



November 26, 2019

Beckman Coulter, Inc.
Jennifer Bennett
Staff Regulatory Affairs
1000 Lake Hazeltine Drive
Chaska, Minnesota 55318-1084

Re: K192271

Trade/Device Name: Access PCT, Access PCT Calibrators

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: PTF

Dated: August 21, 2019

Received: August 22, 2019

Dear Jennifer Bennett:

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. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm> identifies combination product submissions. 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 Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

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 <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems>.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance>) and CDRH Learn (<https://www.fda.gov/training-and-continuing-education/cdrh-learn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice>) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Kristian Roth, Ph.D.
Branch Chief
Bacterial Multiplex and Medical Counter Measures
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)

K192271

Device Name

Access PCT, Access PCT calibrators

Indications for Use (Describe)

The Access PCT assay is a paramagnetic, chemiluminescent immunoassay for in vitro quantitative determination of procalcitonin (PCT) levels in human serum and plasma (lithium heparin and EDTA) using the Access Immunoassay Systems. Measurement of PCT in conjunction with other laboratory findings and clinical assessments aids in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock.

The Access PCT Calibrators are intended to calibrate the Access PCT assay for the quantitative determination of procalcitonin levels in human serum and plasma (lithium heparin and EDTA) using the Access Immunoassay Systems.

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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Immunodiagnostic Development Center

1000 Lake Hazeltine Drive
Chaska, Minnesota 55318-1084

510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92(a)(1).

The assigned 510(k) number is _____

Submitted By:

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Date Prepared:

August 22, 2019
November 18, 2019 (Updated)

Device Name:

Proprietary / Trade Name: Access PCT Reagent Common
Name: Procalcitonin Immunoassay
Classification Name: Device to detect and measure non-microbial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis
Classification Regulation: 21 CFR 866.3215
Classification Product Code: PTF

Predicate Device:

The Access PCT Reagent claims substantial equivalence to the VIDAS[®] B·R·A·H·M·S PCT^{®†} assay kit by Biomerieux, FDA 510(k) Number K162827, cleared May 31, 2017.

Device Description:

The Access PCT assay is a paramagnetic, chemiluminescent immunoassay for *in vitro* quantitative determination of procalcitonin (PCT) levels in human serum and plasma using the Access Immunoassay Systems. Measurement of PCT in conjunction with other laboratory findings and clinical assessments aids in the risk assessment of critically ill patients on their first day of ICU admission for progressive to severe sepsis and septic shock.

A description of the reagent pack is provided below.

- R1a: Dynabeads* paramagnetic particles coated with mouse anti-human Procalcitonin monoclonal antibody in a TRIS buffer with surfactant, protein (bovine), ≤ 0.1% sodium azide, and 0.1% ProClin**300
- R1b: 0.10 N Sodium Hydroxide
- R1c: MOPS Buffer with surfactant and protein (bovine, murine), ≤ 0.1% sodium azide, and 0.1% ProClin 300
- R1d: Rat anti-Procalcitonin recombinant alkaline phosphatase conjugate in a MOPS buffer with surfactant and protein (bovine, murine, recombinant), ≤ 0.1% sodium azide, and 0.1% ProClin 300

*Dynabead[®] is a registered trademark of Dynal A.S., Oslo, Norway

**ProClin[™] is a trademark of The Dow Chemical Company ("Dow") or an affiliate company of Dow.

Intended Use:

The Access PCT assay is a paramagnetic, chemiluminescent immunoassay for *in vitro* quantitative determination of procalcitonin (PCT) levels in human serum and plasma (lithium heparin and EDTA) using the Access Immunoassay Systems. Measurement of PCT in conjunction with other laboratory findings and clinical assessments aids in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock.

Comparison to the Predicates:

The Access PCT Assay and the predicate device, VIDAS[®] B·R·A·H·M·S PCT^{®†} assay (K162827), were compared. The information for the predicate device was derived from the predicate device 510(k) Summary and product labeling.

[†] VIDAS[®] is a registered trademark of bioMérieux SA. B·R·A·H·M·S PCT[®] is a registered trademark of B·R·A·H·M·S GmbH.

