K070319

# 510(k) SUMMARY

MAR 31 2008

## General Information

Submitted by: B·R·A·H·M·S Aktiengesellschaft
Neuendorfstrasse 25
D-16761 Henningsdorf near Berlin
Germany

Contact Person: Jonas Leichtner
B·R·A·H·M·S USA, Inc.
2568A Riva Road, Suite 207
Annapolis, MD 21401

Phone: (410) 897 9960
Fax: (410) 972 2452
Email: j.leichtner@brahms-usa.com

Date Prepared: February 14, 2008

## Device Name

Trade Name: B·R·A·H·M·S PCT sensitive KRYPTOR® Test System
Common Name: Inflammatory Response Marker
Classification Name: Antigen, Inflammatory Response Marker, Sepsis, 21 CFR 866.3210

## Predicate Device

| Manufacturer | Product Name | 510(k) No. |
|---|---|---|
| B·R·A·H·M·S Aktiengesellschaft | B·R·A·H·M·S PCT LIA | K040887 |

## Device Description

The B·R·A·H·M·S PCT sensitive KRYPTOR® assay is a homogeneous sandwich immunoassay for detection of PCT in human serum or plasma. The B·R·A·H·M·S KRYPTOR® analyzer is a fully automated system. The B·R·A·H·M·S KRYPTOR® analyzer is a closed system and can only operate utilizing special reagents provided by B·R·A·H·M·S Aktiengesellschaft. The measuring principle is based on Time-Resolved Amplified Cryptate Emission (TRACE®) technology, which measures the signal that is emitted from an immunocomplex with time delay.

The basis of the TRACE® technology is a non-radiative energy transfer from a donor [a cage-like structure with a europium ion in the center (cryptate)] to an acceptor (XL 665). The proximity of donor (cryptate) and acceptor (XL 665) in a formed immunocomplex and the spectral overlap between donor emission and acceptor absorption spectra on the one hand intensifies the fluorescent signal and on the other hand extends the life span of the acceptor signal, allowing for the measurement of temporally delayed fluorescence.

After the sample to be measured has been excited with a nitrogen laser at 337 nm, the donor (cryptate) emits a long-life fluorescent signal in the milli-second range at 620 nm, while the acceptor (XL 665) generates a short-life signal in the range of nano-seconds at 665 nm. When both components are bound in an immunocomplex, both the signal amplification and the prolonged life span of the acceptor signal occur at 665 nm, and the life is in the microsecond range. This delayed acceptor signal is proportional to the concentration of the analyte to be measured.

The specific fluorescence which is proportional to the antigen concentration is obtained through a double selection: spectral (separation depending on wave-length) and temporal (time resolved measurement). This enables an exclusive measurement of the signal emitted by the immunological complex and the ratio between the two wave-lengths (665/620) allows a real-time correction of the variations in optic transmission from the medium.

The contents of the B·R·A·H·M·S PCT sensitive KRYPTOR® assay are:

| **Reagent** | **Quantity for 50 determinations** | **Content** |
|---|---|---|
| Cryptate Conjugate | 1 bottle lyophilized | Cryptate conjugate, cryptate labeled, anti-PCT antibody (polyclonal, sheep), 3.2 ml after reconstitution with KRYPTOR® Solution 1 and KRYPTOR® Solution 2 |
| XL665 Conjugate | 1 bottle lyophilized | XL665 conjugate, XL665 labeled, anti-PCT antibody (monoclonal, mouse), 3.95 ml after reconstitution with KRYPTOR® Solution 1 and KRYPTOR® Solution 2 |
| Diluent | 1 bottle | Defibrinated human plasma, for diluting samples above 50 ng/ml, ready to use |

Controls, Calibrator, and Consumables are provided separate from the reagent unit.

## Intended Use

The B·R·A·H·M·S PCT sensitive KRYPTOR® is an immunofluorescent assay used to determine the concentration of PCT (procalcitonin) in human serum and plasma. The B·R·A·H·M·S PCT sensitive KRYPTOR® 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.

## Technological Comparison

The B·R·A·H·M·S PCT sensitive KRYPTOR® and the B·R·A·H·M·S PCT LIA have similar indications for use, are quantitative assays, and are used to determine the concentration of PCT in human serum and plasma The devices utilize different technologies and instruments to obtain the results. TRACE® technology (immunofluorescence) is used with the B·R·A·H·M·S KRYPTOR® analyzer and chemiluminescence is used with a luminometer for B·R·A·H·M·S PCT LIA. Each device uses 2 antibodies, one of which is the same for both devices. The monoclonal antibody used in both devices binds to Katacalcin. For the second antibody, the B·R·A·H·M·S PCT sensitive KRYPTOR® uses a polyclonal antibody, which is directed against Calcitonin. The B·R·A·H·M·S PCT LIA uses a monoclonal antibody directed against Calcitonin instead of a polyclonal antibody. Although the antibodies directed against Calcitonin come from different origin they bind to the same epitopes. Therefore they will bind to the same PCT molecule.

