

AccuSign® DOA 6

THC/COC/MET/AMP/OPI/BZO

One-Step Panel Assay for Drugs of Abuse

For *In Vitro* Use Only

Simple One-Step Immunoassay for the Qualitative Detection of THC, Cocaine, Methamphetamine, Amphetamine, Opiates, Benzodiazepines and/or their Metabolites in Urine

PBM

Catalog No.	DOA-260	35 Test Kit
	DOA-260-10	10 Test Kit

Intended Use

AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO test is a simple, one-step, immunochromatographic assay for the rapid, qualitative detection of THC, cocaine, methamphetamine, amphetamine, opiates, benzodiazepines, and/or their metabolites present in human urine at the cutoff concentration of the drug specified.

*The AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO test provides only a preliminary analytical result. A more specific alternative chemical method must be used in order to obtain a confirmed analytical result. Gas chromatography, mass spectrometry (GC/MS) is the preferred confirmatory method. Other chemical confirmatory methods are available. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are used.*²

Summary and Explanation

THC (Δ^9 -tetrahydrocannabinol) is the primary active ingredient in cannabinoids (marijuana). When ingested or smoked, it produces euphoric effects. Users experience impairment of short term memory and THC use slows learning. Also, it may cause transient episodes of confusion, anxiety, or frank toxic delirium. Long term, relatively heavy use may be associated with behavioral disorders. The peak effect of smoking THC 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.¹

Cocaine, derived from the leaves of coca plant, is a potent central nervous system (CNS) stimulant and a local anesthetic. Cocaine induces euphoria, confidence and a sense of increased energy in the user; these psychological effects are accompanied by increased heart rate, dilation of the pupils, fever, tremors and sweating. Cocaine is used by smoking, intravenous, intranasal or oral administration, and excreted in the urine primarily as benzoylecgonine in a short time. Benzoylecgonine has a longer biological half-life (5–8 hours) than cocaine (0.5–1.5 hours) and can generally be detected for 24–60 hours after cocaine use or exposure.^{3,5}

Methamphetamine is a potent sympathomimetic agent with therapeutic applications. 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 include 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 amphetamine and oxidized and deaminated derivatives. However, 10–20% of methamphetamine is excreted unchanged. Thus, the presence of the parent compound in the urine indicates methamphetamine use. Methamphetamine is generally detectable in the urine for 3–5 days, depending on urine pH level.⁴

