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K000851

Psychemedics RIA Opiate Assay

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

A.

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Date prepared:	7 December 2000

B.

Device Generic Name:	Analytical Service: RIA Opiate Assay
Proprietary Name:	Psychemedics RIA Opiate Assay
Classification Name:	91 (Toxicology) CFR 862.3650
Product Codes of Devices to Which Equivalence is Claimed:	DJG (K971596, K974840)

II. INTENDED USE

The Psychemedics Opiate Assay is a radioimmunoassay (RIA) for the qualitative and semi-quantitative detection of morphine in hair samples at concentrations at or above 2 ng/10 mg hair for the purpose of identifying heroin 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.

The Psychemedics Opiate Assay provides only a preliminary analytical test result. For a quantitative analytical result or to confirm positive results via the presence of the heroin metabolite, 6-monoacetylmorphone (6-MAM), a more specific alternate chemical method must be used in order to obtain a confirmed analytical result. 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 opiates is based upon the competitive binding of ^{125}I-radiolabeled morphine and unlabeled morphine, in proportion to their relative concentrations in the reaction mixture. An aliquot of a solution of enzymatically-digested hair is added to a test tube with a fixed amount of radiolabeled morphine, primary antibody (antiserum against opiates), 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. For the screening assay, a B/Bo x 100 less than or equal to the B/Bo x 100 of the 2 ng morphine/10 mg hair cut-off calibrator is indicative of the presence of opiates.

The urinalysis predicate devices used in the present study were the SYVA Emit or the Roche Abuscreen systems. A Substantial Equivalence Comparison of hair analysis with these predicate devices is shown in Section VIII.

IV. PRECAUTIONS AND WARNINGS

This assay, designed for use with human hair, was evaluated using vertex head hair samples only. Positive screening results only indicate the presumptive presence of morphine requiring additional analysis by mass spectrometry for confirmation of the presence of 6-MAM before declaring the sample as positive for heroin. The assay cutoff level of 2ng/10 mg hair was determined using populations of heroin users in treatment programs. A negative screening test result does not necessarily rule out the possibility of heroin use during the previous 90 days, i.e. time of collection, frequency of use, dosage used and other factors may influence results. It is not possible to document all possible concentration reduction effects due to treatments, hair types, frequency of use variations, dosages, demographics and combinations thereof. Therefore, all possible factors that may reduce heroin metabolite levels to below cutoff within heroin user populations have not been determined. Codeine and morphine users have not been characterized with this screening assay. 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. The rate of false negatives with the Quick digest has not been characterized.

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 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. An additional problem with urinalysis is its hypersensitivity to small doses of drug, which gives rise to such problems as (i) poppy seed ingestion causing a morphine-positive sample and (ii) positive results due to passive ("sidestream" or environmental) exposure to drugs.

VI. MARKETING HISTORY

The analytic service of detecting drugs in hair began with the 1986 founding of Psychemedics Corporation, a public company dedicated exclusively to hair analysis for drugs of abuse. As the world's first commercial hair testing laboratory for drugs of abuse, Psychemedics focused on workplace testing of the NIDA-5 drugs (cocaine, marijuana, opiates, methamphetamine, and phencyclidine). Since its founding, Psychemedics has performed hair analysis on over 2 million individuals (10 million tests). Test results have routinely been upheld in the courts.

Psychemedics is a California clinical reference laboratory and is licensed under the terms of the Clinical Laboratories Improvement Act (CLIA) of 1988 to engage in interstate commerce for the purpose of performing clinical tests on human subjects (toxicology/drugs of abuse). Psychemedics is also licensed by the numerous State licensing authorities.

