DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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Silver Spring, MD 20993-0002

May 22, 2017

bioMérieux, Inc.
John Albright
Regulatory Affairs Manager
595 Anglum Rd.,
Hazelwood, MO 63042 US

Re: K162827
Trade/Device Name: VIDAS B.R.A.H.M.S. PCT (PCT)
Regulation Number: 21 CFR 866.3215
Regulation Name: Device to detect and measure non-microbial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis
Regulatory Class: Class II
Product Code: PRI, PMT, NTM
Dated: January 25, 2017
Received: January 25, 2017

Dear Mr. Albright:

This letter corrects our substantially equivalent letter of February 23, 2017.

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 regulation 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" (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 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,

Steven R. Gitterman -S for

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiological 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)*
K162827

Device Name
VIDAS B•R•A•H•M•S PCT (PCT)

Indications for Use *(Describe)*
VIDAS® B•R•A•H•M•S PCT™ (PCT) is an automated test for use on the instruments of the VIDAS® family for the determination of human procalcitonin in human serum or plasma (lithium heparinate) using the ELFA (Enzyme-Linked Fluorescent Assay) technique.

Used in conjunction with other laboratory findings and clinical assessments, VIDAS® B•R•A•H•M•S PCT™ is intended for use as follows:
• to aid in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock,
• to aid in assessing the cumulative 28-day risk of all-cause mortality for patients diagnosed with severe sepsis or septic shock in the ICU or when obtained in the emergency department or other medical wards prior to ICU admission, using a change in PCT level over time,
• to aid in decision making on antibiotic therapy for patients with suspected or confirmed lower respiratory tract infections (LRTI) – defined as community-acquired pneumonia (CAP), acute bronchitis, and acute exacerbation of chronic obstructive pulmonary disease (AECOPD) – in an inpatient setting or an emergency department,
• to aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.

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

This 510(k) summary of safety and effectiveness information is being submitted in accordance with the requirement of Safe Medical Devices Act of 1990 and 21 CFR 807.92.

VIDAS® B·R·A·H·M·S PCT™

A. Submitter Information

Submitter's Name:	bioMérieux, Inc.
Address:	595 Anglum Road Hazelwood, MO 63042
Contact Person:	John Albright
Phone Number:	314-731-8546
Fax Number:	314-731-8689
Date of Preparation:	October 6, 2016

B. Device Name

Trade Name:	VIDAS® B·R·A·H·M·S PCT™ (PCT)
Common Name:	Endotoxin Assay
Classification Names:	Device to detect and measure procalcitonin (pct) in human clinical specimens (21 CFR 866.3215, Product Code PMT) Procalcitonin assay (21 CFR 866.3215, Product Code PRI)

C. Predicate Devices

VIDAS® B·R·A·H·M·S PCT™ (K160911)

D. Device Description

The assay principle combines a one-step immunoassay sandwich method with a final fluorescent detection (ELFA).
The Solid Phase Receptacle (SPR®), serves as the solid phase as well as the pipetting device. Reagents for the assay are ready-to-use and pre-dispensed in the sealed reagent strips.
All of the assay steps are performed automatically by the instrument. The sample is transferred into the wells containing anti-procalcitonin antibodies labeled with alkaline phosphatase (conjugate). The sample/conjugate mixture is cycled in and out of the SPR® several times. This operation enables the antigen to bind with the immunoglobulins fixed to the interior wall of the SPR® and the conjugate to form a sandwich. Unbound compounds are eliminated during washing steps.
Two detection steps are performed successively. During each step, the substrate (4-Methyl-umbelliferyl phosphate) is cycled in and out of the SPR®. The conjugate enzyme catalyzes the hydrolysis of this substrate into a fluorescent product (4-Methyl-umbelliferone) the fluorescence of which is measured at 450 nm. The intensity of the fluorescence is proportional to the concentration of antigen present in the sample.
At the end of the assay, results are automatically calculated by the instrument in relation to two calibration curves corresponding to the two detection steps. A fluorescence threshold value determines the calibration curve to be used for each sample. The results are then printed out.

E. Intended Use

VIDAS® B·R·A·H·M·S PCT™ (PCT) is an automated test for use on the instruments of the VIDAS® family for the determination of human procalcitonin in human serum or plasma (lithium heparinate) using the ELFA (Enzyme-Linked Fluorescent Assay) technique.

