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

September 18, 2015

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

Re: K142293
Trade/Device Name: Rapidfret Oral Fluid Assay for Methamphetamine
Rapidfret Oral Fluid Methamphetamine Calibrators
Rapidfret Oral Fluid Methamphetamine Controls
Regulation Number: 21 CFR 862.3610
Regulation Name: Methamphetamine test system
Regulatory Class: II
Product Code: LAF, DLJ, LAS
Dated: September 11, 2015
Received: September 14, 2015

Dear Dr. 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,

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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k142293

Device Name
RapidFRET Oral Fluid Assay for Methamphetamine, RapidFRET Oral Fluid Methamphetamine Calibrators, RapidFRET Oral Fluid Methamphetamine Controls

Indications for Use *(Describe)*
The RapidFRET Oral Fluid Assay for Methamphetamine 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 methamphetamine 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 Methamphetamine Calibrators and RapidFRET Oral Fluid Methamphetamine Controls are intended for use only with appropriate RapidFRET Oral Fluid Assay products 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)

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)*

This section applies only to requirements of the Paperwork Reduction Act of 1995.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

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

September 11, 2015

The assigned 510(k) number is: k142293

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 Methamphetamine (Methamphetamine Test System)
RapidFRET Oral Fluid Methamphetamine Calibrators (Drug Specific Calibrator)
RapidFRET Oral Fluid Methamphetamine Controls (Drug Specific Control Materials)

Product	Code	Class	Regulation Section	Panel
RapidFRET Oral Fluid Assay for Methamphetamine	LAF	II	862.3610	91 - Toxicology
RapidFRET Oral Fluid Methamphetamine Calibrators	DLJ	II	862.3200	91 - Toxicology
RapidFRET Oral Fluid Methamphetamine Controls	LAS	I	862.3280	91 - Toxicology

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

Lin-Zhi International, Inc., LZI Oral Fluid Methamphetamine Enzyme Immunoassay (k131652).

807.92(a)(4): Device Description

The RapidFRET Oral Fluid Assay for Methamphetamine is an In Vitro Diagnostic competitive immunoassay used to detect methamphetamine 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 Methamphetamine 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 Methamphetamine 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 Methamphetamine Calibrators and RapidFRET Oral Fluid Methamphetamine Controls are intended for use only with appropriate RapidFRET Oral Fluid Assay Products 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 MET)	**Predicate Device (Lin-Zhi MET, K131652)**
Indications for Use	Qualitative determination of methamphetamine in human oral fluid in clinical setting.	Qualitative determination of methamphetamine 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.	A drug specific antibody reagent (R1) and a drug conjugate reagent (R2).
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 Methamphetamine.
Safety and	Demonstrated in bench testing and	Demonstrated in bench testing and

	Candidate Device (RapidFRET MET)	**Predicate Device (Lin-Zhi MET, K131652)**
Effectiveness	described in PI, equivalent to predicate.	described in PI.
Neat Oral Fluid Cutoff Level	50 ng/mL neat oral fluid.	50 ng/mL neat oral fluid.
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 LZI Oral Fluid collector.
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 competition of drugs in a sample and drug labeled G6PDH. Drug in the sample binds to the drug specific antibody leaving G6PDH active to produce assay signal. If no drug is present in sample, it binds to the labeled G6PDH enzyme inhibiting activity. The amount of drug in the specimen is proportional to the assay signal as measured by absorbance.
Controls and Calibrator Levels	Calibrators are available at effective concentrations of 0 ng/mL and 50 ng/mL. Controls are available at effective concentrations of 25 ng/mL and 75 ng/mL.	Calibrators are available at 0 ng/mL, 20 ng/mL, 50 ng/mL, 100 ng/mL and 140 ng/mL. Controls are available at 37.5 ng/mL and 62.5 ng/mL.

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 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 Methamphetamine were analyzed for a minimum of 20 non-consecutive days. Negative oral fluid was spiked with d-methamphetamine to 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. Samples were then processed through a RapidEASE Oral Fluid Collector. Three lots of reagents were used to analyze samples on the RapidFRET Integrated Workstation. The

aggregate data is summarized in the tables below:

Summary Precision Data – 3 Lots									
	0%	25%	50%	75%	100%	125%	150%	175%	200%
POS	0	0	0	0	47	264	264	264	264
NEG	264	264	264	264	217	0	0	0	0
N	264	264	264	264	264	264	264	264	264

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 methamphetamine. The samples (n=92) were randomized and blinded to the instrument operator and assayed using RapidFRET MET reagents. Following screening, positive and negative samples were sent for confirmatory testing. The summarized data are shown below.

Accuracy Summary Data				
Range	< 50% of Cutoff	50% to 100% of Cutoff	100% to 150% of Cutoff	>150% of Cutoff
RapidFRET POS	8†	2‡	5	39
RapidFRET NEG	33	3	0	2*

†Six samples contained MDMA at 241, 1940, 211, 2020, 4310, and 250 ng/mL; a seventh sample contained MDMA at 10 ng/mL, methylone at 47,000 ng/mL and 4-methethylcathinone at 7,240 ng/mL; the eighth sample contained MDMA at 13.6 ng/mL, and methylone at 8,920 ng/mL. ‡One sample contained MET at 40.4 ng/mL and MDMA at 1,880 ng/mL; a second sample contained MET at 36.8 ng/mL and MDMA at 439 ng/mL. *One sample contained 150 ng/mL l-methamphetamine; a second sample contained 28.4 ng/mL d-methamphetamine and 114 ng/mL l-methamphetamine.

Cross Reactivity and Analytical Specificity

A compound library of 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 methamphetamine equivalent, processed with the RapidEASE Collector, and tested with the RapidFRET MET 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 (20) structurally related compounds were determined to cross-react below 30,000 ng/mL in the absence of methamphetamine with 3 cross-reacting below 30,000 ng/mL in the presence of 25 ng/mL methamphetamine.

Structurally Related Cross Reactants		
Compound	**Cutoff Equivalent Concentration (ng/mL)**	**Percent Cross-Reactivity**
Structurally Related Compounds That Cross React in Neat Oral Fluid Pool with No Added Methamphetamine		
(–) Ephedrine	5,100	1.0%

Structurally Related Cross Reactants		
Compound	**Cutoff Equivalent Concentration (ng/mL)**	**Percent Cross-Reactivity**
Benzodioxolylbutanamine (BDB)	16,000	0.3%
Phenethylamine	5,700	0.9%
Chloroquine	2,300	2.2%
d-Amphetamine	3,500	1.4%
Fenfluramine	290	17%
l-Methamphetamine	300	17%
l-Phenylephrine	9,400	0.5%
N-methyl-1,3-benzodioxolylbutanamine (MBDB)	28	179%
Methylenedioxyamphetamine (MDA)	12,700	0.4%
Methylenedioxyethamphetamine (MDEA)	1,100	4.5%
Methylenedioxymethamphetamine (MDMA)	126	40%
Mephentermine	1,500	3.3%
4-Methylethcathinone (4-MEC)	4,555	1.1%
Methylone	3,438	1.5%
para-Methoxyamphetamine (PMA)	9,100	0.5%
para-Methoxymethamphetamine (PMMA)	87	57%
Procaine	24,000	0.2%
Ranitidine	8,300	0.6%
Trimethobenzamide	730	6.8%
Structurally Related Compounds That Cross React in Oral Fluid Pool Spiked with 25 ng/mL Methamphetamine		
d-Ephedrine	23,000	0.2%
l-Amphetamine	25,000	0.2%
Procainamide	23,000	0.2%

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

807.92(b)(3): Conclusions

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