Table 4. Non Cross-Reacting Compounds

Acetaminophen	Guaifenesin	Oxymetazoline
Acetophenetidin (Phenacetin)	Hippuric acid	Oxymorphone
N-Acetylprocainamide	Hydralazine	Papaverine
Acetylsalicylate	Hydrochlorothiazide	Penicillin-G
Aminopyrine	Hydrocodone	Pentazocaine
Amitryptyline	Hydrocortisone	Pentobarbital
Amobarbital	Hydromorphone	Perphenazine
Amoxapine	O-Hydroxyhippuric acid	Phencyclidine
Amoxicillin	p-Hydroxymetham phetamine	Phendimetrazine
D,L-Amphetamine	3-Hydroxytyramine	Phenelzine
L-Amphetamine	Ibuprofen	Phenobarbital
Apomorphine	Imipramine	Phentermine
Aspartame	Iproniazid	Phentoin
Atropine	(–) Isoproterenol	L-Phenylephrine
Benzilic acid	Isoxsuprine	ß-Phenylethylamine
Benzoic acid	Ketamine	Phenylpropanola-mine
Benzphetamine	Ketoprofen	Prednisolone
Butabarbital	Labetalol	Prednisone
Cannabidiol	Levorphanol	Procaine
Chloralhydrate	Lidocaine	Promazine
Chloramphenicol	Loperamide	Promethazine
Chlordiazepoxide	Loxapine succinate	D,L-Propanolol
Chlorothiazide	Maprotiline	Propiomazine
Chlorpromazine	Meperidine	D-Propoxyphene
Chlorquine	Meprobamate	D-Pseudoephedrine
Cholesterol	Methadone	Quinidine
Clomipramine	Methaqualone	Quinine
Clonidine	Methoxyphenamine	Rantidine
Codeine	(±) 3,4-Methylene-dioxyamphetamine	Salicylic acid
Cortisone	(±) 3,4-Methylenedioxy methamphetamine	Secobarbital
(–) Cotinine	Methylphenidate	Serotonin
Creatinine	Methyprylon	Sulfamethazine
Deoxycorticosterone	Morphine-3-ß-D glucuronide	Sulindac
Dextromethorphan	Nalidixic acid	Temazepam
Diazepam	Nalorphine	Tetracycline
Diclofenac	Naloxone	Tetrahydrocortisone
Diethylpropion	Naltrexone	Δ^9-Tetrahydrocanna binol carboxylic acid
Diflunisal	Naproxen	Tetrahydrozoline
Digoxin	Niacinamide	Thebaine
Diphenhydramine	Nifedipine	Thiamine
Domperidone	Norcodein	Thioridazine
Doxylamine	Norethindrone	D,L-Thyroxine
Ecgonine methylester	Noroxymorphone	Tolbutamide
(+) Ephedrine	D-Norpropoxyphene	Triamterene
(±) Ephedrine	(–) Norpseudoephedrine	Trifluoperazine
(–) Ephedrine	Noscapine	Trimethoprim
(–) Ψ Ephedrine	Nylidrin	Trimipramine
Erythromycin	D,L-Octopamine	Tryptamine
ß-Estradiol	Oxalic acid	D,L-Tryptophan
Estrone-3-sulfate	Oxazepam	Tyramine
Ethyl-p-aminobenzoate	Oxolinic Acid	D,L-Tyrosine
Fenoprofen	Oxycodone	Uric acid
Furoxmide		Verapamil
Gentisic acid		Zomepirac
Glucuronide		
Glutethimide		

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Symbols Key

	Manufactured by
CE	CE Mark
EC REP	Authorized Representative
IVD	*In Vitro* Diagnostic Medical Device
REF	Catalog Number
	Consult Instructions for Use
LOT	Batch Code
EXP YYYY-MM-DD	"Use By" date in year-month-day format
2°C (35°F) Min / 30°C (86°F) Max	Temperature Limitation
Σ n	Contains sufficient for <n> tests
	Do not reuse
CONT	Contents
DEV	Test Device
PIP	Transfer Pipette
IFU	Instructions for Use
TEST DRUG	One-step immunochromatographic Assay for the Detection of Drugs of Abuse in Urine
TEST COC	Cocaine Test

