

MEDTOX®

PROFILE®-IV VISUAL PRODUCT INSERT

The **PROFILE®-IV VISUAL** products are one-step qualitative screening assays for the detection of one or more of the following: Amphetamines, Barbiturates, Benzodiazepines, Cocaine, Methamphetamine/ 3,4 Methylendioxyamphetamine, Methadone, Opiates, Oxycodone, Phencyclidine, Propoxyphene, THC (Cannabinoids) and Tricyclic Antidepressants or their metabolites in human urine. **All PROFILE®-IV VISUAL product(s) are covered by this insert. Refer to product labeling for the actual drugs assayed by the kit configuration.**

1. INTENDED USE

The PROFILE®-IV VISUAL Drugs of Abuse Test is a one-step immunochromatographic test for the rapid, qualitative detection of one or more of the following: Amphetamines, Barbiturates, Benzodiazepines, Cocaine, Methamphetamine/ 3,4 Methylendioxyamphetamine, Methadone, Opiates, Oxycodone, Phencyclidine, Propoxyphene, THC (Cannabinoids), and Tricyclic Antidepressants in human urine. It is not for over-the-counter sale. The test detects drug classes at the following cutoff concentrations:

AMP	Amphetamine (d-Amphetamine)	1000 ng/mL	OPI2	Opiates (Codeine/Morphine)	2000 ng/mL
BAR	Barbiturates (Butalbital)	200 ng/mL	OPI3	Opiates (Codeine/Morphine)	300 ng/mL
BZO	Benzodiazepines (Nordiazepam)	300 ng/mL	OXY	Oxycodone	100 ng/mL
COC	Cocaine (Benzoylecgonine)	300 ng/mL	PCP	Phencyclidine (Phencyclidine)	25 ng/mL
MAMP	Methamphetamine (d-Methamphetamine)	1000 ng/mL	PPX	Propoxyphene (Norpropoxyphene)	300 ng/mL
MDMA	3,4 Methylendioxyamphetamine	1500 ng/mL	THC	Cannabinoids (11-nor-9-carboxy- Δ^9 -THC)	50 ng/mL
MTD	Methadone (Methadone)	300 ng/mL	TCA	Tricyclic Antidepressants (Desipramine)	300 ng/mL

THE PROFILE®-IV VISUAL DRUGS OF ABUSE TEST PROVIDES ONLY A PRELIMINARY ANALYTICAL TEST 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) IS 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 OBTAINED.

2. SUMMARY AND EXPLANATION OF THE TEST

Qualitative PROFILE®-IV VISUAL Drugs of Abuse screens utilize a one-step, solid-phase immunoassay technology to provide a very rapid test requiring no instrumentation. This test may be used to screen urine samples for one or more of the following drug classes prior to confirmatory testing:

The "Amphetamines" are a group of drugs that are central nervous system stimulants. This group includes 'amphetamine' and 'methamphetamine', and related designer drugs like '3,4 Methylendioxyamphetamine', (better known as Ecstasy or MDMA, a psychoactive drug with hallucinogenic effects).

The drug 'Amphetamine' (d-amphetamine) is detected on the device only at the (AMP) position. Both the designer drug Ecstasy (MDMA) 'Methylendioxyamphetamine' and methamphetamine (d-methamphetamine) are detected on the device at the (MAMP) position. The (MAMP) antibody does not differentiate between methamphetamine and ecstasy.

Barbiturates (BAR) are a group of structurally related prescription drugs that are used to reduce restlessness and emotional tension, induce sleep and to treat certain convulsive disorders.

Benzodiazepines (BZO), a group of structurally related central nervous system depressants, are primarily used to reduce anxiety and induce sleep.

Cocaine (COC) is a central nervous system stimulant. Its primary metabolite is benzoylecgonine.

Methadone (MTD) is a synthetic opioid used clinically as a maintenance drug for opiate abusers and for pain management.

Opiates (OPI) are a class of natural and semi-synthetic sedative narcotic drugs that include morphine, codeine and heroin.

Oxycodone (OXY) (Oxycontin®, Percodan, Percocet) is a semi synthetic narcotic analgesic that is prescribed for moderately severe pain. It is available in both standard and sustained release oral formulations. Oxycodone is metabolized to Oxymorphone and Noroxycodone.

Phencyclidine (PCP) is a hallucinogenic drug.

Propoxyphene (PPX) is a narcotic analgesic. Its primary metabolite is norpropoxyphene.³

Marijuana (THC) is a hallucinogenic drug derived from the hemp plant. Marijuana contains a number of active ingredients collectively known as Cannabinoids.

Tricyclic Antidepressants (TCA) are a group of structurally related prescription drugs that are used to manage depression.

Many factors influence the length of time required for drugs to be metabolized and excreted in the urine. A variety of factors influence the time period during which drug metabolites are detected in urine; the rate of urine production, the volume of fluid consumption, the amount of drug taken, the urine pH, and the length of time over which drug was consumed. Drinking large volumes of liquid or using diuretics to increase urine volume will lower the drug concentration in the urine and may decrease the detection period. Although the detection period for these drugs varies widely depending upon the compound taken, dose and route of administration and individual rates of metabolism, some general times have been established and are listed below.^{1-3, 4, 6}

<u>Drug</u>	<u>Detection Period</u>	<u>Drug</u>	<u>Detection Period</u>
Amphetamine Acid Conditions	1-3 days	Opiates Heroin	1 day
Alkaline Condition	3-10 days	Morphine	1-3 days
		Codeine	1-3 days
Barbiturates Short-Acting	Up to 6 days	Oxycodone	1-3 days
Long-Acting	Up to 16 days		
Benzodiazepines	1-12 days	PCP Single Use	1-8 days
		Chronic Use	Up to 4 weeks
Cocaine metabolite	Up to 5 days 1 to 3 days typical	Propoxyphene	Up to 1 week
Methadone	1-3 days	THC Single Use	1-7 days
		Chronic Use	Less than 30 days typical
Methamphetamine Acid Conditions	1-3 days	Tricyclic Antidepressants	1-7 days
Alkaline Conditions	3-10 days		

3. PRINCIPLES OF THE PROCEDURE

The PROFILE®-IV VISUAL Drugs of Abuse Test is a one-step, competitive, membrane-based immunochromatographic assay. A single urine sample can be evaluated for the presence of each of the specified classes of drugs in a single device. The device consists of antibody-colloidal gold, drug-conjugates and a control line.

1. ANTIBODY-COLLOIDAL GOLD Mouse monoclonal drug antibodies were developed. Each antibody only binds drugs from the drug class tested. Antibody-colloidal gold solutions were prepared by absorbing each of the individual monoclonal antibodies to colloidal gold. The colloidal gold solutions were applied to the sample well pad in the drugs of abuse test.

2. DRUG-CONJUGATES Drug from the class tested was individually conjugated to bovine serum albumin (BSA) or IgG. Each drug conjugate was immobilized as a line at a labeled location on the membrane strip.

3. CONTROL LINE Each test strip has anti-mouse immunoglobulin antibody immobilized as a line on the membrane at the Control (C) location on the device window. The anti-mouse immunoglobulin antibody can bind to any of the mouse antibodies coated on the colloidal gold.

The device can be used to detect specific classes of drugs in urine because drug(s) in the urine and the drug(s) conjugated to the protein compete to bind to the antibody-colloidal gold in a highly specific reaction. When the urine sample is placed in the sample well(s), the dried antibody-colloidal gold on the sample pad(s) dissolves and the urine wicks up the white strips carrying the reddish-purple antibody-colloidal gold as a solution with it.

Negative Samples

When no drug(s) is present in the urine sample, the reddish purple antibody-colloidal gold solutions migrate along the strip then binds to the appropriate drug conjugate immobilized on the membrane. The binding of the antibody-colloidal gold to the drug conjugate generates an easily visible reddish-purple line at the appropriate "T" location on the device. Each strip has up to 4 drug test lines labeled T1 – T4. The table directly above the strips shows which drug test is located at which position. The column above each strip corresponds to the drug tests for that strip. A blank space in the table indicates that no drug test is present at that position and that absence of a line at that position does not indicate a positive result for any drug. Negative results can be reported as soon as a line is visible, and a control line has formed (see below).

