510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

k101754

B. Purpose for Submission:

New device

C. Measurand:

Opiates in oral fluid

D. Type of Test:

Qualitative immunoassay

E. Applicant:

Microgenics Corp.

F. Proprietary and Established Names:

Thermo Scientific CEDIA Opiate OFT Assay

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.3650, opiate test system

2. Classification:

   Class II

3. Product code:

   DJG, enzyme immunoassay, opiates

4. Panel:

   Toxicology (91)

H. Intended Use:

1. Intended use(s):

   See indications for use below.

2. Indication(s) for use:

   The CEDIA® Opiate OFT Assay is intended for use in the qualitative determination of opiates at a cutoff of 30.0 ng/mL in neat oral fluid. The specimen must be collected exclusively with the Oral-Eze™ Saliva Collection System. The assay is calibrated against morphine and performed on the MGC 240. This in vitro diagnostic device is intended for clinical laboratory use only.

   The CEDIA Opiate OFT Assay provides only a preliminary analytical test result. A more specific alternative method must be used to obtain a confirmed analytical result. Gas Chromatography/Mass Spectrometry (GC/MS) and Liquid Chromatography-Tandem Mass Spectrometry (LC-MS/MS) are the preferred confirmatory methods. Clinical consideration and professional judgment should be applied to any drug of abuse test result particularly when preliminary positive results are used.

3. Special conditions for use statement(s):

   For prescription use only
   The assay is not designated for use in point-of-care settings.

4. Special instrument requirements:

   MGC 240 analyzer

I. Device Description:

Oral-Eze Saliva Collection System

The Oral-Eze Saliva Collection System consists of Oral-Eze saliva collector and collection tube with preservative buffer. Oral-Eze saliva collector consists of an absorbent pad attached to a plastic handle. The saliva collector is provided with a volume adequacy indicator. The plastic handle has a round window where blue color will appear when sufficient volume of oral fluid is collected. Samples are collected by placing the collector pad and plastic shield between lower cheek and gum with the plastic shield facing the cheek. Oral fluid collection is done when blue color appears in the window of the handle. The pad is ejected in to the collection tube by placing thumb on the ridges on the handle and pushing the thumb forward. The collection tube is capped and sent to the laboratory for processing and testing

CEDIA® Opiate OFT Assay Reagents

1. EA Reconstitution Buffer
   Contains buffer salts, mouse monoclonal anti-amphetamine antibody, stabilizer, and preservative

1a EA Reagent
   Contains Enzyme Acceptor (microbial), buffer salts and preservative

2. ED Reconstitution Buffer
   Contains buffer salts, stabilizers, and preservative

2a ED Reagent
   Contains Enzyme Donor (microbial) conjugated to amphetamine derivative, chlorophenol red- β -D-galactopyranoside, stabilizers, detergent and preservative

Additional Materials Required (sold separately):

10014954 CEDIA Multi-Drug OFT Negative Calibrator
10014955 CEDIA Multi-Drug OFT Cutoff Calibrator
10014956 CEDIA Multi-Drug OFT High Calibrator
10014957 CEDIA Multi-Drug OFT Controls Kit

Calibrators are cleared under k101752

J. Substantial Equivalence Information:

1. Predicate device name (s):

   OTI Opiates Micro-Plate EIA

2. Predicate 510(k) number(s):

   k981341

3. Comparison with predicate:

Items	CEDIA Opiate OFT Assay (Candidate Device)	OTI Opiates Micro-Plate EIA (Predicate Device)
Similarity		
Intended use /Indication for use	Same	For use in the qualitative determination of opiates in oral fluid samples. For In Vitro Diagnostic Use.
Sample type	Same	Oral fluid
Calibrated against	Same	Morphine
Difference		

Cutoff	30 ng/mL in Neat Oral Fluid	10 ng/mL when oral fluid collected with the Oral Specimen Collection Device
Collection Device	Oral-Eze	OraSure®
Instrument	MGC 240 analyzer	Micro-plate reader
Measuring wavelength	570 nm (primary) 670 (secondary)	450 nm

K. Standard/Guidance Document Referenced (if applicable):

None were referenced.

