510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K201326

B Applicant

Psychemedics Corporation

C Proprietary and Established Names

Psychemedics Homogeneous Enzyme Immunoassay for Opiates in Hair
Psychemedics Homogeneous Enzyme Immunoassay for Oxycodone in Hair

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
DJG	Class II	21 CFR 862.3650 - Opiate Test System	TX - Clinical Toxicology

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Opiates, Oxycodone

C Type of Test:

Qualitative screening test: homogeneous enzyme immunoassay
Quantitative confirmatory test: LC-MS/MS

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 opiates is an enzyme immunoassay for the preliminary qualitative detection of opiates in human head and body hair using a morphine calibrator at 2 ng morphine/10 mg hair for the purpose of identifying opiate use. This is an in vitro diagnostic device intended exclusively for Psychemedics use only and is not intended for sale to anyone. The Psychemedics 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. Liquid Chromatography/Mass Spectrometry/Mass Spectrometry (LC/MS/MS) is the preferred confirmatory method.

The Psychemedics homogeneous enzyme immunoassay (HEIA) for oxycodone is an enzyme immunoassay for the preliminary qualitative detection of oxycodone in human head and body hair using an oxycodone calibrator at 2 ng oxycodone/10 mg hair for the purpose of identifying opioid use. This is an in vitro diagnostic device intended exclusively for Psychemedics use only and is not intended for sale to anyone. The Psychemedics 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. Liquid Chromatography/Mass Spectrometry/Mass Spectrometry (LC/MS/MS) is the preferred confirmatory method.

C Special Conditions for Use Statement(s):

OTC - Over The Counter

The Psychemedics homogeneous enzyme immunoassay (HEIA) for opiates and homogeneous enzyme immunoassay (HEIA) for oxycodone combine a screening method (immunoassay) with a confirmation method (LC/MS/MS) in one test system.
The assay is to be performed only at Psychemedics Corporation.

D Special Instrument Requirements:

Performance data for the Psychemedics homogeneous enzyme immunoassay (HEIA) for opiates in hair and Psychemedics homogeneous enzyme immunoassay (HEIA) for oxycodone in hair screening assays was collected on the Olympus AU 640 analyzer.

The confirmation assay consists of an AB Sciex 3200 LC/MS/MS linked to two Perkin Elmer Series 200 Micro pumps and a Perkin Elmer Series 200 autosampler.

IV Device/System Characteristics:

A Device Description:

The homogeneous enzyme immunoassay (HEIA) test (screening assay) consists of two parts; a pre-analytical hair treatment procedure (to extract opiates from the solid hair matrix to form a measurable liquid matrix) and the screening assay, the Psychemedics Opiates HEIA and the Psychemedics Oxycodone HEIA.

The Psychemedics Opiates HEIA consists of reagents R1 (anti-opiates monoclonal antibody with substrate) and R2 (morphine labeled recombinant G6PDH). The Psychemedics Oxycodone HEIA consists of reagents R1 (anti-oxycodone monoclonal antibody with substrate) and R2 (oxycodone labeled recombinant G6PDH).

The confirmation assay consists of an AB Sciex 3200 LC/MS/MS linked to two Perkin Elmer Series 200 Micro pumps and a Perkin Elmer Series 200 autosampler.

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 opiates antibody and opiate-labeled G6PDH or oxycodone antibody and oxycodone-labeled G6PDH using a chemistry autoanalyzer. The cutoff calibrator and controls are also processed through the extraction and autoanalyzer steps.

The immunoassay is based on competition between the morphine-labeled G6PDH or oxycodone-labeled G6PDH and free drug from the extracted hair sample for a fixed amount of specific antibody binding sites. In the absence of free drug from the samples, the specific antibody binds the opiate- G6PDH or oxycodone-G6PDH and causes a decrease in enzyme activity. This phenomenon creates a direct relationship between the drug concentration in hair and enzyme activity. The enzyme activity is determined spectrophotometrically at 340 nm by measuring the conversion of nicotinamide adenine dinucleotide (NAD) to NADH.

