



September 25, 2024

Abionic SA
Iwan Märki
Chief Technology Officer
Route de la Corniche 5
Epalinges, 1066
Switzerland

Re: K240041

Trade/Device Name: IVD CAPSULE PSP; abioSCOPE

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: SCX

Dated: January 3, 2024

Received: January 5, 2024

Dear Iwan Märki:

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.

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 System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

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 systems (QS) regulation (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**

Digitally signed by Bryan
M. Grabias -S
Date: 2024.09.25 14:03:14
-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

Indications for Use

510(k) Number (if known)

K240041

Device Name

IVD CAPSULE PSP / abioSCOPE

Indications for Use (Describe)

The IVD CAPSULE PSP is a single-use, rapid in vitro diagnostic immunofluorescence assay for the semi-quantitative determination of the concentration of pancreatic stone protein (PSP) in human K2-EDTA (arterial and venous) and K3-EDTA (venous) anticoagulated whole blood.

The IVD CAPSULE PSP is to be used on the abioSCOPE in vitro diagnostic analyzer. This diagnostic test is used in conjunction with other clinical assessments and laboratory findings to aid in the early detection of sepsis manifesting within the first 3 days after testing. IVD CAPSULE PSP generates PSP values that fall within one of three discrete Interpretation bands based on increasing likelihood of sepsis.

The test is intended for professional use in clinical laboratory settings. It is indicated for use in adult patients at high risk of sepsis presenting to intensive care units (ICUs).

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

IVD CAPSULE PSP on abioSCOPE®

This summary has been prepared in accordance with the requirements of 21 CFR 807.92.

1. 510(k) Number: K240041

2. Submitter

Abionic SA
Route de la Corniche 5
CH-1066 Epalinges
Switzerland

Contact Person: Iwan Märki
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Date of Summary preparation: September 25, 2024

3. Regulatory Information

Subject Device

Device Trade Name:	IVD CAPSULE PSP
Device Reference Number:	P02.00026
Device Common Name:	Pancreatic Stone Protein biomarker for sepsis detection
Regulation Number:	21 CFR 866.3215
Classification Name:	Device to detect and measure non-microbial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis.
FDA Classification:	Class II
Product Code:	SCX
Name of reading platform:	abioSCOPE®
Reference number of platform:	P01.00007

Predicate Device

Device Name: B.R.A.H.M.S PCT sensitive KRYPTOR® Test System
510(k) Number: K070310
Applicant: B.R.A.H.M.S Aktiengesellschaft
Manufacturer: B.R.A.H.M.S GmbH, part of Thermo Fisher Scientific

4. Device Description

IVD CAPSULE PSP (diagnostic assay kit)

The **IVD CAPSULE PSP** is a single-use, semi-quantitative immunofluorescence assay used to determine the concentration of the pancreatic stone protein (PSP) in a human whole blood sample. The test kit contains the following components:

- Capsule
- Special pipette (abioPIPETTE)
- Vial containing a detection reagent (abioMIX)
- Desiccant bag (auxiliary item to reduce moisture within the blister)

The main component of the test kit is the capsule. The capsule is a high impact polystyrene plastic cartridge similar in shape to a domino tile albeit smaller. The capsule allows the user to dispense the blood-abioMIX solution onto the loading port with the aid of the abioPIPETTE. The loading port has a membrane separator that excludes cells and other large particulates from the capsule interior. A second membrane drives the sample by capillary force to the entrance of nanofluidic biosensors containing a read-out area where the PSP is captured by specific antibodies and fluorescently detected.

The concentration of the captured PSP is proportional to the fluorescence generated by the fluorophore conjugated to the detection antibody. Therefore, the measured fluorescence signal is proportional to the concentration of PSP within the sample. The capsule also contains a RFID tag that is programmed with the capsule biosensor configuration and lot-specific information.

abioSCOPE (reading platform, analyzer)

The **abioSCOPE** is a tabletop diagnostic device that measures analytes in biological samples, using test-specific capsules (IVD CAPSULE) intended for use with this instrument. It is operated easily through a high-resolution touchscreen.

It is composed of a fully automated fluorescence microscope and a tray onto which is placed a single-use disposable IVD CAPSULE. The abioSCOPE uses a laser to excite the molecular complexes inside the biosensors which leads to the emission of a fluorescence signal. The abioSCOPE then calculates the concentration of the analyte in the patient sample.

5. Intended use

The **IVD CAPSULE PSP** is a single-use, rapid *in vitro* diagnostic immunofluorescence assay for the semi-quantitative determination of the concentration of pancreatic stone protein (PSP) in human K₂-EDTA (arterial and venous) and K₃-EDTA (venous) anticoagulated whole blood.

