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

A. 510(k) Number:

k111927

B. Purpose for Submission:

New device

C. Measurand:

Methamphetamine

D. Type of Test:

Qualitative enzyme immunoassay (EIA)

E. Applicant:

Psychemedics Corporation

F. Proprietary and Established Names:

Psychemedics Microplate EIA for Methamphetamine in Hair

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LAF	II	Methamphetamine Test System. 21 CFR §862.3610	Toxicology (91)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indications(s) for use:

   The Psychemedics Microplate EIA for Methamphetamine is an enzyme immunoassay (EIA) for the preliminary qualitative detection of methamphetamine in human head and body hair samples using a methamphetamine calibrator at 5 ng /10 mg hair cutoff for the

purpose of identifying methamphetamine use. This product is intended exclusively for in-house professional use only and is not for sale to anyone.

The Psychemedics Microplate EIA for Methamphetamine in Hair provides only a preliminary analytical test result. To confirm a presumptive screen positive result, a more specific alternate chemical method such as LC/MS/MS (liquid chromatography/mass spectrometry/mass spectrometry) must be used. Clinical consideration and professional judgment must be applied to the interpretation of any drug-of-abuse test result.

3. Special conditions for use statement(s):

   Over the Counter use

4. Special instrument requirements:

   The device is for use with a microplate reader capable of measuring at 450 and 630 nm.

   Plate washing also requires an instrument specifically designed to effectively and reproducibly wash all wells uniformly.

I. Device Description:

The test consists of two parts; a pre-analytical hair treatment procedure (to convert the solid matrix of hair to a measurable liquid matrix) and the screening assay, the Psychemedics Microplate EIA for Methamphetamine. The test system consists of microplate wells coated with multiple antigens including methamphetamine conjugated to bovine serum albumin (BSA). Hair samples are extracted by incubation with dithiothreitol and then neutralized. Samples are incubated in the wells with goat anti-methamphetamine. The wells are emptied and washed once, followed by addition of donkey anti-goat conjugated with horseradish peroxidase (HRP), followed by washing and incubation with substrate trimethylbenzidine (TMB), acidification and reading using a microplate absorbance reader at 450 nm with background set at 630 nm.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Psychemedics RIA Methamphetamine/MDMA Assay

2. Predicate 510(k) number(s):

   k011185

3. Comparison with predicate:

Item	Psychemedics Cocaine EIA (Candidate Device)	Psychemedics RIA Cocaine Assay (Predicate- K010868)
Indication for Use	The Psychemedics Microplate EIA for Methamphetamine is an enzyme immunoassay (EIA) for the preliminary qualitative detection of methamphetamine in human head and body hair samples using a methamphetamine calibrator at 5 ng /10 mg hair cutoff for the purpose of identifying methamphetamine use. This product is intended exclusively for in-house professional use only. The test is not intended for over the counter sale to non-professionals.	Same
Method of Measurement	Microplate reader	Gamma counter
Cutoff Concentration	5 ng methamphetamine /10 mg hair	Same
Test Principle	Enzyme Immunoassay (EIA)	Radioimunoassay (RIA)
Extraction Method	The hair sample preparation for the EIA screening assay is a pH 9.5 digestion of the hair in 0.3% dithiothreitol for 2 hours at 37oC (patent pending). After digestion, the sample is neutralized and diluted 1:4 in 0.05 M phosphate buffer, pH 7 prior to the EIA.).	An 8 mg aliquot of the hair segment is weighed and enzymatically digested in 1.6 ml, of pH- 9.5 digest for 2 hours at 37 'C. After incubation, 130 µL, of neutralizing solution is added, the mixture vortexed, the undigested hair is removed and the solution centrifuged.
Sample matrix	Hair	Same

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

None were referenced.

L. Test Principle:

The components of the assay comprise (1) antigen-coated 96-well microplates, (2) sample, (3) primary antibody directed against the antigen, (4) secondary antibody conjgated with horseradish peroxidase (HRP), and (5) substrate, 3,3',5,5' tetramethylbenzidine (TMB). Hair sample extracts (25 µl) and primary antibody (sheep (polyclonal) anti-methamphetamine antibody) 75 µl, are combined in the wells, and the plate rotated gently at ambient temperature for one hour. The wells are then emptied and washed once with wash buffer.

Next, 100 ml of Rabbit-anti-goat-HRP is added, and the plates rotated gently for one hour. The wells are then emptied and washed with wash buffer three times, after which 100 µl of substrate (TMB) is added. After 30 minutes, the plate is read at 450 nm with background set at 630 nm. Results are normalized by expression as B/B_0 x 100. If methamphetamine is present in the sample, less primary antibody will be bound to the solid-phase antigen, thereby resulting in less binding of HRP-labeled secondary antibody; the absorbance produced is inversely proportional to the amount of methamphetamine in the sample (specimen, calibrator or control).