A change in milli-absorbance units (ΔmAU) greater than or equal to the ΔmAU of the 2 ng morphine/10 mg hair cutoff calibrator is indicative of the presence of opiates; a change in milli-absorbance units (ΔmAU) greater than or equal to the ΔmAU of the 2 ng oxycodone/10 mg hair cutoff calibrator is indicative of the presence of oxycodone.

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 opioids, extracted by a different procedure and confirmed by LC/MS/MS for the presence of opioids or oxycodone.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Psychemedics Microplate EIA for Opiates in Hair, Psychemedics Microplate EIA for Oxycodone in Hair

B Predicate 510(k) Number(s):

K111926, K123799

C Comparison with Predicate(s):

Device & Predicate Device(s):	K201326	K111926
Device Trade Name	Psychemedics Homogeneous Enzyme Immunoassay for Opiates in Hair	Psychemedics Microplate EIA for Opiates in Hair
General Device Characteristic Similarities		
Intended Use/Indications For Use	Same	The Psychemedics Microplate EIA for Opiates is an enzyme immunoassay (EIA) for the preliminary qualitative detection of opiates in human head and body hair samples using a morphine calibrator at 2 ng/10 mg hair cutoff for the purpose of identifying opiate use.
Sample Matrix	Human Hair	Same
General Device Characteristic Differences		
Method of Measurement	Automated Clinical Chemistry Analyzer at 340 nm	Microplate Reader at 450 nm
Antibody	Mouse monoclonal	Rabbit polyclonal

Device & Predicate Device(s):	K201326	K123799
Device Trade Name	Psychemedics Homogeneous Enzyme Immunoassay for Oxycodone in Hair	Psychemedics Microplate EIA for Oxycodone in Hair
General Device Characteristic Similarities		
Intended Use/Indications For Use	Same	The Psychemedics Microplate EIA for Oxycodone is an enzyme immunoassay (EIA) for the preliminary qualitative detection of oxycodone in human head and body hair samples using an oxycodone

Device & Predicate Device(s):	K201326	K123799
		calibrator at 2 ng/10 mg hair cutoff for the purpose of identifying oxycodone use.
Sample Matrix	Same	Human hair
General Device Characteristic Differences		
Method of Measurement	Automated Clinical Chemistry Analyzer at 340 nm	Microplate Reader at 450 nm
Antibody	Mouse monoclonal	Rabbit polyclonal

VI Standards/Guidance Documents Referenced:

CLSI EP06-A: Evaluation of Linearity of Quantitative Measurement Procedures - 2nd Edition

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Opiates Screening Assay

Precision studies were performed by spiking negative hair with previously LC/MS/MS validated calibrator and control solutions to achieve concentrations of negative, the cutoff calibrator of 2 ng morphine/10 mg hair or 2 ng oxycodone/10 mg hair, and +/- 75%, +/-50% and +/-25% of the cutoff calibrator.

Intra-assay precision for both screening assays was performed on a single day in two replicates of four.

Opiates HEIA Intra-assay Precision Results			
Concentration (ng/10 mg)	% of cutoff	# of determinations	Total Result
0	-100	8	0 Positive / 8 Negative
0.5	-75	8	0 Positive / 8 Negative
1.0	-50	8	0 Positive / 8 Negative
1.5	-25	8	0 Positive / 8 Negative
2.0	Cutoff	8	4 Positive / 4 Negative
2.5	+25	8	8 Positive / 0 Negative
3.0	+50	8	8 Positive / 0 Negative
3.5	+75	8	8 Positive / 0 Negative
4.0	+100	8	8 Positive / 0 Negative

Oxycodone HEIA Intra-assay Precision Results			
Concentration (ng/10 mg)	% of cutoff	# of determinations	Total Result
0	-100	8	0 Positive / 8 Negative
0.5	-75	8	0 Positive / 8 Negative
1.0	-50	8	0 Positive / 8 Negative
1.5	-25	8	0 Positive / 8 Negative
2.0	Cutoff	8	5 Positive / 3 Negative
2.5	+25	8	8 Positive / 0 Negative
3.0	+50	8	8 Positive/ 0 Negative
3.5	+75	8	8 Positive/ 0 Negative
4.0	+100	8	8 Positive/ 0 Negative

Inter-assay precision for both screening assays was performed for 10 days, 2 runs per day in replicates of 4 for a total of 80 results per sample.