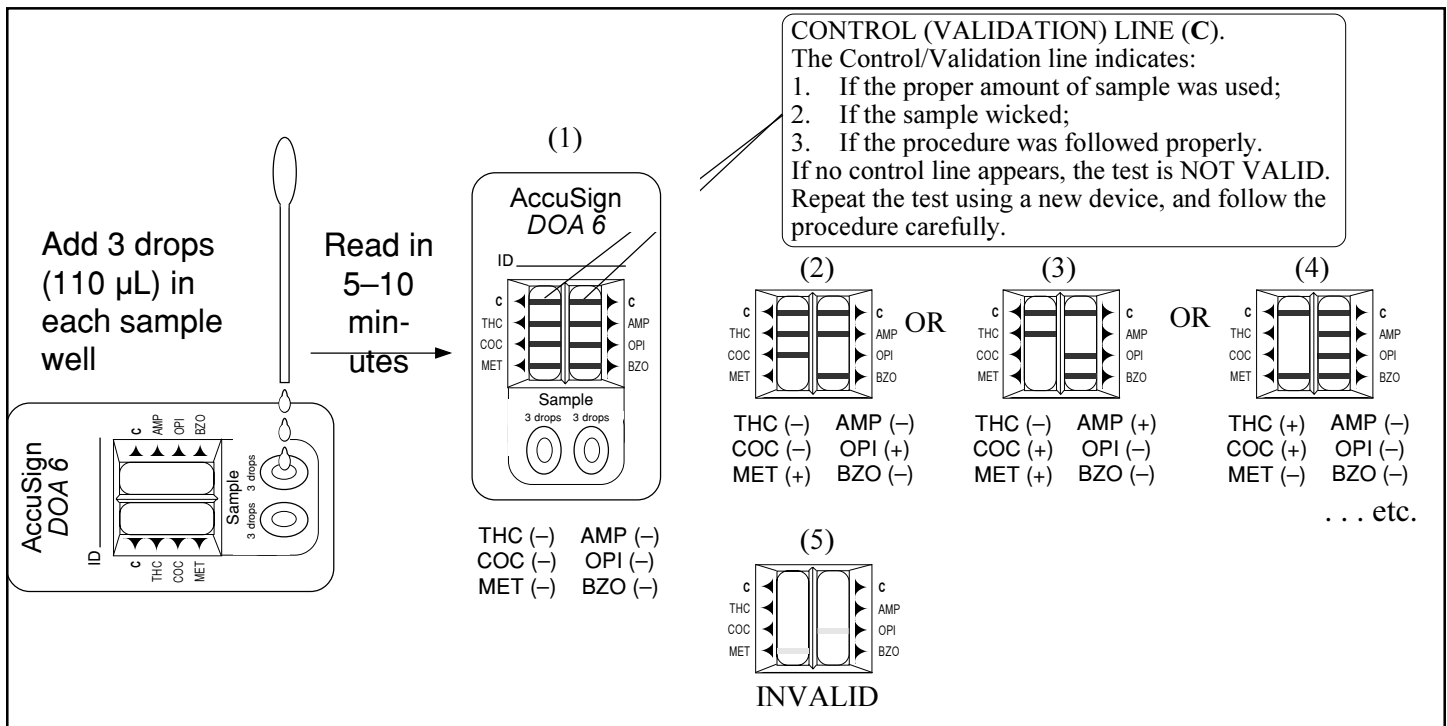
Amphetamine is a potent sympathomimetic agent with therapeutic applications. The drug can be taken orally, injected, or inhaled. Acute higher doses lead to enhanced stimulation of the central nervous system and induce euphoria, alertness, reduced appetite, and a sense of increased energy and power.⁵ Cardiovascular responses to amphetamine include increased blood pressure and cardiac arrhythmias. More acute responses include anxiety, paranoia, hallucinations, psychotic behavior, and eventually, depression and exhaustion. The effects of amphetamine generally last 2–4 hours, and the drug has a half-life of 9–24 hours in the body. Amphetamine is excreted in the urine in unchanged form and also as hydroxylated and deaminated derivatives.^{3,6}

Morphine, codeine, and semisynthetic derivatives of morphine belong to the class of drugs called opiates. An opiate exerts its effects on the central nervous system and can produce euphoria, respiratory depression and coma when it is abused. Morphine is the prototype compound of opiates. Morphine is excreted in the urine as morphine-3-glucuronide, unchanged morphine, and other minor metabolites. Heroin is metabolized to morphine and codeine and excreted in the urine with a small amount of unchanged form. Codeine is also excreted as morphine and in the form of conjugates. Although some opiate metabolites appear in the feces, urinary excretion is the primary route of elimination.^{1,2,3}

Benzodiazepines are a class of widely prescribed central nervous system (CNS) depressants and include widely used drugs such as chlordiazepoxide, diazepam, and oxazepam. They have medically useful properties, including antianxiety, sedative, anticonvulsant, and hypnotic effects. They are taken orally or sometimes by injection, and have a low potential for physical or psychological dependence. Benzodiazepines induce drowsiness and muscle relaxation; however, their use can also result in intoxication, similar to drunken behavior except without evidence of alcohol use, and the loss of inhibitions. Chronic abuse can result in addiction and tardive dyskinesia (involuntary muscle movements of the face, limbs, and trunk). Overdose can result in coma and possible death. Withdrawal syndrome includes anxiety, insomnia, tremors, delirium, and convulsions. The effects of benzodiazepine use last 4–8 hours. The different benzodiazepines are absorbed at different rates, and the timing of their psychoactive effects varies with the absorption rate. The drugs are excreted in the urine primarily as the parent compounds or as oxazepam glucuronide, an inactive metabolite, (in the case of chlordiazepoxide and diazepam) and are detectable for 1–2 days. Oxazepam may be detectable in the urine for up to 7 days.^{2,3}

