JAN 2 4 2014

510(k) Summary for the RapidFRET Oral Fluid Assay for OPIATES

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92

The assigned 510(k) number is: k133642

807.92(a)(1): Contact Information

Name: Biophor Diagnostics, Inc.
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807.92(a)(2): Device Name, Common Name and Classification

RapidFRET Oral Fluid Assay for OPIATES (Enzyme Immunoassay for Opiates)
RapidFRET Oral Fluid Calibrator Set (Clinical Toxicology Calibrator)
RapidFRET Oral Fluid Control Set (Drug Mixture Control Materials)

Product	Code	Class	Regulation Section	Panel
RapidFRET Oral Fluid Assay for OPIATES	DJG	II	862.3650	91 - Toxicology
RapidFRET Oral Fluid Calibrator Set	DKB	II	862.3200	91 - Toxicology
RapidFRET Oral Fluid Control Set	DIF	I	862.3280	91 - Toxicology

807.92(a)(3): Identification of Legally Marketed Predicate Devices

Thermo Scientific CEDIA® Opiates OFT Assay (k101754).

807.92(a)(4): Assay Principle

The RapidFRET Oral Fluid Assay for OPIATES is an In Vitro Diagnostic competitive immunoassay used to detect opiates in human oral fluid. This is a ready-to-use homogenous system that involves energy transfer between an acceptor fluorophore labeled to an antibody and a donor fluorophore labeled to drug. The assay is based on competition between drug in the sample and drug labeled with the donor fluorophore for a fixed number of binding sites on the antibody reagent. When acceptor and donor fluorophores are brought into close proximity through a binding event, energy transfer occurs. The fluorescence resonance energy transfer (FRET) signal is measured at the wavelength of the acceptor fluorophore and is inversely proportional to the amount of drug in the sample. A Cutoff Calibrator is used to translate the sample measurement into a positive or negative result. Controls are used to establish and monitor precision and accuracy.

Device Description

The RapidFRET Oral Fluid Assay for Opiates is provided in an all liquid, ready to use format. Two reagents are provided included a drug specific reagent and a second competitive donor reagent. The kit is provided with reagents and microtiter plates. A Cutoff Calibrator is used to translate the sample measurement into a positive or negative result. Controls are used to establish and monitor precision and accuracy. Calibrators and controls are sold separately.

807.92(a)(5): Intended Use

The RapidFRET Oral Fluid Assay for OPIATES is a homogeneous time-resolved fluorescence assay that is intended for prescription use in central laboratories only on the RapidFRET Integrated Workstation. The assay is used to perform a qualitative screen for Opiates at 40 ng/mL in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector. This assay is calibrated against Morphine. This assay provides only a preliminary result. To obtain a confirmed analytical result, a more specific alternate chemical method such as GC/MS or LC/MS/MS is required. Professional judgment should be applied to any drug test result, particularly when using preliminary positive results. For In Vitro Diagnostic Use Only.

The RapidFRET Oral Fluid Calibrator Set and RapidFRET Oral Fluid Control Set are intended for use only with the RapidFRET Oral Fluid Assay for OPIATES and samples collected with the RapidEASE Oral Fluid Collector. The cutoff calibrator is used to determine the cutoff level and translate the assay measurement into a positive or negative result. The positive and negative controls are used to monitor laboratory systems, operators, precision, accuracy and assay conditions. For In Vitro Diagnostic Use Only.

807.92(a)(6): Technological Similarities and Differences to the Predicate

	Candidate Device (RapidFRET OPIATES)	**Predicate Device (Thermo Opiates, K101754)**
Indications for Use	Qualitative determination of opiates in human oral fluid in central labs. Prescription use only.	Qualitative determination of opiates in human oral fluid in clinical setting.
Methodology	Competitive homogeneous immunoassay.	Competitive homogeneous immunoassay.
Kit Components	1 Drug specific antibody reagent in liquid, ready to use format. 1 Drug conjugate reagent in liquid, ready to use format.	1 Drug specific antibody reagent (marketed in combination as a lyophilized reagent and reconstitution buffer). 1 Drug conjugate reagent (marketed in combination as a lyophilized reagent and reconstitution buffer).