Opiates HEIA Inter-assay Precision Results			
Concentration (ng/10 mg)	% of cutoff	# of determinations	Total Result
0	-100	80	0 Positive / 80 Negative
0.5	-75	80	0 Positive / 80 Negative
1.0	-50	80	0 Positive / 80 Negative
1.5	-25	80	0 Positive / 80 Negative
2.0	Cutoff	80	50 Positive/ 30 Negative
2.5	+25	80	80 Positive / 0 Negative
3.0	+50	80	80 Positive / 0 Negative
3.5	+75	80	80 Positive/ 0 Negative
4.0	+100	80	80 Positive/ 0 Negative

Oxycodone Inter-assay Precision Results			
Concentration (ng/10 mg)	% of cutoff	# of determinations	Total Result
0	-100	80	0 Positive / 80 Negative
0.5	-75	80	0 Positive / 80 Negative
1.0	-50	80	0 Positive / 80 Negative
1.5	-25	80	0 Positive / 80 Negative
2.0	Cutoff	80	52 Positive / 28 Negative
2.5	+25	80	80 Positive/ 0 Negative
3.0	+50	80	80 Positive/ 0 Negative
3.5	+75	80	80 Positive/ 0 Negative
4.0	+100	80	80 Positive/ 0 Negative

LC-MS/MS confirmation method

Intra-assay Precision around the Cutoff

Morphine	1.0	1.5	2.0	2.5	3.0
Mean	0.988	1.468	1.942	2.418	2.788
SD	0.046	0.016	0.094	0.073	0.049
%CV	4.694	1.119	4.822	3.031	1.746

Oxycodone	1.0	1.5	2.0	2.5	3.0
Mean	0.975	1.496	1.912	2.458	2.88
SD	0.0475	0.0568	0.0823	0.0536	0.0938
%CV	4.867	3.799	4.303	2.180	3.257

Intra-assay Precision over the range of the Assay

Morphine	0.25	0.5	1	75	100
Mean	0.206	0.449	0.8546	62.52	82.94
SD	0.0044	0.0139	0.0278	0.5805	0.8264
%CV	2.15	3.10	3.25	0.93	1.00
Oxycodone	0.25	0.5	1	75	100
Mean	0.2404	0.48	1.0286	68.34	89.58
SD	0.0170	0.0239	0.0542	0.6066	3.0351
%CV	7.08	4.97	5.27	0.89	3.39

Inter-assay Precision around the cutoff

Morphine			
Target concentration (ng/10 mg hair)	1.00	2.00	3.00
Mean	0.98	1.94	2.89
SD	0.05	0.11	0.13
%CV	4.97	5.68	4.58

Oxycodone			
Target concentration (ng/10 mg hair)	1.00	2.00	3.00
Mean	1.05	2.11	3.09
SD	0.07	0.13	0.16
%CV	6.25	6.20	5.17

2. Linearity:

The screening immunoassays are qualitative tests. An evaluation of linearity is not applicable.

The linearity of the LC-MS/MS confirmation method for the calibrator drugs morphine and oxycodone was evaluated as follows. Morphine concentrations at 0.0, 0.25, 0.50, 1.0, 1.5, 2.0, 2.5, 3.0, 10.0, 25.0, 50.0, 100.0, 125.0, and 150.0 ng/per 10 mg hair and oxycodone concentrations of 0.0, 0.25, 0.50, 1.0, 1.5, 2.0, 2.5, 3.0, 10.0, 25.0, 50.0, 100.0, 125.0, and 150.0 ng per 10 mg hair were evaluated.

All concentrations for the morphine and oxycodone samples demonstrated percent recoveries within ± 20 % of the expected value.

The LC-MS/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:

Opiates Immunoassay: Cross-reactivity with structurally related compounds

The cross-reactivity characteristics of the opiates screening immunoassay were evaluated by spiking various concentrations of potential cross-reactants into drug-free hair samples and comparing the result to the cutoff calibrator. The table below lists the percent cross-reactivity and the approximate concentration of each compound required to produce a response approximately equivalent to the cutoff concentration of the assay.