VII. POTENTIAL ADVERSE EFFECTS ON HEALTH

Not Applicable

VIII. EQUIVALENCE COMPARISON

	SYVA EMIT II (K971596)	**Roche Abuscreen Online (K974840)**	**Psychemedics RIA Opiate Assay**
Type of Product	**Analytical Reagents**	**Analytical Reagents**	**Analytical Service**
Measured Analytes	Morphine Codeine Dihycodeine Hydromorphone Levorphanol 6-Acetylmorphine Morphine-3-glucuronide	Morphine Codeine Ethylmorphine Diacetylmorphine 6-Acetylmorphine Dihydrocodeine Morphine-3-glucuronide	Morphine
Test Medium	Urine	Urine	Hair
Cut-off levels	300 ng morphine/mL	300 ng morphine/mL	2 ng morphine/10 mg hair
Test System	Competitive Enzyme Immunoassay	Competitive Microparticle Immunoassay	Competitive Radioimmunoassay
Materials	Polyclonal primary antibody; enzyme-labeled morphine; optical assay of enzyme substrate	Monoclonal primary antibody; soluble drug conjugate; microparticle-bound antibody; optical measurement of aggregation	Polyclonal primary antibody; isotopically labeled morphine; double antibody precipitation
Indications for Use	Identify Opiate Use	Identify Opiate Use	Identify Opiate Use
Target Population	Workplace; criminal justice; medical	Workplace; criminal justice; medical	Workplace; criminal justice; medical
GC/MS Confirmation	Yes	Yes	Yes

VIX. SUMMARY OF ANALYTICAL STUDIES

1. Limit of Detection (LOD) and Precision at Zero Morphine Concentration

Five different solutions are utilized in the analytical service: Quick and Long Hair Digests, Quick and Long artificial (BSA) matrix digests, and phosphate buffer wash medium. For both hair digests, matrix effects at zero opiate concentration among 100 different hair samples were determined. For all five systems, precision studies at zero opiate concentration were performed. From these studies, the LOD (or minimum detectable analyte concentration, MIN) was determined for each solution using the formula: $(Bo/Bo \times 100)_{MIN} = (Bo/Bo \times 100)_{MEAN}$ - 3 Standard Deviations.

For hair digests, the standard deviations (SD) due to matrix effects were slightly greater than those measured in the precision tests; thus the LOD=s for the hair digests are determined from the matrix effects studies. For the phosphate buffer wash, in which a single uniform matrix is utilized throughout an assay, the LOD was determined from the precision studies.

Limits of Detection of the Hair Digests and Wash Solution Used in the Analysis of Opiates in Hair

	LOD (ng/10 mg hair)
Quick Hair Digest	0.43
Long Hair Digest	0.35
Wash Buffer Solution	0.02

Intra-Assay Precision Studies at Zero Opiate Concentration with Hair and BSA Digests

	Sample Size (N)	Mean ($B_0/B_0 \times 100$)	SD ($B_0/B_0 \times 100$)	% CV
Quick Hair Digest	20	101.5	1.13	1.13
Long Hair Digest	20	98.8	1.37	1.39
Quick BSA Digest	20	101.8	1.74	1.71
Long BSA Digest	20	102.2	1.29	1.26

2. Matrix Effects and Intra-Assay Precision at the Cut-Off with Hair and BSA Quick and Long Digests and Wash Buffer

Variable matrix effects of different hair samples in Quick and Long Hair Digests were also measured at the cut-off concentration of 2 ng morphine / 10 mg hair. The same 100 negative samples analyzed for the matrix study at zero morphine concentration were spiked at the cut-off level concentration and assayed.

Matrix Effects of 100 Different Hair Samples at the Cut-Off Concentration

	Sample Size (N)	Mean ($B_0/B_0 \times 100$)	SD ($B_0/B_0 \times 100$)	% C.V.	SD (ng/10 mg hair)	% CV
Quick Hair Digest	96	73.5	3.68	4.99	0.348	17.4
Long Hair Digest	100	65.8	3.79	5.76	0.278	13.9

The intra-assay analytical precision around the cut-off (2 ng/10 mg hair) was determined for Quick and Long Digests of both hair and BSA. For the hair digest studies, a pool of negative hair digests was prepared. For both pooled hair digests and BSA digests, 20 replicates each were spiked at + 25%, + 50%, and 100% of the cutoff concentration of 2 ng morphine / 10 mg hair.

