510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K212952

B Applicant

Psychemedics Corporation

C Proprietary and Established Names

Psychemedics Homogeneous Enzyme Immunoassay (HEIA) for Phencyclidine in Hair

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LCM	Unclassified		

II Submission/Device Overview:

A Purpose for Submission:
New device

B Measurand:
Phencyclidine

C Type of Test:
Qualitative homogenous enzyme immunoassay (HEIA)

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:

The Psychemedics homogeneous enzyme immunoassay (HEIA) for phencyclidine in hair is an enzyme immunoassay system for the preliminary qualitative detection of phencyclidine in human head and body hair using a phencyclidine calibrator at 3 ng phencyclidine/10 mg hair for the purpose of identifying phencyclidine use.

This is an in vitro diagnostic device intended exclusively for Psychemedics use only and is not intended for sale to anyone. The Psychemedics phencyclidine homogeneous enzyme immunoassay provides only a preliminary analytical test 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.

C Special Conditions for Use Statement(s):

OTC - Over The Counter

The Psychemedics Homogenous Enzyme Immunoassay (HEIA) for Phencyclidine in Hair combine a screening method (immunoassay) with a confirmation method (GC/MS) in one test system.

The assay is to be performed only at Psychemedics Corporation.

D Special Instrument Requirements:

The Psychemedics HEIA for phencyclidine in hair requires the use of an automated clinical chemistry analyzer at 340 nm. The Olympus AU 640 analyzer was used for validation of the candidate assay.

The GC/MS confirmation assay uses either 1) Agilent GC/MS System consisting of an MSD 5975C linked to an Agilent 6890N GC equipped with a split/splitless injector, a Hewlett-Packard 7683B autosampler, and a capillary column or 2) Agilent GC/MS System consisting of an MSD 5977A linked to an Agilent 7890B GC equipped with a split/splitless injector, a Hewlett-Packard 7693 autosampler, and a capillary column. The carrier gas for both systems is Ultra High Purity Helium.

IV Device/System Characteristics:

A Device Description:

The Psychemedics homogenous enzyme immunoassay (HEIA) test for phencyclidine in hair (also referred to as Phencyclidine HEIA) consists of two parts: a pre-analytical hair treatment procedure (to extract phencyclidine from the solid hair matrix to a measurable liquid matrix) and the screening assay, the Psychemedics Phencyclidine Homogeneous Enzyme Immunoassay (HEIA).

Performance of the Psychemedics Phencyclidine HEIA requires a sample extract solution and Phencyclidine-Glucose-6-phosphate dehydrogenase (G6PDH) conjugate. The Psychemedics Phencyclidine HEIA consists of reagents R1 (anti-phencyclidine monoclonal antibody with substrate) and R2 (phencyclidine labeled recombinant G6PDH).

The confirmation assay consists of either 1) an Agilent GC/MS System consisting of an MSD 5975C linked to an Agilent 6890N GC equipped with a split/splitless injector, a Hewlett-Packard 7683B autosampler, and a capillary column or 2) an Agilent GC/MS System consisting of an MSD 5977A linked to an Agilent 7890B GC equipped with a split/splitless injector, a Hewlett-Packard 7693 autosampler, and a capillary column.

B Principle of Operation:

Hair specimens are extracted in a phosphate buffer solution at an acidic pH at high temperature. After the extraction, the sample is analyzed with phencyclidine (PCP) antibody and phencyclidine-labeled G6PDH using a chemistry autoanalyzer. The cutoff calibrator and controls are also processed through the extraction and autoanalyzer steps.

The screening portion of the test system is based on competition for antibody binding sites between drug in the measurable liquid matrix and drug-labeled recombinant glucose-6-phosphate dehydrogenase (G6PDH). As the antibody binds labeled G6PDH, enzyme activity decreases. When phencyclidine is present in the sample, enzyme activity increases in direct proportion to the drug concentration. Active enzyme reduces nicotinamide adenine dinucleotide (NAD) to NADH in the presence of glucose-6-phosphate (G6P), resulting in an absorbance change that is measured spectrophotometrically at 340 nm. A change in milliabsorbance units (ΔmAU) greater than or equal to the ΔmAU of the 3 ng phencyclidine/10 mg hair cutoff calibrator is indicative of the presence of phencyclidine.

