# 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
# DECISION SUMMARY
ASSAY AND INSTRUMENT

## I Background Information:

### A 510(k) Number

K240041

### B Applicant

Abionic SA

### C Proprietary and Established Names

IVD CAPSULE PSP; abioSCOPE

### D Regulatory Information

| Product Code(s) | Classification | Regulation Section | Panel |
|---|---|---|---|
| SCX | Class II | 21 CFR 866.3215 - Device to detect and measure non-microbial analyte(s) in human clinical specimens to aid in assessment of patients with suspected sepsis | MI - Microbiology |

## II Submission/Device Overview:

### A Purpose for Submission:

To obtain a substantial equivalence determination for the IVD CAPSULE PSP assay on the abioSCOPE instrument as an aid to diagnose sepsis.

### B Measurand:

Pancreatic Stone Protein (PSP)

### C Type of Test:

Immunofluorescence assay

## III Intended Use/Indications for Use:

### A Intended Use(s):

See Indications for Use below.

### B Indication(s) for 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 (venous and arterial) and K3-EDTA (venous) 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).

### C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

### D Special Instrument Requirements:

abioSCOPE

## IV Device/System Characteristics:

### A Device Description:

The IVD CAPSULE PSP is a sandwich immunofluorescence assay used on the abioSCOPE instrument and is intended to measure the concentration of pancreatic stone protein (PSP) in human K2-EDTA (venous and arterial) and K3-EDTA (venous) whole blood. The IVD CAPSULE PSP is a single use test kit containing the following four components:

- The abioCAPSULE, a polystyrene plastic cartridge which consists of membranes that filter the sample and drive the sample to the biosensors by capillary force. The abioCAPSULE also includes an RFID tag containing relevant information of the test.
- The abioMIX, a screw-top microtube containing an antibody specific to human PSP in an optimized buffered solution.
- An abioPIPETTE, used to mix 50 µL specimen with abioMIX and load the mixture on abioCAPSULE.
- A desiccant, used to protect the contents of the sealed IVD CAPSULE from any potential detrimental effects of ambient humidity during transportation and storage.

The abioSCOPE is a benchtop diagnostic device that measures analytes in biological samples. It is composed of a fully automated fluorescence microscope and is operated through a high-resolution touchscreen. The abioSCOPE uses a laser to excite the molecular complexes inside the biosensors which leads to the emission of a fluorescence signal.

## B Principle of Operation:

*Test principle*: The blood sample is mixed with a solution composed of a fluorescently labelled monoclonal antibody specific to human PSP. The blood sample, now containing the PSP-antibody complex, is loaded onto the capsule where it is drawn through the capsule by capillary action and passes through a built-in separator that excludes particles from the measurement area. After passing through the separator, the PSP-antibody complex is captured by anti-PSP monoclonal antibodies immobilized within the read-out area of the capsule. The concentration of the captured PSP is proportional to the fluorescence generated by the fluorophore conjugated to the detection antibody.

*Test procedure*: Briefly, 50 µL of patient blood sample is mixed with the provided reagent, abioMIX, which contains fluorochrome labeled, mouse anti-human PSP antibody. The sample-reagent mixture is then loaded into the port of the abioCAPSULE. Patient material is drawn through the capsule by capillary action and passes through a built-in separator that excludes particles from the measurement area. After passing through the separator, the PSP-antibody complex is bound by capture antibodies (anti-human PSP) immobilized within the read-out area of the capsule. The abioCAPSULE is inserted into the into the abioSCOPE to read the fluorescent signal. The concentration of the PSP in the sample is proportional to the fluorescence generated by the abioSCOPE in the reading area. The abioSCOPE uses the calibration information encoded in the abioSCOPE and in the capsule along with the measured fluorescent signal to quantify the level of PSP in the patient's blood sample and express the PSP concentration in ng/mL.

The IVD CAPSULE PSP test results are interpreted using the following bin assignment indicating level of sepsis risk for different PSP level ranges:

- PSP value ≥300 ng/ml: Increased risk of sepsis
- PSP value 100-299 ng/ml: Slightly increased risk of sepsis
- PSP value <100 ng/ml: Decreased risk of sepsis

## C Instrument Description Information:

1. Instrument Name:

   abioSCOPE

2. Specimen Identification:

   The IVD CAPSULE PSP to be used on the abioSCOPE in vitro diagnostic analyzer is validated for use with human K2-EDTA (venous and arterial) and K3-EDTA (venous) whole blood specimens. The whole blood specimen must be tested and analyzed within twenty-four hours of blood draw.

