

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

A. 510(k) Number:

k101742

B. Purpose for Submission:

New Device

C. Measurand:

Cocaine in oral fluid

D. Type of Test:

Qualitative immunoassay

E. Applicant:

Microgenics Corporation, Thermo Fisher Scientific Clinical Diagnostic Division

F. Proprietary and Established Names:

CEDIA Cocaine OFT Assay

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
DIO	Class II	21 CFR § 862.3250	91, Toxicology

H. Intended Use:

1. Intended use(s):

See Indications for use below.

2. Indication(s) for use:

The CEDIA® Cocaine OFT Assay is intended for use in the qualitative determination of cocaine and cocaine metabolites at a cutoff concentration of 15 ng/mL in neat oral fluid. The specimen must be collected exclusively with the Oral-Eze™ Saliva Collection System. The assay is calibrated against benzoylecgonine and performed on the MGC 240. This *in vitro* diagnostic device is intended for clinical laboratory use only.

The CEDIA® Cocaine 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):

The CEDIA® Cocaine OFT Assay is for prescription professional use only in clinical chemistry laboratories. It is not for use in Point of Care settings.

4. Special instrument requirements:

MGC 240 analyzer

I. Device Description:

The CEDIA® cocaine OFT Assay uses recombinant DNA technology to produce a homogeneous enzyme immunoassay system. The assay is based on the bacterial enzyme β -galactosidase, which has been genetically engineered into two inactive fragments (enzyme acceptor and enzyme donor). These fragments spontaneously re-associate to form fully active enzyme that cleaves a substrate and then generates a color change that can be measured spectrophotometrically.

The CEDIA® cocaine OFT Assay utilizes the Oral-Eze™ Saliva Collection System consisting of the 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 a blue color will appear when sufficient volume of oral fluid is collected. Samples are collected by placing the collector pad and plastic shield between the lower cheek and gum with the plastic shield facing the cheek. The pad is ejected into 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.

J. Substantial Equivalence Information:

1. Predicate device name:
OTI Cocaine Metabolite Intercept ® MICRO-PLATE EIA
2. Predicate 510(k) number:
k001197
3. Comparison with predicate:

Comparison	Device - CEDIA® Cocaine OFT Assay	Predicate – k001197 OTI Cocaine Metabolite Intercept ® MICRO-PLATE EIA
Intended Use	Same	The OTI Cocaine Metabolite Intercept® MICRO-PLATE EIA is intended for use by clinical laboratories in the qualitative determination of cocaine and cocaine metabolites in oral fluid collected with the Intercept® Drugs of Abuse (DOA) Oral Specimen Collection Device. For in Vitro Diagnostic Use.
Measurement Mode	Same	Qualitative measurements only
Sample Matrix	Same	Oral Fluid
Calibrator levels	0, 5.0, 50.0 ng/mL	0, 5 ng/mL
Cutoff level	15 ng/mL in neat oral fluid	5 ng/mL when oral fluid collected with the Oral Specimen Collection Device

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

CLSI Documents:

Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline (EP05-A2)

Method Comparison and Bias Estimation Using Patient Samples; Approved Guideline (EP09-A2)

L. Test Principle:

In the assay, analyte in the sample competes with analyte conjugated to one inactive fragment of β -galactosidase for antibody binding site. If analyte is present in the sample, it binds to antibody, leaving the inactive enzyme fragments free to form active enzyme. If analyte is not present in the sample, antibody binds to analyte conjugated on the inactive fragment, inhibiting the reassociation of inactive β -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 drug present in the sample.

The Oral-Eze Saliva Collection System contains a preservative buffer that dilutes the neat oral fluid sample. The assay result is reported as a positive or negative result relative to the neat oral fluid cutoff of 15 ng/mL.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Negative neat oral fluid samples were collected into a sample cup. Oral fluid samples were spiked with benzoylecgonine at three times the final concentration into negative neat oral fluid resulting in concentrations at -25%, -50%, -75% below the cutoff, cutoff, and +25%, +50%, +75% and +100% above the cutoff. All spiked neat oral fluid samples (3X) were confirmed by LC-MS/MS. Neat oral fluid samples were applied onto the Oral-EZE collection device pad (n=2 pad/level) until the blue color appeared in the round (sample adequacy) window of the handle. The pads were then ejected into vials containing 2.2 mL of the preservative buffer. All the diluted spiked samples (1X) were then confirmed by LC-MS/MS. Samples were tested using one lot of reagent on three different MGC 240 instruments by three different operators. Five replicates of each sample were tested per run, 2 runs per day for five non-consecutive days, with a total of N=50/level.