L. Test Principle:

Microgenics CEDIA® Opiate OFT Assay uses recombinant DNA technology to produce a unique homogeneous enzyme immunoassay system. The assay is based on the bacterial enzyme ß-galactosidase, which has been genetically engineered into two inactive fragments. These fragments spontaneously re-associate to form fully active enzyme that, in the assay format, cleave a substrate, generating a color change that can be measured spectrophotometrically.

In the assay, analyte in the sample competes with analyte conjugated to one inactive fragment (enzyme donor) of ß-galactosidase for antibody binding site. If analyte is present in the sample, it binds to antibody, leaving the inactive enzyme fragment free to form active enzyme. If the analyte is not present in the sample, antibody binds to analyte conjugated on the inactive fragment, inhibiting the re-association of inactive ß -galactosidase fragments, and no active enzyme is formed. The amount of active enzyme formed and resultant absorbance change are directly proportional to the amount of analyte present in the sample.

The Oral-Eze Saliva Collection System consists of Oral-Eze saliva collector and collection tube with preservative buffer. Oral-Eze saliva collector consists of an absorbent pad attached to a plastic handle. The saliva collector is provided with a volume adequacy indicator. The assay result is reported as a positive or negative result relative to the neat oral fluid cutoff of 30 ng/mL

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M. Performance Characteristics (if/when applicable):

1. <u>Analytical performance:</u>

   All analytical performance data was collected on human oral fluid samples collected with the Oral-Eze Saliva Collection System and analyzed on the MGC 240 analyzer. The collection device includes a diluent that results in a dilution of approximately 1/3. The assay cannot be used to measure undiluted (neat)

samples. Analyte concentrations refer to the neat oral fluid concentration, unless otherwise noted.

a. Precision/Reproducibility:

Negative neat oral fluid samples were collected by spitting into a cup. Testing samples were prepared by spiking morphine into the negative neat oral fluid. The samples were applied onto the pad of Oral-Eze collection device (n=2 pad/level) and eluted following the instruction menu. Precision were evaluated following randomized CLSI (EP5-A2) precision protocol as in study 1.

Note: The values obtained in this study were collected from samples containing opiates prior to the collection step. Therefore the results reflect the performance of the entire system including the collection step.

The results are summarized in the table below:

Analyte	Concentration of sample	**Opiate OFT Assay # Neg / # Pos**
Morphine	Negative	50 Neg / 0 Pos
Morphine	-75%	50 Neg / 0 Pos
Morphine	-50%	50 Neg / 0 Pos
Morphine	-25%	50 Neg / 0 Pos
Morphine	Cutoff	0 Neg / 50 Pos
Morphine	25%	0 Neg / 50 Pos
Morphine	50%	0 Neg / 50 Pos
Morphine	75%	0 Neg / 50 Pos

b. Linearity/assay reportable range:

Not applicable. This is a qualitative assay.

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

See k101752 decision summary for information on calibrators.

Reagent stability:

Real time testing is on-going to support the product shelf life of 3 years. The stability protocol was reviewed and found acceptable. The current test results support the stability at 2-8^{o}C for 24 months. The on board stability of reconstituted reagents is 60 days (2-8^{o}C).

Sample storage and stability:

The stability of oral fluid samples in the preservative buffer was evaluated in real time. The stability protocol was reviewed and found acceptable. Oral fluid samples in the preservative buffer can be stored at 2-8º C or at room temperature (21-25°C) for 21 days.

Sample shipment/travel stability:

Conditions simulating ground shipping, air shipping and various climate conditions (desert, tropical) were tested. Neat samples spiked at concentrations below the cutoff recovered as negative for both the control and shipped samples. Samples spiked at concentrations above the cutoff recovered as positive for both the control and shipped samples.

d. Detection limit:

Analytical performance of the device around the cutoff is described in the precision section 1.a above.

e. Analytical specificity:

Cross-reactivity:

Pooled neat drug-free oral fluid samples were collected by spitting into a cup. The cross-reactant solutions were prepared by adding the compounds to neat oral fluid samples at the concentration listed in the table below. The neat oral fluid samples were processed using the Oral-Eze device to obtain diluted oral fluid samples which were tested in the CEDIA Opiate OFT Assay. The table below lists the concentrations of each compound that gave a response approximately equal to the cutoff.