Compound	Percent Cross-reactivity	Expected Concentration Equivalent to 2 ng morphine / 10 mg hair
Codeine	100	2.0
6-Acetylmorphine	80	2.5
Hydrocodone	20	10
Morphine 3-Glucuronide	20	10
Hydromorphone	13	15
Buprenorphine	10	20
Atropine	2.7	75
Oxycodone	<2	>100
Oxymorphone	<2	>100
Methadone	<2	>100
Naloxone	<2	>100
Naltrexone	<2	>100
Propoxyphene	<2	>100
Meperidine	<2	>100

Opiates Immunoassay: potential interference from structurally unrelated compounds

Potentially interfering compounds at a concentration of 100 ng/10 mg hair were added individually to spiked hair samples at +/- 50% of the morphine cutoff to evaluate which of them might interfere in the assay. The following compounds did not cause any positive or negative interference with the opiates screening assay.

Anhydroecgonine Methyl Ester, Homovanillic Acid, Bupropion, Cotinine, Cannabinol, O- Desmethylvenlafaxine, Desipramine, Doxylamine succinate, 1S, 2R Ephedrine, Naproxen, Nicotine, Nortriptyline, H-Propoxyphene, R,R-Pseudoephedrine, Thioridazine, Cis-Tramadol, Venlafaxine, (±)-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 (designer drug), JWH-019 (naphthoylindole), JWH-081 (naphthoylindole), JWH-122 (Synthetic Cannabimimetic), Imipramine, Acetaminophen, Caffeine, Dyphylline, Methaqualone, Theophylline. CP47.497 (Cannabinoid Receptor Agonist Drug), CP47.497 C8 Homologue, HU-211 (Dexanabinol), JWH-200, JWH-250, Ibuprofen, Ethosuximide, (±)-Epinephrine, Norepinephrine, Barbital, Metanephrine, Normetanephrine, Methocarbamol, Alprazolam, Citicoline, Citalopram, Clopidogrel, Bisulfate, Fluconazole, Hydrochlorothiazide, Lamotrigine, L-Thyroxine, MethylPhenidate, Omeprazole, Amlodipine Besylate, Atorvastatin, Azithromycin, Bupivacaine, Cetirizine, Dimenhydrinate, Lisinopril, Methsuximide, Phensuximide, N-Normethyl Suximide, Butabarbital, Amobarbital, Secobarbital, Hexobarbital, Phenobarbital, Mephenytoin, Ethotoin, Mephobarbital, PEMA (phenylethylmalonamide), 10, 11-Dihydrocarbamazepine, Medazepam, Chlorpromazine, Flurazepam, Lorazepam, Temazepam, Bromazepam, Primidone, 5,5-Diphenyl Hydantoin, Triamterene, Nordoxepin, Oxazepam, Levetiracetam, Metformin, Phenytoin, R-Phenylephrine, Sertraline, Topiramate, Zolpidem Tartrate, Vanillylmandelic acid, 5-Hydroxy Indole-3-Acetic Acid

Opiates Immunoassay: Effect of cosmetic treatments

Hair samples negative for opiates and hair samples positive for opiates 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 opioids analysis and assayed by the opiates screening assay. The screening results with and without treatment were compared to evaluate any interference in the assay or loss of drug due to the treatments. Fifteen (15) hair samples negative for opiates were evaluated before and after the following cosmetic treatments: permanent wave, relaxer, dye (which includes bleach), and shampoo. Nine of the samples were described as brown, four as dark brown, and two as light brown.

All fifteen of the opiates negative samples produced a negative result both before and after the cosmetic treatments.

Forty (40) samples (ten for each of the four cosmetic treatments) positive for opiates were evaluated before and after the following cosmetic treatments: permanent wave, relaxer, dye (which includes bleach), and shampoo. Thirty-one of the samples were described as black, seven as brown, and two as salt and pepper.

All forty of the opiates positive samples produced a positive result both before and after the cosmetic treatments.

Oxycodone Immunoassay: Cross-reactivity with structurally related compounds

The cross-reactivity characteristics of the oxycodone screening immunoassay were evaluated by spiking various concentrations of potential cross-reactants into drug-free hair samples and comparing the result to the cutoff calibrator. The table below lists the percent cross-reactivity and the approximate concentration of each

compound required to produce a response approximately equivalent to the cutoff concentration of the assay.