Comparison of Technological Characteristics to the Predicate (Assay)

Characteristic	Predicate Device VIDAS [®] B·R·A·H·M·S PCT ^{®†} k162827	Proposed Device Access PCT Assay on Access 2 Immunoassay System
Intended Use/ Indications for Use	<p>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:</p> <ul style="list-style-type: none"> · 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. 	<p>The Access PCT assay is a paramagnetic, chemiluminescent immunoassay for <i>in vitro</i> quantitative determination of procalcitonin (PCT) levels in human serum and plasma (lithium heparin and EDTA) using the Access Immunoassay Systems. Measurement of PCT in conjunction with other laboratory findings and clinical assessments aids in the risk assessment of critically ill patients on their first day of ICU admission for progression to severe sepsis and septic shock.</p>

[†] VIDAS[®] is a registered trademark of bioMérieux SA. B·R·A·H·M·S PCT[®] is a registered trademark of B·R·A·H·M·S GmbH.

Characteristic	Predicate Device VIDAS[®] B·R·A·H·M·S PCT^{®†} k162827	Proposed Device Access PCT Assay on Access 2 Immunoassay System
Analyte Measured	Procalcitonin (PCT)	Same
Sample Type	Human serum or plasma (lithium heparinate)	Human Serum or Plasma (LiHep and EDTA)
Method	Automated Assay	Same
Format	ELFA (Enzyme-Linked Fluorescent Assay) technique	Chemiluminescent
Technology	Immunoassay based on sandwich principle	Same
Primary Reagent Materials	Solid Phase: Mouse monoclonal anti-procalcitonin immunoglobins coated on interior of the SPR Conjugate: Alkaline phosphatase-labeled mouse monoclonal anti-human procalcitonin immunoglobins	Dynabeads* paramagnetic particles coated with mouse anti-human procalcitonin monoclonal antibody
Assay Duration	Approximately 20 minutes	Same
Sample Volume	200 µL	35 µL
Measuring Range	0.05 ng/mL to 100 ng/mL	0.05 ng/mL to 100 ng/mL
LoB	0.01 ng/mL	0.005 ng/mL
LoD	0.03 ng/mL	0.01 ng/mL
LoQ	0.05 ng/mL	0.02 ng/mL
Hook	No hook effect up to procalcitonin concentrations of 2,600 ng/mL	No hook effect up to procalcitonin concentrations of 5,000 ng/mL
Expected Results (Upper Reference Limit)	99 th percentile 0.09 ng/ml 95 th percentile < 0.05 ng/mL	95 th percentile of 0.065 ng/mL with a 95% Confidence Interval (CI) of 0.054 – 0.085 ng/mL

*Dynabead[®] is a registered trademark of Dynal A.S., Oslo, Norway

[†] VIDAS[®] is a registered trademark of bioMérieux SA. B·R·A·H·M·S PCT[®] is a registered trademark of B·R·A·H·M·S GmbH.

Summary of Studies

Method Comparison: A comparison of approximately 207 serum samples with PCT concentrations ranging from approximately 0.05 ng/mL to 100 ng/mL were run on both the Access PCT assay and the predicate VIDAS[®] B-R-A-H-M-S PCT^{®†} assay. The results were compared using Passing-Bablok regression and Pearson correlation with the predicate on the x-axis. The observed linear fit had a slope = 0.96 with 95% confidence interval of 0.94 to 0.99, an intercept = 0.02 ng/mL and a correlation coefficient (r) = 0.99. The slope specification is set at 0.90 ± 0.10 with correlation coefficient (r) ≥ 0.95.

Imprecision: The Access PCT assay exhibits total imprecision of ≤ 8.0% CV at concentrations ≥ 0.150 ng/mL, and standard deviation (SD) ≤ 0.012 ng/mL at concentrations < 0.150 ng/mL.

The Access PCT assay exhibits within run imprecision of ≤ 6.0% CV at concentrations ≥ 0.150 ng/mL, and a standard deviation (SD) ≤ 0.009 ng/mL at concentrations < 0.150 ng/mL.

High-dose Hook Effect: The Access PCT assay demonstrated no high-dose hook effect at concentrations up to at least 5,000 ng/mL.

Linearity: The Access PCT assay has demonstrated to be linear across the range of the assay (0.05 ng/mL to approximately 100 ng/mL).

Dilution Recovery: The Access PCT assay has been demonstrated to dilute recover across the range of the assay (0.05 ng/mL to approximately 100 ng/mL) in serum, lithium heparin plasma, and EDTA plasma samples. Samples containing procalcitonin concentrations up to 1,000 ng/mL can be diluted 10-fold with an overall average recovery of 100 ± 10% and an individual sample dose recovery within ± 15%.