Non-Negative Samples

When drug(s) is present in the urine sample the antibody-colloidal gold binds to the drug(s) before it migrates along the strip. However, when the antibody-colloidal gold binds to the drug(s) in the urine, the antibody colloidal gold cannot bind to the drug conjugate immobilized on the membrane. When the drug concentration is at or above the cutoff concentration, the majority of the antibody-colloidal gold is bound to the drug from the urine. Therefore, as the drug bound antibody-colloidal gold migrates along the strip(s), it is unable to bind to the appropriate drug conjugate immobilized on the membrane. Therefore no line is generated at the drug-specific location in the result window for a positive sample. Read non-negative results at 10 minutes. The control line should be present for the test to be valid. The test result after 10 minutes may not be consistent with the original reading.

Control Line

Each test strip has an internal procedural control. A line must form at the Control (C) position in the result window to indicate that the proper sample volume was used and that the reagents are migrating properly. If a Control line does not form, the test is considered invalid. A Control line forms when the antibody-colloidal gold binds to the anti-mouse immunoglobulin antibody immobilized on the membrane at the (C) location(s) near the top of the device window.

4. MATERIALS PROVIDED/STORAGE CONDITIONS

Each PROFILE®-IV VISUAL Drugs of Abuse Test System contains all the reagents necessary to test one urine sample simultaneously for one or more drugs.

1. The test device contains one or more test strips composed of a membrane strip coated with drug conjugate and a pad coated with antibody dye complexes in a protein matrix.

Kit Contents

1. Twenty-five (25) test devices in individual foil packages.
2. Twenty-five (25) transfer pipettes.
3. One reference guide.

Storage Conditions

The kit, in its original packaging, should be stored at 2-25°C (36-77°F) until the expiration date on the label.

5. PRECAUTIONS

1. Urine specimens and all materials coming in contact with them should be handled and disposed of as if infectious and capable of transmitting infection. Avoid contact with broken skin.
2. Avoid cross-contamination of urine samples by using a new urine specimen container for each urine sample.
3. The device should remain in its original sealed foil pouch until ready to use. If the pouch is damaged, do not use the test.
4. Do not store the test kit at temperatures above 25°C (77°F).
5. If devices have been stored refrigerated, bring to ambient temperature (18-25°C/ 64-77°F) prior to opening foil pouch.
6. Do not use tests after the expiration date printed on the package label.
7. The drug screen portion of the device is for in vitro diagnostic use only.

6. SAMPLE COLLECTION AND PREPARATION

The urine sample should be collected. No preservatives should be added. Urine may be tested immediately following collection. If it is necessary to store the urine, store under refrigeration for no more than one day. Urine may be frozen for longer storage. Stored urine must be brought to ambient temperature (18 to 25°C/64 to 77°F) and mixed well to assure a homogeneous sample prior to testing.

7. MATERIALS REQUIRED BUT NOT PROVIDED

1. Urine collection container.

NOTE: Specimen containers, disposable gloves and urine temperature strips are available from MEDTOX Diagnostics, Inc.

TEST PROCEDURE

1. Open one pouch for each sample to be tested and mark the device with the patient or sample identification (ID). (You may notice a reddish-purple color in the sample well. This is normal, do not discard the test).
2. Apply two drops (75 µl) of urine to sample well (indicated by ▽).
 - Hold the pipette by the bulb.
 - Lower the tip of the pipette into the urine sample.
 - Squeeze the bulb then release to fill the pipette with urine.
 - Hold the pipette vertically above the sample well and lightly squeeze the bulb till two drops of urine have been added.
3. Repeat Step 2 for all sample wells with a ▽ above them.
4. Read the results at 10 minutes after application.

8. READING THE TEST RESULTS

Negative: The appearance of a reddish-purple line at both the control area (C) and appropriate test area (T#) indicates a negative test result. **The color intensities of the control lines (C) and test lines (T#) may not be equal and may vary from test to test. The test line and control line positions may vary slightly from test strip to test strip. Any line of reddish-purple color, even those of faint intensity, indicates a negative test result.**

Non-Negative: The appearance of a control line and the absence of a test line indicate a preliminary positive test result for that drug.

Invalid: The control line must be present for the test to be valid. The absence of a control line indicates the test is invalid. The urine sample should be retested on a new device.

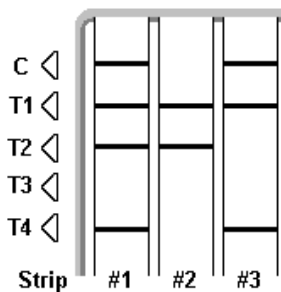
9. INTERPRETATION OF TEST RESULTS

A NEGATIVE test result for a specific drug indicates that the sample does not contain the drug/drug metabolite above the cutoff level.

A NON-NEGATIVE test result for a specific drug indicates that the sample may contain drug/drug metabolite near or above the cutoff level. It does not indicate the level of intoxication or the specific concentration of drug in the urine sample. Non-negative samples or those with abnormal LFAS tests should be sent to a reference laboratory for more definitive testing. Examples of Negative and Non-Negative results are shown below.

C	CTRL	CTRL	CTRL
T1	Drug1	Drug4	Drug6
T2	Drug2	Drug5	Drug7
T3			Drug8
T4	Drug3		Drug9

Interpretation of Results



Strip #1	Strip #2	Strip #3
Control Valid	Control Invalid	Control Valid
Drug1 = Negative	Drug4 = Invalid	Drug6 = Negative
Drug2 = Negative	Drug5 = Invalid	Drug7 = Non-Negative
Blank	Blank	Drug8 = Non-Negative
Drug3 = Negative	Blank	Drug9 = Negative

10. QUALITY CONTROL

An internal procedural control is included on each device. A line must form at the Control (C) position in the result window to indicate that the proper sample volume was used and that the reagents are migrating properly. If a Control line does not form, the test is considered invalid. The Control line consists of immobilized anti-mouse antibody that reacts with the antibody-colloidal gold as it passes this region of the membrane. Formation of a visible line verifies the Control line antibody antigen reaction occurred. This line may be considered an internal negative procedural control. In addition, if the test has been performed correctly and the device is working properly, the background will clear such that result lines are distinct. The cleared background may be considered an internal positive procedural control. The visible Control line (C) should always be present regardless of whether drug is absent or present in the sample.

The purpose of quality control in laboratory testing is to ensure accuracy, reliability of results and to detect errors. Because the devices are self-contained, single use tests, traditional quality control programs do not apply. The Quality Control program MEDTOX recommends for these non-instrumented test devices includes a combination of the internal device controls and external controls to ensure accuracy, reliability and to detect possible errors. The on-board reactive device controls may be one aspect of the quality program utilized by a laboratory to satisfy the daily quality control requirement established by the Laboratory Director. Another aspect of a quality control program includes an external negative control containing no drug and a positive drug control challenging to the assay cutoff concentration. These controls may be used to initially test each shipment of product received by the laboratory or to verify appropriate storage conditions and long-term stability of the test reagent. To follow good laboratory practices, we

recommend that the user document the receipt of each new lot number of devices, the results of external controls performed initially and periodically thereafter, and the results of the internal controls within each device.

It is the responsibility of each Laboratory Director to demonstrate and document the validity of the alternate QC procedure they choose to use in their laboratory. For additional information or forensic and workplace testing requirements, users should contact and follow the appropriate federal, state, and local guidelines. Quality control materials are available from MEDTOX and commercial sources. Contact MEDTOX for further information.

11. LIMITATIONS OF THE PROCEDURE

1. The PROFILE®-IV VISUAL Drugs of Abuse Test is only for use with unadulterated human urine samples. Urine samples which are either extremely acidic (below pH 4.0) or basic (above pH 9.0) may produce erroneous results.
2. A positive result for any drug(s) does not indicate or measure intoxication. It only indicates the presence of specific drug(s) in the urine specimen.
3. Test results interpreted after 10 minutes may not be consistent with the original result obtained at 10 minutes.
4. The PROFILE®-IV VISUAL Drugs of Abuse Test was not evaluated in point-of-care settings.
5. There is a possibility that other substances and/or factors, e.g. technical or procedural errors, may interfere with the test and cause false results.

