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

A. 510(k) Number:

k101744

B. Purpose for Submission:

New device

C. Measurand:

Cannabinoids in oral fluid

D. Type of Test:

Qualitative enzyme immunoassay

E. Applicant:

Microgenics Corporation, Thermo Fisher Scientific Clinical Diagnostic Division

F. Proprietary and Established Names:

Thermo Scientific CEDIA® Cannabinoids OFT Assay

Thermo Scientific CEDIA® THC OFT Calibrators

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LDJ	II	21 CFR 862.3870– Cannabinoid test system	91-Toxicology
DLJ	II	21 CFR 862.3200– Clinical toxicology calibrator	91-Toxicology

H. Intended Use:

1. Intended use(s):

   See indications for use below

2. Indication(s) for use:

   The CEDIA® Cannabinoids OFT Assay is intended for use in the qualitative determination of Cannabinoids in human oral fluid at a cutoff concentration of 3.0 ng/mL in neat oral fluid. The specimen must be collected exclusively with the Oral-Eze™ Saliva Collection System. The assay is calibrated against l-Δ^9 THC and performed on the MGC240. This in vitro diagnostic device is intended for clinical laboratory use only.

   The CEDIA® THC OFT Calibrators are intended for use in the calibration of l-Δ^9 THC when used with the CEDIA® Cannabinoids OFT Assay. This in vitro diagnostic device is intended for clinical laboratory use only.

   The CEDIA® Cannabinoids 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):

   This is an in vitro diagnostic device.
   For prescription use
   For use in the clinical laboratory
   Not for use in the Point-of-Care settings

4. Special instrument requirements:

   For use with the MGC240 analyzer

I. Device Description:

The assay consists of lyophilized reagent and liquid reconstitution Buffer. Reagent 1 (EA Reconstitution Buffer) contains buffer salts, rabbit monoclonal anti-THC antibody, stabilizer and preservative, Reagent 1(a) (EA Reagent) contains Enzyme Acceptor (microbial), buffer salts and preservative. Reagent 2 (ED Reconstitution Buffer) contains buffer salts, stabilizers and preservative, Reagent 2(a) (ED Reagent) contains Enzyme Donor (microbial) conjugated to cannabinoid derivative, chlorophenol red-β-D-galactopytanoside, stabilizers, detergent and preservative.

Calibrators: Qualitative assay required calibrators Negative Calibrator (0 ng/mL), Cutoff Calibrator (1.0 ng/mL) and High Calibrator (10.0 ng/mL).

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.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   STC Cannabinoids Intercept Micro-plate EIA, OTI, Orasure Technologies Inc

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

   k002375

3. Comparison with predicate:

Similarities/Differences		
Item	Device	Predicate
Intended Use	Qualitative detection of cannabinoids	Same
Assay Type	Enzyme immunoassay	Same
Matrix	Oral Fluid	Same
Cutoff	3.0 ng/mL in Neat Oral Fluid	1.0 ng/mL when oral fluid collected with the Oral Specimen Collection Device
Calibrators	0, 1.0, 10.0 ng/mL	0, 1.0 ng/mL

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

CLSI EP05-A2 Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guidelines - 2nd edition

CLSI EP09-A2 Method Comparison and Bias Estimation Using Patient Samples; Approved Guidelines - 2nd edition

L. Test Principle:

CEDIA Cannabinoids OFT Assay uses recombinant DNA technology to produce a unique homogenous enzyme immunoassay system. The assay is based on the bacterial enzyme β-galactosidase, which has been genetically engineered into two inactive fragments. Analyte in the sample competes with analyte conjugates to one inactive fragment (enzyme donor) of β-galactosidase for antibody binding site. The amount of active enzyme formed (color change) is measured spectrophotometrically at 570 nm which is directly proportional to the amount of analyte present in the sample.

The Oral-Eze Saliva Collection System contains a preservative buffer that dilutes the neat oral fluid sample. The calibrator levels are set at diluted levels so that sample absorbance values can be compared directly to the absorbance values of the calibration curve. The assay result is reported as a positive or negative result relative to the neat oral fluid cutoff of 3.0 ng/mL.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   All analytical performance data was collected on neat human oral fluid samples and processed through the Oral-Eze Saliva Collection System and analyzed on the MGC 240 instrument. The Oral-Eze 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:

   Precision studies were performed by spiking an l-isomer-Δ^9 THC solution into neat oral fluid pools at concentrations of 0, 0.75, 1.50, 2.25, 3.00, 3.75, 4.50, 5.25 and 6.00 ng/mL. Concentrations were confirmed by LC-MS/MS. Each sample was then processed through the Oral-Eze Saliva Collection system to obtain a final concentration at approximately negative, -75%, -50%, -25%, cutoff, +25% and 50%, 75% and 100% of the calibrator cutoff. Testing was performed in replicates of 5, twice a day over 5 non-consecutive days for all concentrations. The results are presented in the table below:

Drug	Concentration of sample	Number of determinations	Results # Neg/ #Pos
l-isomer-Δ^9 THC	Negative	50	50/0
	-75%	50	50/0
	-50%	50	50/0
	-25%	50	50/0
	Cutoff	50	2/48
	25%	50	0/50
	50%	50	0/50
	75%	50	0/50

b. Linearity/assay reportable range:

Not applicable, this is a qualitative assay

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

Calibrator:

Traceability:
Calibrators are specified in the labeling but are supplied separately from the reagents. Calibrators consist of a synthetic oral fluid matrix spiked with known concentrations of l-isomer-Δ^9THC.