3. Specimen Sampling and Handling:

   The patient's specimen is mixed with the provided abioMIX reagent and pipetted by the user into the designated specimen loading port of the abioCAPSULE using the abioPIPETTE provided with the kit. The users are instructed to pipette 50 µL of sample into the cartridge.

Each single-use kit package contains all necessary components for testing a single patient specimen.

4. Calibration:

A calibration is unique to reagent and abioCAPSULE cartridge lot. The calibration process assures that the unique characteristics of each device and the unique state of each cartridge lot are accounted for in the calibration and that the concentration results are consistent and accurate.

5. Quality Control:

The abioSCOPE evaluates internal quality controls at power-on and during measurement after insertion of a capsule. If these internal controls fail, the abioSCOPE displays a specific error message and the abioSCOPE user manual must be consulted.

Additionally, two quality control products (IVD CAPSULE Control PSP and abioSCOPE Control) are available through Abionic SA. These quality controls can be used to verify that both the IVD CAPSULE PSP and abioSCOPE, respectively, work properly. It is recommended to use these quality controls:

- at least on a monthly basis;
- during training of new operators;
- anytime an unexpected test result with the IVD CAPSULE PSP kit is obtained;
- in compliance with the local regulatory requirements for quality control testing.

## V Substantial Equivalence Information:

### A Predicate Device Name(s):
BRAHMS PCT Sensitive Kryptor

### B Predicate 510(k) Number(s):
K070310

### C Comparison with Predicate(s):

| **Device & Predicate Device(s):** | K240041 | K070310 |
|---|---|---|
| Device Trade Name | IVD CAPSULE PSP | BRAHMS PCT Sensitive Kryptor |
| **General Device Characteristics Similarities** | | |
| Intended Use/Indications For Use | The IVD CAPSULE PSP is a single-use, rapid in vitro diagnostic immunofluorescence | The BRAHMS PCT sensitive KRYPTOR is an immunofluorescent assay used to determine |

| | | |
|---|---|---|
| | 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.<br><br>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.<br><br>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 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. |
| Signal | Fluorescence | Same |
| Intended End-user | Trained laboratory professionals | Same |
| **General Device Characteristics Differences** | | |
| Assay Type | Semi-quantitative | Quantitative |

| | | |
|---|---|---|
| Analyte | Pancreatic stone protein (PSP) | Procalcitonin (PCT) |
| Controls | One level (medium concentration) | Two levels (low and high) |
| Sample Matrix | K2-EDTA (venous and arterial), and K3-EDTA (venous) whole blood | EDTA-anticoagulated serum and plasma from venous blood |
| Detection Method | Immunofluorescence assay based on specific microfluidic biosensor design | Immunofluorescence assay based on TRACE technology which measures the signal emitted from an immunocomplex with time delay |
| Measurement Range | 20-600 ng/mL | 0.02-5000 ng/mL |
| Result Output | Fluorescent signal is converted to concentration with the use of a calibration curve that falls within one of three discrete interpretation bands based on likelihood of sepsis within three (3) days of testing. | Concentration of circulating PCT, in units of ng/mL |
| Instrument/Analyzer | abioSCOPE | BRAHMS KRYPTOR |

## VI Standards/Guidance Documents Referenced:

- CLSI EP05-A3 7-251: Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition
- CLSI EP06 2nd Edition 7-306: Evaluation of the Linearity of Quantitative Measurement Procedures
- CLSI EP07 3rd Edition 7-275: Interference Testing in Clinical Chemistry
- CLSI EP14-A3 7-252: Evaluation of Commutability of Processed Samples; Approved Guideline - Third Edition
- CLSI EP17-A2 7-233: Evaluation of Detection Capability for Clinical Laboratory Measurement
- Procedures; Approved Guideline Second Edition
- CLSI EP25-A 7-235: Evaluation of Stability of In Vitro Diagnostic Reagents; Approved Guideline.
- CLSI EP28-A3c 7-224: Defining Establishing and Verifying Reference Intervals in the Clinical Laboratory; Approved Guideline - Third Edition