Used in conjunction with other laboratory findings and clinical assessments, VIDAS® B•R•A•H•M•S PCT™ is intended for use as follows:

- to aid in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock,
- to aid in assessing the cumulative 28-day risk of all-cause mortality for patients diagnosed with severe sepsis or septic shock in the ICU or when obtained in the emergency department or other medical wards prior to ICU admission, using a change in PCT level over time,
- to aid in decision making on antibiotic therapy for patients with suspected or confirmed lower respiratory tract infections (LRTI) – defined as community-acquired pneumonia (CAP), acute bronchitis, and acute exacerbation of chronic obstructive pulmonary disease (AECOPD) – in an inpatient setting or an emergency department,
- to aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.

F. Technological Characteristics Summary

A general comparison of the similarities and differences of the assay with the predicates is presented in the following table.

Item	Proposed Device: VIDAS® B·R·A·H·M·S™ PCT	Predicate device: VIDAS® B·R·A·H·M·S PCT™ (K160911)
Intended Use and indications for use	VIDAS® B·R·A·H·M·S PCT™ (PCT) is an automated test for use on the instruments of the VIDAS® family for the determination of human procalcitonin in human serum or plasma (lithium heparinate) using the ELFA (Enzyme-Linked Fluorescent Assay) technique. Used in conjunction with other laboratory findings and clinical assessments, VIDAS® B•R•A•H•M•S PCT™ is intended for use as follows: • to aid in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock, • to aid in assessing the cumulative 28-day risk of all-cause mortality for patients diagnosed with severe sepsis or septic shock in the ICU or when obtained in the emergency department or other medical wards prior to ICU admission, using a change in PCT level over time, • to aid in decision making on antibiotic therapy for patients with suspected or confirmed lower respiratory tract infections (LRTI) – defined as community-acquired pneumonia (CAP), acute bronchitis, and acute exacerbation of chronic obstructive pulmonary disease (AECOPD) – in an inpatient setting or an emergency department, • to aid in decision making on antibiotic discontinuation for patients with suspected or confirmed sepsis.	VIDAS® B·R·A·H·M·S PCT™ (PCT) is an automated test for use on the instruments of the VIDAS® family for the determination of human procalcitonin in human serum or plasma (lithium heparinate) using the ELFA (Enzyme-Linked Fluorescent Assay) technique. VIDAS® B·R·A·H·M·S PCT™ (PCT) is intended for use in conjunction with other laboratory findings and clinical assessments to aid in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock. VIDAS® B·R·A·H·M·S PCT™ (PCT) is also intended for use to determine the change in PCT level over time as an aid in assessing the cumulative 28-day risk of all-cause mortality in conjunction with other laboratory findings and clinical assessments for patients diagnosed with severe sepsis or septic shock in the ICU or when obtained in the emergency department or other medical wards prior to ICU admission. Procalcitonin (PCT) is a biomarker associated with the inflammatory response to bacterial infection that aids in the risk assessment of critically ill patients on their first day of Intensive Care Unit (ICU) admission for progression to severe sepsis and septic shock. The percent change in PCT level over time also aids in the prediction of cumulative 28-day mortality in patients with severe sepsis and septic shock. PCT levels on the first day of ICU admission above 2.0 ng/mL are associated with a higher risk for progression to severe sepsis and/or septic shock than PCT levels below 0.5 ng/mL. A PCT level that declines ≤ 80% from the day that severe sepsis or septic shock was clinically diagnosed (Day 0) to four days after clinical diagnosis (Day 4) is associated with higher cumulative 28-day risk of all-cause mortality than a decline > 80%. The combination of the first PCT level (≤ 2.0 ng/mL or > 2.0 ng/mL) at initial diagnosis of severe sepsis or septic shock with the patient's clinical course and the change in PCT level over time until Day 4 provides important additional information about the mortality risk. The PCT level on Day 1 (the day after severe sepsis or septic shock is first clinically diagnosed) can be used to calculate the percent change in PCT level at Day 4 if the Day 0 measurement is unavailable.
Specimen	Human serum or plasma (lithium heparinate).	Same as the proposed device
Analyte	Procalcitonin (PCT)	Same as the proposed device

Item	Proposed Device: VIDAS® B·R·A·H·M·S™ PCT	Predicate device: VIDAS® B·R·A·H·M·S PCT™ (K160911)
Automated	Automated assay	Same as the proposed device
Assay Technique	ELFA (Enzyme-Linked Fluorescent Assay) technique.	Same as the proposed device
Assay principle	Immunoassay based on sandwich principle	Same as the proposed device
Detection method	Fluorescence (ELFA) of 4-methyl-umbelliferyl measured at 450 nm	Same as the proposed device

G. Nonclinical Tests

A summary of the non-clinical (analytical) results is presented below.