The results are summarized in the following table:

Analyte	Tested Concentration (ng/mL)	Cocaine OFT Assay # Neg/ # Pos
Benzoyllecgonine	0	50 Neg/ 0 Pos
Benzoyllecgonine	-75%	50 Neg/ 0 Pos
Benzoyllecgonine	-50%	50 Neg/ 0 Pos
Benzoyllecgonine	-25%	50 Neg/ 0 Pos
Benzoyllecgonine	Cutoff	50 Neg/ 0 Pos
Benzoyllecgonine	+25%	0 Neg/50 Pos
Benzoyllecgonine	+50%	0 Neg/50 Pos
Benzoyllecgonine	+75%	0 Neg/50 Pos
Benzoyllecgonine	+100%	0 Neg/50 Pos

b. *Linearity/assay reportable range:*

Not applicable

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

Collection device:

Shipment/Travel Stability:

Oral fluid samples were spiked with benzoyllecgonine. Two sets of identical spiked samples were prepared. One set was kept at room temperature in the lab and used as the unshipped control. The other set was tested through three different stress conditions simulating ground shipping, air shipping and various climate conditions (desert, tropical). The shipping temperature should not exceed >40°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 can be stored at 2-8° C or at room temperature (21-25°C) for 21 days.

Reagent Stability:

Real time stability testing was conducted. The stability protocol was reviewed and found acceptable. The testing supports the stability at 2-8°C for 24 months. The on board stability of reconstituted reagents is 60 days (2-8°C).

d. *Detection limit:*

Sensitivity of this assay is characterized by validating performance around the claimed cutoff concentration of the assay, including a determination of the lowest concentration of drug that is capable of producing a positive result. This information appears in the precision section 1.a., above.

e. *Analytical specificity:*

Cross-reactivity was established by spiking various concentrations of similarly structured compounds into negative neat oral fluid samples. The concentrations in the neat oral fluid were 3 times the final (1X) tested concentration. These samples were applied onto the pad of the Oral-Eze collection device until the blue color appeared in the round (sample adequacy) window of the handle. The pads were then ejected into the vials containing 2.2 mL of the preservative buffer. The final concentrations of drug in the samples were diluted to 1X concentration. The diluted samples were qualitatively tested and the results were compared to the cutoff calibrator. All compounds were tested in duplicate.

Specificity and Cross-Reactivity

Cross-reactivity was evaluated by spiking various concentrations (which could be found in a neat oral fluid sample) of structurally related compounds into drug-free neat oral fluid pool, than added to the oral fluid collection device. The various concentrations were evaluated against the cutoff calibrator. The table below lists the concentration of each compound that gave a response approximately equal to the cutoff.

Compounds	Tested Concentration in Neat Oral Fluid (ng/mL)	Response Equivalent to the cutoff
Cocaethylene	180	Positive
Cocaine	180	Positive
Ecgonine	2,550	Positive
Ecgonine methyl ester	34,500	Negative

Various over-the-counter medications and structurally unrelated compounds were tested for cross-reactivity in the assay. Cross-reactant solutions were prepared by adding the compound to neat oral fluid at the concentrations 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 Cocaine OFT assay. All compounds tested negative and did not show any cross-reactivity.

