FEB 11 2002

# Psychemedics RIA Phencyclidine (PCP) Assay (K011275)

## 510(k) SUMMARY

I. GENERAL INFORMATION

A.
| | |
|---|---|
| Submitter's Name: | Psychemedics Corporation |
| Address: | 5832 Uplander Way, Culver City, California 90230 |
| Telephone Number: | (310) 216-7776; (800) 522-7424 |
| Contact Person: | William R. Thistle, JD |
| Date prepared: | 07 February 2002 |

B.
| | |
|---|---|
| Device Generic Name: | Analytical Service: RIA Phencyclidine Assay |
| Proprietary Name: | Psychemedics RIA Phencyclidine (PCP) Assay |
| Classification Name: | 91 LCL (Toxicology) |

Product Codes of Devices to Which Equivalence is Claimed: Dade Behring (K993983)

### II. INTENDED USE

The Psychemedics Phencyclidine Assay is a radioimmunoassay (RIA) for the qualitative and semi-quantitative detection of phencyclidine in hair through the measurement of phencyclidine at concentrations at or above 3 ng/10 mg hair. This product is intended exclusively for in-house professional use only. The test is not intended for over the counter sale to non-professionals.

The Psychemedics Phencyclidine Assay provides only a preliminary analytical test result. To confirm a screen positive result, a more specific alternate chemical method, such as GC/MS, must be used. Clinical consideration and professional judgement should be applied to any drug of abuse test result, particularly when preliminary positive results are obtained.

### III. DESCRIPTION OF THE PRODUCT

The Psychemedics RIA Assay for phencyclidine is based upon the competitive binding of $^{125}$I-radiolabeled and unlabeled phencyclidine with a PCP-specific primary antibody. An 8 mg specimen of hair is digested in a solution containing dithiothreitol and proteinase K at pH 9.5 for two hours. After the 2-hour digestion, the digest solution is neutralized, vortexed, and centrifuged to remove the melanin. Any remaining undigested hair strands may be removed, prior to centrifugation, with applicator sticks (to avoid clogging of multiprobe pipetting tips). An aliquot of the supernatant is added to a test tube with a fixed amount of radiolabeled phencyclidine, primary antibody (antiserum against phencyclidine), and second antibody. Following incubation, the mixture is centrifuged in the presence of polyethylene glycol, and the unbound fraction is discarded by decanting the supernatants of the precipitated antigen-antibody complex. The pellets containing the bound antigen are counted in a gamma scintillation counter. All cutoffs and controls, as well as a 20% BSA sample used to determine the value of $B_0$, are processed through the digestion, incubation and counting steps. A $B/B_0 \times 100$ less than or equal to the $B/B_0 \times 100$ of the 3 ng phencyclidine/ 10 mg hair cut-off calibrator is indicative of the presence of phencyclidine.

A comparison of hair analysis with the predicate device, Dade Behring's EMIT II urine assay, is shown in Section VI.

### IV. PRECAUTIONS AND WARNINGS

This assay was evaluated using head hair samples from 5 drug abusers in treatment programs. Positive screening results only indicate the presumptive presence of phencyclidine, and require additional analysis by mass spectrometry to obtain a confirmed result. A negative screening test result does not necessarily rule out the possibility of phencyclidine use, i.e., time of collection, frequency of use, mode of ingestion, dosage used, hair types and other factors may influence results. It is not possible to document all possible effects due to treatments such as bleaching, straightening and dying. There is a possibility that other substances and/or factors not listed above may interfere with the test and cause false results that cannot be confirmed by mass spectrometry, e.g. technical or procedural errors.

