

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k091454

B. Purpose for Submission:

Addition of 3 new drugs of abuse tests (oxycodone, tricyclic antidepressants and propoxyphene) to an already cleared reader. Amphetamines, Barbiturates, Benzodiazepines, Cocaine, Methadone, Methamphetamine, Opiates, Phencyclidine and THC assays were previously cleared on the reader.

C. Measurand:

Oxycodone, tricyclic antidepressants, and propoxyphene.

D. Type of Test:

Qualitative immunochromatographic test for drugs of abuse in urine performed on a reader.

E. Applicant:

Medtox Diagnostics, Inc.

F. Proprietary and Established Names:

PROFILE®-V MEDTOXScan®

G. Regulatory Information:

1. Regulation section:
 - 21 CFR 862.3650 Opiate test system
 - 21 CFR 862.3700 Propoxyphene test system
 - 21 CFR 862.3910 Tricyclic antidepressant drugs test system

2. Classification:
 - Class II

3. Product code:
 - DJG, Enzyme Immunoassay Opiates

JXN, Enzyme Immunoassay, Propoxyphene.
LFI, High Pressure Liquid Chromatography, Tricyclic Antidepressant Drugs

4. Panel:

91, Toxicology

H. Intended Use:

1. Intended use(s):

See indications for use statement below.

2. Indication(s) for use:

The PROFILE®-V MEDTOXScan® Drugs of Abuse Test System consists of the PROFILE®-V MEDTOXScan® Test Devices and the MEDTOXScan® Reader. The PROFILE®-V MEDTOX Scan® Test Devices are one-step immunochromatographic tests for the rapid, qualitative detection of one or more of the following in human urine: Amphetamines, Barbiturates, Benzodiazepines, Cocaine, Methadone, Methamphetamine, Opiates, Oxycodone, Phencyclidine, Propoxyphene, THC (Cannabinoids), and Tricyclic Antidepressants or their metabolites. The PROFILE®-V MEDTOXScan® Test Devices can only be used with the MEDTOXScan® Reader. The MEDTOX Scan® Reader is an instrument used to interpret and report the results of the PROFILE®-V MEDTOXScan® Test Device. PROFILE®-V MEDTOXScan® Test Devices cannot be visually read.

The PROFILE®-V MEDTOXScan® Drugs of Abuse Test System is for *in vitro* diagnostic use and is intended for prescription use only. It is not intended for use in point-of-care settings.

The PROFILE®-V MEDTOXScan® Drugs of Abuse Test System detects drug classes at the following cutoff concentrations:

AMP Amphetamine (d-Amphetamine)	500 ng/mL	OPI Opiates (Morphine)	100 ng/mL
BAR Barbiturates (Butalbital)	200 ng/mL	OXY Oxycodone (Oxycodone)	100 ng/mL
BZO Benzodiazepines (Nordiazepam)	150 ng/mL	PCP Phencyclidine (Phencyclidine)	25 ng/mL
COC Cocaine (Benzoyllecgonine)	150 ng/mL	PPX Propoxyphene (Norpropoxyphene)	300 ng/mL
MAMP Methamphetamine (d-Methamphetamine)	500 ng/mL	THC Cannabinoids (11-nor-9-carboxy- r9-THC)	50 ng/mL
MTD Methadone	200	TCA Tricyclic	300 ng/mL

(Methadone)	ng/mL	Antidepressants (Desipramine)	
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Configurations of the PROFILE®-V MEDTOXScan® Test Devices may consist of any combination of the above listed and previously cleared drugs. Refer to specific product labeling for the combination of drug tests included on that test device.

The PROFILE®-V MEDTOXScan® DRUGS OF ABUSE TEST SYSTEM 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), HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC) OR LIQUID CHROMATOGRAPHY / TANDEM MASS SPECTROMETRY (LC/MS/MS) ARE THE PREFERRED CONFIRMATORY METHODS. CLINICAL CONSIDERATION AND PROFESSIONAL JUDGMENT SHOULD BE APPLIED TO ANY DRUG OF ABUSE TEST RESULT, PARTICULARLY WHEN PRELIMINARY POSITIVE RESULTS ARE OBTAINED.

The MEDTOXScan® Reader includes a Positive QC Test Device, a Negative QC Test Device and a Cleaning Cassette. The MEDTOXScan® Positive and Negative QC Test Devices are intended to detect errors associated with the MEDTOXScan® Reader and a contaminated contact imaging sensor (CIS), and to verify that the CIS cleaning procedure using the MEDTOXScan® Cleaning Cassette effectively removed any contamination.

3. Special conditions for use statement(s):

The device is for in vitro diagnostic prescription use.

