October 23, 2026

B·R·A·H·M·S GmbH (part of Thermo Fisher Scientific)
Anja Jagalla
Senior Regulatory Affairs Specialist
Neuendorfstrasse 25
Hennigsdorf, BRANDENBURG 16761
Germany

Re: K260302
Trade/Device Name: B·R·A·H·M·S MR-proADM KRYPTOR; B·R·A·H·M·S MR-proADM KRYPTOR CAL; B·R·A·H·M·S MR-proADM KRYPTOR QC
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 Codes: SJQ, JIT, JJX
Dated: January 28, 2026
Received: January 30, 2026

Dear Anja Jagalla:

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 (the 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 available 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.

Before making any change significantly affecting the safety or effectiveness of the device, you must submit a new premarket notification in accordance with 21 CFR 807.81. Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality Management System Regulation (QMSR) (21 CFR Part 820), which includes, but is not limited to, ISO 13485 clause 7.3 (Design controls), ISO 13485 clause 8.3 (Nonconforming product), ISO 13485 clause 8.5.2 (Corrective action), and ISO 13485 clause 8.5.3 (Preventative action). Please note that regardless of whether a change requires premarket review, the QMSR requires device manufacturers to review and approve changes to device design and production (ISO 13485 clause 7.3 and ISO 13485 clause 7.5) and document changes and approvals in the Medical Device File (ISO 13485 clause 4.2.3).

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 Part 803) for devices or postmarketing safety reporting (21 CFR Part 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 Management System Regulation (QMSR) (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 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,

BRYAN M. GRABIAS -S
2026.10.23 13:18:14
-04'00'

Bryan Grabias, Ph.D.
Acting Branch Chief
Bacterial Respiratory and Medical Countermeasures Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
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: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K260302

Device Name
B·R·A·H·M·S MR-proADM KRYPTOR

Indications for Use *(Describe)*
The B·R·A·H·M·S MR-proADM™ KRYPTOR™ test is an automated immunofluorescent assay using Time-Resolved Amplified Cryptate Emission (TRACE™) technology for the detection of midregional proadrenomedullin (MR-proADM) in human EDTA plasma.

The B·R·A·H·M·S MR-proADM KRYPTOR is intended for use, in conjunction with other laboratory findings and clinical assessments, as an aid in assessing the cumulative 28-day risk of all-cause mortality for patients diagnosed with sepsis or septic shock.

This assessment can be performed at the time of diagnosis or, alternatively, on any of the following four days (days 1–4). The assessment can be performed in the ICU or emergency department and other medical wards prior to ICU admission.

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

B·R·A·H·M·S MR-proADM™ KRYPTOR™

Section 5: 510(k) Summary [21 CFR 807.92]

807.92(a)(1), (2), (3):

Date Prepared: January 29, 2026

Applicant: Anja Jagalla, Senior Regulatory Affairs Specialist
B·R·A·H·M·S GmbH (part of Thermo Fisher Scientific)
Neuendorfstrasse 25
16761 Hennigsdorf, Brandenburg 16761
GERMANY
+49 33 0288 3616

Device Trade Name: B·R·A·H·M·S MR-proADM™ KRYPTOR™

Common Name: MR-proADM

Review Panel: In vitro diagnostics - Microbiology (OHT7)

Classification Name: Device to detect and measure non-microbial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis.

Regulation No.: 866.3215

Classification Code: SJQ

Predicate Device: B·R·A·H·M·S PCT™ sensitive KRYPTOR™: DEN150009
Classification Code: PMT
Regulation No.: 866.3215

Device Description *807.92(a)(4)***:**

The B·R·A·H·M·S MR-proADM KRYPTOR test is an automated immunofluorescent assay for the detection of the concentration of midregional proadrenomedullin (MR-proADM) in human plasma (EDTA). It is intended to be used with the B·R·A·H·M·S KRYPTOR compact PLUS (B·R·A·H·M·S KRYPTOR analyzer family) and B·R·A·H·M·S KRYPTOR calibrators and controls. The B·R·A·H·M·S KRYPTOR analyzer, B·R·A·H·M·S KRYPTOR calibrator and control materials are sold and distributed separately from the B·R·A·H·M·S MR-proADM KRYPTOR test.