Intra-Assay Precision of Hair and BSA Quick and Long Digests around the Cut-Off

	Morphine Concentration	Mean (B_0/B_0 x 100)	SD (B_0/B_0 x100)	% CV	SD (ng/10 mg hair)	% CV
Quick Hair Digest	-50% of cutoff (1.0 ng/10 mg hair)	84.83	1.18	1.39	0.112	11.2
	-25% of cutoff (1.5 ng/10 mg hair)	79.32	1.05	1.32	0.099	6.6
	100% of cutoff (2.0 ng/10 mg hair)	74.27	0.95	1.28	0.090	4.5
	-50% of cutoff (2.5 ng/10 mg hair)	70.82	0.79	1.12	0.075	3.0
	-50% of cutoff (3.0 ng/10 mg hair)	67.94	0.86	1.26	0.081	2.7
Long Hair Digest	-50% of cutoff (1.0 ng/10 mg hair)	76.08	0.91	1.20	0.066	6.6
	-25% of cutoff (1.5 ng/10 mg hair)	68.41	1.03	1.46	0.075	5.0
	100% of cutoff (2.0 ng/10 mg hair)	62.39	0.84	1.35	0.061	3.1
	-50% of cutoff (2.5 ng/10 mg hair)	59.55	0.94	1.58	0.069	2.8
	-50% of cutoff (3.0 ng/10 mg hair)	55.44	0.86	1.55	0.063	2.1

	Morphine Concentration	Mean (B_0/B_0 x 100)	SD (B_0/B_0 x100)	% CV	SD (ng/10 mg hair)	% CV
Quick BSADigest	-50% of cutoff (1.0 ng/10 mg hair)	79.23	1.24	1.56	0.117	11.7
	-25% of cutoff (1.5 ng/10 mg hair)	74.48	0.90	1.21	0.085	5.7
	100% of cutoff (2.0 ng/10 mg hair)	70.26	1.06	1.51	0.100	5.0
	-50% of cutoff (2.5 ng/10 mg hair)	65.74	1.25	1.90	0.118	4.7
	-50% of cutoff (3.0 ng/10 mg hair)	62.34	0.84	1.35	0.080	2.7
Long BSA Digest	-50% of cutoff (1.0 ng/10 mg hair)	74.93	0.77	1.06	0.056	5.6
	-25% of cutoff (1.5 ng/10 mg hair)	69.00	0.70	1.02	0.051	3.4
	100% of cutoff (2.0 ng/10 mg hair)	63.89	0.79	1.24	0.058	5.7
	-50% of cutoff (2.5 ng/10 mg hair)	59.41	0.80	1.35	0.058	5.7
	-50% of cutoff (3.0 ng/10 mg hair)	55.91	0.64	1.15	0.047	4.6

Intra-assay precision of the assay with phosphate buffer wash solution was assessed by assaying wash solution spiked at the calibrator concentrations covering the optimum range of the standard curve. Twenty replicates of each concentration were assayed.

Intra-Assay Precision of Phosphate Wash Buffer at the Concentrations of the Calibrators.

Intra-Assay Precision of the Phosphate Buffer Wash at the Calibrator Concentrations

Calibrator (ng/assay tube)	Mean (B_0/B_0 x 100)	SD (B_0/B_0 x 100)	% CV	SD (ng/10 mg hair)	% CV

0.1	79.00	1.47	1.86	.005	5.0
0.4	54.64	0.94	1.72	.007	1.8
1.0	35.58	1.18	3.30	.041	4.1
3.0	16.20	0.47	2.91	.082	2.7

Interassay precision around the cut-off concentration with Quick and Long Hair and BSA digests was determined among 20 different assays performed twice daily for 10 days. For hair digests, a pool of negative hair digests was prepared, and 2 tubes each were spiked at each concentration of + 25%, + 50%, and 100% of the cutoff concentration (2 ng morphine / 10 mg hair).

Inter-Assay Precision of Hair and BSA Quick and Long Digests around the Cut-Off

	Morphine Concentration	Mean (B_0/B_0 x 100)	SD (B_0/B_0 x 100)	% CV	SD ng/10 mg hair	% CV
Quick Hair Digest	-50% of cutoff (1.0 ng/10 mg hair)	83.63	1.92	3.70	.181	18.1
	-25% of cutoff (1.5 ng/10 mg hair)	78.59	1.53	2.33	.145	9.6
	100% of cutoff (2.0 ng/10 mg hair)	74.27	1.49	2.23	.141	7.1
	-50% of cutoff (2.5 ng/10 mg hair)	70.81	1.45	2.10	.137	5.5
	-50% of cutoff (3.0 ng/10 mg hair)	67.47	1.38	1.92	.131	4.4
Long Hair Digest	-50% of cutoff (1.0 ng/10 mg hair)	76.07	0.96	1.26	.077	7.7
	-25% of cutoff (1.5 ng/10 mg hair)	68.79	0.94	1.37	.069	4.6
	100% of cutoff (2.0 ng/10 mg hair)	64.50	1.01	1.57	.073	3.7
	-50% of cutoff (2.5 ng/10 mg hair)	59.99	1.01	1.68	.073	2.9
	-50% of cutoff (3.0 ng/10 mg hair)	56.03	1.06	1.89	.077	2.6

