

2. Specificity

The following table lists compounds that are detected by DOA panel test, which produced positive results when tested at levels equal or greater than the concentrations listed below:

| Test | Compounds | Cut-off (ng/ml) |
|-------------------------|---|----------------------|
| Amphetamine | D-Amphetamine | 1,000 |
| | D/L-Amphetamine | 2,000 |
| | (±)3,4-Methylenedioxyamphetamine | 2,500 |
| | l-Amphetamine | 30,000 |
| | (+)methamphetamine | > 100 µg/ml |
| | (±)3,4-Methylenedioxymethamphetamine | > 100 µg/ml |
| Methamphetamine | (+)Methamphetamine | 1000 |
| | (±)3,4-Methylenedioxy-methamphetamine (Ecstasy) | > 100 µg/ml |
| | d-Amphetamine | > 100 µg/ml |
| | l-Amphetamine | > 100 µg/ml |
| | (±)3,4-Methylenedi- oxyamphetamine | > 100 µg/ml |
| | Chloroquine | > 100 µg/ml |
| | (-)Ephedrine | > 100 µg/ml |
| | β-Phenylethylamine | > 100 µg/ml |
| | Procaine | > 100 µg/ml |
| | d-Pseudoephedrine | > 100 µg/ml |
| | Randitidinr | > 100 µg/ml |
| Cocaine | Benzoylcegonine | 300 |
| | Cocaine | 30,000 |
| Opiate | Morphine | 2,000 |
| | Codeine | 2,000 |
| | Diacetylmorphine(Heroin) | 2,000 |
| | Ethylmorphine | 600 |
| | Hydromorphone | 15,000 |
| | Hydrocodone | 15,000 |
| | Merperidine | >100,000 |
| | 6-Monoacetylmorphine (6-MAM) | 5,000 |
| | Morphine-3-β-d-glucuronide | 10,000 |
| | Oxycodone | >20,000 |
| | Oxymorphone | >20,000 |
| | Rifampicine | >50,000 |
| | Thebaine | 20,000 |
| | THC | 11-nor-Δ9-THC-9-COOH |
| 11-nor-Δ8-THC-9-COOH | | 37.5 |
| 11-hydroxy-Δ9-THC | | 5000 |
| Δ8-Tetrahydrocannabinol | | 15000 |
| Δ9-Tetrahydrocannabinol | | 25000 |

The following compounds show no cross-reactivity at concentration up to 100 µg/ml unless specified.

| | | | |
|------------------------|---------------------|----------------------|------------------|
| Acetaminophen | 4-Acetamidophenol | Acetylsalicylic acid | Amikacin |
| Amitriptyline | Arterenol | Aspartame | Ascorbic acid |
| Atrophine | Caffeine | Camphor | Chloroquine |
| Chlopheniramine | Cortisone | Deoxyephedrine | Dextromethorphan |
| Diglotxin | Digoxin | Diphenhydramine | Ecgonine |
| Ecgonine methyl ester | Ephedrine | Epinephrine | Gentisic acid |
| Guaiaicol glycer ester | Histamine | Hydrochlorothiazide | Homatrophine |
| Imipramine | Ibuprofen | Isoproterenol | Ketamine |
| Lidocaine | Meperidine | Methaqualon | Methylphenidate |
| Neomycin | Niacinamide | Perphenazine | Penicillin G |
| Phenylethylamine-□ | Phenylpropanolamine | Promethazine | Pseudoephedrine |
| Quinine antidine | Salicylic acid | Tetracycline | Tetrahydrozoline |
| Theophylline | Thioridazine | Trifluoperazine | Tryptophan |

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DTA Pty Ltd, Australia
1066E Beaufort Street, Unit 6-7, Bedford WA 6052
PO Box 109, Inglewood WA 6932
email@drugtesting.com.au
www.drugtesting.com.au

DTA Pty Ltd, South Africa
PO Box 1661, Sun Valley 7985 Cape Town
email@drugtesting.co.za
www.drugtesting.co.za

DTP Ltd, New Zealand
PO Box 5066, Whangarai 0101
email@drugtesting.net.nz
www.drugtesting.net.nz

DTA Pty Ltd, Europe
PO Box 1614, DK- 2720 Vanløse
email@drugtesting.dk
www.drugtesting.dk

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It is highly recommended that these test be performed under the guidance of a registered medical practitioner.