The B·R·A·H·M·S MR-proADM KRYPTOR test contains sufficient reagents for 50 determinations. The reagent unit contains three reagent bottles.

Indications for Use *[Intended Use 807.92(a)(5)]***:**

The B·R·A·H·M·S MR-proADM™ KRYPTOR™ test is an automated immunofluorescent assay using Time-Resolved Amplified Cryptate Emission (TRACE™) technology for the detection of midregional proadrenomedullin (MR-proADM) in human EDTA plasma.

The B·R·A·H·M·S MR-proADM KRYPTOR is intended for use, in conjunction with other laboratory findings and clinical assessments, as an aid in assessing the cumulative 28-day risk of all-cause mortality for patients diagnosed with sepsis or septic shock.

This assessment can be performed at the time of diagnosis or, alternatively, on any of the following four days (days 1–4). The assessment can be performed in the ICU or emergency department and other medical wards prior to ICU admission.

Technological Characteristics *807.92(a)(6)***:**

B·R·A·H·M·S MR-proADM KRYPTOR and the predicate, B·R·A·H·M·S PCT sensitive KRYPTOR granted in DEN150009, are both devices to detect and measure non-microbial analyte(s) in human EDTA plasma to aid in assessment of patients diagnosed with sepsis or septic shock. However, each measures a different analyte associated with sepsis that are both able to aid in assessing the cumulative 28-day risk of all-cause mortality for patients diagnosed with sepsis or septic shock.

The primary difference between the predicate device and the subject device is the analyte and specimen types. The predicate, B·R·A·H·M·S PCT sensitive KRYPTOR, detects and measures procalcitonin (PCT). The subject device, B·R·A·H·M·S MR-proADM KRYPTOR, detects and measures midregional proadrenomedillin (MR-proADM). Despite PCT and MR-proADM being distinct biomarkers, the reference device and the subject device include the same clinical utility in assessing risk.

The B·R·A·H·M·S MR-proADM KRYPTOR has the same fundamental technological characteristics as the primary predicate. The analysis method of both uses Time-Resolved Amplified Cryptate Emission (TRACE) technology based on the formation of a complex comprised of the analyte “sandwiched” between two anti-analyte antibodies. Both devices are intended to be performed on the B·R·A·H·M·S KRYPTOR analyzer family. The subject device and the primary predicate are both provided with one (1) calibrator and two (2) levels of controls that are sold separately.

Summary of Non-Clinical Test - Performance and Safety Testing *807.92(b)(1)***:**

FDA Special Control 3 in regulation 866.3215 was met as shown with the reports contained in the 510(k) submission. Summary data are as follows:

Analytical Sensitivity (Limit of Blank, Limit of Detection, and Limit of Quantification)

The Limit of Blank (LoB), Limit of Detection (LoD) and Limit of Quantitation (LoQ) of the B·R·A·H·M·S MR-proADM KRYPTOR assay were determined following Clinical and Laboratory Standards Institute (CLSI) guideline EP17-A02.

LoB was determined by testing a total of 60 replicates per reagent lot (120 total replicates) obtained from 4 different blank samples over 5 days using 2 reagents lots on 2 B·R·A·H·M·S KRYPTOR compact PLUS instruments. The LoB is the 95th percentile from 60 determinations of 4 analyte-free samples.

LoD was determined based on the LoB and the standard deviation of 4 low level samples from 60 determinations of low analyte samples, per reagent lot. The LoD is the lowest amount of MR-proADM in a sample that can be detected with 95% probability.

LoQ was determined by testing a total of 80 replicates of 9 different samples. The samples measured were prepared from either depleted K2-EDTA human plasma sample from a healthy individual, K2-EDTA human plasma sample from a healthy individual, or partially depleted K2-EDTA human plasma sample from a healthy individual. The samples were tested using 2 reagents lots on 1 B·R·A·H·M·S KRYPTOR compact PLUS instrument by 2 operators over 20 days. The LoQ is calculated with guidance from CLSI EP17-A2, appendix D1 and CLSI EP05-A3, and is the lowest analyte concentration that can be reproducibly measured with an intermediate within-lab precision Coefficient of Variation (CV) of ≤ 20%.