Structurally Related Compounds:

Compounds	**Tested Concentration in Neat Oral Fluid* (ng/mL)**	**Response Equivalent to the cutoff**
Codeine	24	Positive
Diacetylmorphine	42	Positive
Hydrocodone	36	Positive
Hydromorphone	42	Positive
Imipramine	2,100	Positive
Morphine-3-Glucoronide	37.5	Positive
Morphine-6-Glucoronide	75	Positive
6-Monoacetylmorphine	37.5	Positive
Meperidine	18,000	Positive
Oxymorphone	1,800	Positive
Oxycodone	1,050	Positive

*The concentrations listed were the lowest levels yielding positive results in the assay.

Potential interference from structurally unrelated compounds and various common over-the-counter medications were tested by spiking the potentially interfering compound into neat oral fluid, and then processed through the oral fluid collection device.

Compounds E	Tested Concentration In Neat Oral Fluid (ng/mL)	Response Equivalent to the cutoff
Acetaminophen	1,800,000	Negative
Acetylsalicylic Acid	1,800,000	Negative
Alprazolam	30,000	Negative
Amobarbital	30,000	Negative
Amoxicillin	240,000	Negative
Amphetamine	240,000	Negative
Ampicillin	30,000	Negative
Atropine	30,000	Negative
ß-Phenethylamine	30,000	Negative
Buproprion	30,000	Negative
Butabarbital	30,000	Negative
Butalbital	30,000	Negative
Caffeine	60,000	Negative
Captopril	1,800,000	Negative
Chlordiazepoxide	240,000	Negative
Chlorpromazine	30,000	Negative
Cimetidine	600,000	Negative
Clonazepam	30,000	Negative
Clorazepate	30,000	Negative
Codeine	120,000	Negative
Cotinine	30,000	Negative
Cyclizine	6,000	Negative
Dextromethorphan	30,000	Negative
Diazepam	90,000	Negative
Digoxin	120,000	Negative
Diphenhydramine	30,000	Negative
Enalapril	600,000	Negative
Fluoxetine	600,000	Negative
Gentisic Acid	30,000	Negative
Ibuprofen	600,000	Negative
l-Ephedrine	30,000	Negative
Levothyroxine	600,000	Negative
Lidocaine	30,000	Negative
Loperamide	30,000	Negative
Medazepam	30,000	Negative
Methadone	240,000	Negative
Methamphetamine	240,000	Negative
Metoprolol	30,000	Negative
Naproxen	30,000	Negative
Niacinamide	30,000	Negative
Nicotine	30,000	Negative
Nifedipine	3,000,000	Negative
Norchlordiazepoxide	30,000	Negative
Nordiazepam	30,000	Negative

Interference:

The potential interference from several endogenous and exogenous substances, and pH on the detection accuracy of samples containing morphine at +/- 50% of the cutoff concentration were tested in the assay. The interfering substances were added to neat oral fluid at the concentrations listed in the table below. The neat oral fluid samples were processed using the Oral-Eze collection device and tested in the CEDIA Opiate OFT Assay.