The concentration of l-isomer-Δ^9THC in the calibrators is verified by LC/MS/MS.

Stability:

Real-time Stability studies were conducted on two lots of calibrators. The stability protocol was reviewed and found acceptable. The testing supports the stability at 2-8^{o}C for 18 months. The open vial stability of reconstituted reagents is 50 days (2-8^{o}C).

Shipment Stability:

Conditions simulating ground shipping, air shipping and various climate conditions (desert, tropical) were tested. Oral fluid samples were spiked with l-isomer-Δ^9THC to concentrations of -50% of the cutoff and +50% of the cutoff. One set was stored at room temperature and used as the control, while the other set was used for testing. All samples at -50% of the cutoff recovered as negative and all samples at +50% of the cutoff recovered as positive. The shipping temperature should not exceed >40ºC.

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 2-8º 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^{o}C for 24 months. The on board stability of reconstituted reagents is 60 days (2-8^{o}C).

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 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.

Compound	**Tested Concentration (ng/mL)**	**Response equivalent to cutoff**
l-11-nor-Δ^9 THC-COOH	3.0	Positive
11-OH-Δ^9 THC	3.75	Positive
Δ^8 THC	3.75	Positive
Cannabinol	12	Positive
Cannabidiol	3000	Positive

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.

Compound	Tested Concentration in neat Oral Fluid (ng/mL)	Response Equivalent to the cutoff
Acetaminophen	240,000	Negative
Acetylsalicylic acid	240,000	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
Benzoylecgonine	120,000	Negative
Phenethylamine	30,000	Negative
Butabarbital	30,000	Negative
Butalbital	30,000	Negative
Caffeine	24,000	Negative
Captopril	120,000	Negative
Chlordiazepoxide	24,000	Negative
Chlorpromazine	30,000	Negative
Cimetidine	120,000	Negative
Clonazepam	30,000	Negative
Clorazepate	30,000	Negative
Cocaethylene	30,000	Negative
Cocaine	1500	Negative
Codeine	240,000	Negative
Cyclizine	30,000	Negative
Dextromethorphan	240,000	Negative
Diazepam	120,000	Negative
Digoxin	24,000	Negative
Diphenhydramine	30,000	Negative
Enalapril	120,000	Negative
Fluoxetine	120,000	Negative
Gentisic acid	30,000	Negative
Hydrocodone	30,000	Negative
Hydromorphone	30,000	Negative

Compound	Tested Concentration in neat Oral Fluid (ng/mL)	Response Equivalent to the cutoff
Ibuprofen	120,000	Negative
Imipramine	30,000	Negative
l-Ephedrine	30,000	Negative
Levothyroxine	12,000	Negative
Lidocaine	30,000	Negative
Loperamide	30,000	Negative
Medazepam	30,000	Negative
Meperidine	240,000	Negative
Methadone	240,000	Negative
Methamphetamine	240,000	Negative
Metoprolol	30,000	Negative
Morphine	48,000	Negative
Naproxen	240,000	Negative
Niacinamide	30,000	Negative
Nifedipine	120,000	Negative
Norchlordiazepoxide	30,000	Negative
Oxazepam	120,000	Negative
Penicillin	30,000	Negative
Phencyclidine	240,000	Negative
Phenobarbital	240,000	Negative
Phenylephrine	30,000	Negative
Phenylpropanolamine	30,000	Negative
Procainamide	30,000	Negative
Procaine	30,000	Negative
Propoxyphene	240,000	Negative
Pseudoephedrine	30,000	Negative
Quinidine	30,000	Negative
Ranitidine	120,000	Negative
Salbutamol	30,000	Negative
Salicyluric Acid	120,000	Negative
Secobarbital	240,000	Negative
Temazepam	30,000	Negative

Compound	Tested Concentration in neat Oral Fluid (ng/mL)	Response Equivalent to the cutoff
Theophylline	30,000	Negative
Tolmetin	120,000	Negative
Verapamil	120,000	Negative
Zomepirac	30,000	Negative

Potential interference from endogenous and exogenous substances and pH were spiked into neat oral fluid containing l-isomer-Δ^9THC 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)	PCP OFT Assay	
		-50% PCP	+50% PCP
Cotinine	0.03	Negative	Positive
Nicotine	0.03	Negative	Positive
Hemoglobin	0.3	Negative	Positive
Human serum albumin	7.5	Negative	Positive
Sodium Chloride	18	Negative	Positive
Cholesterol	0.45	Negative	Positive
Acetaminophen	0.3	Negative	Positive
Acetylsalicylic Acid	0.3	Negative	Positive
Caffeine	0.3	Negative	Positive
Ibuprofen	0.3	Negative	Positive
Coffee	6% v/v	Negative	Positive
Milk	1.5% 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	3% 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	Cannabinoid OFT Assay Results	
		-50% l-isomer-Δ^9THC	+50% l-isomer-Δ^9THC
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:

Two method comparison studies were performed.

Study 1:

42 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® Cannabinoids 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	3	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 81 samples (40 negative and 41 positive) were evaluated by the candidate device and GC/MS. All samples were collected with the Oral-Eze Saliva collection system.

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	0	4	36
Negative	34	2	4	1	0

% Agreement among positives is 98% (40/41)
% Agreement among negatives is 100% (40/40)

	MGC 240 OFT Assay (POS/NEG)	Drug/Metabolite GC/MS value
Sample	Negative	4.2 (ng/mL) Δ^9 THC

b. Matrix comparison:

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

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.