- CLSI EP35 1st Edition 7-298: Assessment of Equivalence or Suitability of Specimen Types for Medical Laboratory Measurement Procedures
- CLSI EP37 1st Edition 7-284: Supplemental Tables for Interference Testing in Clinical Chemistry
- ISO 14971: 2019 5-125 Medical devices – Application of risk management to medical devices
- ISO TR 24971:2020 - Medical devices - Guidance on the application of ISO 14971
- ISO 23640:2011 In vitro diagnostic medical devices — Evaluation of stability of in vitro diagnostic reagents

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

1. Precision/Reproducibility:

A precision study was conducted to evaluate between-operator, between-device and between -lot precision of the device. The study evaluated five K3-EDTA plasma samples covering the entire assay reportable range of the PSP assay (20 to 600 ng/ml). These samples were tested in triplicate on two separate runs per day (morning and afternoon), separated by at least two hours, for five non-consecutive days. The study included three operators, three abioSCOPE devices and three kit lots. The test measurement procedure followed the instruction for use if the product and the abioSCOPE. Equivalency between K3-EDTA plasma, K3-EDTA whole blood, and K2-EDTA whole blood was established separately in a matrix equivalency study. The study was designed and executed according to the guideline CLSI EP05-A3.

**Table 1: Summary of Between-operator, Between-instrument, and Between-lot Variability – Study 1**

| PSP Level | Mean PSP concentration (ng/mL) | Between Operator | | Between Instrument | | Between Lot | |
|---|---|---|---|---|---|---|---|
| | | SD (ng/mL) | %CV | SD (ng/mL) | %CV | SD (ng/mL) | %CV |
| **Level 1** | 49 | 2.4 | 5.2% | 1.6 | 2.9% | 1.2 | 2.3% |
| **Level 2** | 70 | 0.0 | 0% | 0.0 | 0% | 4.4 | 5.7% |
| **Level 3** | 253 | 0.0 | 0% | 0.0 | 0% | 0.0 | 0% |
| **Level 4** | 326 | 12.2 | 4.1% | 17.8 | 5.1% | 10.3 | 2.9% |
| **Level 5** | 699 | 0.0 | 0% | 49.4 | 7.0% | 0.0 | 0% |

Given the automated nature of the test, site-to-site variability was expected to be minor. An additional precision study was conducted at a different site to evaluate the between-instrument and between-user components of precision with three K2-EDTA plasma samples covering the entire assay reportable range of the IVD CAPSULE PSP product (20 to 600 ng/ml). These samples were tested in triplicate, in two runs per day (morning and afternoon) separated by at least 2 hours, on 5 different (non-consecutive) days and on three abioSCOPE 2.0 devices. The observed between-user and between-instrument precision are summarized in the table below.

**Table 2: Summary of Between-user and Between-instrument Variability – Study 2**

| PSP level | Mean PSP concentration (ng/mL) | External site precision | | | |
|---|---|---|---|---|---|
| | | Between user | | Between instrument | |
| | | SD (ng/mL) | %CV | SD (ng/mL) | %CV |
| **Low** | 72.2 | 4.5 | 6.2% | 3.9 | 5.4% |
| **Intermediate** | 235 | 0.0 | 0.0% | 12.7 | 5.2% |
| **High** | 669 | 56.5 | 8.4% | 0 | 0.0% |

A smaller study was performed to evaluate between-run variability with 23 K2-EDTA anticoagulated whole blood samples spanning the assay reportable range (20 to 600 ng/ml). Each sample was tested twelve times using 4 analyzers and multiple reagent lots during the study. The variability (% CV) observed across the samples within the assay measuring range was acceptable.

An additional 20-day precision study was performed to evaluate between day and between run variability components of the within-laboratory precision by testing eight K3-EDTA plasma samples covering the entire reportable range of the PSP assay (20 to 600 ng/ml). These samples were tested in duplicate, in two runs per day (morning and afternoon) separated by at least 2 hours, on 20 different (non-consecutive) days, on one abioSCOPE 2.0.