Quick BSADigest	-50% of cutoff (1.0 ng/10 mg hair)	83.93	1.31	1.56	.124	12.4
	-25% of cutoff (1.5 ng/10 mg hair)	78.99	1.42	1.80	.134	8.9
	100% of cutoff (2.0 ng/10 mg hair)	74.00	1.37	1.85	.130	6.5
	-50% of cutoff (2.5 ng/10 mg hair)	71.35	1.56	2.19	.148	5.9
	-50% of cutoff (3.0 ng/10 mg hair)	67.91	1.68	2.47	.159	5.3
Long BSA Digest	-50% of cutoff (1.0 ng/10 mg hair)	76.07	0.96	1.26	.070	7.0
	-25% of cutoff (1.5 ng/10 mg hair)	68.79	0.94	1.37	.069	4.6
	100% of cutoff (2.0 ng/10 mg hair)	64.50	1.01	1.57	.074	3.7
	-50% of cutoff (2.5 ng/10 mg hair)	59.99	1.01	1.68	.074	3.0
	-50% of cutoff (3.0 ng/10 mg hair)	56.03	1.06	1.89	.077	2.6

The inter-assay precision of the phosphate buffer wash solution in the morphine RIA assay was measured by performing the assay twice daily for 10 days . In each assay, duplicates of wash buffer solution spiked at each calibrator concentration were assayed.

Morphine (ng/assay tube)	Mean (B_0/B_0 x 100)	SD (B_0/B_0 x 100)	% CV	SD (ng/10 mg hair)	%CV

0.1	71.51	1.23	1.72	.004	4.0
0.4	49.41	2.01	4.07	.029	7.25
1.0	32.01	1.24	3.87	.043	4.3
3.0	14.84	0.89	6.02	.156	5.2

Serial dilutions of the last phosphate buffer washes of 8 opiate-positive hair samples were assayed to test the opiate assay for linearity of results with the hair washes. No deviations from linearity were observed in the dilution study.

A natural positive hair digest from a heroin user was diluted over the range of the assay and found to be linear to the detection limit of 0.35 ng/10 mg hair. Samples with morphine values higher than the highest calibrator must be diluted in negative matrix and re-assayed to obtain a semi-quantitative result.

4. Cross Reactivity

Cross-Reacting Compounds

The compounds listed below were spiked into Quick Digest and assayed in the morphine RIA assay. The B/Bo x 100 responses of the target and cross-reactant compounds were determined and the percent cross-reactivity was calculated by the following equation:

Cross-Reactivity = (Concentration of Target Analyte at 50% B/Bo x 100) divided by
(Concentration of Cross-Reactant at 50% B/Bo)

Cross-Reactivity of Morphine-Related Drugs in Assay

Drug	Percent Cross-Reactivity
Hydromorphone	1.6
Hydrocodone	< 0.25
Codeine	8.0
6-Monoacetylmorphine	1.1
Morphine-∃-glucuronide	< 0.5
Naloxone	~ 0
Naltroxone	~ 0
Propoxyphene	~ 0
Meperidine	~ 0
Methadone	~ 0

The following additional compounds structurally unrelated to morphine were tested in the assay and found to have no cross-reactivity: Cocaine, Cocaethylene, Ecgonine, PCP,Δ-9-tetrahydrocannabinol (THC), Oxazepam; Benzoylecgonine, Methamphetamine, Amphetamine, 11-nor-9-carboxy BΔB9-Carboxy THC, Stimulants (amphetamine, caffeine, cocaine, methamphetamine, methylphenidate) , Tricyclic antidepressants (Trimipramine, Doxepin, Amitriptyline, Imipramine, Nordoxepen, Nortriptyline, Desipramine, protryptyline); Antihistaminics (Pheniramine, Doxylamine, Orphenadrine, Metapyraline, Chlorpheniramine, Diphenopyraline, Promethazine),), Antidepressants (Medazepam, Oxazepam, Lorazepam, Diazepam,

Temazepam, Bromozepam), Anticonvulsants(Ethosuximide, Methsuximide, Normethsuximide, Mephenitoin, PEMA, MPEMA); Depressants (Chlorpromazine, diazepam, flurazepam, glutethimide, methaqualone), and Barbiturates (amobarbital, butabarbitol, hexobarbitol, secobarbital).