12. EXPECTED VALUES

The Substance Abuse and Mental Health Services Administration (SAMHSA) recommends the following screening test cutoffs:

AMP	Amphetamine	1000 ng/mL
COC	Benzoyllecgonine	300 ng/mL
MAMP	Methamphetamine	1000 ng/mL
OPI	Morphine and Codeine	2000 ng/mL
PCP	Phencyclidine	25 ng/mL
THC	11-nor-9-carboxy- Δ^9 -THC	50 ng/mL

There are no SAMHSA recommended screening levels for barbiturates, benzodiazepines, MDMA, methadone, tricyclic antidepressants and propoxyphene and/or their metabolites.

The PROFILE®-IV VISUAL Drugs of Abuse Test qualitatively detects amphetamines, barbiturates, benzodiazepines, cocaine, methamphetamine/MDMA, methadone, opiates, oxycodone, phencyclidine, propoxyphene, THC, tricyclic antidepressants and/or their metabolites as listed (See Specificity).

13. PERFORMANCE CHARACTERISTICS

Sensitivity

The PROFILE®-IV VISUAL Drugs of Abuse Test detects one or more of the following drugs at cutoff levels listed below. Cutoffs for amphetamines, cocaine metabolite, methamphetamines, opiates (OPI2), phencyclidine, and cannabinoids (THC) are based on SAMHSA recommendations for screening of these drugs in human urine. The Opiate (OPI3) test, if present, detects opiates below the SAMHSA recommendations for screening of opiates in human urine. There are no SAMHSA recommended screening cutoff levels for barbiturates, benzodiazepines, MDMA, methadone, oxycodone, tricyclic antidepressants, norpropoxyphene, or propoxyphene.

AMP	Amphetamine	1000 ng/mL
BAR	Barbiturates (Butalbital)	200 ng/mL
BZO	Benzodiazepines (Nordiazepine)	300 ng/mL
COC	Benzoyllecgonine	300 ng/mL
MAMP	Methamphetamine	1000 ng/mL
MDMA	3,4 Methylene-dioxymethamphetamine	1500 ng/mL
MTD	Methadone	300 ng/mL
OPI2	Morphine and Codeine	2000 ng/mL
OPI3	Morphine and Codeine	300 ng/mL
OXY	Oxycodone	100 ng/mL
PCP	Phencyclidine	25 ng/mL
PPX	Propoxyphene (Norpropoxyphene)	300 ng/mL
THC	11-nor-9-carboxy- Δ^9 -THC	50 ng/mL
TCA	Tricyclic Antidepressants (Desipramine)	300 ng/mL

Accuracy

A panel of naturally metabolized urine samples for the following drug(s) was analyzed using the PROFILE® Drugs of Abuse Test and the Boehringer Mannheim qualitative CEDIA® assay or the ROCHE ABUSCREEN ONLINE® for each drug and the results were compared. Results are shown in the following tables.

ACCURACY COMPARED TO THE BOEHRINGER MANNHEIM QUALITATIVE CEDIA® or THE ROCHE ABUSCREEN ONLINE® II ASSAYS

CEDIA AMPHETAMINE (1000 ng/mL cutoff)

		Positive	Negative	TOTAL
AMP (1000 ng/mL cutoff)	Positive	64	0	64
	Negative	2	618	620
	TOTAL	66	618	684

Overall agreement: >99% (682/684). Samples having discrepant results were analyzed by GC/MS. The two false negative samples contained amphetamine at 2353 and 3569 ng/mL.

CEDIA COCAINE (300 ng/mL cutoff)

		Positive	Negative	TOTAL
COC (300 ng/mL)	Positive	96	8	104
	Negative	2	578	580
	TOTAL	98	586	684

Overall agreement: 99% (674/684). Samples having discrepant results were analyzed by GC/MS. Of the eight false positive samples one contained 151 ng/mL while seven did not contain cocaine metabolite detectable at the GC/MS cutoff of 150 ng/mL. The two false negative samples contained cocaine metabolite at 688 and 666 ng/mL.

ROCHE ABUSCREEN ONLINE®-II OPIATE (2000 ng/mL cutoff)

		<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
OPI (2000 ng/mL cutoff)	Positive	68	0	68
	<u>Negative</u>	<u>0</u>	<u>89</u>	<u>89</u>
	TOTAL	68	89	157

Overall agreement: 100% (157/157).

CEDIA OPIATE (300 ng/mL cutoff)

		<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
OPI (300 ng/mL cutoff)	Positive	133	1	134
	<u>Negative</u>	<u>0</u>	<u>550</u>	<u>550</u>
	TOTAL	133	551	684

Overall agreement: >99% (683/684). The discrepant sample was analyzed by GC/MS. The one false positive sample did not contain morphine or codeine detectable at the GC/MS cutoff of 300 ng/mL.

CEDIA PHENCYCLIDINE (25 ng/mL cutoff)

		<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
PCP (25 ng/mL)	Positive	56	2	58
	<u>Negative</u>	<u>1</u>	<u>625</u>	<u>626</u>
	TOTAL	57	627	684

Overall agreement: >99% (681/684). Samples having discrepant results were analyzed by GC/MS. The two false positive samples did not contain phencyclidine detectable at the GC/MS cutoff of 25ng/mL. The one false negative sample contained phencyclidine at 28 ng/mL.

CEDIA MULTI-LEVEL THC (50 ng/mL cutoff)

		<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
THC (50 ng/mL cutoff)	Positive	194	3	197
	<u>Negative</u>	<u>10</u>	<u>477</u>	<u>487</u>
	TOTAL	204	480	684

Overall agreement: 98% (671/684). Samples having discrepant results were analyzed by GC/MS. The three false positive samples were found to contain 16, 28, and 32 ng/mL while the ten false negative samples contained 32, 35, 41, 42, 46, 46, 49, 50, 50, and 90 ng/mL.

RELATIVE SENSITIVITY AND SPECIFICITY COMPARED TO THE BOEHRINGER MANNHEIM QUALITATIVE CEDIA® or THE ROCHE ABUSCREEN ONLINE® II ASSAYS (Amphetamines, Cocaine, Opiates, PCP and THC)

	<u>Relative Sensitivity</u>	<u>Relative Specificity</u>
AMP	97% (64/66)	100% (618/618)
COC	98% (96/98)	99% (578/586)
OPI2	100% (68/68)	100% (89/89)
OPI3	100% (133/133)	>99% (550/551)
PCP	98% (56/57)	>99% (625/627)
THC	95% (94/204)	99% (477/480)

ACCURACY COMPARED to GC/MS

		<u>PROFILE®</u>	<u>GC/MS</u>	<u>Values for discrepant Samples (ng/mL)</u>
AMP	Positive	48	50	
	Negative	52	50	2353 and 3569
COC	Positive	49	50	
	Negative	51	50	666
OPI2	Positive	47	47	
	Negative	0	0	No Discrepant
OPI3	Positive	50	50	
	Negative	50	50	No Discrepant
PCP	Positive	49	50	
	Negative	51	50	28
THC	Positive	48	50	
	Negative	52	50	35 and 46

Precision (Amphetamines, Cocaine, Opiates, PCP, and THC)

Performance around the specific cutoff for each drug was measured by testing standard drug solutions diluted in drug-free urine in replicates of 20 each on 3 different days by 3 operators. Twenty replicates of drug-free urine were also tested on each day. At 25% above the cutoff, the precision of each assay was as follows: AMP=100%, COC=100%, OPI2= 96.7%, OPI3= 100%, PCP=100% and THC= 95%.