The maximum LoB, LoD, and LoQ observed are indicated below:

LoB = 0.03 nmol/L

LoD = 0.06 nmol/L

LoQ = 0.13 nmol/L

Precision

Precision (repeatability, within-laboratory, reproducibility and lot-to-lot precision) was determined following CLSI guideline EP05-A3. The samples measured were either K2-EDTA human plasma sample from a healthy individual, K2-EDTA human plasma sample from a healthy individual spiked with a pool of individual human EDTA plasma samples from patients representative of the intended use, K2-EDTA human plasma sample from a healthy individual spiked with recombinant MR-proADM antigen, K3-EDTA human plasma sample from a healthy individual spiked with recombinant MR-proADM antigen.

Repeatability and within-laboratory precision studies was conducted using 2 reagents lots and 1 B·R·A·H·M·S KRYPTOR compact PLUS instrument by 2 operators. A total of 80 replicates for each sample were tested with 2 replicates per run and 2 runs per day for 20 days. The results obtained were analyzed to determine repeatability (within-run) and precision (within-laboratory, between-day and between-run) for each sample. The assay demonstrated single laboratory repeatability less than 5.0% CV and within-laboratory precision less or equal to 6.0% CV. The least favorable CVs per sample

between the 2 lots as well as the Standard Deviation (SD) are presented in the tables below.

Sample	Mean Value (nmol/L)	Repeatability	
		SD	CV
29PRE01	0.39	0.02	4.9%
29PRE02	0.81	0.02	2.3%
29PRE03	1.59	0.02	1.6%
29PRE04	2.30	0.03	1.4%
29PRE05	4.94	0.08	1.5%
29PRE06	7.00	0.11	1.6%
29PRE07	8.63	0.10	1.2%

Sample	Mean Value (nmol/L)	Within-Laboratory	
		SD	CV
29PRE01	0.38	0.02	6.0%
29PRE02	0.81	0.03	4.1%
29PRE03	1.55	0.04	2.7%
29PRE04	2.24	0.07	3.1%
29PRE05	4.94	0.17	3.5%
29PRE06	7.00	0.29	4.1%
29PRE07	8.63	0.46	5.3%

Lot-to-lot CVs were calculated from the measurement of samples over 5 days, with 5 replicates per day using 3 reagent lots and 1 analyzer. The results are shown below.

Sample	Mean Value (nmol/L)	Lot-to-Lot	
		SD	CV
29PRE01	0.37	0.01	1.5%
29PRE02	0.78	0.02	2.1%
29PRE03	1.47	0.02	1.6%
29PRE04	2.12	0.04	1.9%
29PRE05	4.71	0.09	1.9%
29PRE06	6.71	0.03	0.5%
29PRE07	8.35	0.07	0.8%

For reproducibility, samples have been measured on 5 days, with 1 run per day in 5 replicates using 1 reagent lot at 3 different sites (different analyzers). The results obtained were analyzed to demonstrate the multi-laboratory total repeatability, within-laboratory and reproducibility by combining precision results across the three laboratories. The results are shown below.

Sample	Mean Value (nmol/L)	Repeatability		Between-Day		Within-Laboratory		Between-Site		Reproducibility	
		SD	CV	SD	CV	SD	CV	SD	CV	SD	CV
29PRE01	0.36	0.01	3.6%	0.00	1.1%	0.01	3.8%	0.01	3.1%	0.02	4.8%
29PRE02	0.74	0.01	1.9%	0.02	2.4%	0.02	3.1%	0.04	5.9%	0.05	6.7%
29PRE03	1.44	0.02	1.6%	0.01	0.6%	0.02	1.7%	0.03	2.2%	0.04	2.8%
29PRE04	2.10	0.03	1.3%	0.01	0.5%	0.03	1.4%	0.03	1.6%	0.04	2.1%
29PRE05	4.47	0.07	1.6%	0.13	3.0%	0.15	3.4%	0.16	3.6%	0.22	5.0%
29PRE06	6.51	0.08	1.2%	0.11	1.7%	0.14	2.1%	0.20	3.0%	0.24	3.7%
29PRE07	7.95	0.11	1.4%	0.16	2.0%	0.19	2.4%	0.39	4.9%	0.44	5.5%

Linearity

The linearity study was conducted as described in CLSI EP06 Edition 2. One pool of individual human plasma samples collected from patients representative of the intended use population with MR-proADM concentration of 10.9 nmol/L were serially diluted to create a linearity panel with 15 concentration levels that span a range between 10.9 and 0.11 nmol/L. Each dilution was measured in 5 to 10 replicates, and the mean value was compared to its predicted value for deviation percentage using a weighted least squares regression analysis. The assay demonstrated a linear range from 10.9 nmol/L down to 0.11 nmol/L, where measured concentrations showed ≤ 10% deviation of their predicted concentrations with a mean deviation from linearity of -0.04%. The results are shown below.