The **IVD CAPSULE PSP** is to be used on the **abioSCOPE** *in vitro* diagnostic analyzer. This diagnostic test is used in conjunction with other clinical assessments and laboratory findings to aid in the early detection of sepsis manifesting within the first 3 days after testing. IVD CAPSULE PSP generates PSP values that fall within one of three discrete Interpretation bands based on increasing likelihood of sepsis.

The test is intended for professional use in clinical laboratory settings. It is indicated for use in adult patients at high risk of sepsis presenting to intensive care units (ICUs).

6. Technological Characteristics Comparison

The following table describes the similarities and differences between the IVD CAPSULE PSP (subject device), and the BRAHMS PCT sensitive KRYPTOR (predicate device).

Item	Subject Device	Predicate Device
	IVD CAPSULE PSP on abioSCOPE	BRAHMS PCT sensitive KRYPTOR
Intended Use	The IVD CAPSULE PSP is a single-use, rapid <i>in vitro</i> diagnostic immunofluorescence assay for the semi-quantitative determination of the concentration of pancreatic stone protein (PSP) in human K₂-EDTA (arterial and venous) and K₃-EDTA (venous) anticoagulated whole blood. The IVD CAPSULE PSP is to be used on the abioSCOPE <i>in vitro</i> diagnostic analyzer. This diagnostic test is used in conjunction with other clinical assessments and laboratory findings to aid in the early detection of sepsis manifesting within the first 3 days after testing. IVD CAPSULE PSP generates PSP values that fall within one of three discrete Interpretation bands based on increasing likelihood of sepsis. The test is intended for professional use in clinical laboratory settings. It is indicated for use in adult patients at high risk of sepsis presenting to intensive care units (ICUs).	The BRAHMS PCT sensitive KRYPTOR® is an immunofluorescent assay used to determine the concentration of PCT (procalcitonin) in human serum and plasma. The BRAHMS 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.

Item	Subject Device	Predicate Device
	IVD CAPSULE PSP on abioSCOPE	BRAHMS PCT sensitive KRYPTOR
Detection Method	Immunofluorescence assay based on specific nanofluidic biosensor design	Immunofluorescence assay with measuring principle based on Time-Resolved Amplified Cryptate Emission (TRACE) technology which measures the signal emitted from an immunocomplex with time delay
Assay Type	Semi-quantitative	Quantitative
Result Output	Fluorescent signal is converted with the use of a calibration curve to a concentration that falls within one of three discrete interpretation bands based on likelihood of sepsis within three (3) days of testing.	Fluorescent signal is converted to concentration with the use of a calibration curve.
Sample Volume	50 µl	50 µl
Analyte	PSP (Pancreatic Stone Protein)	PCT (Procalcitonin)
Specimen type	K ₂ -EDTA (arterial and venous) and K ₃ -EDTA (venous) anticoagulated whole blood	EDTA anticoagulated serum and plasma from venous blood
Measuring Range	20-600 ng/ml	0.02-50 µg/L
Assay Time	7.5 minutes	19 minutes
Operating conditions for instrument	Operating temperature (18-28 °C). Relative humidity: 20-80%	Instrument-controlled, 37 °C
Controls	One level (medium concentration at approximately 200 ng/ml))	Two levels (low and high)

Table 1| Comparison table of subject and predicate device for establishing substantial equivalence.

Discussion of main differences:

The main technological differences between the IVD CAPSULE PSP on abioSCOPE and its predicate are not critical and include the following:

- The biomarkers (PSP vs PCT) are different. Reference values as normal range, cut-offs, etc. are different but diagnostic performance is equivalent as shown in clinical studies.
- Both test systems deliver as result biomarker concentration values, but an international reference standard has not yet been established for PSP, therefore, different test methods using PSP may have a certain bias between them and the measurement is indicated as “semi-quantitative”.
- The IVD CAPSULE PSP is currently limited to adult patients since sufficient clinical data is not yet available for younger populations. The indications of use for the subject device fall within the intended use of the predicate device.
- The IVD CAPSULE PSP uses a special nanofluidic biosensor design to shorten the time-to-result and concentrate the labelled measurand proteins, thereby increasing the fluorescence signal. The performance of the (subject and predicate) devices has been validated to be substantially equivalent.

- The systems use different (closed) reading instruments with similar methods (immunofluorescence) to work with specific test kits for measurements. The performance of the devices has been validated to be substantially equivalent.
- The collected specimen types (whole blood vs serum/plasma) are different but do not impact the effectiveness of the device since whole blood (arterial and venous) is easily available by the standard of care in ICUs and the used matrices were properly validated.