The assay is not designated for use in point-of-care settings.

The PROFILE®-V MEDTOXScan® Test Devices cannot be visually read.

The PROFILE®-V MEDTOXScan® Drugs of Abuse Test System 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), high performance liquid chromatography (HPLC) or liquid chromatography/tandem mass spectrometry (LC/MS/MS) are the preferred confirmatory methods. Clinical consideration and professional judgment should be applied to any drug of abuse test result, particularly when preliminary positive results are obtained.

4. Special instrument requirements:

PROFILE®-V MEDTOXScan®

I. Device Description:

The PROFILE®-V MEDTOXScan® Drugs of Abuse Test System includes an instrument and drugs of abuse cassettes that detect specific drugs in urine. The PROFILE®-V MEDTOXScan® Test Device includes antibody-colloidal gold, drug-conjugates and a control line. A test line will form when drug in the sample is below the detection threshold (negative result). The MEDTOXScan® Reader scans the test device and utilizes a contact imaging sensor (CIS) to capture relative line intensities. Software algorithms and barcodes are used to identify the test device, the drug tests associated with the test device and whether the presence or absence of a line is associated with a negative or positive result, respectively.

The MEDTOXScan® Reader includes a Positive QC Test Device, a Negative QC Test Device and a Cleaning Cassette. The MEDTOXScan® Positive and Negative QC Test.

J. Substantial Equivalence Information:

1. Predicate device name(s):

PROFILE®-V MEDTOXScan® Drugs of Abuse Test System, MEDTOX® Oxycodone, VERDICT-II Propoxyphene, PROFILE-ER.

2. Predicate K number(s):

k080635, k060351, k020387 and k002331 respectively.

3. Comparison with predicate:

The submission is the exact device as the predicate.

The differences are the number of drugs detected, calibration points and timing modes-see table below.

Differences		
Item	Device	Predicate
Analytes	Amphetamines, Barbiturates, Benzodiazepines, Cocaine, Methadone, Methamphetamine, Opiates, Phencyclidine, THC, Tricyclics Antidepressants, Propoxyphene and Oxycodone,	Amphetamines, Barbiturates, Benzodiazepines, Cocaine, Methadone, Methamphetamine, Opiates, Phencyclidine and THC.
Calibration	5-point calibration method is used	A single point +3SD threshold calibration is used.
Timing Modes	Clinical samples are run in instrument-time mode only	Clinical samples are run in either instrument-timed or user-times modes.

K. Standard/Guidance Document Referenced (if applicable):

The sponsor references the following guidance document in their submission:

CLSI Guidance EP-12A User Protocol for the Evaluation of Qualitative Test Performance.

L. Test Principle:

The PROFILE®-V MEDTOXScan® Drugs of Abuse Test System includes a competitive, membrane-based immunochromatographic PROFILE®-V MEDTOXScan® Test Device and the MEDTOXScan® Reader.

Antibody-Colloidal Gold: Mouse monoclonal antibodies bind to the drug being tested.

Drug-Conjugates: Each drug to be tested was individually conjugated to bovine serum albumin (BSA) or IgG. Each drug conjugate is immobilized on a test line at a designated position on the membrane strip.

Control Line: Each test strip has anti-mouse antibody immobilized at the Control (C) position of the membrane strip. The anti-mouse antibody will bind excess antibody-colloidal gold, indicating that the reagents are migrating properly. When the urine sample is placed in the sample well of a test strip, the dried antibody-colloidal gold under the sample pad dissolves and the urine wicks up the white strips carrying the reddish-purple antibody-colloidal gold 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 and bind to the respective drug conjugate(s) immobilized on the membrane. Each strip has up to 4 drug test lines labeled T1 – T4. The binding of the antibody-colloidal gold to the drug conjugate generates a line at the corresponding test (T) position on the strip. The MEDTOXScan® Reader will scan each test position and if a line is detected it will return “NEG” on the display screen (or print out) next to the abbreviation for the drug test, indicating a negative result.

Positive 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. When the antibody colloidal gold binds to the drug(s) in the urine, it cannot bind to the drug conjugate immobilized on the membrane and no line is generated at the drug specific position in the result window. The MEDTOXScan® Reader will scan each test position and if no line is detected it will return “POS” on the display screen (or print out) next to the abbreviation for the drug test, indicating a preliminary positive result.