## V. EQUIVALENCE COMPARISON

| | Dade Behring EMIT (K993983) | Psychemedics RIA Phencyclidine Assay |
|---|---|---|
| Type of Product | Analytical Reagents | Analytical Service |
| Measured Analytes | Phencyclidine (PCP) | Phencyclidine (PCP) |
| Test Medium | Urine | Hair |
| Cut-off levels | 25 ng PCP/mL | 3 ng PCP/ 10 mg hair |
| Test System | Competitive Enzyme Immunoassay | Competitive Radioimmunoassay |
| Materials | Polyclonal antibody;<br>enzyme-labeled PCP;<br>optical assay of enzyme substrate | Polyclonal primary antibody; isotopically labeled PCP;<br>double antibody precipitation |
| Indications for Use | Identify PCP Use | Identify PCP Use |
| Target Population | Medical | Workplace; criminal justice; medical |
| Mass Spectrometry Confirmation | Yes | Yes |

## VI. SUMMARY OF ANALYTICAL STUDIES

***1. Sample Preparation and Recovery of Phencyclidine***

The hair sample preparation for the assay is a 2-hour, pH = 9.5, enzymatic digestion of the hair. Under these conditions, 92% of Phencyclidine spiked onto negative hair was recovered at the concentrations of 2.1 and 4.4 ng/10 mg hair.

***2. Matrix Effects***

Variations due to matrix effects among different hair samples were assessed by digestion and assay of 100 phencyclidine-negative hair samples, which had been previously determined by RIA to be negative. The mean $\%B/B_0$ of these samples was 99.2 with a central 95% confidence range of 89-103%.

Similarly, matrix effects at the cutoff were assessed by spiking the same negative hair samples with phencyclidine (3 ng/10 mg hair), digesting and assaying them. The mean $\%B/B_0$ of the spike samples was 61.7, with a central 95% confidence range of 56-68%.

***3. Limit of Detection (LOD)***

At 1.5 ng/ 10 mg hair, the lowest standard concentration for which precision data was generated, the mean ng/ 10 mg hair of 20 assays with samples run in triplicates, was 1.55, with a central 93% confidence range of 1.31 to 1.85 ng/ 10 mg hair.

***4. Precision***

a. Within-Run

The intra-assay analytical precision around the cut-off (3 ng/10 mg hair) was determined. 20 replicate hair samples each were spiked before digestion at + 25%, + 50%, -25%, -50% and 100% of the cutoff concentration of 3 ng phencyclidine per 10 mg hair.

Intra-Assay Precision of the Device

| Phencyclidine Spiked Concentration | Mean (ng/ 10 mg hair) | Central 90% Confidence Interval Lower | Central 90% Confidence Interval Upper |
|---|---|---|---|
| -50% of cutoff | 1.63 | 1.43 | 1.88 |
| -25% of cutoff | 2.56 | 2.22 | 2.92 |
| 100% of cutoff | 3.06 | 2.61 | 3.49 |
| +25% of cutoff | 4.04 | 3.53 | 4.54 |
| +50% of cutoff | 4.32 | 3.72 | 4.82 |

b. Between-Run

Inter-assay precision around the cut-off concentration was determined among 20 different assays performed (2 per day) for 10 days, in triplicate samples. Prior to digestion, hair samples were spiked at each concentration of + 25%, + 50%, -25%, -50% and 100% of the cutoff concentration (3 ng phencyclidine /10 mg hair).

Inter-Assay Precision of Device

| Phencyclidine Spiked Concentration | Mean (ng/ 10 mg hair) | Central 94% Confidence Interval Lower | Central 94% Confidence Interval Upper |
|---|---|---|---|
| -50% of cutoff | 1.55 | 1.31 | 1.85 |
| -25% of cutoff | 2.33 | 2.04 | 2.90 |
| 100% of cutoff | 3.08 | 2.67 | 3.49 |
| +25% of cutoff | 3.87 | 3.42 | 4.53 |
| +50% of cutoff | 4.51 | 3.77 | 5.36 |

*5. Cross Reactivity and Interference*

Hair samples (8 mg each) were spiked before digestion with compounds to be tested for cross-reactivity: After digestion they were assayed by the device and the % $B/B_0$ compared to % $B/B_0$ of 3 ng PCP/10 mg hair.