Proportion in High Sample	Predicted Value (nmol/L)	Measured (nmol/L)	Deviation from Linearity (%)
1.000	11.1	10.9	-2.1%
0.850	9.48	9.34	-1.5%
0.700	7.82	7.77	-0.7%
0.550	6.16	6.14	-0.3%
0.400	4.49	4.64	3.3%
0.250	2.83	3.01	6.4%
0.205	2.33	2.52	8.1%
0.135	1.55	1.63	4.8%
0.100	1.17	1.17	0.6%
0.080	0.94	0.94	-0.7%
0.050	0.61	0.61	-0.9%
0.020	0.28	0.27	-4.4%
0.010	0.17	0.15	-9.4%
0.005	0.11	0.11	-3.9%
		Mean Deviation from Linearity (%)	-0.04%

Extended Measuring Interval

A total of 10 individual EDTA human plasma samples from a patient representative of the intended use with different MR-proADM concentrations were used to assess the Extended Measuring Interval (EMI). The individual samples were measured using the dilution factors established for B·R·A·H·M·S MR-proADM KRYPTOR at 1 to 10. As there are no international standards and no reference methods registered in the USA for MR-proADM measurements, the target concentration of the different samples was established by manual dilution in 4-fold determinations with the dilution factor at 1 to 10. The recoveries between the values obtained by manual dilution and dilution obtained by instrument were calculated, as well as the mean recoveries. The samples

had individual recovery values ranging from 90.8% to 108.8%. The results are shown below.

Sample	Dilution Factor	Manual Dilution - Expected MR-proADM Concentration (nmol/L)	Instrument Dilution - Measured MR-proADM Concentration (nmol/L)	Recovery (%)
29RGE01	1/10	10.2	10.2	99.3
29RGE02	1/10	11.3	10.3	90.8
29RGE03	1/10	12.5	12.6	101.3
29RGE04	1/10	13.5	12.8	94.9
29RGE05	1/10	14.7	14.4	98.2
29RGE06	1/10	15.7	15.6	99.6
29RGE07	1/10	17.5	17.0	97.5
29RGE08	1/10	18.2	18.1	99.6
29RGE09	1/10	19.9	18.6	93.3
29RGE10	1/10	20.2	22.0	108.8

Spike Recovery

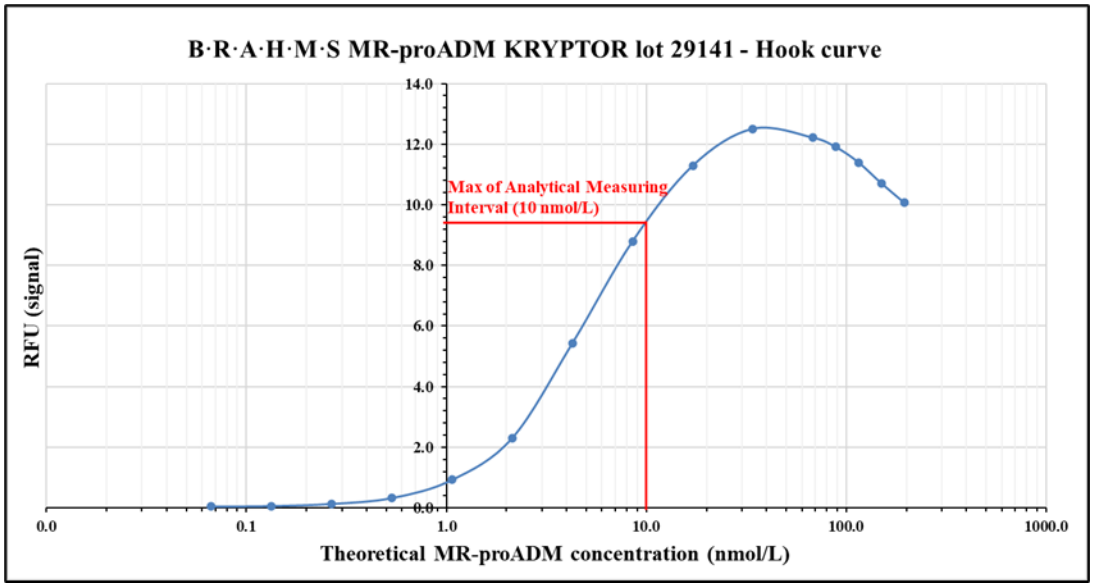
A total of 10 individual EDTA human plasma samples from patients representative of the intended use with different MR-proADM concentrations were used to assess spike recovery of the B·R·A·H·M·S MR-proADM KRYPTOR. The individual samples were spiked with 10% of MR-proADM antigen (targeted at 9 nmol/L). The same individual samples were pooled with the same matrix used for the antigen, with the same proportion. These 2 samples obtained from each of the individual samples were pooled together in 1 to 1 ratio. The 3 samples were measured in 3 replicates with 1 lot of reagents on 1 B·R·A·H·M·S KRYPTOR compact PLUS instrument. Testing was conducted by 1 operator on 1 run. The recoveries between the measured means and the expected concentrations were calculated for the 10 spiked pools. The results are shown below.