7. Analytical Performance Data

The analytical performance characteristics of the IVD CAPSULE PSP were investigated and validated using a series of dedicated individual studies, each of those looking at a particular aspect of the assay. The findings are summarized in the table below.

Inputs	Results
Analytical sensitivity	
Limit of Blank (LoB)	2.6 ng/ml
Limit of Detection (LoD)	9.4 ng/ml
Lower Limit of Quantification (LLoQ)	17.0 ng/ml
Analytical specificity	
Endogenous interferences	8 endogenous substances were assessed for their effect on the assay's performance. All but one (total protein) exhibited an average bias across all three PSP levels below the acceptance limit set at 10% although individual bias was above the limit for 2 substances (HAMA and hemoglobin) at the highest PSP concentration. Following these results, dose-response experiments were conducted on these 3 substances. Only total protein showed doses that were outside the acceptance limits of $\pm 10\%$ at the medium and highest PSP concentrations.
Exogenous interferences	29 exogenous substances were assessed for their effect on the assay's performance. In the initial assessment, all substances exhibited an average bias across all three PSP levels below the acceptance limit set at 10% although some individual biases were above the limit for 10 substances (acetaminophen, dopamine, doxycycline, ethanol, fentanyl, furosemide, heparin, imipenem, salmeterol and tiotropium) at certain PSP concentration. Following these results, dose-response experiments were conducted on these substances. Among the 10 substances tested in these experiments, only fentanyl showed doses that were outside the acceptance limits of $\pm 10\%$ at the highest PSP concentration. It was concluded that all the other interferences are not affecting the assay's performance.
Interference by sample Carryover	By alternating low-dose and high dose samples, the study showed that PSP measurement is not impacted by the previous test and no sample carryover was observed.
Analytical measuring range	
Measuring range	The measuring range of the assay was established and spans from 20 ng/ml to 600 ng/ml.
Linearity	The product showed linearity for the device measuring interval (20 to 600 ng/ml).
High-dose hook effect	No hook effect was observed at 10'000 ng/ml. Of important note, no PSP value above 5'000 ng/ml has been observed so far in clinical samples.
Accuracy	
Trueness of measurement (method comparison)	<i>Not evaluated</i> (there is no established reference method, therefore the test is indicated as semi-quantitative)
Precision	
In clinical laboratory settings	- Between-run and between-day CV% met acceptance criteria. Actual values are all below or equal to 6%. - Reproducibility (device-to-device, lot-to-lot and operator-to-operator precision) fulfilled

Inputs	Results
	the acceptance criteria exhibiting %CV values lower than 7% at the individual PSP concentrations analyzed and with averages across all 5 levels of 3%, 2.2% and 1.8% respectively. - instrument-to-instrument and user-to-user imprecision measured at 3 levels of PSP (low/intermediate/high) proved to be acceptable overall with %CV values not higher than 8.4% at the individual PSP concentrations analyzed. - Whole blood between-run precision was also determined with samples covering the reportable range (20 to 600 ng/ml) and yielded a %CV of 14.8%.
Stability	
Shelf-life	The current claimed shelf-life of the IVD CAPSULE PSP is 9 months at 2-8 °C.
In-Use	An open IVD CAPSULE PSP device can withstand at least 3 hours exposure to room temperature with temperatures reaching up to 30 °C. It is nevertheless recommended to use the device as soon as it is open and limit its exposure to the elements as much as possible.
Shipping	The stability of IVD CAPSULE PSP during transportation was assessed using a simulation approach where the kits were submitted to different temperature sequences to simulate a transport by plane from the manufacturing site to a customer site with the kit's exposure to either high or low temperature. It was shown that the benefit-risk ratio is not impacted by the results of the study.
Calibration and metrological traceability	
Metrological traceability	- No internationally recognized reference standard is available at this point of time. - Abionic has established an in-house higher order calibrator to which the final result in the patient's sample can be traced back through an unbroken chain of interdependence.
Specimen	
Type	The IVD CAPSULE PSP is an assay for the semi-quantitative determination of the concentration of pancreatic stone protein (PSP) in K ₂ -EDTA and K ₃ -EDTA anticoagulated venous and arterial whole blood.
Stability	PSP is stable in K ₂ -EDTA anticoagulated whole blood for up to 24 hours at room temperature and by extension at 2°C to 8°C.

Table 2 | Summary of analytical performance

The analytical performance of IVD CAPSULE PSP was established in accordance with the requirements for special controls imposed by the CFR regulation. The corresponding non-clinical studies were performed in compliance with the applicable CLSI standards, and the applied methods and performance characteristics of the device correspond to the current general state of the art for IVD devices. A direct analytical performance comparison with the predicate has only limited value as both devices use different biomarkers with individual cut-off values.