Reproducibility (Amphetamines, Cocaine, Opiates 300, PCP, and THC)

A panel of 55 naturally metabolized human urine samples was prepared. All samples in the panel had been screened for the presence or absence of AMP, COC, PCP and THC. In addition, each of the 55 samples had also been quantitated by GC/MS conducted at SAMHSA cutoffs for positive samples or at limit of quantitation for negative samples to determine the concentration of a specific drug. Five of the 55 samples were drug-free negatives and 50 of the samples were positive for one or more of the five drugs. The concentration of primary metabolite in the positive samples was between 1056 and 4622 ng/mL for AMP; 487 and 1342 ng/mL for COC; 464 and 2000 ng/mL for OPI3; 32 and 109 ng/mL for PCP and 66 and 198 ng/mL for THC. The panel was used to evaluate the lot-to-lot and lab-to-lab reproducibility.

Lot-to-Lot Reproducibility (Amphetamines, Cocaine, Opiates 300, PCP, and THC)

Three aliquots of each of the 55 samples were prepared and each of the three sets of aliquots was coded and used to evaluate the performance of one of three lots of drug tests for the five drugs above. There was one incorrect result (a false negative on an amphetamine low positive sample) on the 825 tests for a reproducibility of >99%.

Lab-to-Lab Reproducibility (Amphetamines, Cocaine, Opiates 300, PCP, and THC)

Three aliquots of each of the 55 samples were prepared and each of the three sets of aliquots was tested by one of three study participants using one lot of the five drug test panel above. There was >99% agreement between the three participants. Overall, there were three incorrect results, two incorrect results for OPI3 (one false negative on an opiate low positive sample and one false negative on an opiate high positive sample) and one incorrect result for PCP (one false negative a low positive sample), on the 825 tests.

Reproducibility (Opiates 2000)

A panel of 25 naturally metabolized human urine samples was prepared. All samples in the panel had been screened for the presence or absence of opiates. In addition, each of the positive samples had also been quantitated by GC/MS conducted at SAMHSA cutoff for positive samples to determine the concentration of morphine and codeine. The concentration of morphine and/or codeine in the positive samples was between 2000 and 6000 ng/mL. The panel was used to evaluate Opiates 2000 for lot-to-lot and lab-to-lab reproducibility. There were no incorrect results on the 75 tests (25 samples x 3 lots) for a lot-to-lot reproducibility of 100%. There were no incorrect results on the 75 tests (25 samples x 3 study participants) for a lab-to-lab reproducibility of 100%.

Accuracy (Propoxyphene)

One-hundred forty one (141) clinical samples were evaluated by the Roche Abuscreen OnLine Propoxyphene assay, using a 300 ng/mL cut off. Sixty (60) samples were found to be negative and eighty-one (81) samples were found to be positive by the Roche method. Three aliquots of each sample were prepared, and assayed by three operators in a masked manner. There was no significant difference in the results obtained by the three operators, therefore the results of all three operators are included in the table. Results of this comparison are as follows:

	<u>OnLine Positive</u>	<u>OnLine Negative</u>
	238	0
PPX (300 ng/mL cutoff)	5*	180

* GC/MS results are 390, 441, 499, 536 and 679 ng/mL

In addition to the 141 clinical samples, eight additional clinical samples containing only norpropoxyphene were diluted with drug-free urine in order to obtain an adequate number of samples that had concentrations of drug that were challenging to the cutoff. These eight diluted samples, and the 141 clinical samples described above were analyzed by GC/MS for propoxyphene and norpropoxyphene. The level of quantitation of the GC/MS was 30 ng/mL. Only ten of the samples contained propoxyphene, and each of these samples had norpropoxyphene levels greater than 1,647 ng/mL. As in the study above, three aliquots of the 149 samples were prepared, coded, and assayed by three operators in a masked manner. There was no significant difference in the results obtained by the three operators, therefore the results of all three operators are included in the comparison table.

GC/MS Range (ng/mL)	None detected	150-265	339-450	>472
Number of samples	60	8 (Diluted samples)	7	74
Positive	0	12	19	219
Negative	180	12	2	3

Sensitivity/Precision/Distribution of Random Error (Propoxyphene)

Performance around the specific cut-off of 300 ng/ml for norpropoxyphene was evaluated by testing standard drug solutions diluted in drug-free urine in triplicate on 5 different days by 3 operators. Drug-free urine was also tested on each day. There was no significant difference in the results of the three operators so the results were combined and are shown in the following table.

Conc. (ng/mL)	Number Tested	Norpropoxyphene – Cut-off = 300 ng/mL		% Agreement
		Positive	Negative	
0	45	0	45	100
30	45	0	45	100
75	45	1	44	98
150	45	9	36	80
225	45	16	29	64
300	45	37	8	82
375	45	42	3	93
450	45	44	1	98
600	45	45	0	100

Accuracy (Methamphetamine and MDMA)

A panel of naturally metabolized urine samples was analyzed using the PROFILE® MAMP-MDMA and the GC/MS assay for methamphetamine and MDMA. The results obtained in the procedures are shown in the following tables.

GC/MS Methamphetamine (limit of quantitation 50 ng/mL)

	<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
MAMP (1000 ng/mL cut-off) Positive	56	0	56
Negative	2	56	58
TOTAL	58	56	114

Overall agreement: >98% (112/114). Samples having discrepant results were analyzed by GC/MS. The false negative samples contained methamphetamine at 1056 ng/mL and at 1136 ng/mL.

GC/MS MDMA (limit of quantitation 50 ng/mL)

	<u>Positive</u>	<u>Negative</u>	<u>TOTAL</u>
MDMA (1500 ng/mL cut-off) Positive	19	1	20
Negative	4	57	61
TOTAL	23	58	81

Overall agreement: 94% (76/81). The false negative samples contained MDMA concentrations at 1641 ng/mL, 1775 ng/mL, 1800 ng/mL and 2388 ng/mL. The false positive was at 1300 ng/mL.

Percent Agreement of MAMP-MDMA Compared to GC/MS

	<u>POSITIVE</u>	<u>NEGATIVE</u>
MAMP	97% (56/58)	100% (56/56)
MDMA	83% (19/23)	98% (57/58)

Sensitivity/Precision MAMP-MDMA

Performance for methamphetamine and MDMA was evaluated by testing standard drug solutions diluted in drug-free urine in duplicates of 8 drug concentrations on 5 different days by 3 operators. Drug-free urine was also tested on each day. The complete results for both drugs are shown in the tables below.

Conc. (ng/mL)	Methamphetamine Cut-off = 1000 ng/mL				MDMA Cut-off= 1500 ng/mL				
	No. Tested	(+)	(-)	% Agreement	Conc(ng/mL)	No. Tested	(+)	(-)	% Agreement
0	30	0	30	100	0	30	0	30	100
100	30	0	30	100	500	30	0	30	100
250	30	0	30	100	750	30	0	30	100
500	30	26	4	87	1000	30	12	18	60
750	30	27	3	90	1250	30	23	7	77
1000	30	28	2	93	1500	30	25	5	83
1250	30	29	1	97	2000	30	30	0	100
1500	30	30	0	100	2500	30	30	0	100
2000	30	30	0	100	3000	30	30	0	100

Reproducibility (MAMP-MDMA)

A panel of 18 spiked human urine samples, comprised of drug-free and drug standard samples, was prepared. The panel was examined by 3 operators, once a day for 5 days. The concentration of methamphetamine and MDMA had been quantitated by GC/MS in each of the 18 samples. There was 100% agreement between the three operators over the 5 day period at 0 ng/mL, 1500 ng/mL (cut-off + 50%) and 2000 ng/mL (cut-off + 100%) for methamphetamine. There was also 100% agreement between the three operators over the 5 day period for 0 ng/ml, 2000 ng/mL (cut-off +33%), 2500 ng/mL (cut-off + 67%) and 3000 ng/mL (cut-off + 100%) for MDMA.

Accuracy (Barbiturates, Benzodiazepines and Methadone and Tricyclic Antidepressants)

The accuracy was evaluated by assaying a coded panel of clinical urine samples containing varying concentrations of drugs and comparing the results to validated methods. Validated GC/MS assays measured barbiturates, benzodiazepines, and methadone levels. Results are shown in the following tables.