Sample	Expected MR-proADM Concentration of Spiked Sample (nmol/L)	Measured MR-proADM Concentration of Spiked Sample (nmol/L)	Recovery (%)
29REC01	1.51	1.48	98.1
29REC02	1.47	1.48	101
29REC03	1.99	1.95	98.2
29REC04	2.50	2.53	101
29REC05	2.94	2.93	99.7
29REC06	3.37	3.41	101
29REC07	3.80	3.80	99.8
29REC08	4.87	4.88	100
29REC09	5.92	6.01	102
29REC10	6.85	6.85	99.9

High Dose Hook Effect

A high dose hook effect study was conducted with a highly concentrated plasma sample (obtained by spiking recombinant MR-proADM into an individual human EDTA plasma sample from a patient representative of the intended use), serially diluted to

create a range of MR-proADM concentrations to assess assay signal as a function of concentration on the total analytical measurement range. The signal of the sample at 195 nmol/L was higher than the signal for the concentration of 10 nmol/L (upper limit of the analytical measuring interval), indicating there is no high dose hook effect in the assay. As conclusion, No High Dose Hook Effect affects the performance of the B·R·A·H·M·S MR-proADM KRYPTOR assay.



Interference

Interference studies were conducted based on CLSI EP07-A3 and CLSI EP37 2nd Edition. All tested concentrations represented the supplemental amount of respective interfering substance added to the human plasma samples (K2-EDTA human plasma samples from a healthy individual spiked with a pool of individual human EDTA plasma samples from patients representative of the intended use; pool of individual human EDTA plasma samples from patients representative of the intended use; individual human EDTA plasma sample from a patient representative of the intended use).

The following endogenous and exogenous substances, when tested for interference in the B·R·A·H·M·S MR-proADM KRYPTOR at the concentrations indicated in the tables below, resulted in less than or equal to 12% bias in detecting MR-proADM.

Endogenous substances:

Endogenous Interfering Substance	Concentration
Albumin	5.3 g/dL
Bilirubin (conjugated)	30 mg/dL
Bilirubin (unconjugated)	0.6 mg/dL
HAMA	63 ng/mL
Human hemoglobin	750 mg/dL
Rheumatoid factor	1 290 IU/mL
Triglycerides	14 000 mg/dL

Exogenous substances:

Exogenous Interfering Substance	Concentration
Albuterol	0.0045 mg/dL
Acetylsalicylic acid	43.5 mg/dL
Acetaminophen	7.8 mg/dL
Budesonide	0.00063 mg/dL
Caffeine	10.8 mg/dL
Cefotaxime	52.8 mg/dL
Dexamethasone	0.09 mg/dL
Dobutamine	0.121 mg/dL
Dopamine	0.0621 mg/dL
Ethanol	600 mg/dL
Furosemide	1.59 mg/dL
Heparin	330 units/dL
Ibuprofen	36 mg/dL
Ipratropium bromide	0.0003 mg/dL
Meropenem	33.9 mg/dL
Methylprednisolone	0.783 mg/dL
Norepinephrine	0.137 mg/dL
Piperacillin	110 mg/dL
Prednisolone	0.36 mg/dL
Prednisone	0.0114 mg/dL
Tazobactam	8.7 mg/dL
Theophylline	6 mg/dL
Vancomycin	12 mg/dL