5. Analytical Sensitivity and Specificity

Analytical Sensitivity and Analytical Specificity were calculated using data derived from (A) 1048 RIA negative samples and 285 RIA positive results from two combined research studies among drug abusing populations versus confirmation by Mass Spectrometry; and (B) a group of 70 RIA negative samples tested by GCMS. This comparison, under Long Digest, yielded an Analytical Sensitivity (TP x 100/TP + FN) of 100% and an Analytical Specificity (TN x 100/TN + FP) for heroin detection of 94% for the Opiate Assay.

No. of Samples Negative by RIA	No. of Samples Positive by RIA	No. of RIA Positives Negative by GCMS*
1048	285	38

* Includes 7 Codeine samples above 12.1 ng considered as positive (calculated based on using a % cross reactivity factor of 8.0)

No. of RIA Negatives Tested by GCMS	No. of RIA Negatives Positive by GCMS
70	0

6. Stability of the Analyte During Digestion

Morphine, at the level of 2 ng/10 mg hair, was spiked before and after digestion into tubes containing the same opiate-negative hair. The neutralized Quick and Long Digest tubes were assayed by their respective methods. Recovery of analyte after digestion is shown below for both systems.

	Morphine Value After Digestion (ng/10 mg hair)		Morphine Value Before Digestion (ng/10 mg hair)		Percent Recovery
	Mean $_{(n = 10)}$	S.D.	Mean $_{(n = 10)}$	S.D.	
Quick Hair Digest	2.05	0.15	2.17	0.19	94.5
Long Hair Digest	2.09	0.14	2.08	0.13	100.5

7. Stability of the Radioactive Tracer and Antibody Solutions

The stability of the first (morphine-specific) and second (donkey anti-sheep) antibody reagents was tested by comparing various parameters at the time of preparation and after one month of the reagents being in use. The Bo/T x 100, the NSB (as B/Bo x 100) and the B/Bo 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-morphine tracer used in the opiate assay was assessed by comparing the B/Bo x 100 responses of the calibrators and NSB (nonspecific binding) tube and the Bo/T x 100 of the Zero calibrator with fresh and 3-week-old reagent. These indicators did not change with aging of the tracer.

Duplication between Aliquots of Same Hair Sample

Duplicate portions of 31 opiate-positive hair samples were weighed and tested. Of these, 14 were codeine positive, 22 were morphine positive, and 14 were 6-MAM positive. The means of the differences between samples were as follows: morphine, 27.6% (S.D. 13.2); 6-MAM, 30.6% (S.D. 14.1); codeine, 22.8 % (S.D. 14.9).

8. Stability of the Analyte during Storage at Ambient Temperature

Samples first analyzed from 1.3 to 5.3 years in the past were re-analyzed after having been stored in the collection packets at ambient temperatures until the current second testing. The morphine content of the hair samples showed a decrease of 20% (S.D. 13.1%); codeine decreased 13.2% (S.D. 10%) and 6-MAM decreased 26.6% (S.D. 17.4%).

9. Effect of Excessive Washing, Perming, Relaxing and Dyeing on the Analytical Result

Nine morphine-positive hair samples were subjected to three common hair treatments: perming, relaxing, and dyeing. The results with the different hair specimens show that an average of 28.6 % (range of 8.2% B 48%) of drug was removed by perming; 24.6% (5.9 B 39%) by relaxing, and 1.1% (0 B 4.5%) by dyeing.