Cross-Reactivity of Phencyclidine-Related Drugs

| Compound | Amount of Related Compound (ng/ 10 mg hair) Required to Produce a Positive Test at the Cutoff of 3 ng/ 10 mg hair |
|---|---|
| PCP-morpholine analog | 12 |
| 4-hydroxy-PCP | 250 |
| Dextromethorphan | 5000 |

Hair samples were also spiked with 250, 2500 and 10000 ng/10 mg hair of the following compounds unrelated to phencyclidine. None of the compounds showed any reactivity at the 10000 ng/10 mg hair level.

Barbital, 10,11-dihydrocarbamazepine, Ethosuximide, mephenytoin, metharbital, 4-methylprimidone, methsuximide, PEMA, Phensuximide, carbamazepine, 5,5-diphenylhydantoin, ethotoin, mephobarbital, methyl

PEMA, a-methyl-a-propylsuccinimide, N-Normethsuximide, Phenobarbital, Primidone, Codeine, Meperidine, Morphine, Ethylmorphine, Methadone, Hydromorphone, Oxycodone, Diacetylmorphine, Chlorpromazine, Flurazepam, Methaqualone, Diazepam, Glutethimide, Amobarbital, Hexobarbital, Secobarbital, Butabarbital, Phenobarbital, Medazepam, Lorazepam, Temazepam, Oxazepam, Bromazepam, Ethosuximide, Normethsuximide, mephenytoin, Trimipramine, Amitriptyline, Nordoxepin, Desipramine, Doxepin, Imipramine, Nortriptyline, Protriptyline, Benzocaine, Acetaminophen, bupropion, caffeine, l-cotinine, haloperidol, lidocaine, mepivacaine, ibuprofen, naproxin, phenylpropanolamine, procaine, Theophylline, d-pseudoephedrine, (-)-ephedrine, (+)-ephedrine, nicotine, cocaine, glutethimide, EDDP, MDMA, atropine.

The same un-related compounds tested for reactivity were also tested for interference. Negative hair spiked at -50%, cutoff, and +50% were also spiked with the unrelated compounds at a concentration of 1000 ng/10 mg hair. None of the compounds tested revealed an interference effect on the assay.

***6. Performance of The Device with Banked Samples***

Performance of the device was assessed using head hair samples that had previously been found positive for PCP by hair analysis (positive by RIA and confirmed by GC/MS). Twenty six head hair samples, ranging from 4.5 to > 50 ng/10 mg hair, re-analyzed positive by RIA and confirmed positive by GS/MS. Three underarm hair samples, ranging from 3.2 to 4.4 ng/10 mg hair, re-analyzed positive by RIA and confirmed positive by GC/MS. Two leg hair samples, with concentrations of 31.4 and 51.7 ng/10 mg hair, re-analyzed positive by RIA and confirmed positive by GC/MS. An historical analysis of over 1.4 million samples performed at Psychemedics shows that about 0.02% of the work place population test positive by the PCP RIA assay. Of those approximately 35% confirm positive by GC/MS.

***7. Stability of the Radioactive Tracer and Antibody Solutions***

The stabilities of the prepared first (phencyclidine-specific) and second (donkey anti-sheep) antibody reagents were tested by comparing various parameters at the time of preparation and after one month of the reagents being in use. The $B_0/T$ x 100, the NSB (as $B/B_0$ x 100) and the $B/B_0$ x 100 depressions of the standards over the range of the curve were compared. The responses did not change over the one-month use and storage conditions.

The stability of the $^{125}$I-labeled-phencyclidine tracer used in the phencyclidine assay was assessed by comparing the $B/B_0$ x 100 responses of the calibrators and NSB (nonspecific binding) tube and the $B_0/T$ x 100 of the Zero calibrator with fresh and one month old reagent. These indicators did not change with aging of the prepared tracer.