Cross-reactivity

Cross-reactivity study was based on CLSI EP07-A3 as a guideline. Note that tested concentration represented the supplemental amount of respective MR-proANP substance added to the human plasma samples (K2-EDTA human plasma sample from a healthy individual spiked with a pool of individual human EDTA plasma samples from patients representative of the intended use).

The MR-proANP substance, when tested for cross-reactivity in the B·R·A·H·M·S MR-proADM KRYPTOR at the concentrations indicated in the table below, resulted in less than or equal to 12.0% bias in detecting MR-proADM.

Cross Reactant	Maximum Concentration Tested	Maximum Cross Reactivity
MR-proANP	2510 pmol/L	-1.2%

Sample Stability

a. Freezing and Thawing Stability

- Sample stability studies on 21 plasma samples frozen and thawed 4 times support a stability claim of up to 3 freezing thawing cycles.

b. Short-Term Sample Stability at Room Temperature and 2-8 °C

- Sample stability studies on 22 plasma samples stored at room temperature (18-25°C) support a stability claim of up to 24 hours at room temperature.
- Sample stability studies on 22 plasma samples stored at 2-8°C support a stability claim of up to 24 hours at 2-8°C.

c. Long-Term Sample Stability at ≤ -20°C and ≤ -80°C

- Long-term stability study for 22 plasma samples stored at ≤ -20°C is still in process and is currently at 6 months. Long-term stability for plasma samples at ≤ -20°C is claimed at 3 months currently with a final objective at 12 months at the end of the experiment.
- Long-term stability study for 22 plasma samples stored at ≤ -80°C is still in process and is currently at 6 months. Long-term stability for plasma samples at ≤ -80°C is claimed at 3 months currently with a final objective at 12 months at the end of the experiment.

d. Long-Term Sample Stability for Clinical Samples

- Sample stability study of 49 plasma samples stored at -80°C supports a stability claim of up to 8 years. This study confirms the stability of plasma samples from the clinical study stored at -80°C up to 6 years after blood collection before being measured with the B·R·A·H·M·S MR-proADM KRYPTOR assay to assess clinical validity.

Summary of Clinical Tests *807.92(b)(2)*:
FDA Special Control 4 in regulation 866.3215 was met as shown with the reports contained in the 510(k) submission. Summary data are as follows.

Reference Range

The reference range study was conducted in accordance with CLSI EP28-A3c and was established using EDTA plasma samples from 130 self-declared healthy individuals. This study was performed on the B·R·A·H·M·S KRYPTOR compact PLUS. The 97.5th percentile has been found at 0.84 nmol/L. The median is equal to 0.43 nmol/L.

Diagnostic Sensitivity and Specificity

The clinical performance of B·R·A·H·M·S MR-proADM KRYPTOR was evaluated for the prediction of cumulative 28-day all-cause mortality in a study of 530 adult patients diagnosed with sepsis or septic shock that were recruited across 9 investigational sites in the US. A total of 530 subjects were evaluated on day 0, 512 on day 1, 496 on day 2, 472 on day 3 and 437 on day 4.

The analysis population (530 subjects; day 0) comprised 45% female and 55% male patients with a mean age of 67 years. About 78.5% of the patients had sepsis and

17.0% septic shock according to the Sepsis-3 definition. For 4.5% of the patients, the sepsis classification could not be determined.