## Performance Summary

Precision and Reproducibility

Based on CLSI testing, the analytical sensitivity was determined to be 0.02 ng/ml and the functional assay sensitivity (FAS) was determined to be 0.06 ng/ml. In addition, the total precision ranges from 3.2 – 13.4 % CV and the within run precision ranges from 1.0 – 13.6 % CV.

High Dose Hook Effect

The B•R•A•H•M•S PCT sensitive KRYPTOR® assay is homogenous, and does not require separation or washing steps. It is thus possible to obtain data without interrupting the immunological reaction. High concentration samples (> 50 ng/ml) are detected in the first few seconds of incubation and may be diluted by the appropriate dilution factor, then re-assayed automatically. This process allows for sample measurements greater than 50 ng/ml up to 5000 ng/ml.

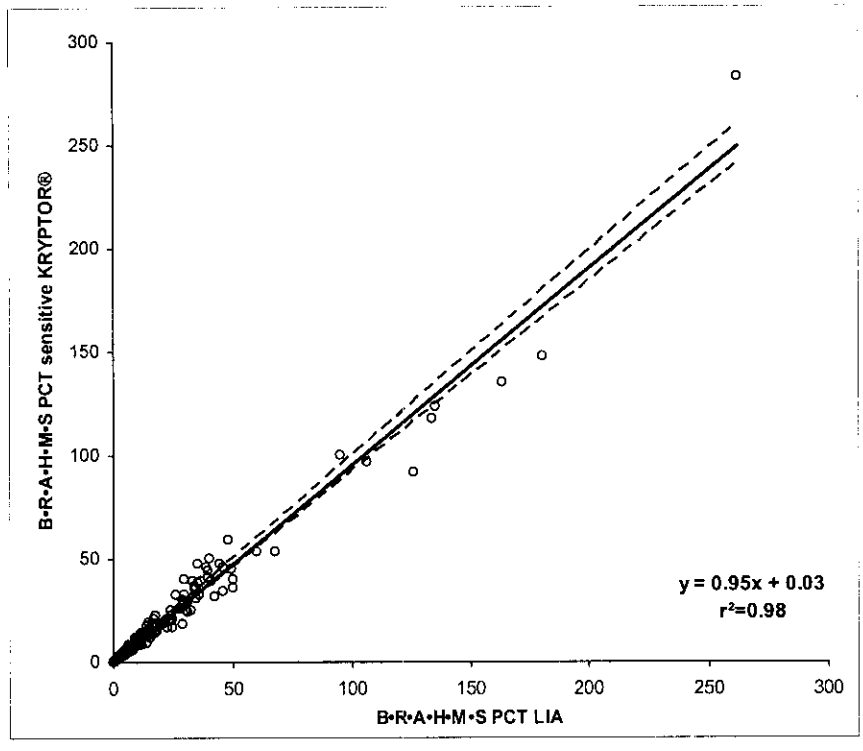
Interference and Cross Reactivity

Based on CLSI testing, the substances evaluated with the B·R·A·H·M·S PCT sensitive KRYPTOR® assay were found not to affect the test performance at concentrations reasonably and consistently found in clinical situations. The substances included the following

- bilirubin,
- hemoglobin,
- triglycerides,
- albumin,
- substances that share amino acid sequences with procalcitonin,
- drugs which are typically used for septic patients in intensive care units, and
- drugs which may be commonly used in subjects at greater risk of developing community acquired pneumonia than the general population, such as in asthma and/or COPD patients.

**Method Comparison Summary**

The B·R·A·H·M·S PCT sensitive KRYPTOR® and the B·R·A·H·M·S PCT LIA both detect procalcitonin (PCT) in human serum or plasma. A correlation study was performed in accordance with CLSI guideline EP9-A, "Method Comparison and Bias Estimation Using Patient Samples" between the B·R·A·H·M·S PCT sensitive KRYPTOR® assay and the B·R·A·H·M·S PCT LIA assay. There were 184 samples from three (3) sites, which had B·R·A·H·M·S PCT LIA measurements of 0.3 ng/ml (the functional assay sensitivity of B·R·A·H·M·S PCT LIA) or higher and/or B·R·A·H·M·S PCT sensitive KRYPTOR® measurements of 0.06 ng/ml (the functional assay sensitivity of B·R·A·H·M·S PCT sensitive KRYPTOR®) or higher. Passing-Bablock analysis shows a nearly perfect correlation of the B·R·A·H·M·S PCT sensitive KRYPTOR® assay and B·R·A·H·M·S PCT LIA assay, as demonstrated in the correlation graph below.