Compounds related to oxycodone and tested for cross-reactivity with the antibody are listed in the table below.

Cross-Reactivity of Compounds structurally related to oxycodone

Compound	Percent Cross-reactivity	Expected Concentration Equivalent to 2 ng oxycodone / 10 mg hair
6-Acetylcodeine	100	2
Hydrocodone	80	2.5
Ethylmorphine	80	2.5
Codeine	67	3.0
Dihydrocodeine	67	3.0
6-Acetylmorphine	27	7.5
Morphine	27	7.5
Dihydromorphine	20	10
Morphine 3-Glucuronide	20	10
Atropine	13	15
Buprenorphine	13	15
Hydromorphone	10	20
Oxymorphone	5	40
Nalorphine	2	100
Imipramine	2	100
Meperidine	<2	>100
Methadone	<2	>100
Naloxone	<2	>100
Naltrexone	<2	>100
Propoxyphene	<2	>100

Oxycodone Immunoassay: Interference Testing

Potentially interfering compounds at a concentration of 100 ng/10 mg hair were added individually to spiked hair samples at +/- 50% of the oxycodone cutoff to evaluate which of them might interfere in the assay. The following compounds did not cause any positive or negative interference with the oxycodone screening assay.

Anhydroecgonine Methyl Ester, Homovanillic Acid, Bupropion, Cotinine, Cannabinol, O- Desmethylvenlafaxine, Desipramine, Doxylamine succinate, 1S, 2R Ephedrine, Naproxen, Nicotine, Nortriptyline, H-Propoxyphene, R,R-Pseudoephedrine, Thioridazine, Cis-Tramadol, Venlafaxine, (±)-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 (designer drug), JWH-019 (naphthoylindole), JWH-081 (naphthoylindole), JWH-122 (Synthetic Cannabimimetic), Acetaminophen, Caffeine, Dyphylline, Methaqualone,

Theophylline, CP47.497 (Cannabinoid Receptor Agonist Drug), CP47.497 C8 Homologue. HU-211 (Dexanabinol), JWH-200, JWH-250, Ibuprofen, Ethosuximide, (±)-Epinephrine, Norepinephrine, Barbital, Metanephrine, Normetanephrine, Methocarbamol, Alprazolam, Citicoline, Citalopram, Clopidogrel, Bisulfate, Fluconazole, Hydrochlorothiazide, Lamotrigine, L-Thyroxine, MethylPhenidate, Omeprazole, Amlodipine Besylate, Atorvastatin, Azithromycin, Bupivacaine, Cetirizine, Dimenhydrinate, Lisinopril, Methsuximide, Phensuximide, N-Normethyl Suximide, Butabarbital, Amobarbital, Secobarbital, Hexobarbital, Phenobarbital, Mephenytoin, Ethotoin, Mephobarbital, PEMA (phenylethylmalonamide), 10, 11-Dihydrocarbamazepine, Medazepam, Chlorpromazine, Flurazepam, Lorazepam, Temazepam, Bromazepam, Primidone, 5,5-Diphenyl Hydantoin, Triamterene, Nordoxepin, Oxazepam, Levetiracetam, Metformin, Phenytoin, R-Phenylephrine, Sertraline, Topiramate, Zolpidem Tartrate, Vanillylmandelic acid, 5-Hydroxy Indole-3-Acetic Acid

Atropine and chlorpheniramine were found to cause positive interference in the Opiates and
Oxycodone screening assays.

Oxycodone Immunoassay: Effect of cosmetic treatments

Hair samples negative for oxycodone and samples positive for oxycodone 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 analysis and assayed by the oxycodone screening assay. The screening results with and without treatment are compared to evaluate any interference in the assay or loss of drug due to the treatments. The study included 15 negative samples and 10 oxycodone-positive samples with each of the treatments.

Fifteen (15) hair samples negative for oxycodone were evaluated before and after the following cosmetic treatments: permanent wave, relaxer, dye (which includes bleach), and shampoo. Nine of the samples were described as brown, four as dark brown, and two as light brown.