For samples that are presumptive positive by the screening assay, a new aliquot of the hair sample is weighed, washed extensively to remove externally derived phencyclidine, extracted by a different procedure, and confirmed by GC/MS for the presence of phencyclidine.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Psychemedics Microplate EIA for Phencyclidine in Hair

B Predicate 510(k) Number(s):
K111928

C Comparison with Predicate(s):

Device & Predicate Device(s):	K212952	K111928
Device Trade Name	Psychemedics Homogeneous Enzyme Immunoassay (HEIA) for Phencyclidine in Hair	Psychemedics Microplate EIA for Phencyclidine in Hair
General Device Characteristic Similarities		

Device & Predicate Device(s):	K212952	K111928
Intended Use/Indications For Use	The Psychemedics homogeneous enzyme immunoassay (HEIA) for phencyclidine in hair is an enzyme immunoassay system for the preliminary qualitative detection of phencyclidine in human head and body hair using a phencyclidine calibrator at 3 ng phencyclidine/10 mg hair for the purpose of identifying phencyclidine use. This is an in vitro diagnostic device intended exclusively for Psychemedics use only and is not intended for sale to anyone. The Psychemedics phencyclidine homogeneous enzyme immunoassay provides only a preliminary analytical test 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.	Same
Product Code	LCM	Same
Measurand	Phencyclidine	Same
Sample Matrix	Human Hair	Same
Type of Test	Enzyme immunoassay	Same
Confirmation method	GC/MS	Same
General Device Characteristic Differences		
Test system	Psychemedics Homogenous Enzyme Immunoassay for Phencyclidine in Hair	Psychemedics Microplate EIA for Phencyclidine in Hair
Method of measurement	Automated Clinical Chemistry Analyzer at 340 nm	Microplate reader at 450 nm
Extraction method	Acidic aqueous buffer	Patented digestion method

VI Standards/Guidance Documents Referenced:

None referenced.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Intra-assay Precision for the Phencyclidine HEIA
Precision studies were run on a single day in 2 replicates of 4 distinct samples using hair previously shown to be negative for phencyclidine. Hair was spiked relative to the calibrator of 3 ng phencyclidine per 10 mg hair as follows: 0 ng/10 mg (-100%), 0.75 ng/10 mg (-75%), 1.5 ng/10 mg (-50%), 2.25 ng/10 mg (-25%), 3 ng/10 mg (cutoff calibrator), 3.75 ng/10 mg (25%), 4.5 ng/10 mg (50%), 5.25 ng/10 mg (75%), 6 ng/10 mg (100%). HEIA extraction and assay was performed on all samples.

Intra-assay Precision Results, Phencyclidine 3 ng per 10 mg Hair Cutoff HEIA			
Concentration (ng/10 mg)	% of cutoff	# of determinations	Total Result
0	-100	8	8 Negative
0.75	-75	8	8 Negative
1.50	-50	8	8 Negative
2.25	-25	8	8 Negative
3.0	Cutoff	8	4 Positive / 4 Negative
3.75	+25	8	8 Positive
4.50	+50	8	8 Positive
5.25	+75	8	8 Positive
6.0	+100	8	8 Positive

Inter-assay Precision for the Phencyclidine HEIA
Precision studies were performed for 10 days, 2 runs per day of 4 distinct samples using hair previously shown to be negative for phencyclidine. Hair was spiked in the same manner as the intra-assay precision study described above. HEIA extraction and assay was performed on all samples.