8. Clinical Performance Data

Normal reference range

The normal PSP concentration [ng/ml] range in adults was determined by the manufacturer on an US adult population. Results are provided in the following table.

Mean	97 ng/ml
5-95% percentiles	89 – 105 ng/ml
Median	81 ng/ml
LRL / URL	29 / 228 ng/ml

Table 3 | Normal PSP values. Values are from 211 healthy donors (Male/Female (%): 35/65, Caucasian/African American/Asian/Other (%): 77/15/7/1).

The distribution of the normal reference values over the established risk interpretation bands is shown in Table 4.

PSP concentration [ng/ml]	Distribution of (normal) reference values: number of subjects (percentage)	
≥ 300	4	(1.9%)
100 – 299	69	(32.7%)
≥200-299	11	(5.2%)
≥100-200	58	(27.5%)
< 100	138	(65.4%)

Table 4 | Distribution of normal PSP values in a (healthy) reference population (n=211).

Normal PSP values in adults aged over 60 are about 30% higher than in adults under 60. Gender or ethnicity/race do not significantly influence normal PSP values. It is recommended that each laboratory establishes its own expected reference ranges for the population it serves.

Clinical performance data

The association between PSP levels and the development of sepsis was demonstrated in a multicentric, prospective, observational clinical study (AB-PSP-002; NCT04105699) conducted across six ICU centers in the U.S., involving 497 patients.

The primary study population consisted of the intention-to-diagnose (ITD) group, representing a typical ICU patient demographic. This group included all participants with a valid PSP determination on day 1 and having an expected ICU stay for at least 3 days according to the study protocol. Participants who withdrew from the study or were discharged from the ICU within the first 24 hours of admission were excluded from the ITD analysis.

The study population closely mirrored the U.S. racial demographics as of July 1st, 2023, with 83% of participants identifying as White, 11.3% as Black or African American, and 1% as Asian. The table below provides a detailed breakdown of the study's demographics and clinical characteristics.

	Full ITD Population N = 497	Sepsis N = 241	No Sepsis N = 256
Age (years)			
Mean ± SD (N)	59.7 ± 16.38 (497)	61.9 ± 15.37 (241)	57.6 ± 17.04 (256)
Median (Q1, Q3)	63.0 (50.0, 71.0)	65.0 (54.0, 72.0)	60.0 (46.0, 71.0)
Min, Max	18.0, 100.0	19.0, 100.0	18.0, 96.0
Sex			
Female	44.3% (220/497)	46.9% (113/241)	41.8% (107/256)
Male	55.7% (277/497)	53.1% (128/241)	58.2% (149/256)
Race			
American Indian or Alaskan Native	0.8% (4/497)	1.2% (3/241)	0.4% (1/256)

	Full ITD Population N = 497	Sepsis N = 241	No Sepsis N = 256
Asian	1.0% (5/497)	0.8% (2/241)	1.2% (3/256)
Black or African American	11.3% (56/497)	10.4% (25/241)	12.1% (31/256)
Native Hawaiian or Other Pacific Islander	0.0% (0/497)	0.0% (0/241)	0.0% (0/256)
White	83.3% (414/497)	84.2% (203/241)	82.4% (211/256)
Other	1.6% (8/497)	1.7% (4/241)	1.6% (4/256)
Unknown/Not Reported	2.8% (14/497)	2.9% (7/241)	2.7% (7/256)
Reason for ICU Admission			
Respiratory Failure	16.3% (81/497)	20.3% (49/241)	12.5% (32/256)
Surgery (trauma)	10.5% (52/497)	3.3% (8/241)	17.2% (44/256)
Infection	7.0% (35/497)	12.4% (30/241)	2.0% (5/256)
Alteration in mental status	6.4% (32/497)	8.7% (21/241)	4.3% (11/256)
Hemodynamic disorders	4.0% (20/497)	4.1% (10/241)	3.9% (10/256)
Vasopressor support	3.8% (19/497)	7.5% (18/241)	0.4% (1/256)
Hematologic problems	3.6% (18/497)	0.8% (2/241)	6.3% (16/256)
Neurological problems	3.4% (17/497)	1.7% (4/241)	5.1% (13/256)
Surgical complications and/or wound care	3.0% (15/497)	2.9% (7/241)	3.1% (8/256)
Metabolic problems	2.0% (10/497)	0.8% (2/241)	3.1% (8/256)
Remaining other	39.8% (198/497)	37.3% (90/241)	42.2% (108/256)
PSP (ng/mL)			
Mean $\pm$ SD (N)	229.4 $\pm$ 201.58 (497)	298.4 $\pm$ 209.82 (241)	164.4 $\pm$ 169.89 (256)
Median (Q1, Q3)	136.0 (68.0, 359.0)	233.0 (113.0, 537.0)	85.0 (56.0, 207.5)

Table 5 | Demographic and clinical characteristics on enrolled patients forming the ITD population of study AB-PSP-002.