Control Line (Valid or Invalid results)

Each test strip has an internal procedural control. A line must form at the Control (C)

position in the result window to indicate that sufficient sample was applied and that the reagents are migrating properly. If a Control line does not form, the test is invalid. The MEDTOXScan® Reader scans each control line and returns “VALID” to the right of the drug test result to confirm that the control line was detected. If no control line is detected it will return “INVALID” on the display screen next to the abbreviation for the invalid drug test, and no result will be given for the drug test.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Urine stock solutions were prepared for each of the test compounds by spiking standard solution of known concentrations into a commercially available negative pool of urine (pH range of 6-7 and Specific Gravity range of 1.012 - 1.018). Each stock solution was assayed by GC/MS or LC/MS/MS. The 150% cutoff sample was serially diluted to form the next lower level in the study. The prepared diluted samples were re-checked additionally by GC/MS or LC/MS/MS to confirm concentrations. A total of 45 results (3 readers x 3 aliquots for 5 days) were obtained for each level.

Oxycodone (Oxycodone) Cutoff=100 ng/ml				
Conc. (ng/mL)	% of Cutoff	Number Tested	Positive	Negative
0	Neg	45	0	45
25	25%	45	0	45
50	50%	45	1	44
75	75%	45	26	19
125	125%	45	45	0
150	150%	45	45	0

Propoxyphene (Norpropoxyphene) Cutoff=300 ng/mL				
Conc. (ng/mL)	% of Cutoff	Number Tested	Positive	Negative
0	Neg	45	0	45
150	50%	45	0	45
225	75%	45	14	31
375	125%	45	43	2
450	150%	45	45	0

Tricyclics Antidepressants (Desipramine) Cutoff=300 ng/mL				
Conc. (ng/mL)	% of Cutoff	Number Tested	Positive	Negative
0	Neg	45	0	45
150	50%	45	0	45
225	75%	45	36	9

375	125%	45	45	0
450	150%	45	45	0

b. *Linearity/assay reportable range:*

Not applicable. This assay is intended for qualitative use.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Profile V quality control materials were previously cleared and are sold separately. The sponsor specifies the quality control product in the “materials required but not provided” section of the labeling.

No calibrators are required. The device is calibrated during the manufacturing process.

d. *Detection limit:*

Sensitivity of qualitative assays may be characterized by validating performance around the claimed cutoff concentration of the assay, and demonstrating the lowest concentration of drug that is capable of or consistently producing a positive result. This information appears in the precision section, *l.a.*, above.

e. *Analytical specificity:*

Cross-reactivity was established by spiking various concentrations of similarly structured drug compounds into drug-free urine. The tables below summarize the results of cross-reactivity studies using various common and structurally similar compounds. Results are expressed as a minimum concentration of metabolite or compound required to produce a response approximately equivalent to the cutoff concentration of the assay. (or, if no cross-reactivity was observed, then “none detected” is reported).

Oxycodone (OXY) (Oxycodone) 100 ng/mL		
Compound	Result	% Cross-Reactive
Codeine	Positive at 5000 ng/mL	2%
Dihydrocodeine	Positive at 25,000 ng/mL	<1%
Ethylmorphine	Positive at 7,500 ng/mL	1%
Hydrocodone	Positive at 50,000 ng/mL	<1%
Hydromorphone	Positive at 50,000 ng/mL	<1%
Morphine	Positive at 25,000 ng/mL	<1%
Morphine 6-β-D-Glucuronide	Positive at 100,000 ng/mL	<1%
Naloxone	Positive at 25,000 ng/mL	<1%
Naltrexone	Positive at 50,000 ng/mL	<1%

Oxycodone (OXY) (Oxycodone) 100 ng/mL		
Norcodeine	Positive at 100,000 ng/mL	<1%
Oxymorphone	Positive at 250 ng/mL	40%
Apomorphine	Negative at 100,000 ng/mL	None Detected
Diacetylmorphine	Negative at 100,000 ng/mL	None Detected
Levorphanol	Negative at 100,000 ng/mL	None Detected
6-Monoacetylmorphine	Negative at 100,000 ng/mL	None Detected
Morphine 3-β-D-Glucuronide	Negative at 100,000 ng/mL	None Detected
Nalorphine	Negative at 100,000 ng/mL	None Detected
Thebaine	Negative at 100,000 ng/mL	None Detected

Propoxyphene-(PPX) (Norpropoxyphene) 300 ng/mL		
Compound	Result	% Cross-Reactive
Propoxyphene	Positive at 50 ng/mL	600%