**Table 3: Summary of 20-Day Within-Laboratory Precision Study**

| PSP Level | Mean PSP concentration (ng/mL) | Between Day | | Between run | |
|---|---|---|---|---|---|
| | | SD (ng/mL) | %CV | SD (ng/mL) | %CV |
| **Level 1** | 46 | 1.4 | 3% | 0.0 | 0% |
| **Level 2** | 62 | 3.0 | 5% | 1.2 | 2% |
| **Level 3** | 131 | 0.0 | 0% | 3.0 | 2% |
| **Level 4** | 173 | 5.3 | 3% | 3.7 | 2% |
| **Level 5** | 217 | 5.3 | 2% | 1.7 | 1% |
| **Level 6** | 392 | 0.0 | 0% | 11 | 3% |
| **Level 7** | 404 | 0.0 | 0% | 21 | 5% |
| **Level 8** | 463 | 29 | 6% | 0.0 | 0% |

Overall, across all of the precision studies, less than 10% variability (%CV) was observed between operators, between runs, between days, between instruments and between lots.

2. Linearity:

A linearity study was conducted evaluating a 13-level dilution series where a high PSP pool (S1) sample was prepared by pooling three K3-EDTA plasma samples. The remaining 12 samples were prepared by dilution of the S1 sample with the PSP-depleted K3-EDTA plasma. Samples (7 replicates/ level) were supplemented with red blood cells to reach a 38% hematocrit (v/v) before testing. Equivalency between K3-EDTA plasma, K3-EDTA whole blood and K2-EDTA whole blood was established in a separate matrix equivalency study.

**Table 4: Linearity Study Results Summary**

| | Measured PSP [ng/ml] | SD [ng/ml] | Imprecision (%CV) | Expected PSP [ng/ml] | Deviation from Expected PSP (%) |
|---|---|---|---|---|---|
| **S1** | 2328.9 | 1134.5 | 48.7% | 2006 | 16.1 |
| **S2** | 1445.6 | 462.3 | 32.0% | 1231 | 17.4 |
| **S3** | 1026.2 | 193.2 | 18.8% | 1017 | 0.9 |
| **S4** | 825.2 | 202.5 | 24.5% | 803 | 2.8 |
| **S5** | 732.8 | 222.6 | 30.4% | 647 | 13.3 |
| **S6** | 508.3 | 67.0 | 13.2% | 508 | 0.1 |
| **S7** | 346.9 | 60.3 | 17.4% | 375 | -7.5 |
| **S8** | 301.4 | 83.0 | 27.5% | 294 | 2.5 |
| **S9** | 158.1 | 24.7 | 15.6% | 161 | -1.8 |
| **S10** | 69.8 | 6.6 | 9.4% | 75 | -6.9 |
| **S11** | 37.5 | 6.9 | 18.4% | 37 | 1.4 |
| **S12** | 20.3 | 1.7 | 8.3% | 19 | 6.8 |
| **S13** | 1.2 | 1.6 | 131.4% | 0 | N/A |

Though significant deviations were observed in S1 and S2 samples, these high concentrations are well outside the assay's claimed measuring range. A regression analysis was also performed with the best fit line having a slope of 0.994 and an intercept of 0.0 ng/ml. The data was found to be linear across the measuring range of the assay (20-600 ng/mL). The percent deviation from expected PSP concentration was found to be within ±10% for all the samples between the established measuring range (20-600 ng/mL).

3. High Dose Hook Effect

A high-dose hook effect study was conducted by evaluating samples spiked at three PSP concentrations: 10,000 ng/mL, 5,000 ng/mL, and 250 ng/mL. Test results for samples containing 5,000 ng/mL and 10,000 ng/mL indicated a PSP concentration that is above the upper limit of the assay reportable range. Thus, no hook effect was observed for the IVD CAPSULE PSP assay at high levels of PSP.

4. Analytical Specificity/Interference:

To evaluate potential interference effects on the IVD CAPSULE PSP from both endogenous and exogenous substances, eight endogenous serum substances and 29 exogenous substances were evaluated. Testing utilized a total of six reagent lots and included four operators across five devices. A substance was considered a potential interferent if the mean percent recovery of PSP in the spiked sample compared to the control sample was greater or lesser than ±10%.