Inter-assay Precision Results, Phencyclidine 3 ng per 10 mg Hair Cutoff HEIA			
Concentration (ng/10 mg)	% of cutoff	# of determinations	Total Result
0	-100	80	80 Negative
0.75	-75	80	80 Negative
1.50	-50	80	80 Negative
2.25	-25	80	80 Negative

3.0	Cutoff	80	47 Positive / 33 Negative
3.75	+25	80	80 Positive
4.50	+50	80	80 Positive
5.25	+75	80	80 Positive
6.0	+100	80	80 Positive

Intra-assay Precision for GC/MS

Intra-assay precision was determined around the cutoff of 3 ng phencyclidine/10 mg hair. PCP standard solution was added to negative hair at each of the following concentrations: ±25 percent of the cutoff, ±50 percent of the cutoff, and at the cutoff concentration. Five distinct hair samples were used at each concentration.

Intra-assay Precision Around the 3 ng Analyte per 10 mg Hair Cutoff					
	ng PCP/10 mg hair				
Phencyclidine	1.5	2.25	3.0	3.75	4.5
Average	1.536	2.262	3.034	3.81	4.49
S.D.	0.033	0.022	0.015	0.052	0.061
%C.V.	2.140	0.958	0.500	1.364	1.364

Intra-assay precision was determined over the range of the assay from lower to upper limit of quantification. Concentrations evaluated were 0, 1, 2, 3, 4, 50, 100, and 150 ng PCP/10 mg hair. Five distinct samples were used at each concentration.

Intra-Assay Precision Over the Range of the Assay							
	ng PCP/10 mg hair						
Phencyclidine	1	2	3	4	50	100	150
Average	0.93	1.94	2.85	3.99	52.66	103.73	156.04
S.D.	0.0134	0.0182	0.0477	0.0110	1.0799	0.6534	1.0478
%CV	1.44	0.94	1.67	0.27	2.05	0.63	0.67

Inter-assay Precision for GC/MS

Inter-assay precision for phencyclidine around the cutoff was determined at 1.5, 3.0 and 4.5 ng analyte per 10 mg of hair. Inter-assay precision was performed over 5 separate days, testing each respective sample concentration in quintuplicate. Five distinct samples were tested at each point over 5 days, yielding 25 total distinct results per sample.

GC/MS Inter-assay Precision			
ng PCP/10 mg hair			
	1.5	**3.0**	**4.5**
Average	1.44	3.06	4.63
S.D.	0.0939	0.1298	0.1420
%CV	6.51	4.25	3.06

2. Linearity:

An evaluation of linearity for the Phencyclydine HEIA is not applicable, as it is a qualitative screening test.

However, linearity was assessed for the GC/MS confirmatory method. The following concentrations of phencyclidine were analyzed: 0.0, 1.0, 2.0, 4.0, 50, 100, and 150 ng/10 mg of hair. All results were within 20 percent of their target concentrations. Agreement of the 5 determinations at each concentration were ≤10% CV. The regression coefficient (R^2) was 1.

The GC/MS assay is used only to determine if the concentration of the target analyte is above or below the cutoff. There are no clinical claims for concentrations other than the cutoff.

3. Analytical Specificity/Interference:

Phencyclidine HEIA Cross Reactivity Studies

The cross-reactivity characteristics of the Phencyclidine HEIA were evaluated by spiking various concentrations of potential cross-reactants into drug-free hair samples and comparing the result to the cutoff calibrator. Two distinct hair samples that were previously tested negative for all phencyclidine-related compounds were used for this study. Phencyclidine HEIA extraction and assay were performed on samples.