The manufacturer, distributor and pharmacy do not accept any liability whatsoever for any consequent actions resulting from the interpretations of the product/s supplied.

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AccuTest™ 5B DOA PANEL TEST

FOR THE QUALITATIVE ASSESSMENT OF DRUGS AND THEIR METABOLITES IN HUMAN URINE



For in vitro Diagnostic and Forensic Use

INTENDED USE

All of DOA Panel Test is an immunochromatography based one step in vitro test. It is designed for qualitative determination of drug substances in human urine specimens. This assay may be used in the point of care setting. Below is a list of cut-off concentrations for each drug using our test.

| | |
|-------------------------------|----------------------------------|
| Amphetamine | 300 ng/ml of d-amphetamine |
| Methamphetamine (Ecstasy/TIK) | 500 ng/ml of (+) methamphetamine |
| Cocaine | 300 ng/ml of benzoylcegonine |
| Opiate* | 2,000 ng/ml of morphine |
| Cannabinoid (THC) | 50 ng/ml of 11-nor-Δ9-THC-9-COOH |

This assay provides only a preliminary analytical test result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. The Substance Abuse Mental Health Services Administration (SAMHSA) has established gas chromatography/ mass spectrometry (GC/MS) as 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 indicated.

* SAMHSA recommends a cut-off concentration of 2000 ng/ml for Opiates Test

Amphetamines are a class of potent sympathomimetic agents with therapeutic applications. The most common amphetamines are d-amphetamine and d,l-amphetamine. Amphetamines are central nervous stimulants that cause the neurotransmitters epinephrine, norepinephrine and dopamine to be released into the brain and body giving users feelings of euphoria, alertness, and increased energy. Chronic abuse of amphetamine leads to tolerance and drug reinforcement effect. Cardiovascular responses to amphetamine include increased blood pressure and cardiac arrhythmias. More acute responses produce anxiety, paranoia, hallucinations and psychotic behavior. Amphetamine is metabolized by a number of pathways. In general, acid urine promotes excretion whereas alkaline urine retards it. In 24 hours, approximately 79% of the amphetamine dose is excreted in acid urine and about 45% in alkaline urine. Typically, about 20% is excreted as unchanged amphetamine. Unchanged amphetamine can be detected up to 1 –2 days after use.

Methamphetamine is the most popular synthetic derivative of the amphetamines. It is a potent sympathomimetic agent with therapeutic applications. Acute large doses lead to enhanced stimulation of the central nervous system and induce euphoria, alertness, reduced appetite, and a sense of increased energy and power. More acute response produces anxiety, paranoia, psychotic behavior, and cardiac dysrhythmias. Methamphetamine is excreted in the urine as amphetamine and oxidized and deaminated derivatives. However, 10-40% of methamphetamine is excreted unchanged. Methamphetamine is generally detectable in the urine for 3 to 5 days after use.

Cocaine Derived from the leaves of cocoa plant, cocaine is a potent central nervous system stimulant as well as a local anesthetic. Some of the psychological effects induced by cocaine are: euphoria, confidence and a sense of increased energy, accompanied by increased heart rate, dilation of the pupils, fever, tremors and sweating. Continued ingestion of cocaine could induce tolerances and physiological dependency; which leads to its abuse. Cocaine is used by smoking, intravenous, intranasal or oral administration and excreted in the urine primarily as benzoylcegonine in a short period. Benzoylcegonine has a biological half-life of 5 – 8 hours, which is much longer than that of cocaine (0.5 – 1.5 hours), and can be generally detected for 12 – 72 hours after cocaine use or exposure.

Opiate Opioid analgesics comprised of a large group of substances that control pain by depressing the central nervous system. Acute high dose used by abusers or addicts can cause depressed coordination, disrupted decision, decreased respiration, hypothermia and coma. Morphine is excreted un-metabolized and is the marker metabolic product of opiates. Morphine and morphine glucuronide is detectable in urine for several days after opiates dose.

THC The agents of Marijuana that cause various biological effects in humans are called cannabinoid. Cannabinoid is a central nervous stimulant that alters mood and sensory perceptions, produces loss of coordination, impairs short term memory, and produces symptoms of anxiety, paranoia, depression, confusion, hallucination, and increased heart rate. Large doses of cannabinoid could cause the development of tolerances and physiological dependency and lead to abuse. A tolerance to the cardiac and psychotropic effects can occur and withdrawal syndrome produces restlessness, insomnia, anorexia and nausea. Δ9-THC is the primary active ingredient in cannabinoids. The main metabolite excreted in the urine is 11-nor -Δ9-THC-9-COOH, which are found within hours of exposure and remain detectable in the urine for 3- 10 days after smoking.