To test the endogenous and exogenous substances, three $K_3$-EDTA anticoagulated plasma pools were prepared containing low, moderate, and high concentrations of PSP (51 ng/mL, 187 ng/mL, and 334 ng/mL, respectively). Aliquots of each plasma pool was prepared then stored at -80°C until use. Each exogenous substance was diluted in an appropriate diluent (ultrapure water, ethanol or DMSO) then spiked at the appropriate test concentration into a low, moderate, and high PSP plasma pool. Each pool was evaluated in replicates of 13 and compared to results from the control samples prepared with the corresponding diluent only.

During the initial interference testing, a bias of more than 10% was observed for Fentanyl (30.0 μg/dL) and total protein (15.0 g/dL). Therefore, additional interference testing was conducted by evaluating serially diluted dose response of the interferants (n=10 replicates). No interference was observed for Fentanyl at concentrations ≤ 7.50 μg/dL and total protein ≤ 7.13 g/dL.

**Table 5. Summary of Interference Study Results**

| Tested substances | Non-interfering concentration |
|---|---|
| Acetaminophen | 15.6 mg/dL |
| Acetylsalicylic acid | 3.00 mg/dL |
| Ascorbic Acid | 5.25 mg/dL |
| Azithromycin | 1.11 mg/dL |
| Caffeine | 10.8 mg/dL |
| Cefotaxime | 52.8 mg/dL |
| Celecoxib | 0.879 mg/dL |
| Cetirizine HCl | 0.435 mg/dL |
| Dextromethorphan | 1.56 μg/dL |
| Dobutamine | 0.121 mg/dL |
| Dopamine | 0.0621 mg/dL |
| Doxycycline | 1.80 mg/dL |
| Epinephrine | 0.01 μg/dL |
| Ethanol | 600.0 mg/dL |
| Furosemide | 1.59 mg/dL |
| Heparin | 330.0 Units/dL |
| Ibuprofen | 21.9 mg/dL |
| Imipenem | 33.9 mg/dL |
| Levofloxacin | 3.60 mg/dL |
| Loratadine | 8.70 μg/dL |
| Nicotine | 96.9 μg/dL |
| Norepinephrine | 0.507 μg/L |
| Oxymetazoline | 0.126 μg/dL |
| Phenylephrine | 3.0 μg/dL |
| Prednisolone | 0.12 mg/dL |
| Salmeterol | 0.273 μg/L |
| Tiotropium | 0.048 μg/L |
| Vancomycin | 12.0 mg/dL |
| Albumin, human | 6.0 g/dL |
| Bilirubin, conjugated | 40.0 mg/dL |
| Bilirubin, unconjugated | 40.0 mg/dL |
| Hemoglobin | 1000.0 mg/dL |
| Rheumatoid factor (RF) | 100 IU/ml |
| Triglycerides | 1500 g/dL |
| HAMA | 35.0 μg/dL |
| Fentanyl | 7.5 μg/dL |
| Total protein | 7.13 g/dL |

5. Assay Reportable Range:

The measuring range of the IVD CAPSULE PSP test is between 20 and 600 ng/mL of PSP. Assay results are intended to be interpreted with respect to three different risk bands for sepsis: decreased risk (<100 ng/mL PSP), slightly increased risk (100-299 ng/mL PSP), and increased risk (≥ 300 ng/mL PSP).

6. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

*Calibrator Traceability*:
An international standard or reference material for PSP is not available. IVD CAPSULE PSP is calibrated by the manufacturer using a purified preparation of recombinant human PSP (purified from *Pichia pastoris* culture by HPLC cation exchange and gel filtration chromatography) based on the mass (concentration) of the analyte present in K3-EDTA anticoagulated venous whole blood matrix. Each batch of IVD CAPSULE PSP is calibrated using a weighted 5 parameter logistic curve fit data reduction method. The instrument automatically reads in the batch-specific calibration data that are embedded within the capsule's chip, eliminating the need for calibration by the user. PSP Values assigned to the calibration materials are directly traceable to the master batch of calibrator (i.e., the primary reference material).