**ACCURACY COMPARED TO GC/MS
(Barbiturates, Benzodiazepines, and Methadone and Tricyclic Antidepressants)**

DRUG CLASS	Concentration Range (ng/mL)	Number of Samples	PROFILE Results
Barbiturates			
Phenobarbital	201 – 27776 155, 155, 156, 158, 161	36 5	36/36 Positive 5/5 Negative
Butalbital	240 - 3814 109, 151, 194	27 3	27/27 Positive 3/3 Positive
Pentobarbital	264	1	1/1 Positive
Benzodiazepines	303 – 30813 234, 236, 238, 250, 283	57 5	57/57 Positive 5/5 Negative
DRUG CLASS	Concentration Range (ng/mL)	Number of Samples	PROFILE Results
Methadone	306 - 70560 224, 226, 227, 230, 232	57 5	57/57 Positive 5/5 Negative
Tricyclic Antidepressants	305 – 19224 228, 235, 238, 238, 246	50 5	49/50 Positive 5/5 Negative

Only one tricyclic antidepressant positive sample containing a combination of nortriptyline and amitriptyline for a combined tricyclic antidepressant concentration of 519 ng/mL tested negative.

Additionally, the accuracy was evaluated in comparison to the Roche Diagnostics Sytems, Inc, ABUSCREEN ONLINE® assays for barbiturates, benzodiazepines and methadone. A panel of clinical urine samples was analyzed and the results obtained in the procedures were compared. Results are shown in the following tables.

**ACCURACY COMPARED TO THE ROCHE ABUSCREEN ONLINE® II OR HPLC ASSAYS
(Barbiturates, Benzodiazepines, Methadone and Tricyclic Antidepressants)**

**ABUSCREEN ONLINE® II Barbiturates Result (Secobarbital)
(300 ng/mL cutoff)**

		<u>Positive</u>	<u>Negative</u>	<u>Total</u>
BAR (200 ng/mL cutoff)	Positive	62	0	62
Butalbital Test	<u>Negative</u>	0	45	45
	Total	62	45	107

Overall agreement: 100% (107/107).

**ABUSCREEN ONLINE® II Benzodiazepines Result
(300 ng/mL cutoff)**

		<u>Positive</u>	<u>Negative</u>	<u>Total</u>
BZO (300 ng/mL cutoff)	Positive	57	0	57
Nordiazepam Test	<u>Negative</u>	0	45	45
	Total	57	45	102

Overall agreement: 100% (102/102).

**ABUSCREEN ONLINE® II Methadone Result
(300 ng/mL cutoff)**

		<u>Positive</u>	<u>Negative</u>	<u>Total</u>
MTD (300 ng/mL cutoff)	Positive	55	0	55
Methadone Test	<u>Negative</u>	<u>0</u>	<u>45</u>	<u>45</u>
	Total	55	45	100

Overall agreement: 100% (100/100).

HPLC Tricyclic Antidepressants (25 ng/mL limit of quantitation)

		<u>Positive</u>	<u>Negative</u>	<u>Total</u>
TCA (300 ng/mL cutoff)	Positive	49	0	49
Desipramine Test	<u>Negative</u>	<u>1</u>	<u>45</u>	<u>46</u>
	Total	50	45	95

Overall agreement: 99% (94/95). Only one tricyclic antidepressant positive sample containing a combination of nortriptyline (499 ng/mL) and amitriptyline (20 ng/mL) for a combined tricyclic antidepressant concentration of 519 ng/mL tested negative.

**PERCENT AGREEMENT COMPARED TO ROCHE ABUSCREEN
ONLINE ASSAYS OR HPLC
(Barbiturates, Benzodiazepines, Methadone and Tricyclic Antidepressants)**

	<u>POSITIVE</u>	<u>NEGATIVE</u>
Barbiturates	100% (62/62)	100% (45/45)
Benzodiazepines	100% (57/57)	100% (45/45)
Methadone	100% (55/55)	100% (45/45)
Tricyclic Antidepressants	98% (49/50)	100% (45/45)

Sensitivity / Precision / Distribution of Random Error (Barbiturates, Benzodiazepines, Methadone and Tricyclic Antidepressants)

Performance around the specific cutoff for each drug was evaluated by testing standard drug solutions diluted in drug-free urine in triplicate on 5 different days by 3 operators. Drug-free urine was also tested on each day. Operator-to-operator agreement was excellent, therefore, the data were combined and summarized in the following tables.

Barbiturates (Butalbital) Cutoff = 200 ng/mL

<u>Conc. (ng/mL)</u>	<u>Number Tested</u>	<u>Positive</u>	<u>Negative</u>	<u>% Agreement</u>
Negative	45	0	45	100
50	45	0	45	100
100	45	0	45	100
150	45	12	33	73
200	45	43	2	96
250	45	45	0	100
300	45	45	0	100

Benzodiazepines (Nordiazepam) Cutoff = 300 ng/mL

<u>Conc. (ng/mL)</u>	<u>Number Tested</u>	<u>Positive</u>	<u>Negative</u>	<u>% Agreement</u>
Negative	45	0	45	100
30	45	0	45	100
75	45	6	39	87
150	45	27	18	60
225	45	41	4	91
300	45	42	3	93
375	45	43	2	96
450	45	45	0	100
600	45	45	0	100

Methadone (Methadone) Cutoff = 300 ng/mL

<u>Conc. (ng/mL)</u>	<u>Number Tested</u>	<u>Positive</u>	<u>Negative</u>	<u>% Agreement</u>
Negative	45	0	45	100
30	45	3	42	93
75	45	28	17	62
150	45	35	10	78
225	45	43	2	96
300	45	45	0	100
375	45	45	0	100
450	45	43	2	96
600	45	44	1	98

Tricyclic Antidepressants (Desipramine) Cutoff = 300 ng/mL

<u>Conc. (ng/mL)</u>	<u>Number Tested</u>	<u>Positive</u>	<u>Negative</u>	<u>% Agreement</u>
Negative	45	0	45	100
30	45	2	43	96
75	45	17	28	62
150	45	33	12	73
225	45	34	11	76
300	45	40	5	89
375	45	41	4	91
450	45	44	1	98
600	45	45	0	100

Accuracy in a Point of Care setting (Oxycodone)

The accuracy was evaluated by assaying a panel of blind coded clinical urine samples containing varying concentrations of drugs and comparing to GC/MS results. The samples were obtained from MEDTOX Laboratories. Samples that screened negative by the predicate device were not confirmed by GC/MS. Positive samples were confirmed by GC/MS. The GC/MS determination included Oxycodone and oxymorphone and a weighted concentration using 100% cross-reactivity for Oxycodone and a 50% cross-reactivity for oxymorphone was calculated. Clinical urine samples containing Oxycodone and oxymorphone at higher concentrations were diluted with negative urine to obtain the desired number of samples with concentrations below and above the cutoff. The testing was performed by nine point of care personnel at three sites.

OXYCODONE Results vs stratified GC/MS Values

MEDTOX® OXYCODONE Results	Negative by Immunoassay (Predicate Device)	Concentration up to 50% below the cutoff	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration)	High Positive (Greater than 50% above the cutoff concentration)
Positive	0	2	2	6	37
Negative	103	5	4	1	1

GC/MS values used to categorize samples in this table are determined by adding together the concentration of Oxycodone plus 50% of the concentration of oxymorphone, based on the OXYCODONE cross-reactivity studies.

% Agreement among positives is 96%
 % Agreement among negatives is 97%

A second, in-house accuracy study was done using many of the same samples as in the POC study above. Results between the two studies were similar.