Principle

The **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** test uses solid-phase chromatographic membrane immunoassay technology for the qualitative, simultaneous detection of THC, cocaine, methamphetamine, amphetamine, opiates, benzodiazepines, and/or their metabolites in human urine. The test is based on the principle of the highly specific immunochemical reactions between antigens and antibodies which are used for the analysis of specific substances in biological fluids. The test relies on the competition between the drug conjugates and the drugs



which may be present in the urine sample, for binding to antibodies. In the test procedure, a sample of urine is placed in the Sample well of the device and is allowed to migrate upward. If the drug is present in the urine sample, it competes with the drug conjugate bound to the dye, for the limited antibodies immobilized on the membrane. If the level of drug or drug metabolite is above the cutoff level, the drug will saturate the antibodies, thus inhibiting the binding of the dye coated with drug conjugates to the antibodies on the membrane. This prevents the formation of a line on the membrane. Therefore, a drug-positive urine sample will not generate a line at the specific drug position in the Result window, indicating a positive result. A negative urine sample will generate a line at the specific drug position in the Result window, indicating a negative result. The same principle of competition is applicable where the drug conjugate is immobilized on the membrane and the antibody is coated on the dye.

In addition to the Test line(s) that may appear in the Result window, a Control line is present to confirm the viability of the test. This Control line (validation line) should always appear if the test is conducted properly. Polyclonal sheep anti-mouse IgG antibody is immobilized on the control line. The monoclonal antibody-dye conjugates that pass the line will be captured and produce a colored line at the Control position (C). This works as a procedural control, confirming that proper sample volume was used and the reagent system at the Control line and the conjugate-color indicator worked properly. If insufficient sample volume is used, there may not be a Control line, indicating the test is invalid.

Materials Provided

The **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** test kit contains all the reagents necessary to perform the assay.

- **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** device. The test device contains membrane strips and dye pads: Membrane strips are coated with THC-protein (a purified bovine protein) conjugate, monoclonal anti-morphine, anti-methamphetamine, anti-benzoylcegonine, anti-amphetamine, as well as polyclonal anti-benzodiazepine antibodies. Dye pads contain dye coated with monoclonal anti-THC antibody as well as conjugates of morphine, benzoylcegonine, amphetamine, and oxazepam (each drug is conjugated with a purified bovine protein).
- Disposable sample dispenser.
- Instructions for use.

Precautions

- For *in vitro* diagnostic use only.
- Avoid cross contamination of urine samples by using a new urine specimen container and dropper for each urine sample.
- The test kit does not contain any HIV or hepatitis infective components.
- Urine specimens are potentially infectious. Proper handling and disposal methods should be established according to good laboratory practices.
- The **AccuSign®** device should remain in its original sealed pouch until ready for use. Do not use the test if the pouch is damaged or the seal is broken.
- Do not use the test kit after the expiration date.

Storage and Stability

The **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** test kit should be stored at 2–30°C (35–86°F) in the original sealed pouch. The expiration dating was established under these storage conditions.

Specimen Collection and Preparation

Approximately 110 µL of urine sample is required for each test sample well. Fresh urine specimens do not require any special handling or pretreatment. Specimens should be collected in a clean glass or plastic container. If testing will not be performed immediately, specimens should be refrigerated (2–8°C) or frozen. Frozen specimens must be completely thawed, and thoroughly mixed before using.

Specimens containing a large amount of particulate matter may give inconsistent test results. Such specimens should be clarified by centrifuging or allowing to settle before testing.

Test Procedure

The test procedure consists of adding the urine sample to the Sample well of the device and watching for the appearance of colored lines in the result window.

Test Protocol

1. For each test, open one AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO pouch and label the AccuSign® device with the patient ID.
2. Holding the dropper vertically, dispense 3 drops (110 µL) of the urine sample into the each Sample well (S).
3. Read the result after 3 minutes, but within 10 minutes of sample addition.

Interpretation of Results

Negative: The appearance of a reddish-purple Control line (C) and a line at a specific drug position indicates a negative test result; i.e., no drug above the cutoff level has been detected. The color intensities of the Control line and a specific drug line may not be equal. *Any faint line at the specific drug position, visible in 10 minutes, should be interpreted as negative. A negative test result does not indicate the absence of drug in the sample, it only indicates the sample does not contain drug above the cutoff level in qualitative terms.*

Positive: The appearance of a reddish-purple Control line and no distinct line next to a specific drug name indicates the test result is positive for that drug (i.e., the specimen contains the drug at a concentration above the cutoff level). *A positive test result does not provide any indication of the level of intoxication or urinary concentration of the drug in the sample, it only indicates the sample contains drug above the cutoff level in qualitative terms.*

Invalid: A distinct Control line (C) should always appear. The test is invalid if no Control line forms at the C position. Such tests should be repeated with a new AccuSign® DOA 6 test device.