*Quality Controls*:
The IVD CAPSULE Control PSP is a single use kit consisting of a control solution vial that contains a known concentration of PSP that is used to perform a quality control of the IVD CAPSULE PSP on the abioSCOPE device and ensuring the accurate quantification of PSP by the user. The acceptable measurement range of the IVD CAPSULE Control PSP is indicated on the label of the primary packaging. The measured value of the abioSCOPE is compared to the lower and upper range limits. If the value is within the acceptable range, the result is displayed as "passed". If the control result is outside of the acceptable range, the result will be displayed as "failed", indicating that the test was not performed properly, or that the test reagents are not functioning properly, or that the abioSCOPE test system is not working properly. Laboratories should follow applicable regulations and guidelines regarding quality control testing frequency.

The abioSCOPE Control is a quality control capsule developed with the objective of ensuring adequate performance of the abioSCOPE instrument. The abioSCOPE Control is a capsule similar to the IVD CAPSULE PSP test except that it is provided closed and with all components already integrated within the capsule. As a self-contained capsule, the abioSCOPE Control can be re-used several times up to a limit indicated on the capsule and programmed in the RFID tag or until its expiration (also programmed in the RFID tag) whichever comes first.

*Specimen Stability*:
A specimen stability study was conducted to identify appropriate handling conditions for the blood samples before testing with the IVD CAPSULE PSP assay. Three unique K2-EDTA whole blood specimens were collected from healthy donors. Two specimens were spiked with recombinant PSP to obtain PSP concentrations around 200 ng/mL and 500 ng/mL while the PSP concentration of the third sample was approximately 80 ng/mL. Single-use aliquots were prepared and stored at 30°C to mimic ambient temperature conditions. The samples

were tested in duplicates using one lot of IVD CAPSULE PSP and three abioSCOPE 2.0 devices at 0 hr, 1 hr, 4 hr, 5 hr, 8 hr, 21 hr, 24 hr and 26 hr time points.

**Table 6. Summary of Specimen stability study**

| Time point | Donor 1 | | | Donor 2 | | | Donor 3 | | |
|---|---|---|---|---|---|---|---|---|---|
| | Mean [ng/ml] | CV [%] | RE [%] | Mean [ng/ml] | CV [%] | RE [%] | Mean [ng/ml] | CV [%] | RE [%] |
| **T0** | 68 | 14.6 | 100 | 209 | 18.3 | 100 | 545.5 | 16.5 | 100 |
| **T1** | 57 | 9.9 | 83.8 | 225 | 1.3 | 107.7 | 525.5 | 4.2 | 96.3 |
| **T4** | 64.5 | 1.1 | 94.9 | 213 | 14.6 | 101.9 | 578 | 16.4 | 106 |
| **T5** | 54.5 | 1.3 | 80.1 | 216 | 5.2 | 103.3 | 616 | 2.8 | 112.9 |
| **T8** | 67 | 14.8 | 98.5 | 243 | 4.7 | 116.3 | 485.5 | 5.4 | 89 |
| **T21** | 60.5 | 31.6 | 89 | 241 | 18.2 | 115.3 | 535 | 19.3 | 98.1 |
| **T24** | 52.5 | 31 | 77.2 | 181 | 0.8 | 86.6 | 441 | 29.5 | 80.8 |
| **T26** | 63 | 15.7 | 92.6 | 232 | 12.8 | 111 | 496.5 | 26.3 | 91 |

Percent recovery (%RE) at each time point was computed from the baseline value at T0. A linear regression analysis of %RE versus time was then conducted, and the slope of regression line evaluated for significance. If the slope was found to be statistically significant (i.e., different from 0 with $p<0.05$), then the stability claim would be based on the intersection of the 95% confidence interval of the curve with the acceptance limits (percent recoveries of either 90% or 110%). Otherwise, the stability claim would be the penultimate time point evaluated in the study. No significant slope was observed in the regression analysis indicating no significant deterioration of analyte stability over the measured interval. Thus, the data supports a stability claim of 24 hr at ambient temperature for whole blood specimens. Equivalency between K2-EDTA and K3-EDTA whole blood specimen types was established in a matrix equivalency study.

