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K010868

Psychemedics RIA Cocaine Assay

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: 17th August 2001

B. Device Generic Name: Analytical Service: RIA Cocaine Assay
Proprietary Name: Psychemedics RIA Cocaine Assay
Classification Name: 91 KLN (Toxicology) **CFR 862.3250**
Product Codes of Devices to Which Equivalence is Claimed: Dade Behring (K993988)

II. INTENDED USE

The Psychemedics Cocaine Assay is a radioimmunoassay (RIA) for the qualitative and semi-quantitative detection of cocaine in head hair, leg hair, underarm hair and chest hair through the measurement of cocaine and cocaine metabolites at concentrations at or above 5 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 Cocaine Assay provides only a preliminary analytical test result. To confirm a screen positive result, a more specific alternate chemical method, such as LC/MS/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 Radioimmunoassay Assay for cocaine is based upon the competitive binding of ^{125}I-radiolabeled cocaine, and unlabeled cocaine and cocaine metabolites. An 8 mg specimen of hair is digested in a solution containing dithiothreitol and proteinase K at pH 9.5 for two hours. During this process, approximately 60% of the cocaine is hydrolyzed to benzoylecgonine. 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 extracted and added to a test tube with a fixed amount of radiolabeled cocaine, primary antibody (antiserum against cocaine), 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 x 100 less than or equal to the B/B_0 x 100 of the 5 ng cocaine/ 10 mg hair cut-off calibrator is indicative of the presence of cocaine.

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

IV. PRECAUTIONS AND WARNINGS

This assay was evaluated using primarily head hair samples from a population of drug abusers in treatment programs. Interpretation of results must take into account that drug concentrations detected in hair from a single individual can vary extensively depending on the site of collection. Positive screening results only indicate the presumptive presence of cocaine, 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 cocaine 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 dyeing. 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. ALTERNATIVE PRACTICES AND PROCEDURES

Blood and urine specimens have figured prominently in efforts to monitor drug use. Problems with the analysis of these specimens relate to evasion by adulteration of the specimen or temporary abstention from drug use; the latter is facilitated by the rapid clearance of drugs from blood or urine, usually 2-3 days after last use. To adequately detect drug intake over extended periods with urine, it is necessary to collect many specimens at short intervals relative to the half lives of the drugs in the body. For illicit drugs this would require multiple samplings per week.

VI. EQUIVALENCE COMPARISON

	Dade Behring EMIT (K993988)	Psychemedics RIA Cocaine Assay
Type of Product	Analytical Reagents	Analytical Service
Measured Analytes	Benzoylecgonine, cocaine and ecgonine	Cocaine, benzoylecgonine and metabolites
Test Medium	Urine	Hair
Cut-off levels	300 ng benzoylecgonine/mL	5 ng cocaine equiv./ 10 mg hair
Test System	Competitive Enzyme Immunoassay	Competitive Radioimmunoassay
Materials	Polyclonal primary antibody; enzyme-labeled benzoylecgonine; optical assay of enzyme substrate	Polyclonal primary antibody; isotopically labeled cocaine; double antibody precipitation
Indications for Use	Identify Cocaine Use	Identify Cocaine Use
Target Population	Workplace; criminal justice; medical	Workplace; criminal justice; medical
Mass Spectrometry Confirmation	Yes	Yes

VI. SUMMARY OF ANALYTICAL STUDIES

1. Sample Preparation and Hydrolysis of Cocaine

The hair sample preparation for the assay is a 2-hour, high pH, enzymatic digestion of the hair. This procedure hydrolyzes about 60% of the cocaine in the sample, standards and controls. Under pH=9.5 at various concentrations (4, 8 and 16 ng/ 10 mg hair), the hydrolysis of cocaine to benzoylecgonine during the digestion procedures has been determined to be approximately 64%.

2. Matrix Effects

Variations due to matrix effects among different hair samples were assessed by digestion and assay of 100 cocaine-negative hair samples, which had been previously determined by RIA to be negative. The mean %B/Bo of the negative samples was 99.1, with a S.D. of 2.4 and %C. V. of 2.41. The 95% confidence interval for the mean was 98.6-99.6.

Similarly, matrix effects at the cutoff were assessed by spiking the same negative hair samples with cocaine, digesting and assaying them. The mean %B/Bo of the spiked samples was 52.4, with a S.D. of 2.1 and %C.V. of 4.0. The 95% confidence interval for the mean was 52.1-52.9.