Examples of possible results are shown in the diagram in Page 2.

- (1) **THC (-), Cocaine (-), Methamphetamine (-), Cocaine (-), Amphetamine (-), Opiates (-), Benzodiazepines (-):** One line each at two C positions and one each at the **THC, COC, MET, AMP, OPI** and **BZO** positions.
- (2) **THC (-), Cocaine (-), Methamphetamine (+), Amphetamines (-), Opiates (+), Benzodiazepines (-):** One line each at two C positions and one line each at the **THC, COC, AMP** and **BZO** positions; no line at the **MET** and **OPI** position.
- (3) **THC (-), Cocaine (+), Methamphetamine (+), Amphetamines (+), Opiates (-), Benzodiazepines (-):** One line each at two C positions and one line each at the **THC, OPI** and **BZO** positions; no line at the **COC, MET** and **AMP** position.
- (4) **THC (+), Cocaine (+), Methamphetamine (-), Amphetamines (-), Opiates (-), Benzodiazepines (-):** One line each at two C positions one line each at the **MET, OPI, AMP** and **BZO** positions; no lines at the **THC** and **COC** positions.
- (5) **Invalid:** No Control line(s) (C).

Limitations

- The test is designed for use with unadulterated urine only. There is a possibility that factors such as technical or procedural errors, as well as other substances in the urine sample which are not listed in Tables 9 below, may interfere with the test and cause erroneous results.
- Adulterants, such as bleach and/or alum, in urine specimens may produce erroneous results regardless of the method of analysis. If

adulteration is suspected, the test should be repeated with a new sample.

- The test result read after 10 minutes may not be consistent with the original reading obtained within the 10 minute reading period. The test must be read within 10 minutes of sample application.

User Quality Control

Internal Control: Each AccuSign® DOA 6 test device has a built-in control. The Control line is an internal positive procedural control. A distinct reddish-purple Control line should appear at the Control position, if the test procedure is performed properly, an adequate sample volume is used, the sample and reagent are wicking on the membrane, and the test reagents at the control line and the conjugate-color indicator are reactive. In addition, if the test is performed correctly and the device is working properly, the background in the Result window will become clear and provide a distinct result. This may be considered an internal negative procedural control.

The positive and negative procedural controls contained in each AccuSign® DOA 6 test device satisfy the requirements of testing a positive control and a negative control on a daily basis. If the Control line does not appear at the Control position, the test is invalid and a new test should be performed. If the problem persists, contact PBM for technical assistance.

External Control: External controls may also be used to assure that the reagents are working properly and that the assay procedure is followed correctly. It is recommended that a control be tested at regular intervals as good laboratory testing practice. For information on how to obtain controls, contact PBM's Technical Services.

Expected Values

AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO is a qualitative test. The amount of THC, cocaine, methamphetamine, amphetamine, opiates, benzodiazepines and/or their metabolites present in the urine cannot be estimated by the test. The test results distinguish positive from negative samples. Positive results indicate the samples contain THC, cocaine, methamphetamine, amphetamine, opiates, benzodiazepines and/or their metabolites above the cutoff concentration. The **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** test has been shown to detect following cutoff level for each drug: 50 ng/mL of THC, 300 ng/mL of benzoylecgonine, 1000 ng/mL of methamphetamine, 1000 ng/mL of amphetamine, 300 ng/mL of morphine, and 300 ng/mL of oxazepam in urine.

Performance Characteristics

The accuracy of **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** test was evaluated with clinical samples in comparison to a commercially available immunoassay AccuSign® THC, AccuSign® COC, AccuSign® MET, AccuSign® AMP, AccuSign® OPI, AccuSign® BZO, which are proven to be substantially equivalent to Syva's Emit II. The results are shown in Tables 1, 2, 3, 4, 5, and 6. The complete agreement (100%) was observed.