PRINCIPLE

Each component strip of DOA Panel is based on the principle of specific immunochemical reaction between antibodies and antigen to analyze particular compound in human urine specimen. The assay relies on the competition for binding antibody. When drug is present

in the urine specimen, it competes with drug conjugate for the limited amount of antibody dye conjugate. When the amount of drug is equal or more than the cut-off, it will prevent the binding of drug conjugate to the antibody. Therefore, a positive urine specimen will not show a colored band on the test line zone, indicating a positive result, while the presence of a colored band indicates a negative result. A control line is present in the test window to work as procedural control. This colored band should always appear on the control line zone if the test device is stored in good condition and the test is performed appropriately.

MATERIAL PROVIDED

1. A DOA Panel Test device..

2. The amount of each coated antigen and/or antibody on the strip is less than 1.0 mg for antigen conjugate and is less than 1.0 mg for goat anti- mouse IgG antibody. Test zone: contains drug bovine protein antigen conjugates Control zone: contains Goat anti-mouse IgG antibody Conjugate pad: contains mice monoclonal anti-drug antibody. Instruction for use.

MATERIAL REQUIRED BUT NOT PROVIDED

1. Urine collection container.
2. Timer or clock.

WARNINGS AND PRECAUTIONS

1. For in vitro diagnostic and professional use only.
2. Do not use the test device beyond the expiration date.
3. Urine specimens may be infectious; properly handle and dispose of all used reaction devices in a biohazard container.
4. Visually inspect the foil package to insure it is intact. If the package is not intact, the integrity of the device might be compromised.
5. Use a new urine specimen cup for each sample to avoid cross contamination.

STORAGE AND STABILITY

The test device should be stored at 2°C to 28°C; **do not freeze** and will be effective until the expiration date stated on the package. The product is humidity-sensitive and should be used immediately after being open. Any improperly sealed product should be discarded.

SPECIMEN COLLECTION AND PREPARATION

Fresh urine does not require any special handling or pretreatment. Specimen should be collected in a clean, dry, plastic or glass container. If the assay is not performed immediately, urine specimen may be refrigerated at 2- 8 °C or frozen up to 7 days. Specimens should be brought to room temperature before testing. Urine specimens exhibiting a large amount of precipitate or turbidity should be centrifuged or allowed to settle before testing. Avoid contact with skin by wearing gloves and proper laboratory attire.

QUALITY CONTROL

Good Laboratory practice recommends the daily use of control materials to validate the reliability of device. Control materials should be assayed as clinical specimen and challenging to the assay cutoff concentration, e.g., 25% above and below cutoff concentration. If control values do not fall within establish range, assay results are invalid. Control materials that are not provided with this test kit are commercially available.

The Rapid Drugs of Abuse Test provides a built-in process control with a different antigen/antibody reaction at the control region (C). This control line should always appear regardless the presence of drug or metabolite. If the control line does not appear, the test device should be discarded and the obtained result is invalid. The presence of this control band in the control region serve as 1) verification that sufficient volume is added, 2) that proper flow is obtained.

PROCEDURE

1. Bring all materials and specimens to room temperature.
2. Remove the test card from sealed foil pouch.
3. Place the sample pad end into the urine specimen being careful to hold each pad in the urine without touching the plastic card.
4. Hold the card in the urine for 10 seconds, remove from the urine and replace the cap.

Do not interpret the result after 5 minutes. Waiting more than five minutes may cause the reading to be inaccurate. To avoid confusion, discard the test device after interpreting the result.

INTERPRETATION OF RESULTS

Negative:

Two colored bands form on any strip of the card. The appearance of two colored bands, one in test line zone and the other in control line zone, indicates negative result for that particular test(s). The negative result does not indicate the absence of drug in the specimen; it only indicates the level of tested drug in the specimen is less than cut-off level.

Positive:

One colored band appears in control line zone. No colored band is found in test line zone. This is an indication the level of tested drug(s) in the specimen is above the cut- off level.