The cross reactivity of the following structurally related compounds were evaluated by determining the concentration that is equivalent to the assay cutoff concentration of 3.0 ng phencyclidine/10 mg hair:

Cross Reactor	% Cross Reactivity	Expected Concentration Equivalent to 3 ng PCP/10 mg hair (ng/10 mg hair)
3-Methoxy-(Aryl Ring) PCP	37.5	8
4-Hydroxy (Cyclohexyl Ring) PCP	12	25
1-(1-Phenylcyclohexyl)-4-hydroxypiperidine	7.5	40
Venlafaxine	6	50
Atropine	3	100
Metaphit	4	75
1-(1-Phenylcyclohexyl) Morpholine (PCM)	6	50
Rolicyclidine HCl	37.5	8

The following compounds were found to have no cross reactivity in the Phencyclidine HEIA at 100 ng/10 mg hair:
Anhydroecgonine Methyl Ester, Bupropion, Cotinine, Cannabinol, Chlorpheniramine maleate, O-Desmethylvenlafaxine, Desipramine, Doxylamine succinate, 1S, 2R-(+)-Ephedrine, Naproxen, Nicotine, Nortriptyline, H-Propoxyphene, R,R-(-)-Pseudoephedrine,

Thioridazine, Cis-Tramadol, (±)-11-nor-9-Carboxy-Δ9-THC, Pentazocine, Amoxicillin, Propanolol, Promethazine, Phenmetrazine, Phendimetrazine, Benzocaine, Ecgonine, Dextromethorphan, Amitriptyline, R-(-)Phenylephrine, Glutethimide, Meprobamate, Lidocaine, Carbamazepine, Diazepam, Nordiazepam, AM-2201, JWH-019, JWH-081,, JWH-122, Acetaminophen, Caffeine, Dyphylline, Methaqualone, Theophylline, CP47.497, CP47.497 C8 Homologue, HU-211, JWH-200, JWH-250, Ibuprofen, Naproxen, Ethosuximide, (±)-Epinephrine, Norepinephrine, Barbital, Metanephrine, Normetanephrine, Methocarbamol, Alprazolam, Cimoticline, Citalopram, Clopidogrel Bisulfate, Fluconazole, Hydrochloro-thiazide, Lamotrigine, L-Thyroxine, Methyl Phenidate, Omeprazole, Amlodipine Besylate, Atorvastatin, Azithromycin, Bupivacaine, Cetirizine, Dimenhydrinate, Lisinopril, Methsuximide, Phensuximide, N-Normethyl Suximide, Butabarbital, Amobarbital, Secobarbital, Hexobarbital, Phenobarbital, Mephyton, Ethotoin, Mephobarbital, PEMA, 10, 11-Dihydro-carbamazepine, Medazepam, Chlorpromazine, Flurazepam, Lorazepam, Temazepam, Bromazepam, Primidone, 5,5-Diphenyl Hydantoin, Triamterene, Nordoxepin, Oxazepam, Levetiracetam, Metformin, Phenytoin, R-Phenyl-Ephrine, Sertraline, Topiramate, Zolpidem Tartrate, Vanilmandelic Acid, 5-Hydroxyindole 3-Acetic Acid, Homovanilic Acid.

Phencyclidine HEIA Interference Study

Potentially interfering compounds at a concentration of 100 ng/10 mg hair were added individually to spiked hair samples at the Phencyclidine HEIA cutoff and at ±50% of the cutoff to determine which of them might interfere in the assay. Three distinct samples were used for +50% and -50% of calibrator. Compounds were tested individually at each of the different spike concentrations.

The compounds atropine, chlorpheniramine maleate, and venlafaxine were interferences in the Phencyclidine HEIA at the tested concentration.