Compounds	**Tested Conc. in Neat Oral fluid**	**Opiate OFT Assay**	
		-50% Morphine	**+50% Morphine**
Cotinine	0.03 mg/mL	Negative	Positive
Nicotine	0.015 mg/mL	Negative	Positive
Hemoglobin	0.6 mg/mL	Negative	Positive
Human serum albumin	24 mg/mL	Negative	Positive
Sodium Chloride	18 mg/mL	Negative	Positive
Cholesterol	45 mg/mL	Negative	Positive
Acetaminophen	0.3 mg/mL	Negative	Positive
Acetylsalicylic Acid	0.3 mg/mL	Negative	Positive
Caffeine	0.06 mg/mL	Negative	Positive
Ibuprofen	0.12 mg/mL	Negative	Positive
Coffee	6% v/v	Negative	Positive
Milk	3% v/v	Negative	Positive
Orange Juice	6% v/v	Negative	Positive
Cranberry Juice	6% v/v	Negative	Positive
Soft drink (Coke)	6% v/v	Negative	Positive
Toothpaste	6% v/v	Negative	Positive
Mouthwash	6% v/v	Negative	Positive
Tea	6% v/v	Negative	Positive
Denture Adhesive	6% v/v	Negative	Positive
Alcohol	6% v/v	Negative	Positive
Baking Soda	6% v/v	Negative	Positive
Cough Syrup	6% v/v	Negative	Positive
Whole Blood	6% v/v	Negative	Positive
Hydrogen Peroxide	6% v/v	Negative	Positive
pH	5-9	Negative	Positive

Potential interference from additional food and dental compounds was tested by collecting neat oral fluid from volunteers after use of the following substances: hard candy, chewing gum, chewing tobacco, cigarettes and tooth whitening strips.

Compounds	Tested Concentration in Neat Oral Fluid	Opiates OFT Assay Results	
		-50% Opiates	+50% Opiates
Water	n/a	Negative	Positive
Chewing Tobacco	n/a	Negative	Positive
Cigarettes	n/a	Negative	Positive
Gum	n/a	Negative	Positive
Hard Candy	n/a	Negative	Positive
Tooth Whitening Strips	n/a	Negative	Positive

f. Assay cut-off:

Characterization of how the device performs analytically around the claimed cutoff concentration appears in the precision above.

2. Comparison studies:

a. Method comparison with predicate device:

Study 1:

Eighty two unaltered neat oral fluid samples were processed using the Oral-Eze collection device. The diluted oral fluid samples after passing the collection device were tested by the CEDIA Opiate OFT Assay and by the GC-MS method.

Note: this study was performed on samples already collected with the Intercept collection device. When the GC-MS values of the diluted samples were compared to the immunoassay values, the following results were obtained. Therefore the results below do not reflect any inaccuracy inherent in the collection process itself.

Candidate Device Result	Negative	Less than half the cutoff concentration by GC-MS analysis	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration)	High Positive (greater than 50% above the cutoff concentration)
Negative	33	4	4	0	0
Positive	0	0	1*	4	36

- Discrepant result – The sample contained 9 ng/mL morphine by GC/MS
- * This sample initially tested positive, but was found to be negative when retested

The overall concordance between CEDIA Opiate OFT Assay (not including the collection step) and GC-MS in diluted oral fluid is 97.6%.

Study 2:

Forty-two natural (unaltered) neat oral fluid samples from rehabilitation clinics were collected. The neat oral fluid samples were processed using the Oral-Eze collection device. Both the neat and diluted oral fluid samples were tested by LC-MS/MS method while only the diluted samples were tested in the CEDIA Opiate OFT Assay.

Note: The values obtained in this study were collected from samples containing opiates prior to the collection step. Therefore the results reflect the performance of the entire system including the collection step.

Candidate Device Result	Less than half the cutoff concentration by LC-MS/MS analysis	Near Cutoff Negative (Between 50% below the cutoff and the cutoff concentration)	Near Cutoff Positive (Between the cutoff and 50% above the cutoff concentration)	High Positive (greater than 50% above the cutoff concentration)
Negative	18	2	1*	0
Positive	0	0	3	18

*Sample was confirmed positive by LC-MS/MS

Discrepant sample:

Discrepant Sample #	OFT assay (POS/NEG)	Neat Sample LC/MS value (ng/mL)
21	Negative	30.39

The overall concordance between CEDIA Opiate OFT Assay (including the collection step) and LC-MS/MS using a cutoff of 30 ng/mL in neat oral fluid is 97.6%.

b. Matrix comparison:

Not applicable. The assay is intended for only one sample matrix.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable. Clinical studies are not typically submitted for this device type.

b. Clinical specificity:

Not applicable. Clinical studies are not typically submitted for this device type.

c. *Other clinical supportive data (when a. and b. are not applicable):*

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Not applicable

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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