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AccuSign® COC

One-Step Cocaine Test

For *In Vitro* Use Only

Simple One-Step Immunoassay for the Qualitative Detection of Cocaine Metabolite in Human Urine

PBM

Catalog No. DOA-200-35 35 Test Kit
DOA-200-10 10 Test Kit

Intended Use

AccuSign® COC is a simple, one-step immunochromatographic assay intended for use in the qualitative detection of the cocaine metabolite, benzoylecgonine, in human urine with a cutoff at 300 ng/mL.

The* AccuSign® COC *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.[1]

Summary and Explanation

Cocaine, derived from the leaves of the 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.[2,3] 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.[3,4]

Principle

The **AccuSign® COC** test uses solid-phase chromatographic membrane immunoassay technology for the qualitative detection of cocaine metabolites. 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 Test (T) position in the Result window, indicating a positive result from positive drug competition. A negative urine sample will generate a line at Test position in the Result window, indicating a negative result from an absence of competition with free drugs.

In addition to the Test line 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.

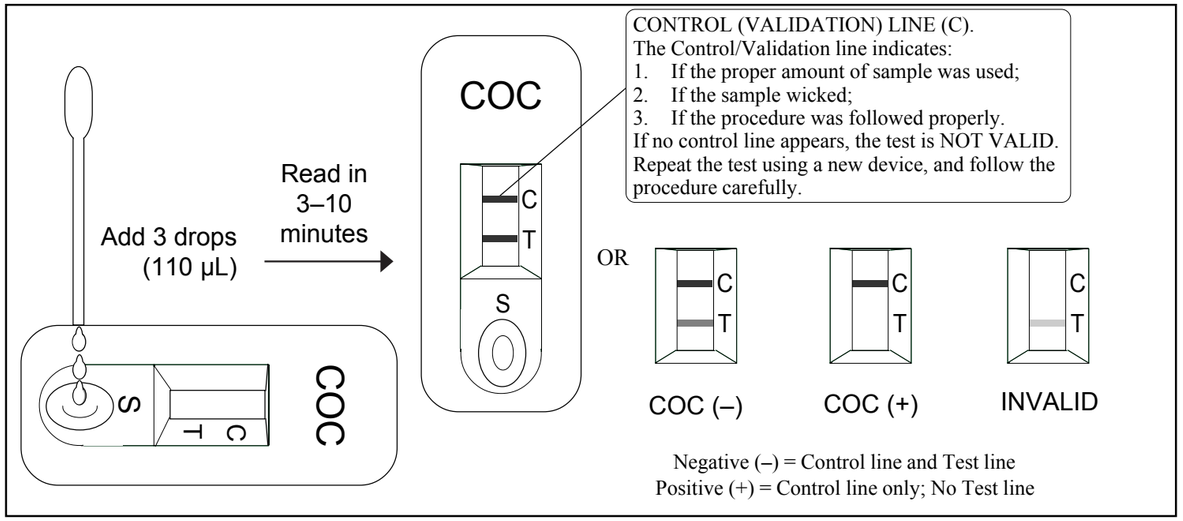
Materials Provided

The **AccuSign® COC** test kit contains all the reagents necessary to perform the tests.

- **AccuSign® COC** device. The test device contains a membrane strip coated with mouse monoclonal anti-benzoylecgonine antibody and a pad containing drug-dye conjugate in a protein matrix.
- Disposable droppers.
- 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® COC** 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. 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. Specimens should be brought to room temperature before testing.

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® COC** pouch and label the **AccuSign®** device with the patient ID.
2. Holding the dropper vertically, dispense 3 full drops (110 µL) of the urine sample into the 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 next to **T** indicates a negative test result; i.e., no drug above the cutoff level has been detected. The color intensities of the Control line and the Test line may not be equal. *Any faint line in the Result window, 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 only a reddish-purple Control line and no distinct line next to **T** indicates the test result is positive for COC (i.e., the specimen contains COC 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® COC** test device.