The following compounds were tested at 100 ng/10 mg hair and found to have no interference with the Phencyclidine HEIA:
Anhydroecgonine methyl ester, Bupropion, Cotinine, Cannabinol, O-Desmethylvenlafaxine, Desipramine, Doxylaminesuccinate, 1S, 2R (+)-Ephedrine, Naproxen, Nicotine, Nortriptyline, H-Propoxyphene, R,R (-)Pseudoephedrine, Thioridazine, cis-Tramadol, (±)-11-nor-9-Carboxy-Δ9-THC, Pentazocine, Amoxicillin, Propranolol, Promethazine, Phenmetrazine, Phendimetrazine, Benzocaine, Ecgonine, Dextromethorphan, Amitriptyline, R-(-)Phenylephrine, Glutethimide, Meprobamate, Lidocaine, Carbamazepine, Diazepam, Nordiazepam, AM-2201, JWH-019, JWH-081, JWH-122, Acetaminophen, Caffeine, Dyphylline, Methaqualone, Theophylline, CP47.497, CP47.497 C8 Homologue, HU-211, JWH-200, JWH-250, Ibuprofen, Naproxen, R,R-(-)-Pseudoephedrine, Ethosuximide, (±) Epinephrine, Norepinephrine, Barbital, Metanephrine, Normetanephrine, Methocarbamol, Alprazolam, Cimetidine, Citalopram, Clopidogrel bisulfate, Fluconazole, Hydrochlorothiazide, Lamotrigine, L-Thyroxine, Methyl Phenidate, Omeprazole, Amlodipine Besylate, Atorvastatin, Azithromycin, Bupivacaine, Cetirizine, Dimenhydrinate, Lisinopril, Methsuximide, Phensuximide, N-Normethyl Suximide, Butabarbital, Amobarbital, Secobarbital, Hexobarbital, Phenobarbital, Mephytoin, Ethytoin, Mephobarbital, PEMA,10,11-Dihydro-carbamazepine, Medazepam, Chlorpromazine, Flurazepam, Lorazepam, Temazepam, Bromazepam, Primodone, 5,5-Diphenyl Hydantoin,

Triamterene, Nordoxepin, Oxazepam, Levitriacetam, Metformin, Phenytoin, R-Phenylephrine, Sertraline, Topiramate, Zolpidem Tartrate, Vanilmandelic acid, 5-Hydroxy Indole 3-Acetic acid, Homovanillic Acid.

Phencyclidine HEIA: Effect of Cosmetic Treatments

Hair samples negative for phencyclidine and samples positive for phencyclidine were treated with the following cosmetic treatments: permanent wave, relaxer, dye (which includes bleach), and shampoo. After the treatments, these samples and an aliquot of the same hair samples untreated were extracted for phencyclidine analysis and then assayed by the Phencyclidine HEIA. The study includes 5 negative samples and 10 phencyclidine-positive samples with each of the treatments. In each case of the 5 negative samples treated with a type of cosmetic treatment, all samples remained negative after the treatments. In each case of the 10 positive samples treated with a type of cosmetic treatment, all samples remained positive after the treatments.

Phencyclidine GC/MS Specificity

An interference study was conducted for the GC/MS method by spiking potential interferents into negative hair specimens that did not contain any drug, and into hair specimens that contained 1.2 ng phencyclidine per 10 mg hair. One distinct sample was used for the interferent alone, and one distinct sample for the interferent plus PCP. This was done for each interferent.

The following compounds were tested at

- **2.5 ng/10 mg hair**: Amlopidine Besylate
- **20 ng/10 mg hair**: Clonazepam, Estazolam, Flurazepam, Flunitrazepam, Midazolam, Nitrazepam, Prazepam, Triazolam, Zolpidem, Phentermine, R,R-(-)-Pseudoephedrine
- **25 ng/10 mg hair**: Cetirizine·2HCl, Prednisolone
- **50 ng/10 mg hair**: Ibuprofen, Meprobamate, Naproxen, (+)-Propoxyphene, Atorvastatin·Ca Salt, Azithromycin·2 H_2O, Bupivacaine HCl·H_2O, Dimenhydrinate, Lisinopril·2H2O, Loratadine, Montelukast·Na Salt, Pioglitazone·HCl, Procainamide·HCl, Simvastatin
- **100 ng/10 mg hair**: Carbamazepine, Levetiracetam, Metformin HCl, Phenobarbital, Phenytoin, R-(-)-Phenylephrine HCl, Sertraline HCl, Topiramate, Zolpidem Tartrate, Zonisamide, (+)-Propoxyphene
- **200 ng/10 mg hair**: Morphine, Oxycodone, Codeine, Cocaine, S-(+) Methamphetamine, S-(+)-Amphetamine, (±)-Methadone, Phenobarbital, Phenytoin, R-(-)-Phenylephrine HCl, Carbamazepine, Salicylic Acid, Valproic Acid, Buprenorphine, Cis-Tramadol HCl, Fentanyl, Hydrocodone, Hydromorphone, Meperidine, Naloxone, Naltrexone, Oxymorphone, Aripiprazole, Lacosamide, Oxocarbazepine, Rufinamide
- **500 ng/10 mg hair**: Oxcarbazepine, Gabapentin, Acetaminophen, (-)-Cotinine, S-(-)-Nicotine, Caffeine, Gabapentin, Pregabalin, Salicylic Acid, Valproic Acid, Vigabatrin
- **2000 ng/10 mg hair:** Warfarin