	Candidate Device (RapidFRET OPIATES)	**Predicate Device (Thermo Opiates, K101754)**
Performance Characteristics	Precision, accuracy, cross reacting/interfering studies demonstrate equivalence to the predicate device.	Precision, accuracy, cross reacting/interfering studies are similar to the RapidFRET Oral Fluid Assay for OPIATES.
Safety and Effectiveness	Demonstrated in bench testing and described in PI, equivalent to predicate.	Demonstrated in bench testing and described in PI.
Neat Oral Fluid Cutoff Level	40 ng/mL neat oral fluid.	30 ng/mL neat oral fluid using a 10 ng/mL cutoff calibrator to account for sample dilution by collection device.
Platform	RapidFRET Integrated Workstation available exclusively from Biophor Diagnostics, Inc.	MGC240 analyzer
Sample Collection	Neat oral fluid is collected with the RapidEASE Oral Fluid Collector via direct expectoration. No diluent is used and sample is stored in glass sample tube with inert screw cap.	Oral fluid is collected with the Oral-Eze Saliva Collection System. This device uses an absorbent swab and diluent. Sample is stored in plastic tube with snap cap.
Principle and Procedure	Drugs in the oral fluid sample compete with the drug conjugate donor fluorophore for a fixed number of binding sites on the individual drug antibody acceptor reagents. When acceptor and donor fluorophores are brought into close proximity, through the binding event, fluorescent energy transfer is measured. The amount of drug in the specimen sample is inversely proportional to the assay signal as measured by time resolved fluorescence.	The assay is based on the sample analytes competing with analyte conjugates to one inactive fragment of β-galactosidase for antibody binding sites. The amount of drug in the specimen is directly proportional to the assay signal as measured by absorbance.
Controls and Calibrator Levels	Calibrators are available at 0 ng/mL and 40 ng/mL. Controls are available at 20 ng/mL and 60 ng/mL.	Calibrators are available at 0 ng/mL, 10 ng/mL, and 80 ng/mL. Controls are available at additional levels.

807.92(b)(1): Brief Description of Study Data:

A series of studies were performed that evaluated the device performance characteristics including precision and analytical sensitivity, correlation with GC/MS and LC/MS/MS, cross reactivity, and analytical specificity that are summarized below.

Precision and Analytical Sensitivity

Three lots of the RapidFRET Oral Fluid Assay for OPIATES were analyzed, four times daily, for a minimum of 20 days. Negative oral fluid pools were spiked with Morphine at 0%, 25%, 50%, 75%, 100%, 125%, 150%, 175% and 200% of the cutoff level corresponding to approximately 0, 10, 20, 30, 40, 50, 60, 70 and 80 ng/mL. The aggregate data is summarized in the table below:

Table 18.2.7. All Lots Precision Results Summary by Data Points

	0%	25%	50%	75%	100%	125%	150%	175%	200%
POS	0	0	0	0	185	278	263	294	278
NEG	279	279	278	279	94	0	0	0	0
N	279	279	278	279	279	278	263	294	278

Table 18.2.8. All Lots Precision Results Summary by Percent Agreement

	0%	25%	50%	75%	100%	125%	150%	175%	200%
POS	0%	0%	0%	0%	66%	100%	100%	100%	100%
NEG	100%	100%	100%	100%	34%	0%	0%	0%	0%
N	279	279	278	279	279	278	263	294	278

The data indicate that the analytical sensitivity is between 75% and 125% of cutoff, and expected results were achieved at a 100% frequency.

Correlation with MS Quantitation

Neat oral fluid was collected with the RapidEASE Oral Fluid Collection Device from volunteers potentially positive and negative for opiates. The samples (n=245) were randomized and blinded to the instrument operator and assayed using RapidFRET Opiates reagents. Following screening, positive and negative samples were sent for confirmatory testing. The summarized data are shown below.

Table of Summary Results

	Negative As determined by the predicate device or less than half the cutoff concentration by GC/MS	**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	1	10	53
Negative	177	4	0	0

Table of Discordant Results

Cutoff Value	Assay (POS / NEG)	Drug / Metabolite LC/MS Value (ng/mL)
40 ng/mL	Positive	Total Opiates = 36.5 ng/mL (26.8 ng/mL Morphine and 9.7 ng/mL Codeine)

The data indicate that the RapidFRET Oral Fluid Assay for OPIATES had an agreement of >98% for RapidFRET positive samples and an agreement of 100% for RapidFRET negative samples in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector.

Cross Reactivity and Analytical Specificity

A compound library of 167 different structurally related and unrelated compounds including metabolites, OTC and prescription medications and drugs of abuse was used to evaluate the device cross reactivity and specificity. Compounds were spiked at 30,000 ng/mL into neat oral fluid pool aliquots with 0 ng/mL, 20 ng/mL and 60 ng/mL of morphine, processed with the RapidEASE Collector, and tested with the RapidFRET OPIATES assay. Those compounds that gave an unexpected result were further titrated to determine the concentration at which the cross-reacting compound yielded a result approximately equivalent to the cutoff. Twenty nine (29) structurally related compounds were determined to cross-react below 30,000 ng/mL in the absence of morphine with twelve cross-reacting at 1000 ng/mL equivalence or less.

Table 18.8.2. Structurally Related Cross Reactants

Compound	Level (ng/mL)	0% Morphine† (0 ng/mL)	50% Morphine† (20 ng/mL)	150% Morphine† (60 ng/mL)
Structurally Related Compounds That Cross React in Neat Oral Fluid Pool with 0 ng/mL Morphine				
6-Monoacetylmorphine	30,000	36 [111%]	POS	POS
Amitriptyline	30,000	12,854 [0.3%]	POS	POS
Chlorpromazine	30,000	12,215 [0.3%]	POS	POS
Clomipramine	30,000	2,017 [2.0%]	POS	POS
Codeine	30,000	31 [129%]	POS	POS
Cyclizine	30,000	10,179 [0.4%]	POS	POS
Cyclobenzaprine	30,000	17,887 [0.2%]	POS	POS
Desipramine	30,000	6,754 [0.6%]	POS	POS
Diacetylmorphine (Heroin)	30,000	40 [100%]	POS	POS
Dihydrocodeine	30,000	32 [125%]	POS	POS
Doxepin	30,000	19,538 [0.2%]	POS	POS
d-Propoxyphene	30,000	23,593 [0.2%]	POS	POS
Ethylmorphine	30,000	31 [129%]	POS	POS
Flurazepam	30,000	5,905 [0.7%]	POS	POS
Hydrocodone	30,000	41 [98%]	POS	POS
Hydromorphone	30,000	35 [114%]	POS	POS