[†] VIDAS[®] is a registered trademark of bioMérieux SA. B-R-A-H-M-S PCT[®] is a registered trademark of B-R-A-H-M-S GmbH.

Limit of Blank (LoB):

The highest measurement result observed with no analyte present in a serum sample is ≤ 0.005 ng/mL.

Limit of Detection (LoD):

The limit of detection (LoD) for the Access PCT assay is ≤ 0.01 ng/mL.

Limit of Quantitation (LoQ): The limit of quantitation (LoQ) based on 20% within-laboratory imprecision for the Access PCT assay is ≤ 0.02 ng/mL.

Total Error: The LoQ was established using a 20% CV acceptance goal as recommended in CLSI guideline EP17-A2 for cases where no generally accepted reference standard is available. To supplement the within-laboratory %CV LoQ analysis, a modeling analysis was performed to estimate the Total Error at each clinical cutoff (0.5 ng/mL and 2.0 ng/mL). The slope and intercept estimates that were derived from the method comparison study were used to obtain estimates of bias and %bias at each concentration listed above. A precision profile model was fit to the estimated within-laboratory %CV values from the imprecision study samples with concentration values covering approximately 0.1 ng/mL to 8 ng/mL. Because the range of samples included in both the method comparison and the imprecision study cover the concentrations 0.1 ng/mL to 2.0 ng/mL, the bias estimates and precision profile estimates can be combined to provide an estimate of total error (TE) and %TE at each medical decision point.

The estimated %TE at the medical decision points 0.5 ng/mL and 2.0 ng/mL is $\leq 9.4\%$ based on estimates from Weighted Deming regression and $\leq 11.3\%$ from Passing Bablok regression.

Percent Total Error Estimates Based on Bias Estimates Using Weighted Deming

Concentration (ng/mL)	Bias (%)	CV (%)	Total Error (%)
0.5	0.6%	4.5%	9.4%
2	0.7%	4.2%	8.9%

Percent Total Error Estimates Based on Bias Estimates Using Passing Bablok

Concentration (ng/mL)	Bias (%)	CV (%)	Total Error (%)
0.5	-0.6%	4.5%	9.4%
2	-3.1%	4.2%	11.3%

Analytical Specificity: Potential cross-reactive substances were added to serum patient samples at three concentrations of procalcitonin (approximately 0.25 ng/mL, 0.5 ng/mL, and 2.0 ng/mL). Stock solutions of potential cross-reactants were prepared volumetrically using calibrated pipettes and the appropriate solvent. This stock solution was added directly to the serum in no more than 5% (v/v) final concentration. Control samples were prepared in the same manner using the solvent, without the cross-reactant added. Control and test samples were tested on the Access 2 instrument within 24 hours of preparation, using three reagent lots. Testing of human calcitonin, human katacalcin, human alpha CGRP and human beta CGRP, with Access PCT found that there is no significant cross-reactivity, as defined by a change in concentration between the diluent control and the test samples within $\pm 10\%$. The acceptance criteria of $\pm 10\%$ was set to ensure that the potential for cross-reactivity is sufficiently mitigated while accommodating the expected imprecision of the assay when performing cross-reactivity testing.

Interfering Substances:

Known concentrations of potential interferents, as per CLSI EP07 (Interference Testing in Clinical Chemistry-Approved Guideline, Third Edition), were added to the patient samples. Results from these spiked test patient samples were evaluated against that of the unspiked control sample. In accordance with CLSI EP07, interference testing was completed on patient serum samples containing four levels of procalcitonin at three clinically relevant concentrations of 0.25 ng/mL, 0.5 ng/mL and 2.0 ng/mL and an additional procalcitonin concentration of approximately 80 ng/mL. See the interfering substance table below for the list of substances and interference concentrations tested.

The study was run at an internal site on three Access 2 instruments, using three reagent pack lots and one calibrator lot. Five replicates were tested for each control sample and each spiked test sample preparation.

Of the substances tested, none were found to cause significant interference, as defined by a change in concentration between the diluent control and test sample within $\pm 10\%$. The acceptance criteria of $\pm 10\%$ was set to ensure that the potential for interference is sufficiently mitigated while accommodating the expected imprecision of the assay when performing interference testing.