Sensitivity/Precision at One Location (Oxycodone)

Performance around the specific cutoff for Oxycodone was evaluated by testing standard drug solutions diluted in drug-free urine in triplicate on 6 different intervals by 3 in-house operators. Drug free urine was also tested on each interval. The results were interpreted at five minutes and are summarized below:

OXYCODONE Precision Study Results

Concentration of sample (ng/mL)	Number of determinations	Results #Neg / #Pos
0	54	54 / 0
25	54	54 / 0
50	54	50 / 4
75	54	14 / 40
100	54	4 / 50
125	54	1 / 53
150	54	0 / 54

Sensitivity/Precision at Point of Care Sites (Oxycodone)

Performance around the cutoff was evaluated by testing standard drug solutions diluted in drug-free urine at the various concentrations listed in the following table. 9 POC users at 3 different sites each tested 5 replicates of the 6 levels. The results obtained from the 3 sites, (Site1, Site2, Site3) are listed below:

OXYCODONE Precision Study Results at Point of Care Sites

Concentration of sample (ng/mL)	Number of determinations			Results #Neg / #Pos		
	Site 1	Site 2	Site 3	Site 1	Site 2	Site 3
0	15	15	15	15 / 0	15 / 0	15 / 0
25	15	15	15	15 / 0	15 / 0	15 / 0
50	15	15	15	13 / 2	15 / 0	14 / 1
100	15	15	15	0 / 15	3 / 12	3 / 12
125	15	15	15	0 / 15	2 / 13	1 / 14
150	15	15	15	0 / 15	0 / 15	0 / 15

Non Crossreactive Endogenous Compounds

Fifteen compounds were dissolved in appropriate solvents at a concentration of at least 1.0 mg/mL. Each compound was further diluted to 100 µg/mL except for albumin (20 mg/mL) and bilirubin (200 µg/mL). None of these compounds showed cross-reactivity at the listed concentrations.

- | | | |
|----------------|-----------------------|---------------------|
| Acetaldehyde | Creatinine | Hemoglobin, Human |
| Acetone | Epinephrine | Sodium Chloride |
| Albumin, Human | β-Estradiol | Tetrahydrocortisone |
| Bilirubin | Estriol | d,1-Thyroxine |
| Cholesterol | Glucose Std. Solution | Uric Acid |

Unrelated Compounds, Prescription and Over-the-Counter Medications

The following compounds were tested for reactivity. Listed compounds were dissolved in appropriate solvents and then added to drug-free urine for testing. Unless otherwise noted, all of the listed compounds were negative in each of the tests at 100 µg/mL. If a drug name is followed by an abbreviation such as "AMP" or "BAR" etc., check the "Related Compounds and Cross Reactants" listing for the drug in question under the appropriate heading (AMP, BAR, etc.). The drug may not cause a presumptive positive drug screen for that drug class.

- | | | |
|-----------------------------------|--------------------------------|--|
| Acecaïnide (N-Acetylprocainamide) | Acetaminophen | Acetylsalicylic Acid |
| Allobarbital- BAR | Alphenal- BAR | Alprazolam- BZO |
| Alprazolam, 1-Hydroxy- BZO | p-Aminobenzoic Acid | 7-Aminoclonazepam- BZO |
| 7-Aminoflunitrazepam- BZO | Amino glutethimide- BAR | l-Aminopyrine (4-(dimethylamino) antipyrine) |

Amitriptyline-**TCA**
 Amoxicillin
 Ampicillin
 Aspartame
 Atropine Sulfate
 Benzilic Acid
 Benzoylcegonine-**COC**
 Brompheniramine
 Butabarbital-**BAR**
 Cannabidiol-**THC**
 Carbamazepine-**TCA**
 Cephalexin
 Chlordiazepoxide-**BZO**
 Chlorpheniramine
 Clobazam-**BZO**
 Clonidine
 Cocaine-**COC**
 Cotinine
 Deoxycorticosterone
 Desmethylchlordiazepoxide-**BZO**
 Dexamethasone
 Diazepam-**BZO**
 Diflunisal
 Dimenhydrinate (Dramamine)
 Domperidone
 Doxepin-**TCA**
 EDDP-(Primary metabolite of methadone) - **MTD**
 Ephedrine-**AMP, MAMP**
 Estrone
 Fenfluramine-**MAMP**
 Flunitrazepam-**BZO**
 Furosemide
 Glutethimide-**BAR**
 Hexobarbital-**BAR**
 Hydrochlorothiazide
 Hydromorphone-**OPI, OXY**
 l-11-Hydroxy- Δ^8 -**THC-THC**
 3-Hydroxytyramine
 Imipramine-**TCA**
 Isoxsuprine
 Labetalol
 Lithium carbonate
 Lorazepam glucuronide-**BZO**
 Lysergic Acid Diethylamide (LSD)
 MDE (MDEA)-**AMP, MAMP**
 Meperidine
 Mesoridazine
 l-Methamphetamine- **AMP, MAMP**
 Methocarbamol
 Methylprylon
 Mirtazapine-**TCA**
 Morphine 3- β -D-Glucuronide-**OPI, OXY**
 Naltrexone-**OPI**
 Naproxen
 Nifedipine
 Norclomipramine-**TCA**
 Nordoxepin-**TCA**
 Normeperidine
 Nortriptyline-**TCA**
 Octopamine
 Omeprazole
 Oxaprosin
 Oxolinic Acid
 Oxymorphone-**OPI, OXY**
 Pentazocine
 Phenacetin (Acetophenetidin)
 Phenelzine
 Phenmetrazine
 Phentermine-**AMP, MAMP**
 Phenylephrine-**MAMP**
 Prazosin
 Procaine-**MAMP**
 Promazine-**TCA**
 Propranolol
 Pyrilamine
 Ranitidine
 Salicylic Acid
 Serotonin (5-Hydroxytryptamine)
 Sulfamethazine
 Temazepam-**BZO**
 Δ^8 -Tetrahydrocannabinol-**THC**
 Thebaine-**OPI, OXY**
 Thiopental
 Tolbutamide
 Triamterene
 Trifluoperazine
 Tripelennamine
 Tyramine-**AMP, MAMP**
 Venlafaxine
 Amobarbital-**BAR**
 d-Amphetamine-**AMP, MAMP**
 Apomorphine-**OPI, OXY**
 Atenolol
 Barbitol-**BAR**
 Benzoic Acid
 Benzphetamine
 Buprenorphine
 Butalbital-**BAR**
 Cannabinol-**THC**
 Carbamazepine- 10,11 epoxide-**TCA**
 Chloral Hydrate
 Chloroquine
 Chlorpromazine
 Clomipramine
 Clorazepate-**BZO**
 Codeine-**OPI, OXY**
 Cyclobenzaprine
 Desalkylflurazepam-**BZO**
 Desmethylflunitrazepam-**BZO**
 Dextromethorphan
 Diclofenac
 Digoxin
 1,3-Dimethylbarbituric acid-**BAR**
 Dopamine
 Doxylamine
 Efavirenz (Sustiva)
 Equilin
 Ethanol
 Fenopropfen
 Fluoxetine (Prozac)
 Fluvoxamine
 Guaiaacol Glyceryl Ether
 Hippuric acid
 Hydrocodone-**OPI, OXY**
 Hydroxybupropion
 p-Hydroxyphenobarbital-**BAR**
 Hydroxyzine
 Iproniazid
 Ketamine
 Levorphanol-**OPI, OXY**
 Loperamide
 Loxapine-**TCA**
 Maprotiline-**TCA**
 MDMA-**AMP, MAMP**
 Mephobarbital-**BAR**
 Methadone-**MTD**
 Methaqualone
 Methoxyphenamine
 Metoprolol
 6-Monoacetylmorphine-**OPI, OXY**
 Morphine 6- β -D-Glucuronide-**OPI, OXY**
 Nalorphine-**OPI, OXY**
 Niacinamide
 Nitrazepam-**BZO**
 Norcodeine-**OPI, OXY**
 Norethindrone
 Norpropoxyphene-**PPX**
 Noscapiene
 Ofloxacin
 Orphenadrine
 Oxazepam-**BZO**
 Oxycodone-**OPI**
 Papaverine hydrochloride
 Pentobarbital-**BAR**
 Phencyclidine-**PCP**
 Phenethylamine-**AMP, MAMP**
 Phenobarbital-**BAR**
 Phenytoin (Diphenylhydantoin)-**BAR**
 Phenylpropanolamine
 Prednisolone
 Procainamide
 Promethazine-**PPX**
 Protriptyline-**TCA**
 Quetiapine (Seroquel)-**TCA**
 Riboflavin
 Secobarbital-**BAR**
 Sertraline (Zoloft)
 Sulindac
 Temazepam glucuronide-**BZO**
 Δ^8 -Tetrahydrocannabinol-**THC**
 Theophylline
 Thioridazine
 Tolmetin (Tolectin)
 Triazolam-**BZO**
 Trimethoprim
 Tryptamine
 Tyrosine
 Verapamil
 Amoxapine
 l- Amphetamine-**AMP, MAMP**
 l-Ascorbic Acid
 Atomoxetine
 Barbituric Acid-**BAR**
 Benzocaine (ethyl-4-aminobenzoate)
 Benztropine
 Bupropion
 Caffeine
 Captopril
 Carisoprodol (Meprobamate)
 Chloramphenicol
 Chlorothiazide
 Chlorprothixene
 Clonazepam-**BZO**
 Clozapine
 Cortisone
 Cyclopentobarbital-**BAR**
 Desipramine
 Desmethylvenlafaxine
 Diacetylmorphine-**OPI, OXY**
 Diethylpropion
 Dihydrocodeine-**OPI**
 Diphenhydramine
 Ecgonine-**COC**
 EMDP-(Secondary metabolite of methadone)-**MTD**
 Erythromycin
 Ethylmorphine-**OPI, OXY**
 Fentanyl (Synthetic opiate)
 Flurazepam-**BZO**
 Genticic Acid (2,5-Dihydroxybenzoic acid)
 Haloperidol
 Hydralazine
 Hydrocortisone
 Hydroxyhippuric Acid
 4-Hydroxyphencyclidine-**PCP**
 Ibuprofen
 (R)-Isoproterenol
 Ketoprofen
 Lidocaine
 Lorazepam-**BZO**
 Lysergic Acid
 MDA-**AMP, MAMP**
 Melanin
 Mepivacaine
 d-Methamphetamine-**AMP, MAMP**
 Methcathinone
 Methylphenidate
 Midazolam-**BZO**
 Morphine-**OPI, OXY**
 Nalidixic Acid
 Naloxone-**OPI, OXY**
 Nicotine
 Nitrofurantoin
 Nordiazepam-**BZO**
 Norlysergic Acid
 l-Norpseudoephedrine
 Nylicrin
 Olanzapine-**TCA**
 Oxalic Acid
 Oxazepam glucuronide-**BZO**
 Oxymetazoline
 Penicillin G
 Perphenazine-**TCA**
 Phendimetrazine
 Pheniramine
 Phenothiazine-**TCA**
 Phenylbutazone
 Piroxicam
 Prednisone
 Prochlorperazine-**TCA**
 Propoxyphene-**PPX**
 d-Pseudoephedrine
 Quinidine
 Rifampin
 Selegiline (Deprenyl)
 Sildenafil (Viagra)
 Talbutal-**BAR**
 Tetracycline
 Tetrahydrozoline
 Thiamine
 Thiothixene-**TCA**
 Trazodone
 Triazolam, 1-hydroxy-**BZO**
 Trimipramine-**TCA**
 Tryptophan
 Valproic Acid
 Zomepirac