7. Detection Limit:

*Limit of blank*:
To identify the limit of blank for IVD CAPSULE PSP, K3-EDTA whole blood samples from four healthy donors was collected, homogenized, and centrifuged as per the supplier's recommendations. Red blood cells were then discarded to collect the K3-EDTA anticoagulated plasma fraction. At least 2 ml of each sample were then PSP-immunodepleted and respectively renamed PS0.1, PS0.2, PS0.3 and PS0.4. After depletion, the PSP concentration of each plasma sample was determined by using an ELISA method. The plasma samples were supplemented with red blood cells to a hematocrit level of 38% (v/v) and analyzed with the IVD CAPSULE PSP assay in duplicate. Measurements were also taken for samples without red blood cells. PSP concentrations were found less than 0.1 ng/ml (undetectable) for the four samples in both sample types, confirming the successful removal of endogenous PSP to an acceptable level.

Thereafter, the samples were tested for 3 days, 5 replicates per day, using 2 lots of IVD CAPSULE PSP, yielding a total of 120 measurements. the rank position corresponding to the 95th percentile for the distribution of blank samples was determined as the highest LoB value

from the two lots tested rounded up to the closed single digit number. Based on the study results, the LoB of the IVD CAPSULE PSP was identified as 2.6 ng/mL of PSP.

*Limit of detection*:
Five K3-EDTA plasma samples containing low concentrations of PSP supplemented with red blood cells to reach a 38% hematocrit level (v/v) were tested for 3 days, 5 replicates per day, on the abioSCOPE using two lots of IVD CAPSULE PSP. Among the 160 results, ten were excluded as invalid due to a human error (the wrong lot of IVD CAPSULE PSP was used). The limit of detection for the IVD CAPSULE PSP assay was calculated based on the remaining 150 valid results following a parametric analysis approach. The highest LoD value between the two lots tested was considered and rounded up to the closed single digit number. Thus, the LoD of the IVD CAPSULE PSP assay was calculated as 9.4 ng/mL.

*Limit of quantitation*:
Two K3-EDTA anticoagulated PSP-immunodepleted ('blank') plasma lots were spiked with recombinant PSP to five levels spanning a concentration range of 12 to 23 ng/mL. The ten spiked panels were supplemented with red blood cells to reach a 38% hematocrit level (v/v) and were run in replicates of five, with one run per day, for five days, using three lots of IVD CAPSULE PSP, and two calibrator lots across two analyzers.

As the IVD CAPSULE PSP lots were calibrated with two batches of calibrators, two sets of calibration parameters were available: the results obtained during the study were back-calculated directly by the abioSCOPE 2.0 onto calibration parameters of the first lot of calibrator. For the other lot, the raw data of the measurements were extracted from the abioSCOPE and back calculated using the parameters of the calibration fit. The mean PSP concentrations and imprecision (%CV) were computed for each PSP concentration level and per lots of IVD CAPSULE PSP. The %CV were then plotted against the mean PSP concentrations with a fitted line to determine the PSP concentration where the upper 95% confidence level crosses the %CV = 20 limit. As described in the CLSI guideline EP17-A2, the LoQ of the IVD CAPSULE PSP was determined as the highest % CV among the three reagent lots, which is 17 ng/mL.

8. Assay Cut-Off:

See section VII.D Clinical Cut-off below.

9. Carry-Over:

Samples containing two different PSP concentrations (Low: approximately 100 ng/mL; High: approximately 450 ng/mL) were prepared by spiking human recombinant PSP in PSP-depleted K3-EDTA anticoagulated plasma. The samples were tested on a single IVD CAPSULE PSP lot and on 3 different abioSCOPE devices. For each abioSCOPE instrument, the first run was performed where both doses were measured one after the other in 10 consecutive replicates. Then, a second run was performed where both doses were re-measured in 10 replicates in an alternating manner to detect potential sample carryover issues. All measurements on each abioSCOPE were performed by the same operator and on the same day. The test measurement procedure followed the instructions for use of the IVD CAPSULE PSP product and the abioSCOPE 2.0.