For samples that are presumptive positive by the screening assay, a new aliquot of the hair sample is weighed, washed extensively to remove and evaluate externally-derived methamphetamine contamination on the hair, digested by a different procedure, and confirmed by LC/MS/MS.

Standard and control stock solutions are purchased from multiple vendors, prepared in the laboratory, and validated by LC/MS/MS confirmation.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   a. Precision/Reproducibility:

Hair samples known to be negative to methamphetamine or related compounds were spiked with methamphetamine to obtain the following concentrations around the cutoff: 0, -75%, -50%, -25%, cutoff, +25%, +50%, +75% and + 100% of the cutoff. The prepared samples were assayed on the Microplate EIA for methamphetamine. Intra-assay precision was performed in 15 replicates in one run and inter-assay precision was performed over 4 non-consecutive days. The results are presented in the tables below:

Summary -Intra-Assay		
LEVEL	NEG	POS
-100%	15	0
-75%	15	0
-50%	15	0
-25%	15	0
Cutoff	5	10
+ 25%	0	15
+ 50%	0	15
+ 75%	0	15
+ 100%	0	15

Summary-Inter-Assay		
LEVEL	NEG	POS
-100%	75	0
-75%	75	0
-50%	75	0
-25%	75	0
Cutoff	39	36
+ 25%	0	75
+ 50%	0	75
+ 75%	0	75
+ 100%	0	75

b. Linearity/assay reportable range:

Not Applicable. This assay is intended for qualitative screening determination.

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

Psychemedics manufactures calibrators and control materials using drug stocks purchased from a commercial vendor. Each lot of drug is received with its specific certificate of analysis. The commercially obtained stock is made into the calibrators and controls to the desired concentrations. The concentrations are confirmed by MS.

Stability studies for both controls and calibrators have been conducted. Protocols and acceptance criteria were described and found to be acceptable. The manufacturer claims the following expiration date for both controls and calibrators:
When stored at less than or equal to 10 ºC product is stable for 12 months.

d. Detection limit:

Not required since this is a qualitative test.

e. Analytical specificity:

Cross-reactivity was evaluated by spiking various concentrations of each substance into drug-free sample. Compounds chemically related to cocaine and its metabolites were tested to determine which of them might react in the EIA cocaine assay. The percent cross-reactivity of those compounds is presented below:

Cross-reactivity of related Compounds in Methamphetamine EIA

Compound	Amount of Compound required to Produce a positive test at the cutoff of 5 ng methamphetamine / 10 mg hair	Percent Cross-reactivity*
Phentermine	>500	< 0.1
Phenylpropanolamine	>500	< 0.1
Ephedrine	750	< 0.1
Pseudoephedrine	>500	< 0.1
Phenylethylamine	>500	< 0.1
d-amphetamine	>800	< 0.1
MDMA	5	100
MDA	3000	< 0.1
MDEA	10	50
L-methamphetamine	29	17
Ranitidine	>500	< 0.1
Fenfluramine	180	2.8
PMA	80	6.2
PMMA	6	83.3
Chloramphetamine	1000	0.5

*Definition of Percent Cross-reactivity: Concentration of Methamphetamine at Cutoff divided by the Concentration of Cross-reactant that gives the same depression as the cutoff (x 100).

Interference by Other Compounds:

Structurally unrelated:

Hair samples were spiked with 2.5, 5.0, and 7.5 ng methamphetamine/10 mg hair (as the reference) and with 2.5 and 7.5 ng/10 mg hair plus an additional compound or mixture of compounds, and assayed by the EIA. The following compounds, added at 100 ng/10 mg hair, caused no interference at +/- 50% of the cutoff.

oxazepam, glutethimide, amitryptyline, trimipramine, doxepin, imipramine, nordoxepin, nortriptyline, desipramine, protryptyline, barbital, phenobarbital, amobarbital, butabarbital, hexobarbital, secobarbital, medazepam, lorazepam, diazepam, flurazepam, medazepam, nordiazepam, temazepam, bromazepam, ethosuximide, methsuximide, a-methyl-a-propylsuccimide, metharbital. phensuximide, normethsuximide, mephenytoin, ethotoin, mephobarbital, PEMA, Methyl-PEMA, 10,11-dihydrocarbamezepine, carbamazepine, primidone, 5,5-diphenylhydantoin, 4-methylprimidone, acetaminophen, caffeine, dyphylline, methaqualone, theophylline, phenmetrazine, phenylpropanolamine, amitriptyline, dextromethorphan, lidocaine, methocarbamol, nordoxepin, pentazocine, phenylephrine, triamterene, meprobromate, methylprylon, Anhydroecgonine methyl ester, Atropine, Bupropion, Cotinine, Cannabinol, Chlorpheniramine maleate, O-Desmethyvenlafaxine, Desipramine, Doxylamine succinate, 1S, 2R Ephedrine, Ethosuximide, Ibuprofen, LSD, Haloperidol, Meperidine, Methadone, Methaqualone, Methyl phenidate, Naloxone, Naltrexone, Nicotine, Naproxen, Nortriptyline,