The performance of the PSP was evaluated by comparing it to the assessment of an External Independent Review Committee (EIRC) consisting of three medical doctors who are experts in critical care medicine and the assessment of infection and sepsis, but who were not otherwise involved in the study. Based on the Sepsis-3 definition the EIRC independently adjudicated all subjects, determining whether each was with or without sepsis at each day within the first 3 days of ICU stay while remaining blinded to the PSP results.

The prevalence of sepsis, as determined by the Sepsis-3 definition, was found to be 48.5%. Patients diagnosed with sepsis exhibited significantly higher average PSP (Pancreatic Stone

Protein) levels (298 ng/ml) compared to those without sepsis (164 ng/ml), confirming the expected relationship between elevated PSP levels and sepsis. The diagnostic performance of PSP was assessed on a patient level, with true positives defined as patients identified with sepsis both by the PSP assay (obtained on day 1) and (any of the daily) clinical diagnosis within the first 72 hours of ICU admission. True negatives were those without sepsis as detected by the PSP assay and clinical diagnosis. False negatives included patients not detected with sepsis by the PSP assay but clinically diagnosed within the first 72 hours, while false positives were those identified with sepsis by the PSP assay but without clinical diagnosis within the same period. A sensitivity analysis was conducted on the ITD population, using cut-off values established from a previous international multicentric observational clinical study, ensuring no influence from this study's patient data on the defined cut-off values and subsequent calculations.

To facilitate practical clinical use of the IVD CAPSULE PSP and provide context for the measured PSP values in relation to sepsis probability, a detailed analysis of predictive values and likelihood ratios was conducted using the study data. The clinical performance characteristics are outlined in Table 8, with PSP concentration thresholds divided into three categories: ≥ 300 ng/mL, 100-299 ng/mL, and < 100 ng/mL. PSP concentrations above 300 ng/ml show a strong correlation with sepsis, with a predictive value of 70.1% and a likelihood ratio of 2.49, highlighting significant risk in this group. PSP levels between 100 and 299 ng/ml also indicate elevated risk, though to a lesser extent, warranting close monitoring. In contrast, PSP concentrations below 100 ng/ml reflect a much lower risk, with only 26.2% of patients in this range diagnosed with sepsis and a likelihood ratio of 0.38. The clear transition of likelihood ratios underscores a meaningful decline in sepsis risk as PSP levels decrease.

PSP Concentration [ng/ml]	Physician Adjudication			Risk (Predictive Value)	Percent of Results	Likelihood Ratio	Lower bound of 95% CI	Upper bound of 95% CI
	Yes	No	Total					
≥ 300	103	44	147	70.10%	29.60%	2.49	1.83	3.38
100-299	88	71	159	55.30%	32.00%	1.32	1.02	1.7
< 100	50	141	191	26.20%	38.40%	0.38	0.29	0.49
Total	241	256	497	Prevalence = 48.5%				

Table 6 | Prevalence, Predictive Value, and LR of PSP Concentration ranges for Sepsis Risk

The following table presents the clinical performance characteristics of the PSP assay, offering a clear interpretation of the sepsis risk associated with specific PSP concentration ranges. Derived from study data and analysis, this information aids clinicians in making informed decisions when assessing sepsis risk, complementing other clinical evaluations and laboratory findings.

PSP concentration [ng/ml]	Result interpretation
≥ 300	Increased risk of sepsis
100 - 299	Slightly increased sepsis risk
< 100	Decreased risk of sepsis

Table 7 | Conversion table of PSP concentrations into classes expressing the risk of sepsis.

Adverse events:

During the US multicentric clinical study no adverse event directly linked to the IVD CAPSULE PSP test was identified.

Benefit-Risk statement:

Safety risks for the patients are essentially linked to potentially false (positive or negative) assay results. Those risks are very similar since both devices have equivalent clinical performance. Therefore, the benefit-risk is substantially equal between the subject and the predicate device.

9. Proposed Labeling

The labeling meets the requirements of 21 CFR Parts 801 and 809, as applicable, and the special controls for this device under 21 CFR 866.3215.

10. Conclusion

The submitted information in this premarket notification is complete and supports a substantial equivalence determination.