3. Limit of Detection (LOD)

At 2.5 ng/ 10 mg hair, the lowest standard concentration for which precision data was generated, the mean ng/ 10 mg hair of 20 assays was 2.57, with a S.D. of 0.12 and %C.V. of 4.66. The 95% confidence interval for the mean of between run precision studies was 2.51-2.62.

4. Precision

a. Within-Run

The intra-assay analytical precision around the cut-off (5 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 5 ng cocaine per 10 mg hair.

Intra-Assay Precision of the Device

Cocaine Spiked Concentration	Mean (ng/ 10 mg hair)	SD (ng/ 10 mg hair)	% CV	95% Confidence Interval Lower	95% Confidence Interval Upper
-50% of cutoff (2.5 ng/ 10 mg hair)	2.40	0.10	4.13	2.35	2.44
-25% of cutoff (3.75 ng/10 mg hair)	3.75	0.24	6.51	3.53	3.97
100% of cutoff (5.0 ng/ 10 mg hair)	5.05	0.25	4.99	4.93	5.17
+25% of cutoff (6.25 ng/ 10 mg hair)	6.13	0.33	5.38	5.98	6.29
+50% of cutoff (7.5 ng/ 10 mg hair)	7.33	0.54	7.4	7.08	7.57

b. Between-Run

Inter-assay precision around the cut-off concentration was determined among 20 different assays performed (2 per day) for 10 days. Prior to digestion, hair samples were spiked at each concentration of + 25%, + 50%, -25%, -50% and 100% of the cutoff concentration (5 ng cocaine /10 mg hair).

Inter-Assay Precision of Device

Cocaine Spiked Concentration	Mean (ng/ 10 mg hair)	SD (ng/ 10 mg hair)	% CV	95% Confidence Interval Lower	95% Confidence Interval Upper
-50% of cutoff (2.5 ng/ 10 mg hair)	2.57	0.12	4.66	2.51	2.62
-25% of cutoff (3.75 ng/10 mg hair)	3.78	0.13	3.55	3.72	3.85
100% of cutoff (5.0 ng/ 10 mg hair)	4.99	0.15	2.94	4.92	5.06
+25% of cutoff (6.25 ng/ 10 mg hair)	6.32	0.19	3.01	6.23	6.41
+50% of cutoff (7.5 ng/ 10 mg hair)	7.35	0.35	4.73	7.16	7.54

5. Cross Reactivity

Before digestion, hair samples (8 mg each) were spiked with the following compounds: Cocaethylene and BE isopropylester (1.75, 2.5, and 3.75 ng/10 mg hair); benzoylecgonine (10, 20, and 40 ng/10 mg hair); hydroxyBE (20, 40, and 80 ng/ 10 mg hair); nor-BE, atropine, norcocaine, nor-CE, ecgonine methyl ester, anhydroecgonine, anhydroecgonine methyl ester (250, 2500, and 10,000 ng/10 mg hair). The samples were digested, neutralized, and tested against standards at 2.5, 5, and 7.5 ng/ 10 mg hair.

Cross-Reactivity of Cocaine-Related Drugs

Compound	Amount of Related Compound (ng/ 10 mg hair) Required to Produce a Positive Test at the Cutoff of 5 ng/ 10 mg hair
Benzoylecgonine	18
m-hydroxybenzoylecgonine	26.5
Norbenzoylecgonine	240
Benzoylecgonine isopropylester	1.35
Atropine	>10,000
Norcocaine	195
Norcocaethylene	200
Cocaethylene	1.73
Ecgonine	2960
Ecgonine methyl ester	2100
Anhydro ecgonine	>10,000
Anhydro ecgonine methyl ester	10,000

Hair samples (8 mg each) were also spiked with 250, 2500 and 10,000 ng/ 10 mg hair of the following compounds unrelated to cocaine. None of the compounds showed any reactivity at the 10,000 ng/ 10 mg hair level: Barbital, 10,11-dihydrocarbamezepine, 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, medazepam, lorazepam, temazepam, oxazepam, diazepam, bromazepam, ethosuximide, normethsuximide, mephenytoin, pheniramine, orphenadrine, chlorpheniramine, promethazine, doxylamine, methapyraline, diphenylpyraline, trimipramine, amitriptyline, nordoxepin, desipramine, doxepin, imipramine; nortriptyline, protriptyline, benzocaine, acetaminophen, buproprion, caffeine, 1-cotinine, haloperidol, lidocaine, mepivacaine, ibuprofen, naproxin, phenylpropanolamine, procaine, d-pseudoephedrine, theophylline, (-)-ephedrine, (+)-ephedrine, nicotine.