Propoxyphene, R,R Pseudoephedrine, Thioridazine, Cis-Tramadol, Venlafaxine hydrochloride, 8(-)-11-nor-9-Carboxy-delta-9 THC, 11-nor-9-Carboxy-delta-9-THC, Delta 8-THC, Streptomycin, Procaine, Benzocaine, Erythromycin, Penicillin G, Mepivacaine, Phendimetrazine bitartrate, Diazepam, Despropionyl fentanyl, Ethylmorphine, Nalorphine, Codeine, Morphine, Hydromorphone, Oxycodone, Cocaethylene, Cocaine, Glutethimide, Meprobamate, Methyprylon, Flurazepam, Lorazepam, Medazepam, Temazepam, Carbamazepine, Diazepam, Nordiazepam, Oxazepam, Acetaminophen, Caffeine, Dyphylline, Methaqualone, Theophylline, Amitriptyline, Dextromethorphan, Lidocaine, Methocarbamol, Nordoxepin, Pentazocine, Phenylephrine, Triamterene, Ethosuximide, a-methyl-a-propylsuccimide, metharbital, barbital, methsuximide, phensuximide, phensuximide, N-Normethsuximide, Mephenytoin, Ethotoin, Mephobarbital, PEMA, Phenobarbital, Methyl PEMA, 10,11-Dihydrocarbamazepine, Primidone, Carbamazepine, 5,5-Diphenylhydantoin, 4-Methylprimidone, Butabarbital, Amobarbital, Secobarbital, Hexobarbital, Phenobarbital, Medazepam, Oxazepam, Lorazepam, Diazepam, Temazepam, Bromazepam, Amitriptyline, Desipramine, Doxepin, Imipramine, Nordoxepin, Nortiptyline, Protriptyline, Trimipramine, Glutethimide, Chlorpromazine, Flurazepam

Effects of Cosmetic Treatments of Hair

Eighty cocaine-negative hair samples were used for this study. The study was conducted with two different hair treatments for each hair sample. No significant differences were observed for the negative hair samples before and after the treatments; all samples remained negative after the treatments.

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Forty eight cocaine-positive hair samples were used in this study. The study was conducted with two different hair treatments for each hair sample. The positive samples showed average changes in the absorbance values of -3.9% for bleach , -3.7% for dye, -14.3% for perm, -7.6% for relaxer, and -1.7% for shampoo, where a negative sign indicates a sample becoming “more negative” due to treatment and a positive sign indicates a sample becoming “more positive.” None of the originally positive samples tested negative after any of the cosmetic treatments.

Environmental Study

Preliminary positive hair sample results by the screening method could be due to environmental contamination. All positive should be sent for confirmation testing on a reference method to distinguish between true positive and those samples that were positive due to external exposure.

f. Assay cut-off:

Analytical performance of the device around the claimed cutoff is described in precision section (1a.) above

2. Comparison studies:

a. Method comparison with predicate device:

The study was performed by comparing ELISA results against the LC/MS/MS results on the same hair sample. A total of 213 donor head and body hair samples were tested. The results are presented in the table below:

Comparison of Positive Samples and Samples around the cutoff by LC/MS/MS

LC/MS/MS	Negative by GC/MS	≥ -50% of Cutoff & < Cutoff	≥ Cutoff, And < +50% of Cutoff	≥ +50% of Cutoff
EIA Positive	0	9	8	86
EIA Negative	105	3	0	2

Discordant Results—EIA *vs.* LC/MS/MS

Cutoff Value (ng/10 mg hair)	Methamphetamine EIA (+/-)	Methamphetamine LC/MS/MS value (ng/10 mg hair)
5	+	3.0
5	+	3.1
5	+	3.1
5	+	3.2
5	+	4.2
5	+	4.5
5	+	4.8
5	+	4.9
5	+	4.9
5	-	7.5
5	-	8.3 (MDMA)

Discussion of Discordant Results
Samples undergoing immunoassay screen testing are not washed prior to analysis. Therefore, unwashed samples containing external drug contamination may be positive in the screening assay and, after washing for the confirmation analysis, confirm negative relative to the cutoff.

b. Matrix comparison:

Not applicable.

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

Specific ranges for each analyte/methodology are listed in the package insert.

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.