Table 18.8.2. Structurally Related Cross Reactants

Compound	Level (ng/mL)	0% Morphine† (0 ng/mL)	50% Morphine† (20 ng/mL)	150% Morphine† (60 ng/mL)
Imipramine	30,000	1,368 [2.9%]	POS	POS
Levorphanol	30,000	348 [11%]	POS	POS
Meperidine	30,000	12,634 [0.3%]	POS	POS
Morphine-3βDG	30,000	31 [129%]	POS	POS
Nalorphine	30,000	37 [108%]	POS	POS
Naloxone	30,000	429 [9.3%]	POS	POS
Naltrexone	30,000	2,720 [1.5%]	POS	POS
Normorphine	30,000	3,318 [1.2%]	POS	POS
Oxycodone	30,000	533 [7.5%]	POS	POS
Oxymorphone	30,000	831 [4.8%]	POS	POS
Rifampin	30,000	8,371[0.5%]	POS	POS
Thioridazine	30,000	18,104 [0.2%]	POS	*
Trimipramine	30,000	1,947 [2.1%]	POS	POS

†Results are presented as either the RapidFRET OPIATES screening result (POS / NEG) or the concentration in ng/mL of the cross-reactant that gives a Cutoff equivalent response. *Due to high cross reactivity at 0 ng/mL morphine, a 60 ng/mL morphine spike was not analyzed.

A second study evaluated common substances such as foods and dental products as well as pH variations. HSA, ethanol, baking soda, whole blood, hemoglobin, hydrogen peroxide, sodium chloride, cholesterol, denture adhesive, ascorbic acid, bilirubin, IgA, IgG and IgM were spiked into neat oral fluid pool aliquots that contained either 20 ng/mL or 60 ng/mL of morphine. Neat oral fluid pool was titrated to pH values of 5, 6, 7, 8 and 9, spiked with morphine to 20 ng/mL or 60 ng/mL and assayed with the RapidFRET OPIATES Assay. The effects of antiseptic mouthwash, cough syrup, cranberry juice, orange juice, tooth paste, chewing tobacco, cigarettes, chewing gum, hard candy, teeth whitening strips, cola, water, antacid, coffee and tea were evaluated by asking volunteers to use a specific item and provide an oral fluid sample. These samples were then spiked with morphine to 20 ng/mL or 60 ng/mL, processed with a RapidEASE Collector and assayed with the RapidFRET OPIATES device. All compounds at the listed concentrations gave a NEG result when spiked with 20 ng/mL morphine and a POS result when spike with 60 ng/mL morphine.

807.92(b)(3): Conclusions

The RapidFRET Oral Fluid Assay for OPIATES including the RapidFRET Oral Fluid Negative and Cutoff Calibrators, the RapidFRET Oral Fluid Negative and Positive Controls and the RapidEASE Oral Fluid Collector were determined to be substantially equivalent in safety and effectiveness for their intended use.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

January 24, 2014

BIOPHOR DIAGNOSTICS, INC.
NATHANIEL BUTLIN
VICE PRESIDENT
1201 DOUGLAS AVE
REDWOOD CITY CA 94063

Re: K133642
Trade/Device Name: RapidFRET Oral Fluid Assay For Opiates
RapidFRET Oral Fluid Calibrator Set
RapidFRET Oral Fluid Control Set
Regulation Number: 21 CFR 862.3650
Regulation Name: Opiate test system
Regulatory Class: II
Product Code: DJG, DKB, DIF
Dated: November 26, 2013
Received: November 27, 2013

Dear Mr. Butlin:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and 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) that do not require approval of a premarket approval application (PMA). 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. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: December 31, 2013
See PRA Statement on last page.

510(k) Number *(if known)*
k133642

Device Name
RapidFRET Oral Fluid Assay for OPIATES; RapidFRET Oral Fluid Calibrator Set; RapidFRET Oral Fluid Control Set

Indications for Use *(Describe)*

The RapidFRET Oral Fluid Assay for OPIATES is a homogeneous time-resolved fluorescence assay that is intended for prescription use in central laboratories only on the RapidFRET Integrated Workstation. The assay is used to perform a qualitative screen for Opiates at 40 ng/mL in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector. This assay is calibrated against Morphine. This assay provides only a preliminary result. To obtain a confirmed analytical result, a more specific alternate chemical method such as GC/MS or LC/MS/MS is required. Professional judgment should be applied to any drug test result, particularly when using preliminary positive results. For In Vitro Diagnostic Use Only.

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Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Avis T. Danishefsky -S