Interfering Substances

Substance	Interferent Concentration Tested	Substance	Interferent Concentration Tested
Acetaminophen	20 mg/dL	Hemoglobin	400 mg/dL
Acetylsalicylic Acid	100 mg/dL	Heparin	8000 IU/L
Azithromycin	1.20 mg/dL	Human Serum Albumin	12 g/dL
Bilirubin (Conjugated)	40 mg/dL	Ibuprofen	50 mg/dL
Bilirubin (Unconjugated)	40 mg/dL	Imipenem	18 mg/dL
Caffeine	6.0 mg/dL	Levofloxacin	1.75 mg/dL
Cefotaxime/Cefotaxin	90 mg/dL	Loratadine	0.03 mg/dL
Celecoxib	24 mg/dL	Naproxen	50 mg/dL
Cetirizine HCL	0.36 mg/dL	Nicotine	0.1 mg/dL
Dextromethorphan	0.14 mg/dL	Noradrenaline	0.2 mg/dL
Dobutamine	1.12 mg/dL	Oxymetazoline HCL	0.009 mg/dL
Dopamine	13 mg/dL	Phenylephrine	0.018 mg/dL
Doxycycline	5.0 mg/dL	Prednisolone	0.3 mg/dL
Epinephrine (adrenaline)	0.18 mg/dL	Salmeterol	0.006 mg/dL
Ethanol	400 mg/dL	Theophylline	10 mg/dL
Fentanyl	1.0 mg/dL	Tiotropium	0.0022 mg/dL
Furosemide	5.98 mg/dL	Triglycerides (Intralipids)	3000 mg/dL

Expected Reference Intervals: Samples were prospectively procured from two hundred and two (202), apparently healthy individuals ≥ 21 years of age, that were not experiencing an acute bacterial or viral illness. The established Reference Interval (RI) is consistent with commonly used reference intervals for apparently healthy individuals of PCT ≤ 0.1 ng/mL.

PCT Sample Statistics			
Number of Subjects	Median ng/mL	95th Percentile Upper Reference Range	95% Nonparametric CI of 95th percentile Reference Range
202	0.025	0.065 ng/mL	[0.054 - 0.085 ng/mL]

Matrix Comparison: A comparison of forty-three (43) matched sets of serum gel, serum no gel, plasma lithium heparin, and plasma EDTA samples with procalcitonin concentrations ranging from approximately 0.19 to 86 ng/mL were compared using Passing-Bablok linear regression analysis.

The observed linear fit for serum (gel) vs. serum (no gel) had an estimated slope = 0.99 with a 95% confidence interval (CI) of 0.98 to 1.00. The observed linear fit for lithium heparin plasma vs. serum (no gel) had an estimated slope = 0.96 with a 95% CI of 0.95 to 0.97. The observed linear fit for EDTA plasma vs. serum (no gel) had an estimated slope of 1.03, with a 95% CI of 1.01 to 1.04. The observed linear fit for lithium heparin plasma vs. serum gel had an estimated slope of 0.97 with a 95% CI of 0.96 to 0.99. The observed linear fit of EDTA plasma vs. serum gel had an estimated slope = 1.04 with a 95% CI of 1.03 to 1.05. The observed linear fit of EDTA plasma vs. lithium heparin plasma had an estimated slope = 1.06 with a 95% CI of 1.05 to 1.08.

Carryover Study: The PCT assay utilizes a sodium hydroxide wash between tests to mitigate the potential occurrence of carryover. Based on the expectation that carryover is minimized by this design feature, the acceptance criteria of $\pm 10\%$ was set to ensure that the potential for carryover is sufficiently mitigated while accommodating the expected imprecision of the assay when performing carryover testing.

Verification studies were performed to determine potential assay carryover for the Access PCT assay on the Access 2 instrument. The test used samples at 0.25 ng/mL and the medical decision points of 0.5 ng/mL and 2.0 ng/mL. Testing alternated low samples with high samples for each level tested and used a serum sample spiked with antigen and the highest calibrator. Testing met result criteria as all results had a shift of $\leq 10\%$ for assay carryover.

Individual estimates of carryover ranged from -6% to +8% and indicate no clear trend of positive or negative shifts. This observation provides additional evidence that the potential

for carryover is sufficiently mitigated. If carryover of a high sample into a lower sample were present, we would expect to observe a positive bias only.

Conclusion:

The Access PCT assay is substantially equivalent to the currently marketed VIDAS® B•R•A•H•M•S PCT®† assay (K162827). The verification and validation data provided in this submission demonstrates that the safety and efficacy of this device is substantially equivalent to the predicate device.

† VIDAS® is a registered trademark of bioMérieux SA. B•R•A•H•M•S PCT® is a registered trademark of B•R•A•H•M•S GmbH.