6. Effect of Interfering Compounds

The same un-related compounds tested for cross 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.

7. Stability of the Radioactive Tracer and Antibody Solutions

The stabilities of the prepared first (cocaine-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 $B_0/T \times 100$, the NSB (as $B/B_0 \times 100$) and the $B/B_0 \times 100$ 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-cocaine tracer used in the cocaine assay was assessed by comparing the $B/B_0 \times 100$ responses of the calibrators and NSB (nonspecific binding) tube and the $B_0/T \times 100$ of the Zero calibrator with fresh and one month old reagent. These indicators did not change with aging of the prepared tracer.

X. CONFIRMATION OF PRESUMPTIVE POSITIVE SAMPLES

Screen positive samples from the device are confirmed by first weighing out a new portion of the sample (approximately 12 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 5.5 for 6 hours. Digested samples are extracted and prepared for subsequent analysis by

LC/MS/MS for cocaine, benzoylecgonine, cocaethylene and nor-cocaine. The criteria for reporting a positive is given below:

Cocaine ng/10 mg hair	Benzoylecgonine % of Cocaine	Cocaethylene ng/10 mg hair	Norcocaine ng/10 mg hair	Wash Rule*	Specimen result
5	5%	Not applicable	Not applicable	PASS	Positive
5	< 5%**	0.5 on-column	Not applicable	Not applicable	Positive
5	< 5%**	< 0.5	1.1 and 0.5 after applying Norcocaine Wash Rule***	Not applicable	Positive

* Wash Rule: PASS = (Cocaine LC/MS/MS result) – 5 X (RIA result for last wash) 5 ng/10 mg hair.
** Benzoylecgonine must be present above the limit of detection, 0.5 ng/10 mg hair.
*** Norcocaine Wash Rule: (Norcocaine LC/MS/MS result) – 5 X (Norcocaine LC/MS/MS result for last wash).

XI. 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.

1. Positive Percent Agreement

Studies on drug using subjects were conducted at four rehabilitation clinics. A total of 107 individuals who tested positive for cocaine by EMIT (300 ng/mL cutoff) in at least one of two urine samples, contributed hair samples. Of those, urine from only 75 individuals were confirmed by GC/MS. All tested positive at a 150 ng /mL cutoff. Of the 75 volunteers 18 were Caucasian, 38 African American, 18 Hispanic, and 1 Asian American. They ranged in ages from 20 to 72. Of the 75 hair samples 31 were black hair, 24 brown hair, 18 salt and pepper hair, and 2 gray. These 75 individuals provided hair samples. 73 screened positive by the device. Of the 73 screen positives, 70 confirmed above the confirmation cutoff, and 3 contained cocaine below the cutoff.

Twelve male participants with a positive urine test provided 29 body hair samples (11 leg hair, 12 underarm hair, 6 chest hair) along with head hair samples. All head hair and 28 out of 29 body hair samples were positive when analyzed by the RIA device. Seven head hair samples and fifteen of the body hair samples were carried forward to confirmation. After application of confirmation criteria, 6 of the 7 head hair samples and 14 of the 15 body samples had the presence of cocaine confirmed above 5 ng/10 mg hair. Two out of seven individuals had drug concentrations in one sample varying across the cutoff, such that a positive in one hair type was a negative in another.

2. Negative Percent Agreement

A total of 73 enrollees provided 2 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 100.50, with a 95% confidence interval range of 99.40 to 101.60. All hair samples were found to be negative during confirmation testing (LC/MS/MS). One of the samples contained cocaine, but the concentration fell below the cut-off level.

A total of 21 male participants also provided body hair samples (30 leg hair, 40 under arm hair, and 17 chest hair). A majority of the participants provided body hair twice with a lapse of at least 6 months between sample collections. All 87 samples were negative by RIA and confirmation testing. All B/B_0 results fell within the 95% confidence range noted in the head hair study.