The binary test results (MR-proADM > 1.5 nmol/L or ≤ 1.5 nmol/L) were significantly associated with 28-day cumulative mortality. For measurement of MR-proADM on the day of diagnosis (day 0) of sepsis or septic shock and 1 to 4 days thereafter, the results of the univariate cox proportional hazard regression analysis were as follows:

28-Day mortality hazard ratios with MR-proADM measurements on days 0–4: MR-proADM ≤ 1.5 nmol/L and MR-proADM > 1.5 nmol/L were compared			
	No. of patients	**No. of deceased**	**Hazard ratio (95% Confidence Interval)**
Day 0	530	112	2.89 (1.39, 5.98)
Day 1	512	95	5.60 (2.35, 13.37)
Day 2	496	85	4.35 (2.04, 9.30)
Day 3	472	78	3.87 (1.94, 7.73)
Day 4	437	72	4.77 (2.14, 10.64)

Clinical performance measures and risk of mortality within 28 days were calculated for binary test results of MR-proADM on the day of diagnosis (day 0) of sepsis or septic shock and 1 to 4 days thereafter. Mean estimates and 95% confidence intervals are presented:

28-Day clinical performances and mortality risk with MR-proADM measurements on days 0–4: MR-proADM ≤ 1.5 nmol/L = test negative and MR-proADM > 1.5 nmol/L = test positive						
	Sensitivity	**Specificity**	**PPV**	**NPV**	**Mortality risk test-negative**	**Mortality risk test-positive**
Day 0	92.7% (87.8, 97.5)	20.1% (16.2, 24.0)	23.7% (19.7, 27.7)	91.1% (85.2, 97.0)	8.9% (3.0, 14.8)	23.7% (19.7, 27.7)
Day 1	93.5% (88.3, 98.7)	30.2% (25.8, 34.7)	23.4% (19.1, 27.7)	95.3% (91.6, 99.1)	4.7% (0.9, 8.4)	23.4% (19.1, 27.7)
Day 2	89.0% (81.7, 96.2)	37.0% (32.0, 41.9)	22.6% (18.1, 27.1)	94.2% (90.3, 98.1)	5.8% (1.9, 9.7)	22.6% (18.1, 27.1)
Day 3	87.1% (79.5, 94.7)	38.6% (33.6, 43.6)	21.9% (17.3, 26.5)	93.8% (90.0, 97.6)	6.2% (2.4, 10.0)	21.9% (17.3, 26.5)
Day 4	89.0% (81.4, 96.7)	39.2% (34.0, 44.4)	22.4% (17.5, 27.3)	94.8% (91.0, 98.5)	5.2% (1.5, 9.0)	22.4% (17.5, 27.3)

Patients with a positive MR-proADM test on day 0 had a 2.7-fold higher 28-day mortality risk than the patients with a negative MR-proADM. Patients with a positive test on days 1 to 4 had a 5.0-fold, 3.9-fold, 3.5-fold and 4.3-fold higher risk, respectively.

Conclusion *807.92(b)(3)***:**

B·R·A·H·M·S MR-proADM KRYPTOR and the predicate, B·R·A·H·M·S PCT sensitive KRYPTOR (DEN150009) are both tests designed to detect and measure non-microbial analyte(s) in human EDTA plasma to aid in assessment of patients diagnosed with sepsis or septic shock. The intended use and key technological characteristics of the tests using the KRYPTOR TRACE technology are substantially equivalent.

The subject device and the predicate device share the same intended use, patient population (patients diagnosed with sepsis or septic shock), fundamental technology, and are both for quantitative determination of analytes to aid in assessing the cumulative 28-day risk of all-cause mortality for patients with sepsis or septic shock. The subject device and predicate device both achieve their intended use as a system with B·R·A·H·M·S MR-proADM analyzer family, controls and calibrators.

MR-proADM complies with the special controls for 866.3215 including applicable analytical standards. The risks identified in the special controls have been mitigated through the completion of performance studies and through labeling. Substantial equivalence of the subject assays clinical performance and the predicate was demonstrated through the conduct of a clinical study. A technical method comparison was not performed, as the analytes PCT and MR-proADM differ in their molecular composition and physiological characteristics. Both the subject device and predicate device are substantially equivalent in meeting the special controls including sensitivity, precision, reproducibility, analytical measuring range, interference, cross reactivity and specimen stability.

The results of performance testing demonstrate that the device functions as intended, and the differences between the B·R·A·H·M·S MR-proADM KRYPTOR and the predicate do not raise new or different questions of safety and effectiveness. The predicate comparison and performance testing provided in this 510(k) is sufficient to demonstrate that the MR-proADM test is substantially equivalent to the legally marketed predicate device, B·R·A·H·M·S PCT sensitive KRYPTOR granted de novo classification in DEN150009.