10. Studies of Washing to Remove External Contamination

To test the efficacy of the wash procedures, 33 opiate-negative samples were contaminated with morphine by the most severe method of soaking in a concentrated solution of morphine. These samples were then washed for 15 minutes at 37°C with dry isopropanol, then three times for 30 minutes and twice for 60 minutes in phosphate buffer (.01 M, pH 5.5) containing 0.1% albumin. The hair was then digested by the Long Digest method. The morphine content of the washes and the digest was determined by the Wash and Long Digest RIA assays, respectively. After subtraction of 5 times the drug content of the 5th wash from the digest, all contaminated samples were below the cut-off value of 2 ng/10 mg hair.

In an experiment to test the effects of sweat on drug-contaminated hair, morphine and 6-MAM were deposited on 13 different hair samples, and kept moist with a simulated sweat solution for 1, 2 and 6 hours. After washing by the standard 3.75 hour wash procedure, both the morphine and the 6-MAM in all 13 samples fell below the 2 ng/10 mg hair cut-off after the standard wash kinetic criteria were applied. The same wash procedure as that applied to the contaminated samples was applied to 66 positive samples from a user population. All of these samples, after the subtraction of 5 times the 5th wash, remained above the cut-off level.

11. Poppy Seed Ingestion

In a controlled study, 10 subjects ingested 150 gm of poppy seed over 3 weeks. Urine samples were collected on the days of poppy seed ingestion, and hair samples were taken in the 5th week of the study. The range among the 10 subjects of the highest urine value for each subject was 2929 to 13,857 ng morphine/mL by mass spectrometry (average 7183 ng/mL); hair morphine concentrations on 1.3 cm sections ranged from 0.05 to 0.48 ng/10 mg hair (average 0.17 ng / 10 mg hair). No 6-MAM was detected in any of the hair samples.). Most of the Long Digest hair morphine concentrations on 1.3 cm sections were below the limit of detection and all were below 0.48 ng/10 mg hair. No 6-MAM was detected in any of the hair samples.

X. SUMMARY OF FIELD STUDIES

Because of ethical impediments preventing the conduct of a controlled clinical trial, five field studies with heroin users in treatment programs were substituted.

1. Determination of Minimum Detectable Drug Use Identified by Hair Analysis

Twenty-two drug users from the Drug Treatment Center of the City of Long Beach and the Federal Probation Office of the Central District of California voluntarily and confidentially provided self reports of their heroin use in terms of number of Adime bags@ (($10 packets). Entry in to the treatment clinic was contingent upon a positive urinalysis result. The minimum detectable heroin use at the cut-off level concentration, calculated for each participating individual by the method described in this submission, was 5 to 6.5 mg per day. The positive percent agreement was 91%.

2. Positive Percent Agreement

a. Methadone Treatment Patients

In a study with the National Development and Research Institute (NDRI), a total of 93 heroin users who had previously been admitted to a methadone program and who were being followed up 12 months later, self-reported the extent of their heroin use during the previous 30 days and provided a hair specimen, of which the first 1.3 cm from the root (approx. a 30-day window of detection) was analyzed for presence of opiates. Positive self reports of heroin use were supported by a positive urinalysis result. The SYVA EMIT opiate assay system served as the predicate device with a cut-off of 300 ng/mL. Nine of the 93 subjects self-reporting heroin use had hair analysis results below the cut-off level. Positive percent agreement was 90.3%.

b. Treatment Initiative Study (DCI)

In a study among 97 intake clients who provided urine and hair specimens and self-reports of heroin use within the past 30 days, the clinical sensitivity was 90.4% (FN = 0, TP = 85). Positive self reports of heroin use were supported by a positive urinalysis result. The SYVA EMIT opiate assay system served as the predicate device with a cut-off of 300 ng/mL.

Results from the post-discharge portion of the study yielded 39 clients completing a telephone interview and hair specimen collection. Sixty-two percent of the follow-up clients had samples which were positive for

opiates by hair testing, and only 36 percent of these had reported opiate use of the drug within the past 30 days. A total of 200 clients were tested by hair analysis in the study.

c. Methadone Maintenance Program Patients
A second study performed by NDRI included 20 methadone-maintenance patients who had positive urinalysis results and self-reported heroin use. Of these, 16 had morphine-positive hair samples. Some of the reports were over a period of 90 days, corresponding to a 3.9-cm segment, and some were 30-day self reports for which a 1.3-cm hair segment was analyzed. The positive percent agreement calculated for this study was 80%. Hair samples from a total of 159 patients were tested for opiates in the study.