Invalid:

If there is no colored band in control line zone of any strip, the test result is invalid. Retest the sample with a new device.

Note: A borderline(+/-) in test line zone should be considered negative result.

LIMITATION 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 processed urine error as well other substances in certain foods and medicines may interfere with the test and cause false results. Please refer "SPECIFICITY" section for lists of substances that will produce either positive results, or that do not interfere with test performance. If a drug/metabolite is found present in the urine specimen, the assay does not indicate frequency of drug use or distinguish between drug of abuse and certain foods and medicines.

EXPECTED RESULTS

The DOA Panel Test is a qualitative assay. It identifies the drug(s) in human urine at its cut-off concentration or higher. The concentration of the drug(s) cannot be determined by this assay. The test is intended to distinguish negative result from presumptive positive result. All positive results must be confirmed using an alternate method, preferably GC/MS.

PERFORMANCE CHARACTERISTICS

A. Accuracy

The accuracy of the DOA test panels were evaluated in each component strip and in comparison to GC/MS method at the following concentration: d-amphetamine 1000ng/ml (AMP), oxazepam, 300 ng/ml (BZO), benzoylcegonine 300ng/ml (COC), morphine 300 ng/ml (OPI), and 11-nor-?9-THC-9-COOH 50ng/ml (THC). The results of each component strip are listed as follows:

1. **Amphetamine** The accuracy of the amphetamine test was evaluated in comparison to GC/MS method at a cut-off of 1000 ng/ml. Eighty one (81) urine specimens with GC/MS confirmed d-amphetamine concentration were evaluated in this study. The results are summarized and presented below:

| Rapid AMP Test | (-) | | (+)) | | Percent agreement with GC/MS |
|----------------|---|--|---|--|------------------------------|
| | GC/MS Negative (Less than -25% cut off) | Near cutoff Negative (between - 25% and cut off) | Near cutoff positive (between cut off & +25%) | GC/MS Positive (Greater than +25% cut off) | |
| Positive | 2 | 1 | 8 | 26 | 92 |
| Negative | 43 | 0 | 1 | 0 | 98 |
| Total | 45 | 1 | 9 | 26 | N=81 |

Positive % agreement: 92, Negative % agreement: 98

Four specimens were found discrepant between the RapidAMP and the GC/MS method. When compared those data, 50% (2 out of 4) of the discrepancy specimens were found between +25% to -25% of cutoff concentration (750-1250 ng/ml).

2. **Methamphetamine** The accuracy of the methamphetamine test was evaluated in comparison to GC/MS at a cut-off of 1000 ng/ml of (+) methamphetamine. Eighty (80) urine specimens with GC/MS confirmed (+) methamphetamine concentration were evaluated in this study. The results are summarized and presented below.

| Rapid MET Test | (-) | | (+)) | | Percent agreement with GC/MS |
|----------------|---|---|---|--|------------------------------|
| | GC/MS Negative (Less than -25% cut off) | Near cutoff Negative (between -25% and cut off) | Near cutoff positive (between cut off & +25%) | GC/MS Positive (Greater than +25% cut off) | |
| Positive | 0 | 2 | 4 | 31 | 95% |
| Negative | 40 | 3 | 0 | 0 | 100% |
| Total | 40 | 5 | 4 | 31 | N = 80 |

Positive % agreement: 95, Negative % agreement: 100

Two specimens were found discrepant between the Rapid MET and GC/MS method. When compared those data, 100% (2 out of 2) of the discrepancy specimens were found between -25% and cut-off concentration (750 – 1000 ng/ml).

3. **Cocaine** The accuracy of the cocaine test was evaluated in comparison to GC/MS at a cut-off of 300 ng/ml of benzoylcegonine. Eighty-one (81) urine specimens with GC/MS confirmed benzoylcegonine concentration was valuated in this study. The results are summarized and presented below:

| Rapid COC Test | (-) | | (+)) | | Percent agreement with GC/MS |
|----------------|---|---|---|--|------------------------------|
| | GC/MS Negative (Less than -25% cut off) | Near cutoff Negative (between -25% and cut off) | Near cutoff positive (between cut off & +25%) | GC/MS Positive (Greater than +25% cut off) | |
| Positive | 0 | 2 | 3 | 31 | 94 |
| Negative | 41 | 4 | 0 | 0 | 100 |
| Total | 42 | 6 | 3 | 31 | N = 81 |

Positive % agreement: 94, Negative % agreement: 100

Two specimens were found discrepant between the RapidCOC and GC/MS method. When compared those data, 100% (2 out of 2) of the discrepancy specimens were found between -25% and +25% cut-off concentration (225 – 375 ng/ml).