A. Head Hair Percent Agreement:

Head Hair Analysis RIA + LC/MS/MS	Urine Analysis EMIT + GC/MS Positive	Urine Analysis EMIT + GC/MS Negative
Positive	70	0
Negative	5	73

Positive Percent Agreement for RIA Screening Assay relative to urine = 73/75 = 97.3%
[95% confidence intervals: 90.7% to 99.7%]

Positive Percent Agreement for Hair Analysis (RIA + LC/MS/MS) relative to urine = 70/(70 + 5) = 70/75 = 93.3%
[95% confidence intervals: 85.1% to 97.8%%]

Negative Percent Agreement = 100%
[95% confidence intervals: 95.1% to 100%]

B. Leg Hair Percent Agreement

Leg Hair Analysis RIA + LC/MS/MS	Urine Analysis EMIT + GC/MS Positive	Urine Analysis EMIT + GC/MS Negative
Positive	7	0
Negative	0	30

Leg Hair Analysis RIA + LC/MS/MS	Head Hair Analysis RIA + LC/MS/MS Positive	Head Hair Analysis RIA + LC/MS/MS Negative
Positive	6	1
Negative	0	30

Positive Percent Agreement for leg hair analysis (RIA+ LC/MS/MS) relative to urine = 7/7 = 100%
[95% confidence intervals: 59.0% to 100%]

Positive Percent Agreement for leg hair analysis relative to head hair analysis = 6/6 = 100%
[95% confidence intervals: 54.1% to 100%]

Negative Percent Agreement for leg hair analysis relative to head hair analysis = 30/31 =96.8%
[95% confidence intervals: 83.3% to 99.9%]

C. Underarm Hair Percent Agreement

Underarm Hair Analysis RIA + LC/MS/MS	Urine Analysis EMIT + GC/MS Positive	Urine Analysis EMIT + GC/MS Negative
Positive	5	0
Negative	1	40

Underarm Hair Analysis RIA + LC/MS/MS	Head Hair Analysis RIA + LC/MS/MS Positive	Head Hair Analysis RIA + LC/MS/MS Negative
Positive	4	1
Negative	1	40

Positive Percent Agreement for under arm hair analysis (RIA+ LC/MS/MS) relative to urine = 5/6 = 83.3%
[95% confidence intervals: 35.9% to 99.6%]

Positive Percent Agreement for under arm hair analysis relative to head hair analysis = 4/5 = 80.0%
[95% confidence intervals: 28.4% to 99.5%]

Negative Percent Agreement for under arm hair analysis relative to head hair analysis = 40/41 = 97.6%
[95% confidence intervals: 87.1% to 99.9%]

D. Chest Hair Percent Agreement

Underarm Hair Analysis RIA + LC/MS/MS	Urine Analysis EMIT + GC/MS Positive	Urine Analysis EMIT + GC/MS Negative
Positive	2	0
Negative	0	17

Underarm Hair Analysis RIA + LC/MS/MS	Head Hair Analysis RIA + LC/MS/MS Positive	Head Hair Analysis RIA + LC/MS/MS Negative
Positive	2	0
Negative	0	17

Positive Percent Agreement for chest hair analysis (RIA+ LC/MS/MS) relative to urine = 2/2 = 100%
[95% confidence intervals: 15.8% to 100%]

Positive Percent Agreement for chest hair analysis relative to head hair analysis = 2/2 = 100%
[95% confidence intervals: 15.8% to 100%]

Negative Percent Agreement for chest hair analysis relative to head hair analysis = 17/17 = 100%
[95% confidence intervals: 80.5% to 100%]

<end> Submitted 17 August 2001/TCairns

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV - 6 2001

Thomas Cairns, Ph.D., DSc
Senior Scientist
Psychemedics Corporation
5832 Uplander Way
Culver City, CA 90230

Re: k010868
Trade/Device Name: Psychemedics RIA Cocaine Assay
Regulation Number: 21 CFR 862.3650
Regulation Name: Opiate test system
Regulatory Class: Class II
Product Code: KLN
Dated: August 17, 2001
Received: August 20, 2001

Dear Dr. Cairns:

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

NOV 0 6 2001

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STATEMENT OF INDICATIONS FOR USE

510(K) Number: K010868

Device Name: **Psychemedics RIA Cocaine Assay**

Indications for Use:

The Psychemedics Cocaine Assay is a radioimmunoassay, (RIA), for the qualitative and semi-quantitative detection of cocaine in head hair, leg hair, underarm hair and chest hair through the measurement of cocaine and cocaine metabolites at concentrations at or above a 5 ng/10 mg hair cutoff. For a quantitative analytical result or to confirm positive results via the presence of cocaine and cocaine metabolites, 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)

Jean Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K010868

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