Interpretation of Results

The B·R·A·H·M·S PCT sensitive KRYPTOR® is intended 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.

SIRS, Sepsis, Severe Sepsis, and Septic Shock were categorized according to the criteria of the consensus conference of the American College of Chest Physicians/Society of Critical Care Medicine.

PCT should always be interpreted in the clinical context of the patient. Therefore, clinicians should use the PCT results in conjunction with other laboratory findings and clinical signs of the patient.

Data support the following interpretative risk assessment criteria:

**PCT > 2 ng/ml**

PCT levels above 2.0 ng/ml on the first day of ICU admission represent a high risk for progression to severe sepsis and/or septic shock.

**PCT < 0.5 ng/ml**

PCT levels below 0.5 ng/ml on the first day of ICU admission represent a low risk for progression to severe sepsis and/or septic shock.

**Note:** PCT levels below 0.5 ng/ml do not exclude an infection, because localized infections (without systemic signs) may also be associated with such low levels. If the PCT measurement is done very early after the systemic infection process has started (usually < 6 hours), these values may still be low.

As various non-infectious conditions are known to induce PCT as well, PCT levels between 0.5 ng/ml and 2.0 ng/ml should be reviewed carefully to take into account the specific clinical background and condition(s) of the individual patient.

Expected Values

In normal subjects, PCT concentrations are < 0.1 ng/ml. In a population of 151 subjects, 146 had a PCT value < 0.1 ng/ml.

Specimen Collection and Handling

Serum or plasma may be used. B·R·A·H·M·S recommends the use of only one matrix, i.e., use the same material (either serum or plasma [EDTA or heparin]) throughout the patient's clinical course. It is recommended that citrate plasma not be used, since concentrations were underestimated with citrate plasma.

CLSI guidelines should be followed for collecting, transporting, and processing patient samples. The sample volume needed for an assay is 50 µl. Testing demonstrated that there is no difference between the use of glass and plastic collecting tube types and that filling volume has no impact on the result. In any case, the results of the B·R·A·H·M·S PCT sensitive KRYPTOR® assay should be evaluated in context of all laboratory findings and the total clinical status of the patient. In cases where the laboratory results do not agree with the clinical picture or history, additional tests should be performed.

Samples may be stored up to 5 days at 2 - 8°C. Samples may be frozen (-20 °C) and thawed four times.

## Conclusions

The B·R·A·H·M·S PCT sensitive KRYPTOR® Test System is substantially equivalent to legally marketed Inflammatory Response Markers.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

Mr. Jonas Leichtner
Director of Marketing
B·R·A·H·M·S Aktiengelsellschaft
2568A Riva Road, Suite 207
Annapolis, MD 21401

MAR 31 2008

Re: K070310
Trade/Device Name: B·R·A·H·M·S PCT sensitive KRYPTOR® Test System
Regulation Number: 21 CFR 866.3210
Regulation Name: Antigen, Inflammatory Response Marker, Sepsis
Regulatory Class: Class II
Product Code: NTM
Dated: February 20, 2008
Received: February 20, 2008

Dear Mr. Leichtner:

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.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).
This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of In Vitro Diagnostic Device Evaluation and Safety at 240-276-0450. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding postmarket surveillance, please contact CDRH's Office of Surveillance and Biometric's (OSB's) Division of Postmarket Surveillance at 240-276-3474. For questions regarding the reporting of device adverse events (Medical Device Reporting (MDR)), please contact the Division of Surveillance Systems at 240-276-3464. You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (240) 276-3150 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

# INDICATIONS FOR USE

510(k) Number (if known): K070310

Device Name: B·R·A·H·M·S PCT sensitive KRYPTOR® Test System

Sponsor Name: B·R·A·H·M·S Aktiengesellschaft

Indications for Use:

The B·R·A·H·M·S PCT sensitive KRYPTOR® is designed for automated detection of PCT (procalcitonin) in human serum or plasma (EDTA, heparin) samples by the immunofluorescent B·R·A·H·M·S PCT sensitive KRYPTOR® assay.

The B·R·A·H·M·S PCT sensitive KRYPTOR® 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.

Prescription Use ☒ (21 CFR 801 Subpart D) And/Or Over-The-Counter Use ☐ (21 CFR 807 Subpart C)

**Do Not Write Below This Line – Continue on Another Page if Needed**

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K070310