Related Compounds and Cross Reactants

The following metabolites and compounds were tested. Reference standards for the various metabolites and compounds were prepared in negative urine samples. None of the compounds reacted with the remaining tests in the panel. Results are expressed as the minimum concentration required to produce a positive result in the indicated assay.

Amphetamines-(AMP)(d-Amphetamine) 1000 ng/mL

l-Amphetamine
Ephedrine
MDA
MDMA
MDE (MDEA)
l-Methamphetamine
d-Methamphetamine
Phenethylamine
Phentermine
Tyramine

Result

Positive at 100 µg/mL
Negative at 100 µg/mL
Positive at 400 ng/mL
Negative at 100 µg/mL
Negative at 100 µg/mL
Negative at 100 µg/mL
Negative at 100 µg/mL
Positive at 10 µg/mL
Negative at 100 µg/mL

Barbiturate-(BAR) (Butalbital) 200 ng/mL

Allobarbital
Alphenal
Amino glutethimide
Amobarbital
Barbital
Barbituric Acid
Butobarbital
Cyclopentobarbital
1,3 Dimethylbarbituric Acid

Result

Positive at 500 ng/mL
Positive at 100 ng/mL
Negative at 100,000 ng/mL
Positive at 2500 ng/mL
Positive at 2500 ng/mL
Negative at 100,000 ng/mL
Positive at 750 ng/mL
Positive at 250 ng/mL
Negative at 100,000 ng/mL

Glutethimide
Hexobarbital
p-Hydroxyphenobarbital
Mephobarbital
Pentobarbital
Phenobarbital
Phenytoin (Diphenylhydantoin)
Secobarbital
Talbutal

Negative at 100,000 ng/mL
Negative at 100,000 ng/mL
Positive at 500 ng/mL
Negative at 100,000 ng/mL
Positive at 500 ng/mL
Positive at 800 ng/mL
Positive at 2500 ng/mL
Positive at 75 ng/mL
Positive at 50 ng/mL

Benzodiazepine-(BZO) (Nordiazepam) 300ng/mL

Alprazolam
Alprazolam, 1-OH
7-Aminoclonazepam
7-Aminoflunitrazepam
Chlordiazepoxide
Clobazam
Clonazepam
Clorazepate
Desalkylflurazepam
Desmethylchlordiazepoxide
Desmethylflunitrazepam
Diazepam
Flunitrazepam
Flurazepam
Lorazepam
Lorazepam glucuronide
Midazolam
Nitrazepam
Oxazepam
Oxazepam glucuronide
Temazepam
Temazepam glucuronide
Triazolam
Triazolam, 1-OH

Result

Positive at 250 ng/mL
Positive at 25 µg/mL
Negative at 100 µg/mL
Negative at 100 µg/mL
Negative at 100 µg/mL
Positive at 50 ng/mL
Positive at 250 ng/mL
Positive at 250 ng/mL
Positive at 250 ng/mL
Positive at 500 ng/mL
Positive at 75 ng/mL
Positive at 50 ng/mL
Positive at 75 ng/mL
Negative at 100 µg/mL
Positive at 2.5 µg/mL
Positive at 1 µg/mL
Positive at 5 µg/mL
Positive at 50 ng/mL
Positive at 500 ng/mL
Positive at 2.5 µg/mL
Positive at 50 ng/mL
Positive at 750 ng/mL
Positive at 750 ng/mL
Negative at 10 µg/mL

Cocaine-(COC) (Benzoylcegonine) 300 ng/mL

Cocaine
Ecgonine
Ecgonine Methyl Ester

Result

Positive at 800 ng/mL
Negative at 100 µg/mL
Negative at 100 µg/mL

Methamphetamine-(MAMP) (d-Methamphetamine) 1000 ng/mL, (MDMA) 1500 ng/mL

d-Amphetamine
l-Amphetamine
Ephedrine
Fenfluramine
MDA
MDE (MDEA)
l-Methamphetamine
Phenethylamine
Phentermine
Phenylephrine
Procaine
Pseudoephedrine
Tyramine

Result

Negative at 100 µg/mL
Negative at 100 µg/mL
Positive at 2.5 µg/mL
Positive at 25 µg/mL
Negative at 100 µg/mL
Positive at 5 µg/mL
Positive at 7.5 µg/mL
Positive at 2.5 µg/mL
Negative at 100 µg/mL
Positive at 25,000 ng/mL
Positive at 7,500 ng/mL
Negative at 100 µg/mL
Negative at 100 µg/mL

Methadone-(MTD) (Methadone) 300 ng/mL

Primary metabolite (EDDP)
Secondary metabolite (EMDP)

Result

Negative at 100 µg/mL
Negative at 100 µg/mL

Opiates(2000)-(OPI) (Codeine/Morphine) 2000ng/mL

Apomorphine
Diacetylmorphine
Dihydrocodeine
Ethylmorphine
Hydrocodone
Hydromorphone
Levorphanol
6-Monoacetyl Morphine

Result

Negative at 100µg/mL
Positive at 2.0 µg/mL
Positive at 3 µg/mL
Positive at 400 ng/mL
Positive at 2.0 µg/mL
Positive at 3 µg/mL
Positive at 12.5 µg/mL
Positive at 3 µg/mL