Limits of detection and quantitation

The Limit of Blank (LoB), the Limit of Detection (LoD) and the Limit of Quantitation (LoQ) were determined on the VIDAS® and VIDAS®3 instruments according to the CLSI® EP17-A2 recommendations. The limits reported below apply for all the instruments of the VIDAS family:

Limit of Blank (LoB)	0.01 ng/mL
Limit of Detection (LoD)	0.03 ng/mL
Limit of Quantitation (LoQ)	0.05 ng/mL

The LoQ was determined to be 0.05 ng/mL (with bias ≤ 10%, %CV ≤ 20% and Total Error ≤ 50%.)

Precision

The study was performed according to the recommendations of CLSI® document EP5-A3. A panel of 11 human samples covering the measuring range were tested in duplicate in 2 runs per day, over 20 days using 3 VIDAS® and 3 VIDAS® 3 instruments (N=240 values for each sample) at 3 sites (one instrument per site). Two reagent lots were used: 10 days of tests and 6 calibrations were performed for each lot. The repeatability, between-day precision, within-laboratory precision and reproducibility/total precision (between-laboratory precision) were estimated for each sample and are reported in the following tables:

VIDAS®

Sample	N	Mean concentration (ng/mL)	Repeatability		Between-Day precision		Within-Laboratory precision		Reproducibility / Total precision	
			Standard Deviation (ng/mL)	CV (%)	Standard Deviation (ng/mL)	CV (%)	Standard Deviation (ng/mL)	CV (%)	Standard Deviation (ng/mL)	CV (%)
PP12	240	0.08	0.011	14.6%	0.012	15.9%	0.015	20.2%	0.015	20.2%
PP16	240	0.10	0.009	9.0%	0.011	10.4%	0.016	15.9%	0.016	15.9%
PS01	240	0.12	0.011	8.9%	0.013	10.8%	0.017	14.2%	0.017	14.2%
PS02	240	0.15	0.010	6.5%	0.014	8.9%	0.019	12.3%	0.019	12.3%
PP14	240	0.23	0.009	4.0%	0.011	4.9%	0.016	7.1%	0.016	7.1%
PS04	240	0.53	0.013	2.4%	0.021	4.0%	0.023	4.2%	0.023	4.2%
PS05	240	2.14	0.027	1.3%	0.063	3.0%	0.083	3.9%	0.083	3.9%
PS06	240	23.12	0.504	2.2%	0.882	3.8%	1.020	4.4%	1.020	4.4%
PS07	240	92.30	3.113	3.4%	5.972	6.5%	6.423	7.0%	6.423	7.0%
PS08	240	128.56	5.275	4.1%	9.562	7.4%	11.087	8.6%	11.087	8.6%
PS11	240	162.99	7.308	4.5%	11.377	7.0%	16.082	9.9%	16.082	9.9%

VIDAS® 3

Sample	N	Mean concentration (ng/mL)	Repeatability		Between-Day precision		Within-Laboratory precision		Reproducibility / Total precision	
			Standard Deviation (ng/mL)	CV (%)	Standard Deviation (ng/mL)	CV (%)	Standard Deviation (ng/mL)	CV (%)	Standard Deviation (ng/mL)	CV (%)
PP13	240	0.08	0.008	9.4%	0.009	10.4%	0.015	18.2%	0.015	18.2%
PP16	240	0.10	0.009	9.7%	0.010	10.9%	0.015	15.9%	0.015	15.9%
PS01	240	0.12	0.010	8.7%	0.011	9.4%	0.015	12.5%	0.015	12.5%
PS02	239	0.15	0.013	8.3%	0.014	9.3%	0.017	11.2%	0.017	11.2%
PP14	240	0.22	0.010	4.3%	0.011	4.9%	0.015	6.8%	0.015	6.8%
PS04	239	0.52	0.020	3.8%	0.024	4.6%	0.026	5.0%	0.032	6.1%
PS05	240	2.06	0.041	2.0%	0.073	3.5%	0.098	4.8%	0.102	5.0%
PS06	240	21.85	0.583	2.7%	0.814	3.7%	0.860	3.9%	0.946	4.3%
PS07	240	83.60	3.372	4.0%	4.445	5.3%	4.895	5.9%	5.785	6.9%
PS08	240	110.83	5.495	5.0%	7.091	6.4%	7.927	7.2%	8.525	7.7%
PS11	240	140.34	6.450	4.6%	10.611	7.6%	11.253	8.0%	12.596	9.0%

Study of drugs and other potentially interfering substances

Following the recommendations of CLSI® document EP7-A2, the potential interferences with the following drugs and potentially interfering substances were studied. No interference was observed at the concentration tested.