Quantitations of phencyclidine in the presence of the potentially interfering compounds listed above were within ± 20% of 1.2 ng/10 mg hair of phencyclidine. In the absence of

phencyclidine analyte and presence of interfering compounds, quantitations of phencyclidine analyte were below the limit of detection.

4. Assay Reportable Range:

   Not applicable for the Phencyclidine HEIA because it is a qualitative test only.

   Refer to the linearity study for the GC/MS method reportable range. The highest concentration tested in linearity studies was 150 ng PCP/10 mg hair and the lowest concentration tested was 1 ng PCP/10 mg hair.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Traceability

The sponsor has provided a Certificate of Analysis for the PCP Primary Standard used, which states that the standard meets the requirements of a Certified Reference Material and a Primary Standard as defined by ISO and is traceable to the SI and higher order standards through an unbroken chain of comparisons.

Sample Storage and Shipping Stability for the Phencyclidine HEIA

Samples containing phencyclidine were initially identified by screening with the Phencyclidine HEIA and confirmed via GC/MS.

PCP in hair samples remained positive after storage for at least 8 months and after shipping round-trip across the United States.

6. Detection Limit:

   The Phencyclidine HEIA is a qualitative test only; therefore, a detection limit evaluation is not applicable. See section VII.A.1. above for performance around the device cutoff.

   The sponsor referenced their GC/MS linearity studies for limit of detection (LoD). The LoD is the lowest concentration that meets chromatographic and retention time criteria, and that can be quantitated within 20% of the target value. The LoD was determined to be 1 ng PCP/10 mg hair. The high concentration tested in linearity studies was 150 ng PCP/10 mg hair.

7. Assay Cut-Off:

   Analytical performance of the device around the claimed cutoff is described in the precision section above.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Accuracy of the immunoassay screening method

A total of 84 samples (40 negative, 44 positive) were utilized for the study. All samples were confirmed by the Psychemedics GC/MS confirmatory assay. The source, gender, and hair color of the samples were as follows:

	Hair Source		Gender		Hair Color			
	Head	Body	Male	Female	Brown	Black	Salt/Pepper	Grey
Number of samples	46	38	67	17	22	56	5	1

A comparison between the Phencyclidine HEIA (screening) results and GC/MS confirmatory results for the samples is summarized in the table below. The calibrator was 3 ng phencyclidine/10 mg hair. There were no discordant results between Phencyclidine HEIA screening results and GC/MS results.

	GC/MS Result, ng Phencyclidine/10 mg hair (% of cutoff calibrator)			
PCP HEIA Result	<1.5 (<50% below cutoff)	1.5-2.99 (≥50% below cutoff to cutoff)	3.0-4.5 (cutoff to ≥50% above cutoff)	>4.5 (>50% above cutoff)
Positive	0	0	4	40
Negative	36	4	0	0

Recovery from GC/MS Analysis

Psychemedics conducted a study to evaluate recovery for phencyclidine at a concentration of 10 ng/10 mg hair. Five distinct samples were prepared and analyzed by GC/MS. The recovery of phencyclidine ranged from 97.3 to 101.8%.

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Not applicable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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