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

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

December 18, 2014

Re: K133047

Trade/Device Name: RapidFRET Oral Fluid Assay for MDMA
RapidFRET Oral Fluid MDMA Calibrator Set
RapidFRET Oral Fluid MDMA Control Set
Regulation Number: 21 CFR 862.3610
Regulation Name: Methamphetamine test system
Regulatory Class: II
Product Code: LAF, DLJ, DIF
Dated: November 18, 2014
Received: November 19, 2014

Dear Dr. Nathaniel 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 Industry and Consumer Education 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" (21 CFR 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 Industry and Consumer Education 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,

Katherine Serrano -S

For: 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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k133047

Device Name
RapidFRET Oral Fluid Assay for MDMA
RapdFRET Oral Fluid MDMA Calibrator Set
RapidFRET Oral Fluid MDMA Control Set

Indications for Use *(Describe)*
The RapidFRET Oral Fluid Assay for MDMA 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 Methylenedioxymethamphetamine at 50 ng/mL in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector. 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 MDMA Calibrator Set and RapidFRET Oral Fluid MDMA Control Set are intended for use only with the RapidFRET Oral Fluid Assay for MDMA 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.

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)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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

December 15, 2014

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: k133047

807.92(a)(1): Contact Information

Name: Biophor Diagnostics, Inc.
Address: 1201 Douglas Avenue
Redwood City, CA 94063

Contact: Nathaniel G. Butlin, Ph.D.
Phone: 650-367-4954
Fax: 650-364-4985

807.92(a)(2): Device Name, Common Name and Classification

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

Product	Code	Class	Regulation Section	Panel
RapidFRET Oral Fluid Assay for MDMA	LAF	II	862.3610	91 - Toxicology
RapidFRET Oral Fluid MDMA Calibrator Set	DLJ	II	862.3200	91 - Toxicology
RapidFRET Oral Fluid MDMA Control Set	DIF	I	862.3280	91 - Toxicology

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

CEDIA Methamphetamine OFT Assay and CEDIA Methamphetamine OFT Calibrators (k101753)
Salivabuse Liquid Oral Fluid Control (k132688)

807.92(a)(4): Device Description

The RapidFRET Oral Fluid Assay for MDMA is an In Vitro Diagnostic competitive immunoassay used to detect MDMA 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.

807.92(a)(5): Intended Use

The RapidFRET Oral Fluid Assay for MDMA 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 Methylenedioxymethamphetamine at 50 ng/mL in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector. 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 MDMA Calibrator Set and RapidFRET Oral Fluid MDMA Control Set are intended for use only with the RapidFRET Oral Fluid Assay for MDMA 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

Similarities		
Item	Predicate CEDIA Methamphetamine OFT assay and CEDIA Methamphetamine OFT Calibrators k101753	Device RapidFRET Oral Fluid Assay for MDMA and RapidFRET Oral Fluid MDMA Calibrator Set k133047
Intended Use	Assay: Qualitative detection of methamphetamine based analyte in neat oral fluid. Calibrators: Calibration of d-methamphetamine for assay system	Same except analyte is MDMA
Methodology	Homogenous competitive immunoassay	Same
Kit Components	1 specific antibody reagent and 1 drug conjugate reagent	Same

Differences		
Item	Predicate CEDIA Methamphetamine OFT assay and CEDIA Methamphetamine OFT Calibrators k101753	Device RapidFRET Oral Fluid Assay for MDMA and RapidFRET Oral Fluid MDMA Calibrator Set k133047
Analyte	Methamphetamine	MDMA
Sample Collection	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.	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.
Sample dilution	Yes	No
Neat Oral Fluid Cutoff	120 ng/mL neat oral fluid using a 40 ng/mL cutoff calibrator to account for sample dilution by collection device.	50 ng/mL neat oral fluid.
Platform	MGC 240 Analyzer	RapidFRET Integrated Workstation from Biophor Diagnostics
Reagent Format	Lyophilized reagent with reconstitution buffer	Liquid, ready to use
Calibrator Levels	Calibrators at 0, 40, and 200 ng/mL	Calibrators at 0 and 50 ng/mL.

Similarities and Differences		
Item	Predicate Salivabuse Liquid Oral Fluid Control k132688	Device RapidFRET Oral Fluid MDMA Control Set k133047
Intended Use	Quality control material for oral fluid drugs of abuse assays to monitor system performance	Same
Control Levels	Negative, -60% cutoff, ±50% cutoff, -30% cutoff, ±25% cutoff, 2X cutoff, and 3x cutoff	25 ng/mL and 75 ng/mL
Analyte	Multiple drugs of abuse	MDMA
Stability	Shelf: 12 months frozen or refrigerated Open: 31 days refrigerated	Shelf: 12 months refrigerated Open: 30 days refrigerated

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 MDMA were analyzed, four times daily, for a minimum of 20 days. Negative oral fluid pools were spiked with MDMA at 0%, 25%, 50%, 75%, 100%, 125%, 150%, 175% and 200% of the cutoff level corresponding to approximately 0, 12.5, 25, 37.5, 50, 62.5, 75, 87.5 and 100 ng/mL. The aggregate data is summarized in the table below:

	0%	**25%**	**50%**	**75%**	**100%**	**125%**	**150%**	**175%**	**200%**
POS	0	0	0	0	266	278	263	294	278
NEG	279	279	278	279	13	0	0	0	0
N	279	279	278	279	279	278	263	294	278

