methamphetamine Screen Test Card and Test Strip devices.

SPECIFICITY STUDY

Device specificity was tested against compounds related to, or not associated with, methamphetamine, prepared in drug-free, normal human urine. The following compounds produced positive results with the DRG® Methamphetamine Screen Test at levels at or greater than the concentrations listed below.

(+)-Methamphetamine	1,000ng/ml
(±) 3,4-Methylenedioxymethamphetamine	2,500ng/ml
Procaine	10,000ng/ml
(-)-Methamphetamine	25,000ng/ml
D-(+)-Amphetamine	50,000ng/ml
Chloroquine	50,000ng/ml
(±)-Ephedrine	50,000ng/ml
β-Phenylethylamine	50,000ng/ml
Ranitidine	50,000ng/ml

The following compounds were found not to have any impact on negative results when tested at levels of up to 100 µg drug/ml (100,000 ng drug/ml).

Acetaminophen (N-Acetyl-p-aminophenol)
Acetone
Albumin
Amitriptyline
L-Amphetamine
Ampicillin
Aspartame (Asp-Phe Methyl Ester)
Aspirin (Acetylsalicylic Acid)
Atropine
Benzocaine (Ethyl p-Aminobenzoate)
Benzoylecgonine
Bilirubin
Caffeine
(+)-Chlorpheniramine
(+/-)-Chlorpheniramine
Creatine
Dexbrompheniramine ([+]-Brompheniramine)
Dextromethorphan
Diazepam
4-Dimethylaminoantipyrine
Dopamine (3-Hydroxytyramine)
Erythromycin
Ethanol
Furosemide
Glucose
Guaiacol glyceryl ether
Hemoglobin
Imipramine
(+/-)-Isoproterenol
(+)-Naproxen
(+/-)-Norephedrine
Oxalic Acid
Penicillin-G (Benzylpenicillin)
Pheniramine
Phenothiazine (Thiodiphenylamine)
Quinidine
Sulindac
Thioridazine
Trifluoperazine
Tyramine
Vitamin C (L-Ascorbic Acid)

ASSAY COMPARISONS & EQUIVALENCY

Accuracy and equivalency comparisons of both the DRG® Methamphetamine Screen Test Card and Test Strip were evaluated against 120 individual in-house laboratory urine samples, as well as against 300 individual external SAMHSA-certified clinical laboratory urine samples. The results have been tabulated below.

Table 1. DRG® Methamphetamine Card vs. Emit® II

DRG	EMIT II (+)	EMIT II (-)	Row Totals
(+)	201	3	204
(-)	5	211	216
Col. Totals	206	214	420

When compared to Emit® II, the percent agreement with DRG® Methamphetamine Screen Test Card positive samples was 201/206 or 97.6%. Negative samples recovered at 211/214 or 98.6%, while the overall relative accuracy obtained was 412/420 or 98.1%.

Table 2. DRG Methamphetamine Strip vs. Emit® II

DRG	EMIT II (+)	EMIT II (-)	Row Totals
(+)	205	3	208
(-)	1	211	212
Col. Totals	206	214	420

When compared to Emit® II, the percent agreement with the DRG® Methamphetamine Screen Test Strip positive samples was 205/206 or 99.5%. Negative samples recovered at 211/214 or 98.6%, while the overall relative accuracy obtained was 416/420 or 99.1%.

Table 3. DRG Methamphetamine Card vs. GC/MS

DRG®	GC/MS (+)	GC/MS (-)	Row Totals
(+)	133	3	136
(-)	0	164	164
Col. Totals	133	167	300

When compared to the GC/MS data, the relative sensitivity or percent agreement of DRG Methamphetamine Screen Test Card positive samples with the external clinical study was 133/133 or 100%. Negative samples recovered a relative specificity of agreement of 164/167 or 98.2%. Finally, the overall relative accuracy obtained was 297/300 or 99.0%.

Table 4. DRG Methamphetamine Strip vs. GC/MS

DRG®	GC/MS (+)	GC/MS (-)	Row Totals
(+)	133	5	138
(-)	0	162	162
Col. Totals	133	167	300

When compared to the GC/MS data, the relative sensitivity or percent agreement of DRG® Methamphetamine Screen Test Strip positive samples with the external clinical study was 133/133 or 100%. Negative samples recovered a relative specificity of agreement of 162/167 or 97.0%. Finally, the overall relative accuracy obtained was 295/300 or 98.3%.

LIMITATIONS OF PROCEDURE

This diagnostic test is designed for the medical or forensic in vitro detection of methamphetamine and its metabolites in human urine.
This diagnostic test only provides a qualitative screening for methamphetamine in urine. It is not to be used for the quantitative determination of methamphetamine in urine. A positive result with this test indicates only the presence of methamphetamine and its metabolites and should be confirmed by GC/MS. It does not indicate intoxication.
There is a possibility of false positive results due to user error or the presence of interfering factors in urine. See "SPECIFICITY STUDY" for substances that produce positive results at high concentrations and those substances that do not interfere with test performance.
Adulterants, such as bleach or other strong oxidizing agents, may produce erroneous test results when added to urine specimens, regardless of the analysis method used. If an adulteration is suspected, a fresh urine specimen should be used.

BIBLIOGRAPHY

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