d. Criminal Justice Population
In a study with 201 subjects of pretrial, probation and parole populations, of 16 clients who reported heroin use retrospectively, 12 were morphine-positive by hair analysis, giving a positive percent agreement of 75%. Positive self reports were supported by positive urinalysis results at a cut-off level of 300 ng/mL measured with the SYVA/EMIT predicate device. These results yield a positive percent agreement of 81%. A prospective side-by-side comparison of urine and hair analysis was performed with 112 test subjects. Eleven individuals were identified as opiate users by 1783 urine tests, whereas 15 individuals were so identified by 187 hair tests.

e. Long Beach Drug Rehabilitation Center
Sixty patients at the Long Beach Drug Rehabilitation Center self-reported heroin use. All sixty of these patients had morphine-positive hair results, giving a positive percent agreement of 100%.

3. Negative Percent Agreement
A total of 81 hair specimens from Psychemedics Corporation employees were tested by the opiate RIA assay. At the time of hair collection, the employees also provided a urine sample which was analyzed, at a cut-off level of 300 ng/mL, by the SYVA/EMIT predicate device. All 81 urine and hair samples tested negative, providing a negative percent agreement of 100%.

X. Conclusions Drawn from the Studies

The heroin metabolites, morphine and 6-MAM, accumulate by endogenous mechanisms in the hair of heroin users. Endogenously produced morphine can be distinguished from morphine contaminants deposited externally on hair by effective wash procedures. Morphine and 6-MAM are released from the protein matrix of hair effectively by the enzymatic digestion of hair. No significant loss of morphine occurs during the enzymatic digestion of hair. The RIA assay is subject to only small matrix effects. The RIA assay exceeds the required sensitivity to produce accurate results at the chosen cut-off level of 2.0 ng/10 mg hair. False positive results due to cross reactivity effects are reduced to an insignificant level by the high morphine specificity of the antibody used in the RIA assay. False positives due to cross reactivity effects are completely avoided by the GC/MS confirmation of all positive RIA results. In most instances, perming, relaxing, dyeing and excessive washing of hair remove insufficient quantities of morphine from hair to serve as effective evasive tactics. No significant loss of morphine occurs when hair is stored at ambient temperatures for 1 to 5 years. Different field studies with independent investigators demonstrated the safety, effectiveness and utility of the chosen cut-off level. The average minimum amount of heroin use that can be detected at the cut-off level is 5 to 6.5 mg heroin per day. A field study with 81 non-drug-using employees yielded a negative percent agreement of 100%. Additional safety is provided by mass spectral confirmation and by the use of effective wash procedures. Field studies demonstrated the general utility of hair testing in a variety of settings.

On the basis of these results, it is concluded that the assay is a safe and effective method for the preliminary identification of morphine and subsequent identification of heroin via mass spectrometry.

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Revision 2:
Submitted 8th December 2000
TCairns

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Cambridge, Massachusetts 02138

Re: K000851
Trade Name: Psychemedics Analysis of Morphine in Hair
Regulatory Class: II
Product Code: DJG
Dated: September 11, 2000
Received: September 12, 2000

Dear Mr. Thistle:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we 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). 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 (Premarket Approval), 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 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

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.

This device was reviewed at our FDA Advisory Panel on November 14, 2000. The panel recommended post-marketing studies. FDA agrees with these recommendations and requests that they be performed. These studies should evaluate the following: (1) rates of false positive and false negative screening results; (2) the percent positive and negative agreement with clinical samples; (3) demographic features with potential impact on testing results including gender, melanin content, hair color, and cross-cultural differences; (4) hair sample variability; and (5) the wash-to-wash extraction variables.

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"(21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers 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,

S. 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

STATEMENT OF INDICATIONS FOR USE

510(K) Number (if known): K000851

Device Name: **Psychemedics RIA Opiate Assay**

Indications for Use:

The Psychemedics Opiate Assay is a radioimmunoassay (RIA) for the preliminary qualitative and semi-quantitative detection of morphine in human hair samples using a 2 ng/10 mg hair cutoff for the purpose of identifying heroin use. For a quantitative analytical result or to confirm positive results via the presence of the heroin metabolite, 6-monoacetylmorphone (6-MAM), 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 OF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Jean Cooper

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K000851

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