## VII. CONFIRMATION OF PRESUMPTIVE POSITIVE SAMPLES

Screen positive samples from the device are confirmed by first weighing out a new portion of the sample (approximately 10-16 mg). The samples are washed for 15 minutes at 37 °C with dry isopropanol, then three times for 30 minutes and twice for 60 minutes in phosphate buffer (0.01 M, pH 6.0) containing 0.1% albumin. The hair is then digested at pH 6.5 for 6 hours. Digested samples are extracted and prepared for subsequent analysis by GC/MS for phencyclidine. The criteria for reporting a positive is one in which the PCP concentration is 3 ng or greater per 10 mg hair after subtracting five time the RIA result of the last wash. Contamination below the wash RIA limit of quantitation (0.5 ng phencyclidine/10 mg hair) may not be accounted for. Any value below the limit of quantitation will be read as zero.

## VIII. PERCENTAGE AGREEMENT STUDIES

Clinical performance was evaluated with two studies, one involving individuals from treatment programs and one with individuals from a population of non-drug users. Clinical sensitivity for non-head hair was not determined.

***Positive Percent Agreement***

Studies on drug using subjects were conducted at four rehabilitation clinics. A total of 6 individuals who tested positive for phencyclidine by EMIT (25 ng/mL cutoff) in at least one of two urine samples, contributed hair samples. Five individuals were included in the study. Of the 5 volunteers one was Caucasian, two Hispanic, and two African American. Of the 5 hair samples 4 were black hair, and one was brown hair. All samples were determined to be from straight hair. Four (4) of the 5 hair samples screened positive by the device, and all four samples confirmed positive by GC/MS above 3 ng/10 mg hair after five times the RIA value for the last wash is subtracted.

***Negative Percent Agreement***
Sixty-six subjects provided two urine samples per week for 5 weeks. All urine samples were negative by EMIT and confirmatory testing. Hair samples were collected from each enrollee during the sixth week of the study. All samples were negative by RIA. The mean B/Bo result of the samples was 99.0, with a central 94% confidence interval range of 93.8 to 103.4. All hair samples were found to be negative during confirmation testing (GC/MS).

***Head Hair Percent Agreement:***

| Head Hair Analysis RIA + GC/MS | Urine Analysis EMIT + GC/MS Positive | Urine Analysis EMIT + GC/MS Negative |
|---|---|---|
| Positive | 4 | 0 |
| Negative | 1 | 66 |

Positive Percent Agreement for RIA Screening Assay relative to urine = 80%
[95% confidence intervals: 28.4% to 99.5%]

Positive Percent Agreement for Hair Analysis (RIA + GC/MS) relative to urine = 80%
[95% confidence intervals: 28.4% to 99.5%]

Negative Percent Agreement = 100%
[95% confidence intervals: 94.6% to 100%]

Prepared by: TCairns/Feb0702
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DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

FEB 11 2002

Mr. William R. Thistle, JD
Vice President, General Counsel
Psychemedics Corporation
1280 Massachusetts Avenue, Suite 200
Cambridge, MA 02138

Re: k011275
Trade/Device Name: Psychemedics RIA Phencyclidine Assay
Regulatory Class: Class II
Product Code: LCL
Dated: November 12, 2001
Received: November 13, 2001

Dear Mr. Thistle:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory-Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

## STATEMENT OF INDICATIONS FOR USE

510(K) Number: **K 011275**

Device Name: **Psychemedics RIA Phencyclidine Assay**

Indications for Use:

The Psychemedics PCP Assay is a radioimmunoassay (RIA) for the preliminary qualitative and semi-quantitative detection of phencyclidine (PCP) in hair using a 3 ng/10 mg hair cutoff for the purpose of identifying PCP use. For a quantitative analytical result or to confirm positive results via the presence of PCP, a more specific alternate chemical method must be used in order to obtain a confirmed analytical result.

**(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)**

**Concurrence of CDRH, Office of Device Evaluation (ODE)**

Sean Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K011275

**Prescription Use** ✓ **OR** **Over-the-Counter Use** _____
**(Per 21 CFR 801.109)**