Tested drug	Tested concentration
Acetominophen	20 mg/dL
Acetylsalicylic Acid	65.2 mg/dL
Alcohol	400 mg/dL
Amoxicillin	7.53 mg/dL
Ampicillin	5.31 mg/dL
Azithromycin	1.15 mg/dL
Beclometasone dipropionate	0.1 mg/dL
Caffeine	5.98 mg/dL
Cefotaxime	32.13 mg/dL
Ceftriaxone	93.7 mg/dL
Celecoxib	24 mg/dL
Cetirizine HCl	0.36 mg/dL
Cromolyn	2.4 mg/dL
Dextromethorphan	0.14 mg/dL
Dobutamine	0.15 mg/dL
Dopamine	0.11 mg/dL
Epinephrine (adrenaline)	0.18 mg/dL
Fluticasone	0.03 mg/dL

Tested drug	Tested concentration
Formoterol	0.0029 mg/dL
Furosemide	5.98 mg/dL
Heparin sodium	3000 UI/L
Ibuprofen	50 mg/dL
Imipenem	18 mg/dL
Levoflaxacin	1.75 mg/dL
Linezolid	48 mg/dL
Loratadine	0.03 mg/dL
Naproxen	50 mg/dL
Nicotine	0.1 mg/dL
Noradrenaline	0.00021 mg/dL
Oxymetazoline HCl	0.009 mg/dL
Phenylephrine	0.018 mg/dL
Prednisolone	0.3 mg/dL
Salmeterol	0.006 mg/dL
Theophylline	4 mg/dL
Tiotropium	0.0022 mg/dL
Vancomycin	10.25 mg/dL

Tested Substances	Tested concentrations
Protein (albumin)	6.5 g/dL
Hemoglobin	600 mg/dL
Triglycerides	3000 mg/dL
Bilirubin	33 mg/dL

H. Clinical performance data

A summary of the clinical performance data is presented below.

Decision making on antibiotic therapy for patients with suspected or confirmed LRTI

Two systematic literature reviews were performed along with study and patient-level meta-analyses, which are studies that combine and contrast data from multiple sources to identify patterns among study results. The study-level meta-analysis encompassed 11 randomized control trials (RCTs) which were published between 2004-2016, and included 4090 patients. The patient-level meta-analysis encompassed 13 RCTs which were published between 2004-2011, and included 3142 patients.

These meta-analyses concluded that PCT guided antibiotic therapy resulted in:

- 19.2% reduction in relative antibiotic initiation for all patients
- 38% reduction in overall antibiotic exposure (i.e. total days of antibiotic therapy) for inpatients
- 51% reduction in overall antibiotic exposure (i.e. total days of antibiotic therapy) for patients in emergency departments*
- 2.9 day reduction in antibiotic duration [1.25 day reduction in study-level]
- 3.6 day reduction in total antibiotic exposure [2.79 day reduction in study-level]
- No negative effects in regards to mortality, complications, or length of stay.

*Patients who presented to the Emergency Department and other associated clinics, but were not admitted.

Additionally, a modified DOOR/RADAR analysis, in which patient outcomes were ranked by clinical severity, was conducted on the patient level data, and found that PCT-guided management had a statistically significant improvement in ranked patient outcomes compared to standard management.

Decision making on antibiotic discontinuation for septic patients

Two systematic literature reviews were performed along with study and patient-level meta-analyses, which are studies that combine and contrast data from multiple sources to identify patterns among study results. The study-level meta-analysis encompassed 10 RCTs which were published between 2008-2016, and included 3489 patients. The patient-level meta-analysis encompassed 5 RCTs which were published between 2008-2010, and included 598 patients.

These meta-analyses concluded that PCT guided antibiotic therapy resulted in:

- 1.5 day reduction in antibiotic duration
- 3.2 day reduction in total antibiotic exposure
- 23% reduction in overall antibiotic exposure (i.e. total days of antibiotic therapy)
- No negative effects in regards to mortality, hospital length of stay, or ICU length of stay.

I. Conclusion

The results from the non-clinical and clinical performance data submitted in this premarket notification are complete and demonstrate that the VIDAS® B·R·A·H·M·S PCT assay is substantially equivalent to the predicate device.