Limitations

- The test is designed for use with human 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 Table 4 below, may interfere with the test and cause erroneous results.
- Adulterants, such as bleach and/or alum, in urine specimens may produce erroneous results. If adulteration is suspected, the test should be repeated with a new sample.
- The test must be read within 10 minutes of sample application. The test result read after 10 minutes may not be consistent with the original reading obtained within the 10 minute reading period.
- Foods and tea containing coca leaves may produce a positive result.

User Quality Control

Internal Control: Each **AccuSign®** test device has built-in controls. The Control line is an internal positive procedural control. A distinct reddish-purple Control line should always appear at the C 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 has been 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®** 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 process. For information on how to obtain controls, contact PBM's Technical Services.

Expected Values

AccuSign® COC is a qualitative assay. The amount of cocaine metabolites present in the urine cannot be estimated by the assay. The assay results distinguish positive from negative samples. Positive results indicate the samples contain cocaine metabolites above the cutoff concentration.

Performance Characteristics

Substance Abuse and Mental Health Services Administration has suggested that the screening cutoff for positive samples be 300 ng/mL for cocaine. The **AccuSign® COC** test has been shown to detect cocaine metabolites in urine at an average cutoff of 300 ng/mL.

The accuracy of **AccuSign® COC** was evaluated in comparison to a commercially available immunoassay (Syva® EMIT® II) at a cutoff of 300 ng/mL. A total of 1023 samples was tested by both procedures. Complete agreement was observed in 98% of the samples as shown below (Table 1).

Table 1. Accuracy: Comparison of AccuSign® COC **with Syva® EMIT® II**

		Syva® EMIT® II (COC)		
		Positive	Negative	TOTAL
AccuSign® COC	Positive	369	3	372
	Negative	16	635	651
TOTAL		385	638	1023
		Relative Sensitivity	Relative Specificity	
Cocaine		95.8% (369/385)	99.5% (635/638)	

In a separate study, **AccuSign® COC** was evaluated against specimens confirmed as positive by GC/MS. The results below demonstrate the excellent correlation of **AccuSign® COC** with GC/MS (99% agreement, Table 2).

Table 2. Accuracy: Comparison of AccuSign® COC **with GC/MS Assay**

	AccuSign®	GC/MS
Positive	77	78
Negative	1	0

Precision and Accuracy

The precision of the **AccuSign® COC** assay was determined by carrying out the test with serially diluted standard drug solutions. Ninety-five percent (95%) of the samples containing drug concentrations 25% over the cutoff level consistently showed positive results.

The study also included over 40 samples ± 25% cutoff level. These results were found to be consistently in agreement with predicate test results.

Distribution of Random Error:

Twenty (20) blind samples prepared by spiking various concentrations of cocaine were separately tested by two operators. The test results from the two operators showed complete agreement.

Reproducibility

The reproducibility of the test results of the **AccuSign® COC** assay was examined at three different sites using a total of 15 blind controls, consisting of 5 negative samples, 5 moderately positive samples (a concentration 1.5 times the cutoff level), and 5 strongly positive samples (i.e., a concentration 3 times the cutoff level). The results obtained at these three sites with these controls demonstrated 100% agreement with each other.

Specificity

The **AccuSign® COC** test detects the cocaine metabolite, benzoylecgonine, in urine.

The following table lists compounds that are detected by the **AccuSign® COC** test. The specificity of the **AccuSign® COC** test was determined by adding the drugs and drug metabolites listed to drug-negative urine specimens and testing with the **AccuSign® COC** test kit. The results are expressed in terms of the concentration required to produce a positive result (Table 3).

Table 3. Specificity

Compound	**Concentration (ng/mL)**
Benzoylecgonine	300
Cocaine HCl	>100,000
Ecgonine HCl	>100,000

The following compounds show no cross-reactivity when tested with **AccuSign® COC** at a concentration of 100 µg/mL (Table 4).