5. **Opiate** The accuracy of the opiates test was evaluated in comparison to GC/MS at a cut -off of 300 ng/ml of morphine. One hundred and twenty three (123) urine specimens with GC/MS confirmed morphine and codeine concentrations were evaluated in this study. The results are summarized and presented:

| Rapid OPI Test | (-) | | (+)) | | Percent agreement with GC/MS |
|----------------|---|--|---|--|------------------------------|
| | GC/MS Negative (Less than -25% cut off) | Near cutoff Negative (between - 25% and cut off) | Near cutoff positive (between cut off & +25%) | GC/MS Positive (Greater than +25% cut off) | |
| Positive | 0 | 2 | 5 | 70 | 97.4% |
| Negative | 35 | 7 | 1 | 3 | 91.3% |
| Total | 35 | 9 | 6 | 73 | N = 125 |

Positive % agreement: 97.4, Negative % agreement: 91.3

Six specimens were found discrepant between the Rapid OPI and GC/MS method. When compared those data, 50% (3 out of 6) of the discrepancy specimens were found between -25% and +25% cut-off concentration (225 – 375ng/ml).

5. **THC** The accuracy of the THC test was evaluated in comparison to GC/MS at a cut-off of 50 ng/ml of 11-nor-?9-THC-9-COOH. Eighty-eight (88) urine specimens with GC/MS confirmed 11-nor-?9-THC-9-COOH concentration were evaluated in this study. The results are summarized and presented below:

| Rapid THC Test | (-) | | (+)) | | Percent agreement with GC/MS |
|----------------|---|--|---|--|------------------------------|
| | GC/MS Negative (Less than -25% cut off) | Near cutoff Negative (between - 25% and cut off) | Near cutoff positive (between cut off & +25%) | GC/MS Positive (Greater than +25% cut off) | |
| Positive | 1 | 1 | 3 | 35 | 95% |
| Negative | 44 | 4 | 0 | 0 | 100% |
| Total | 45 | 5 | 3 | 35 | N = 88 |

Positive % agreement: 95, Negative % agreement: 100

Two specimens were found discrepant between the Rapid THC and GC/MS method. When compared those data, 50% (1 out of 2) of the discrepancy specimens were found between -25% and cut-off concentration (37.5 – 50 ng/ml).

B. Sensitivity

The cut-off concentrations (sensitivity level) of DOA panel test are determined to be:

- AMP 1000 ng/ml,
- MET 1000 ng/ml
- COC 300 ng/ml
- OPI 300 ng/ml
- THC 50 ng/ml.

C. Precision

The precision of DOA panel tests were determined by conducting the test with spiked controls and interpreted the results by three individuals to verify the random error of visual interpretation. The results of 50% above and 50% below cut-off specimens are 100% agreed by three observers:

| Tested Drug | Concentration (ng/ml) | Number Tested | Corrected Result | % Corrected Result |
|-------------|-----------------------|---------------|------------------|--------------------|
| AMP | 500 | 40 | 40 | 100 |
| | 1500 | 40 | 40 | 100 |
| MET | 500 | 40 | 40 | 100 |
| | 1500 | 40 | 40 | 100 |
| COC | 150 | 40 | 40 | 100 |
| | 450 | 40 | 40 | 100 |
| OPI | 150 | 40 | 40 | 100 |
| | 2150 | 40 | 40 | 100 |
| THC | 25 | 40 | 40 | 100 |
| | 75 | 40 | 40 | 100 |

D. Specificity

The specificity for adding various drugs, drug metabolites tested DOA panel test, and other compounds that are likely to be present in urine. All compounds were prepared in drug -free normal human urine.

1. Interference testing

The DOA panel test performance at cut-off level is not affected when pH and Specific Gravity ranges of urine specimen are at 4.5 to 9.0 and 1.005 to 1.035.

The following substances were tested and confirmed did not interfere with DOA panel tests at the listed concentrations.

- Glucose 2000 mg/dl
- Human albumin 2000 mg/dl
- Human hemoglobin 10 mg/dl
- Urea 4000 mg/dl
- Uric acid 10 mg/dl