All fifteen of the oxycodone negative samples produced a negative result both before and after the cosmetic treatments.

Forty (40) samples (ten for each of the four cosmetic treatments) positive for oxycodone were evaluated before and after the following cosmetic treatments: permanent wave, relaxer, dye (which includes bleach), and shampoo. Thirty-one of the samples were described as black, seven as brown, and two as salt and pepper. All forty of the oxycodone positive samples produced a positive result both before and after the cosmetic treatments.

Specificity of the LC-MS/MS method

An interference study was conducted for the LC-MS/MS method by spiking potential interferents into negative hair specimens that did not contain any drug, and individually into hair specimens containing 0.8 mg/10 mg hair of morphine, codeine 6-AM, hydrocodone, hydromorphone, oxycodone, and oxymorphone. All of the samples spiked with interferent but no drug produced a negative result and all of the samples spiked at 0.8 ng / 10 mg hair quantitated at ± 20% of the target value in the presence of interfering substances. The sponsor concluded that the potentially interfering compounds listed below did not cross-react or cause interference with the LC-MS/MS assay.

The following potential interferents were tested at a concentration of 2.5 ng/10 mg hair: Amlodipine besylate, Bupivacaine HCl•H20.

The following potential interferents were tested at a concentration of 20 ng/10 mg hair: Clonazepam, Estazolam, Flurazepam, Flunitrazepam, Midazolam, Nitrazepam, Prazepam, Triazolam, Zolpidem, Phentermine, R,R-(-)-Pseudoephedrine.

The following potential interferents were tested at a concentration of 25 ng/10 mg hair: Cetirizine dihydrochloride, Prednisolone, Prednisone.

The following potential interferents were tested at a concentration of 50 ng/10 mg hair: Ibuprofen, Meprobamate, Naproxen, (+)-Propoxyphene, Atorvastatin calcium salt, Azithromycin dihydrate, Dimenhydrinate, Lisinopril dihydrate, Loratadine, Montelukast sodium salt, Pioglitazone hydrochloride, Procainamide HCl, Simvastatin.

The following potential interferents were tested at a concentration of 100 ng/10 mg hair: Carbamazepine, Levetiracetam, Metformin HCl, Phenobarbital, Phenytoin, R (-)-Phenylephrine HCl, Sertraline hydrochloride, Topiramate, Zolpidem tartrate, Zonisamide.

The following potential interferents were tested at a concentration of 200 ng/10 mg hair: Morphine, Oxycodone, Codeine, Phencyclidine, S-(+)-Methamphetamine, S-(+)-Amphetamine, (±)-Methadone, Phenobarbital, Phenytoin, R-(-)-Phenylephrine HCl, Carbamazepine, Salicylic Acid, Valproic Acid, Buprenorphine (SYN), cis-Tramadol HCl, Fentanyl, Hydrocodone, Hydromorphone, Meperidine, Naloxone, Naltrexone, Oxymorphone, Aripiprazole, Lacosamide, Oxcarbazepine, Rufinamide.

The following potential interferents were tested at a concentration of 500 ng/10 mg hair: Oxcarbazepine, Gabapentin, Acetaminophen, (-)-Cotinine, S- (-)-Nicotine, Caffeine, Pregabalin, Salicylic acid, Valproic acid, Vigabatrin.

The following potential interferents were tested at a concentration of 2000 ng/10 mg hair: Warfarin.

4. Assay Reportable Range:

An assay reportable range is not applicable for the opiates and oxycodone screening assays because they are qualitative only.

The claimed reportable range for the analytes measured by the LC-MS/MS method are as follows:

Morphine: 0.25 ng/10 mg hair to 100 ng/10 mg hair

Codeine, 6-Acetylmorphine, Hydrocodone, Hydromorphone, Oxycodone, and Oxymorphone: 0.25 ng/10 mg hair to 150 ng/10 mg hair

These reportable ranges are supported by the linearity, precision, and lower limit of quantitation (LLOQ) studies.

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

Traceability:

Calibrators and control materials are prepared using drug stocks purchased from a commercial vendor with a certificate of analysis. The commercially obtained stock is made into calibrators and controls to the desired concentrations, which are confirmed by LC/MS/MS.