Table 1. THC Accuracy: Comparison of AccuSign® DOA 6 with AccuSign® THC

		AccuSign® THC		Total
		Positive	Negative	
AccuSign® DOA 6 (THC/COC/MET/ AMP/OPI/BZO)	Positive	150	0	150
	Negative	0	200	200
Total		150	200	350

Table 2. Cocaine Accuracy: Comparison of AccuSign® DOA 6 with AccuSign® COC

		AccuSign® COC		Total
		Positive	Negative	
AccuSign® DOA 6 (THC/COC/MET/ AMP/OPI/BZO)	Positive	150	0	150
	Negative	0	200	200
Total		150	200	350

Table 3. Methamphetamine Accuracy: Comparison of AccuSign® DOA 6 with AccuSign® MET

		AccuSign® MET		Total
		Positive	Negative	
AccuSign® DOA 6 (THC/COC/MET/ AMP/OPI/BZO)	Positive	96	0	96
	Negative	0	150	150
Total		96	150	246

Table 4. Amphetamine Accuracy: Comparison of AccuSign® DOA 6 with AccuSign® AMP

		AccuSign® AMP		Total
		Positive	Negative	
AccuSign® DOA 6 (THC/COC/MET/ AMP/OPI/BZO)	Positive	98	0	98
	Negative	0	200	200
Total		98	200	298

Table 5. Opiates Accuracy: Comparison of AccuSign® DOA 6 with AccuSign® OPI

		AccuSign® OPI		Total
		Positive	Negative	
AccuSign® DOA 6 (THC/COC/MET/ AMP/OPI/BZO)	Positive	150	0	150
	Negative	0	200	200
Total		150	200	350

Table 5. Benzodiazepine Accuracy: Comparison of AccuSign® DOA 6 with AccuSign® BZO

		AccuSign® BZO		Total
		Positive	Negative	
AccuSign® DOA 6 (THC/COC/MET/ AMP/OPI/BZO)	Positive	174	0	174
	Negative	0	200	200
Total		174	200	374

In a separate study, **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** test was evaluated against specimens confirmed as positive by GC/MS, for each of the 6 drugs; 37 samples for THC, 41 samples for COC, 15 samples for MET, 40 samples for AMP, 31 samples for OPI, 28 samples for BZO. The results demonstrate the excellent correlation (100%) of **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** with GC/MS.

Precision

The precision of the **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** test was determined by two people performing the test on four different days with serially diluted each standard drug solutions. All samples containing 50% below cutoff level of the drug showed negative results. All samples containing 50 % above cutoff level of the drug showed positive results. The study also included 20 samples of 25% below cutoff level and 20 samples of 25 % above cutoff level for each of the 6 drugs. The results were found to be consistently in agreement with expected test results.

Distribution of Random Error

Forty (40) blind samples for each drug were prepared by spiking various concentrations of each of the 6 drugs and separately tested by two operators. The tested concentrations were 0, 50% below cutoff, 50% above cutoff and 100% above cutoff for each drug. The test results from the two operators showed complete agreement.

Reproducibility

The reproducibility of the test results of the **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** test was examined at three different sites using a total of 35 blind controls. These consisted of five negative samples, five 50% below cutoff level samples, five 100% above cutoff level samples for each of the 6 drugs. The results obtained at these three sites with these controls demonstrated 100% agreement with each other.

Specificity

The following table lists compounds that are detected by the **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** test. The specificity of the **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** test was determined by adding various drugs and drug metabolites to drug-negative urine specimens and testing with the **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** test. The results are expressed in terms of the concentration required to produce a positive result (Table 7).

Table 7. Specificity

Compound	Concentration (ng/mL)
THC	
Cannabinol	50,000
11-nor- Δ^8 -THC-9-COOH	250
11-nor- Δ^9 -THC-9-COOH	50
Δ^8 -THC	25,000
Δ^9 -THC	15,000
11-hydroxy- Δ^9 -THC	10,000
COC	
Benzoylcegonine	300
Cocaine HCl	300
Ecgonine HCl	>100,000

MET

D-Amphetamine	200,000
D,L-Amphetamine	> 200,000
(-)-Ephedrine	> 200,000
(+)-Ephedrine	200,000
D-Methamphetamine	1,000
p-OH-Methamphetamine	> 200,000
Methylenedioxyamphetamine	> 200,000
Methylenedioxymethamphetamine	2,000

AMP

D-Amphetamine	1,000
D,L-Amphetamine	1,500
L-Amphetamine	60,000
Benzphetamine	>100,000
d-Methamphetamine	>100,000
p-OH-Methamphetamine	>100,000
Methylenedioxyamphetamine	700
Methylenedioxymethamphetamine	>100,000
β-Phenethylamine	60,000
Phentermine	350
Tryptamine	50,000
Tyramine	70,000
3-OH-Tyramine	>100,000