Morphine 3-β-D-Glucuronide	Positive at 3 µg/mL
Morphine 6-β-D-Glucuronide	Positive at 25 µg/mL
Nalorphine	Negative at 100 µg/mL
Naloxone	Negative at 100 µg/mL
Naltrexone	Negative at 100 µg/mL
Norcodeine	Positive at 25 µg/mL
Oxycodone	Negative at 100 µg/mL
Oxymorphone	Negative at 100 µg/mL
Thebaine	Positive at 50 µg/mL

Opiates(300)-(OPI) (Codeine and Morphine) 300ng/mL

Apomorphine	Negative at 100 µg/mL
Diacetylmorphine	Positive at 200 ng/mL
Dihydrocodeine	Positive at 400 ng/mL
Ethylmorphine	Positive at 200 ng/mL
Hydrocodone	Positive at 800 ng/mL
Hydromorphone	Positive at 800 ng/mL
Levorphanol	Negative at 100 µg/mL
6-Monoacetylmorphine	Positive at 200 ng/mL
Morphine 3-β-D-Glucuronide	Positive at 200 ng/mL
Morphine 6-β-D-Glucuronide	Positive at 12.5 µg/mL
Nalorphine	Positive at 75 µg/mL
Naloxone	Negative at 100 µg/mL
Naltrexone	Negative at 100 µg/mL
Norcodeine	Positive at 12.5 µg/mL
Oxycodone	Negative at 100 µg/mL
Oxymorphone	Negative at 100 µg/mL
Thebaine	Positive at 12.5 µg/mL

Result

Oxycodone (OXY) cutoff= 100 ng/mL

Apomorphine	Negative at 100,000 ng/mL
Codeine	Positive at 2,500 ng/mL
Diacetylmorphine	Negative at 100,000 ng/mL
Dihydrocodeine	Positive at 2,500 ng/mL
Ethylmorphine	Positive at 2,500 ng/mL
Hydrocodone	Positive at 10,000 ng/mL
Hydromorphone	Positive at 10,000 ng/mL
Levorphanol	Negative at 50,000 ng/mL
Morphine	Positive at 5,000 ng/mL
6-Monoacetylmorphine	Negative at 100,000 ng/mL
Morphine 3-β-D-Glucuronide	Negative at 100,000 ng/mL
Morphine 6-β-D-Glucuronide	Negative at 10,000 ng/mL
Nalorphine	Negative at 100,000 ng/mL
Naloxone	Positive at 10,000 ng/mL
Naltrexone	Positive at 25,000 ng/mL
Norcodeine	Positive at 50,000 ng/mL
Oxymorphone	Positive at 200 ng/mL
Thebaine	Negative at 100,000 ng/mL

Result

Propoxyphene-(PPX)(Norpropoxyphene) 300 ng/mL

Promethazine	Positive at 100,000 ng/mL
Propoxyphene	Positive at 50 ng/mL

Result

Phencyclidine-(PCP) (Phencyclidine) 25 ng/mL

4-Hydroxyphencyclidine	Positive at 5 µg/mL
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Result

Cannabinoids-(THC) (11-nor-9-carboxy-Δ⁹-THC) 50 ng/mL

Cannabidiol	Negative at 100 µg/mL
Cannabinol	Negative at 100 µg/mL
l-11 Hydroxy-Δ ⁹ -THC	Negative at 50 µg/mL
Δ ⁸ -Tetrahydrocannabinol	Negative at 100 µg/mL
Δ ⁹ -Tetrahydrocannabinol	Negative at 100 µg/mL

Result

Tricyclic Antidepressant-(TCA) (Desipramine) 300 ng/mL

Amitriptyline	Positive at 500 ng/mL
Carbamazepine	Negative at 100 µg/mL
Carbamazepine-10, 11 epoxide	Negative at 100 µg/mL
Chlorpromazine	Negative at 100 µg/mL
Chlorprothixine	Negative at 100 µg/mL
Clomipramine	Negative at 100 µg/mL
Clozapine	Positive at 2.5 µg/mL
Cyclobenzaprine	Positive at 750 ng/mL
Doxepin	Positive at 750 ng/mL
Imipramine	Positive at 250 ng/mL
Loxapine	Negative at 100 µg/mL
Maprotiline	Positive at 750 ng/mL
Mirtazapine	Negative at 100 µg/mL
Norclomipramine	Negative at 100 µg/mL
Nordoxepin	Positive at 500 ng/mL
Nortriptyline	Positive at 500 ng/mL
Olanzapine	Positive at 75 µg/mL
Perphenazine	Negative at 100 µg/mL
Phenothiazine	Negative at 100 µg/mL
Prochlorperazine	Positive at 5,000 ng/mL
Promazine	Positive at 250 ng/mL
Protriptyline	Negative at 100 µg/mL
Thiothixene	Negative at 100 µg/mL
Trimipramine	Positive at 5 µg/mL
Quetiapine (Seroquel)	Positive at 5 µg/mL

Result

Interference-Oxycodone

pH and Specific Gravity:

The OXYCODONE test was assayed with six negative clinical samples with pH values of 4.0, 5.0, 6.0, 7.0, 8.0 and 9.0 ± 0.1. Each sample was assayed in triplicate. The pH samples were fortified with Oxycodone to the concentrations of 25 ng/mL and 150 ng/mL. All the pH levels gave negative results when fortified to 25 ng/mL, and all pH levels gave positive results when fortified to 150 ng/mL.

The OXYCODONE test was assayed with eight samples with specific gravity values of 1.003, 1.005, 1.010, 1.015, 1.020, 1.025, 1.030 and 1.035 ± 0.001. Each sample was assayed in triplicate. The specific gravity samples were fortified with Oxycodone to the concentrations of 25 ng/mL and 150 ng/mL. All the specific gravity levels gave negative results when fortified to 25 ng/mL, and all specific gravity levels gave positive results when fortified to 150 ng/mL.

Common Drugs:

Following the study of M.L. Smith, et. al.⁵ drug free urine samples were spiked with Oxycodone to the concentrations of 25 ng/mL and 150 ng/mL. 100 µg/mL of the common drugs were then added to the preparation and assayed by the OXYCODONE test. Samples were evaluated in triplicate by in-house operators. None of the common drugs listed in the following table affected the expected results.

COMMON DRUGS EVALUATED WITH OXYCODONE TESTS

Acetylsalicylic Acid	Chlorpheniramine	Ibuprofen
Acetaminophen	Cocaine	Morphine- OXY
Brompheniramine maleate	Dextromethorphan	Phenobarbital-
Caffeine	Diphenylhydantoin	d-Pseudoephedrine
Carbamazepine	Doxylamine	Salicylic Acid

Interference Methamphetamine Only

Following the study of M.L. Smith, et. al.⁵ the following drugs were tested to determine the degree of interference they may have on the test. Commercial negative urine was spiked with 100 µg/mL of each of these drugs and with 600 ng/mL of methamphetamine. Each spiked sample was tested in triplicate on the test. None of these drugs affected the expected negative or positive results with the 600 ng/mL fortified samples. The drugs are listed below.

Acetylsalicylic Acid	Chlorpheniramine	Ibuprofen
Acetaminophen	Cocaine	Morphine
Brompheniramine maleate	Dextromethorphan	Phenobarbital
Caffeine	5,5 Diphenylhydantoin	d-Pseudoephedrine
Carbamazepine	Doxylamine	Salicylic Acid

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15. LIMITED EXPRESS WARRANTIES

The manufacturer makes no express warranty other than the diagnostic test kit will measure certain drugs and/or drug metabolites when used in accordance with the manufacturer's printed instructions. The use of the kit for any other purpose is outside the intended use of this product. The manufacturer gives no express warranty as to what the legal or clinical significance is of the levels of drug(s)/drug metabolites detected by the PROFILE®-IV VISUAL Drugs of Abuse Test. The manufacturer disclaims any and all implied warranties of merchantability, fitness for use or implied utility for any other purposes. Any and all damages for failure of the kit to perform to its instructions are limited to the replacement value of the kit.

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U.S. Patent Nos. 5,202,268, 6,566,051, 6,376,251, 6,653,139

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