Sample shipping and storage stability:

Seven hair samples containing morphine, 6-AM, and codeine and six samples containing oxycodone and hydrocodone were stored in the same collection foil and card-envelope provided with the hair collection kit.

After a period of two months, the samples containing morphine, 6-AM, codeine, and hydrocodone were shipped overnight to another location and returned to the original location by overnight shipping. Samples were tested by the routine LC-MS/MS procedure both before being shipped and after their return. The sponsor stated that all samples that tested positive via the HEIA device and confirmed positive via LC-MS/MS before shipping and storage remained positive after shipping and storage.

After a period of four months, the samples containing oxycodone were shipped overnight to another location and returned to the original location by overnight shipping. Samples were tested by the routine LC-MS/MS procedure both before being shipped and after their return. The sponsor stated that all samples that tested positive via the HEIA device and confirmed positive via LC-MS/MS before shipping and storage remained positive after shipping and storage.

6. Detection Limit:

The screening immunoassays are qualitative tests only; therefore, a detection limit evaluation is not applicable. See section VII.A.1. above for performance around the immunoassay device cutoff.

The sponsor performed a study to determine the lower limit of quantitation (LLOQ) of the LC-MS/MS assay for morphine, codeine, 6-acetylmorphine, hydrocodone, hydromorphone, oxycodone and oxymorphone.

The LLOQ is the lowest concentration that meets chromatographic and retention time criteria, and that can be quantitated within 20% of the expected value. The method LLOQ was determined to be 0.25 ng/10 mg for morphine, codeine, 6-MAM, oxycodone, oxymorphone, hydrocodone and hydromorphone. The LLOQ for this method has been administratively raised to 0.5 ng/10 mg for codeine, oxycodone, oxymorphone, hydrocodone, and hydromorphone.

7. Assay Cut-Off:

Analytical performance of the devices around the claimed cutoff is described in precision section VII.A.1 above.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Accuracy of the immunoassay screening methods

A total of 230 de-identified hair samples were analyzed for the opiates immunoassay and 219 samples were analyzed for the oxycodone assay. These samples were compared with results from the LC-MS/MS confirmatory assay. Results are summarized in the tables below:

	LC/MS/MS Result			
Opiates Immunoassay Result	< 1.0 (< 50% below cutoff)	1.0 – 2.0 (≥ 50% below cutoff to cutoff)	2.0 – 3.0 (cutoff to ≤ 50% above cutoff)	> 3.0 (> 50% above cutoff)
Positive	43	3	14	42
Negative	118	10	0	0

The source, gender, and hair color of the opiates samples were as follows:

Source		Gender		Color				
Head	Body	Male	Female	Brown	Black	Salt/Pepper	White/Gray	Blonde
158	72	158	72	88	127	13	1	1

The presence of codeine, 6-AM, and morphine was detected by LC-MS/MS in the 46 discordant results observed, and the presence of these analytes contributed to the positive results observed by the screening assay.

	LC/MS/MS Result			
Oxycodone Immunoassay Result	< 1.0 (< 50% below cutoff)	1.0 – 2.0 (≥ 50% below cutoff to cutoff)	2.0 – 3.0 (cutoff to ≤ 50% above cutoff)	> 3.0 (> 50% above cutoff)
Positive	48	8	15	31
Negative	103	14	0	0

The source, gender, and hair color of the oxycodone samples were as follows:

Source		Gender		Color			
Head	Body	Male	Female	Brown	Black	Salt/Pepper	White/Gray
152	67	152	67	108	97	13	1

The presence of hydrocodone was detected by LC-MS/MS in the 56 discordant results observed, and the presence of this analyte contributed to the positive results observed by the screening assay.

Recovery from LC-MS/MS Analysis

The sponsor conducted a study to evaluate recovery for morphine, codeine, 6-acetylmorphine, hydrocodone, hydromorphone, oxycodone, and oxymorphone at a concentration of 2 ng/10 mg hair. Fifteen tubes were prepared and analyzed by LC/MS/MS. The recovery of the analytes ranged from 94.9% to 104.1%.

2. Matrix Comparison:

Not applicable. The assay is intended for only hair samples.

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.