OPI

Codeine	300
Hydrocodone	500
Hydromorphone	600
Levophanol	5,000
Meperidine	80,000
Morphine	300
Morphine-3-β-D-glucuronide	500
Nalorphine	100
Naloxane	100,000
Norcodeine	60,000
Oxycodone	20,000
Oxymorphone	60,000
Procaine HCl	100,000
Thebaine	5,000

BZO

Alprazolam	10,000
Bromazepam	2,500
Chlordiazepoxide	1,000
Clobazam	10,000
Clonazepam	10,000
Clorzepate dipotassium	250
Delorazepam	1,000
N-Desalkylflurazepam	1,250
N-Desmethyldiazepam	500
Diazepam	2,000
Estazolam	500
Flunitrazepam	>10,000
7-amino flunitrazepam	4,000
a-Hydroxyalprazolam	250
a-Hydroxytriazolam	2,500
Lorazepam	750
Lormetazepam	8,000
Medazepam	2,500
Midazolam	4,000
Nitrazepam	2,500
Nordiazepam	500
Oxazepam	300
Prazepam	9,000
Temazepam	800
Triazolam	>10,000

Interfering Substances**Exogenous compounds:**

The **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** test showed no interference when the endogenous compounds were added at the concentrations given below to urine samples which had $\pm 25\%$ cutoff concentration of each of the 6 drugs.

Table 8. Endogenous Compounds

Substance Added	Concentration Added
Bilirubin	2 mg/dl
Creatinine	20 mg/dl
Glucose	1500 mg/dl
Hemoglobin	25 mg/dl
Ketones	100 mg/dl
Protein	2000 mg/dl
Sodium Chloride	1500 mg/ml
Sodium Nitrite	100 mg/dl

Exogenous compounds:

The following compounds show no cross-reactivity when tested with the **AccuSign® DOA 6 THC/COC/MET/AMP/OPI/BZO** at a concentration of 100 µg/mL (Table 9).

Table 9. Non Cross-Reacting Compounds

4-Acetamidophenol	Gentisic acid	Oxymetazoline
Acetophenetidin	Glutethimide	Papaverine
(Phenacetin)	Guaifenesin	Penicillin-G
N-Acetylprocainamide	Hippuric acid	Pentazocaine
Acetylsalicylic acid	Hydralazine	Phendimetrazine
Aminopyrine	Hydrochlorothiazide	Phenelzine
Amoxapine	Hydrocortisone	Phentoin
Amoxicillin	O-Hydro-	Prednisolone
Apomorphine	xyhippuric acid	Prednisone
Aspartame	Iproniazid	Promethazine
Atropine	(-) Isoproterenol	D,L-Propranolol
Benzilic acid	Isoxsuprine	Propiomazine
Benzoic acid	Ketoprofen	D-Propoxyphene
Benzphetamine	Labetalol	Quinidine
Chloralhydrate	Lidocaine	Quinine
Chloramphenicol	Loperamide	Rantidine
Chlorothiazide	Loxapine succinate	Salicylic acid
Chlorquine	Meprobamate	Serotonin
Cholesterol	Methadone	Sulfamethazine
Clonidine	Methaqualone	Sulindac
Cortisone	Methoxyphenamine	Tetracycline
(-) Cotinine	Methylphenidate	Tetrahydrocortisone
Deoxycorticosterone	Methypylon	Tetrahydrozoline
Dextromethorphan	Nalidixic acid	Thiamine
Diclofenac	Naltrexone	Thioridazine
Diethylpropion	Naproxen	D,L-Thyroxine
Diflunisal	Niacinamide	Tolbutamide
Digoxin	Nifedipine	Triamterene
Domperidone	Norethindrone	Trifluoperazine
Doxylamine	Noroxymorphone	Trimethoprim
Erythromycin	D-Norpropoxyphene	D,L-Tryptophan
β-Estradiol	(-) Norpseudoephedrine	D,L-Tyrosine
Estrone-3-sulfate	Noscapine	Uric acid
Ethyl-p-	Nylidrin	Verapamil
aminobenzoate	D,L-Octopamine	Zomepirac
Fenoprofen	Oxalic acid	
Furoximide	Oxolinic acid	

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The logo for Princeton BioMeditech Corporation, consisting of the letters 'PBM' in a bold, stylized, blocky font.

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Patent No.: 5,559,041

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Printed in U.S.A.
P-5861

Printed April 2001

0430b1