Tricyclic Antidepressant-(TCA) (Desipramine) 300 ng/mL		
Compound	Result	% Cross-Reactive
Amitriptyline	Positive at 500 ng/mL	60%
Clozapine	Positive at 7,500 ng/mL	4%
Cyclobenzaprine	Positive at 20,000 ng/mL	2%
Doxepin	Positive at 1,300 ng/mL	23%
Imipramine	Positive at 250 ng/mL	120%
Maprotiline	Positive at 300 ng/mL	100%
Nordoxepin	Positive at 700 ng/mL	43%
Nortriptyline	Positive at 500 ng/mL	60%
Perphenazine	Positive at 75,000 ng/mL	<1%
Prochlorperazine	Positive at 50,000 ng/mL	<1%
Promazine	Positive at 900 ng/mL	33%
Protriptyline	Positive at 50,000 ng/mL	<1%
Quetiapine (Seroquel)	Positive at 10,000 ng/mL	3%
Trimipramine	Positive at 5,000 ng/mL	6%
Carbamazepine	Negative at 100,000 ng/mL	None Detected
Carbamazepine-10, 11 epoxide	Negative at 100,000 ng/mL	None Detected
Chlorpromazine	Negative at 100,000 ng/mL	None Detected
Clomipramine	Negative at 100,000 ng/mL	None Detected
Loxapine	Negative at 100,000 ng/mL	None Detected
Mirtazapine	Negative at 100,000 ng/mL	None Detected
Norclomipramine	Negative at 100,000 ng/mL	None Detected
Olanzapine	Negative at 100,000 ng/mL	None Detected
Phenothiazine	Negative at 100,000 ng/mL	None Detected

Thiothixene	Negative at 100,000 ng/mL	None Detected
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Non Cross-reactive endogenous compounds

The following compounds were evaluated for reactivity with the Profile V device at 100 ug/mL (albumin was evaluated at 20 mg/mL and bilirubin was evaluated at 200 ug/mL). Samples were evaluated in triplicate by in-house operators. The listed compounds gave negative results with the Profile V device.

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

Unrelated Compounds, Prescription and Over-the-counter Medication

Common compounds were evaluated for reactivity at 100 ug/mL. Samples were evaluated in triplicate by in-house operators and the list of compounds evaluated appears in the package insert.

Common Drugs

Drug free urine samples were spiked with the Profile V targeted drugs to the concentrations of 50% and 125% of the cutoff concentrations. 100 ug/mL of the common drugs listed below, were then added to the preparation and assayed. Evaluations were performed in triplicate by in-house operators. None of the common drugs listed in the following table affected the expected results.

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

There is the possibility that other substances and/or factors not listed above may interfere with the test and cause false results.

pH and Specific Gravity:

To test for possible positive and/or negative interference from pH, the sponsor prepared two study control samples. The control samples consisted of drug free urine spiked with the calibrator drugs at 50% and 125% of the chosen cutoffs.

Aliquots of the control samples and samples with no drug present were adjusted to a pH of 4.0, 7.0, and 9.0. Each sample was assayed in triplicate. No negative interference due to pH was observed.

To test for possible positive and/or negative interference from specific gravity the sponsor, prepared two study control samples. The control samples consisted of drug free urine spiked with the calibrator drugs at negative and positive concentrations. Aliquots of the control samples were altered to span the specific gravity range of 1.003 to 1.030. No positive or negative interference due to specific gravity was observed.

f. Assay cut-off:

Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision section, 1.a, above.

2. Comparison studies:

a. Method comparison with predicate device

Performance was evaluated by assaying a panel of blind coded unaltered clinical urine samples containing varying concentrations of drugs with the Profile V device. In-house results (obtained at 10 minutes) were then compared to GC/MS or LC/MS/MS results. Study results are reported in the table below. –

Drug ng/mL	Candidate Device Results	Negative	Less than half the cutoff concentration by GC/MS or LC/MS/MS	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)
OXY (100)	Positive	0	0	0	3	36
	Negative	40	3	4	1	0
PPX (300)	Positive	0	0	4	4	40
	Negative	45	1	2	0	0
TCA (300)	Positive	0	0	3	4	36
	Negative	40	2	1	0	0

The summary of discordant results is listed in the table below:

Assay	Cutoff Value (ng/mL)	Profile V Assay Pos/Neg	GC/MS or LC/MS/MS value (ng/mL)
OXY	100	Negative	Oxycodone at 71 ng/mL and Oxymorphone at 31 ng/mL.
PPX	300	Positive	Norpropoxyphene at 172 ng/mL
PPX	300	Positive	Norpropoxyphene at 194 ng/mL
PPX	300	Positive	Norpropoxyphene at 228 ng/mL
PPX	300	Positive	Norpropoxyphene at 271 ng/mL.
TCA	300	Positive	Nortriptyline at 194 ng/mL
TCA	300	Positive	Nortriptyline at 217 ng/mL
TCA	300	Positive	Desipramine at 287 ng/mL.

b. Matrix comparison:

Not applicable. The assay is intended for only one sample matrix, urine.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Not applicable.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.