Compounds	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
β-Phenethylamine	30,000	Negative
Bupropion	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	30,000	Negative
Dextromethorphan	30,000	Negative
Diacetylmorphine	30,000	Negative
Diazepam	120,000	Negative
Digoxin	120,000	Negative
Diphenhydramine	30,000	Negative
Enalapril	120,000	Negative
Fluoxetine	600,000	Negative
Gentisic Acid	30,000	Negative
Hydrocodone	30,000	Negative
Ibuprofen	600,000	Negative
Imipramine	24,000	Negative
l-Ephedrine	30,000	Negative
Levothyroxine	600,000	Negative
Lidocaine	30,000	Negative
Loperamide	30,000	Negative
Medazepam	30,000	Negative
Meperidine	30,000	Negative
Methadone	240,000	Negative
Methamphetamine	240,000	Negative

Metoprolol	30,000	Negative
Morphine	60,000	Negative
Naproxen	30,000	Negative
Niacinamide	30,000	Negative
Nicotine	30,000	Negative
Nifedipine	1,500,000	Negative
Norchlordiazepoxide	30,000	Negative
Nordiazepam	30,000	Negative
Penicillin	30,000	Negative
Pentobarbital	30,000	Negative
Phencyclidine	15,000	Negative
Phenobarbital	120,000	Negative
Phenylephrine	30,000	Negative
Phenylpropanolamine	30,000	Negative
Procainamide	30,000	Negative
Procaine	30,000	Negative
Propoxyphene	120,000	Negative
Pseudoephedrine	30,000	Negative
Quinidine	30,000	Negative
Ranitidine	600,000	Negative
Salbutamol	30,000	Negative
Salicylic Acid	300,000	Negative
Secobarbital	240,000	Negative
Temazepam	30,000	Negative
Δ 9-THC	30,000	Negative
11-nor- Δ 9-THC-COOH	15,000	Negative
Theophylline	30,000	Negative
Tolmetin	30,000	Negative
Verapamil	600,000	Negative
Zomepirac	30,000	Negative

Potential interference from endogenous and exogenous substances and pH were spiked into neat oral fluid containing benzoylecgonine at +/- 50% of the cutoff, and then processed through the oral fluid collection device. No interference was observed with the interfering substances and pH 5-9. The results are presented in the table below:

Compounds	Tested Conc. in Neat Oral Fluid (ng/mL)	Cocaine OFT Assay	
		-50% benzoylecgonine	+50% benzoylecgonine
Cotinine	0.03	Negative	Positive
Nicotine	0.015	Negative	Positive
Hemoglobin	0.6	Negative	Positive
Human serum albumin	24	Negative	Positive
Sodium Chloride	18	Negative	Positive
Cholesterol	45	Negative	Positive
Acetaminophen	0.3	Negative	Positive
Acetylsalicylic Acid	0.3	Negative	Positive
Caffeine	0.06	Negative	Positive
Ibuprofen	0.12	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	Cocaine OFT Assay Results	
		-50% Cocaine	+50% Cocaine
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 section, 1.a, above.

2. Comparison studies:

a. *Method comparison with predicate device:*

Two method comparison studies were performed.

Study 1:

41 unaltered neat oral fluid samples were collected from rehabilitation clinics. The neat oral fluid samples were processed using the Oral-Eze collection device. The diluted samples were tested in the CEDIA Cocaine OFT Assay and compared to the neat and diluted oral fluid samples tested by LC/MS/MS. The results reflect the performance of the entire system including the collection step.

Candidate Device Results	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)
Positive	0	0	2	18
Negative	19	2	0	0

% Agreement among positive and negative is 100%

LC/MS/MS values used to categorize samples in this table are based on the concentration found in the neat oral fluid sample.

Study 2:

A total of 82 samples (41 negative and 41 positive) were evaluated by the candidate device and GC/MS. This study was performed on samples already collected with the Oral-Eze Saliva collection device. When the GC/MS values of the diluted samples were compared to the candidate device, the following results were obtained. Therefore the results below do not reflect any inaccuracy inherent in the collection process itself.

Note: this study was performed on samples already collected with the Intercept collection device. When the LC/MS/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 Results	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)
Positive	0	0	1	4	36
Negative	32	4	4	1	0

% Agreement among positives is 97.6% (40/41)

% Agreement among negatives is 97.6% (40/41)

Discordant sample:

Discordant Sample #	OFT assay (POS/NEG)	Neat Sample LC/MS value (ng/mL)
29	Negative	18.9
80	Positive	9.0

b. *Matrix comparison:*

Not Applicable

3. Clinical studies:

a. *Clinical Sensitivity:*

Not Applicable

b. *Clinical specificity:*

Not Applicable

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.