	0%	**25%**	**50%**	**75%**	**100%**	**125%**	**150%**	**175%**	**200%**
POS	0%	0%	0%	0%	95%	100%	100%	100%	100%
NEG	100%	100%	100%	100%	5%	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 MDMA. The samples (n=325) were randomized and blinded to the instrument operator and assayed using RapidFRET MDMA reagents. Following screening, positive and negative samples were sent for confirmatory testing. The summarized data are shown below.

n = 325	MS POS	MS NEG
RapidFRET POS	119	6[†]
RapidFRET NEG	0	200
% Agreement	100%	97%

[†]Samples contained compounds at concentrations that are known to cross react including d-methamphetamine, l- methamphetamine, d-amphetamine, l-amphetamine, 4-Methylethcathionone (4-MEC) and Methylone.

The data indicate that the RapidFRET Oral Fluid Assay for MDMA was accurate 99% of the time in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector.

Cross Reactivity and Analytical Specificity

A compound library of more than 170 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, 25 ng/mL and 75 ng/mL MDMA, processed with the RapidEASE Collector, and tested with the RapidFRET MDMA 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 structurally related compounds were determined to cross-react below 30,000 ng/mL in the absence of MDMA with twelve cross-reacting at 1000 ng/mL or less. An additional four compounds were determined to cross react below 30,000 ng/mL in the presence of 25 ng/mL MDMA.

Compound	Level (ng/mL)	0% MDMA† (0 ng/mL)	50% MDMA† (25 ng/mL)	150% MDMA† (75 ng/mL)
Structurally Related Compounds That Cross React in Neat Oral Fluid Pool with 0 ng/mL MDMA				
(–) Ephedrine	30,000	9000 [0.6%]	POS	POS
(R, 2R) Pseudoephedrine	30,000	2800 [1.8%]	POS	POS
Amitriptyline	30,000	1900 [2.6%]	POS	POS
Benzodioxolylbutanamine	30,000	390 [13%]	POS	POS
Phenethylamine	30,000	15,500 [0.3%]	POS	POS
d-Amphetamine	30,000	16,900 [0.2%]	POS	POS
d-Ephedrine	30,000	4800 [1.0%]	POS	POS
d,l-Amphetamine	9,000	6,500 [0.7%]	ND[1]	ND[1]
d,l-Ephedrine	66,000	11,000 [0.5%]	ND[1]	ND[1]
d-Methamphetamine	30,000	1200 [4.2%]	POS	POS
Doxepin	30,000	11,000 [0.5%]	POS	POS
Fenfluramine	30,000	37 [135%]	POS	POS
Imipramine	30,000	26,000 [0.2%]	POS	POS
Isoxsuprine	30,000	100 [50%]	POS	POS
l-Amphetamine	30,000	2100 [2.4%]	POS	POS
l-Methamphetamine	30,000	90 [56%]	POS	POS
l-Phenylephrine	30,000	16,600 [0.3%]	POS	POS
MBDB	30,000	42 [119%]	POS	POS
MDA	30,000	130 [38%]	POS	POS
MDEA	30,000	40 [125%]	POS	POS
4-Methylethcathinone (4-MEC)	30,000	7,839 [0.6%]	ND[1]	ND[1]
Mephentermine	30,000	120 [42%]	POS	POS
Methylone	30,000	3,783 [1.3%]	ND[1]	ND[1]
Nortriptyline	30,000	23,100 [0.2%]	POS	POS
Phentermine	30,000	1000 [5%]	POS	POS
PMA	30,000	350 [14%]	POS	POS
PMMA	30,000	39 [128%]	POS	POS
Dihydrobupropion	30,000	460 [10.9%]	POS	POS
Verapamil	60,000	1,800 [2.7%]	ND[1]	ND[1]
Structurally Related Compounds That Cross React in Neat Oral Fluid Pool with 25 ng/mL MDMA				
(+/–) Pseudoephedrine	30,000	NEG	>20,000 [< 0.3%]	POS
Cyclobenzaprine	30,000	NEG	>10,000 [< 0.5%]	POS
Fentanyl	30,000	NEG	4,000 [1.3%]	POS
Buproprion	30,000	NEG	>20,000 [< 0.3%]	POS

(1) ND – Not Determined. †Results are presented as either the RapidFRET MDMA screening result (POS / NEG) or the concentration in ng/mL of the cross-reactant that gives a Cutoff equivalent response.

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 25 ng/mL or 75 ng/mL of MDMA. Neat oral fluid pool was titrated to pH values of 5, 6, 7, 8 and 9, spiked with MDMA to 25 ng/mL or 75 ng/mL and assayed with the RapidFRET MDMA 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 MDMA to 25 ng/mL or 75 ng/mL, processed with a RapidEASE Collector and assayed with the RapidFRET MDMA device. All compounds at the listed concentrations gave a NEG result when spiked with 25 ng/mL MDMA and a POS result when spike with 75 ng/mL MDMA.

807.92(b)(3): Conclusions

The RapidFRET Oral Fluid Assay for MDMA including the RapidFRET Oral Fluid Negative and Cutoff MDMA Calibrators, the RapidFRET Oral Fluid Negative and Positive MDMA Controls and the RapidEASE Oral Fluid Collector were determined to be safe and effective for their intended use.