**Table-7: Summary of Carry-over Study Results**

| | Run# | Sample ID | Mean PSP [ng/ml] | SD [ng/ml] | CV [%] |
|---|---|---|---|---|---|
| **Analyzer#1** | 1 | Low | 122.5 | 15.1 | 12.3 |
| | 1 | High | 451.9 | 52 | 11.5 |
| | 2 | Low | 112.2 | 6.7 | 6 |
| | 2 | High | 437.5 | 62.1 | 14.2 |
| **Analyzer#2** | 1 | Low | 123.2 | 6.7 | 5.4 |
| | 1 | High | 388 | 62.4 | 16.1 |
| | 2 | Low | 116.4 | 6.1 | 5.2 |
| | 2 | High | 387.5 | 65 | 16.8 |
| **Analyzer#3** | 1 | Low | 124.5 | 6.5 | 5.2 |
| | 1 | High | 465 | 66.5 | 14.3 |
| | 2 | Low | 123.3 | 12.3 | 10 |
| | 2 | High | 462.3 | 83.6 | 18.1 |

For both runs evaluated, no significant difference was observed in PSP measurements for either the high or low PSP specimens. These data support that no carry over occurs in the abioSCOPE instrument with the IVD CAPSULE PSP assay cartridges.

## B Comparison Studies:

1. Method Comparison with Predicate Device:

   Not applicable.

2. Matrix Comparison:

   A study was conducted to establish equivalent performance of IVD CAPSULE PSP assay with venous K2-EDTA whole blood, K3-EDTA whole blood and K3-EDTA plasma specimen types. This study supported the use of alternative sample matrices in some analytical studies. Fifty-one unique matched venous K2-EDTA and K3-EDTA whole blood specimens were collected for this study. An aliquot of each K3-EDTA whole blood specimen was also used to isolate matched K3-EDTA plasma specimens. The samples from each donor were tested in duplicates on the same day as the respective blood collections using one lot of IVD CAPSULE PSP reagents and three abioSCOPE 2.0 devices.

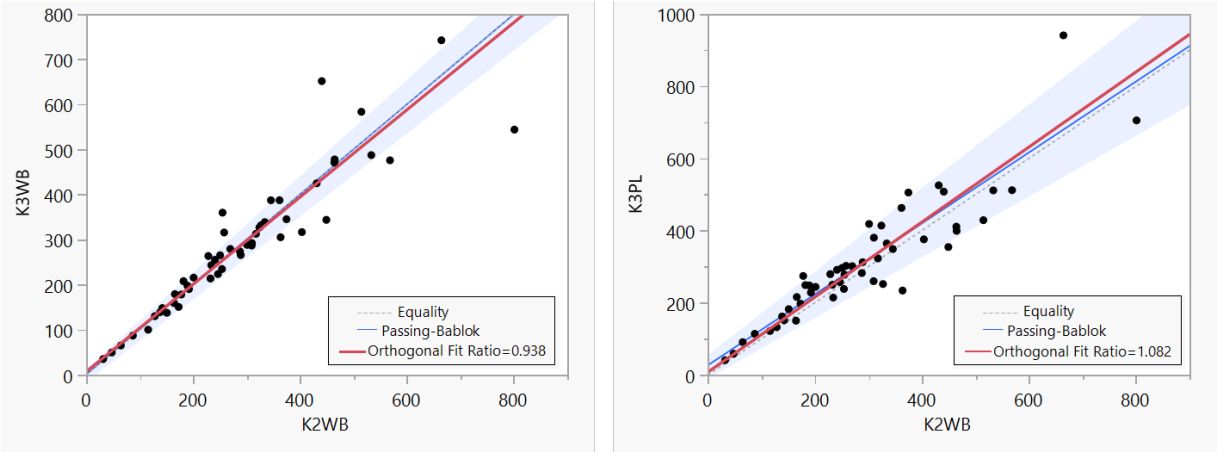


**Figure 1: Regression analysis Scatter plot for different matrices in comparison to venous K2-EDTA whole blood**

Potential differences in assay measurements across different matrices were assessed by Passing/Bablok regression analysis. The Pearson correlation coefficient for K3-EDTA whole blood when compared to K2-EDTA whole blood was 0.92 with a slope of 1.0 (95% CI: 0.92-1.17) and intercept of 0.68 (95% CI: -16.73 – 12.99). The Pearson correlation coefficient of K3-EDTA plasma when compared to K2-EDTA whole blood was 0.91 with a slope of 0.98 (95% CI: 0.84-1.16) and intercept of 26.6 (95% CI: -10.73 – 54.82).

Another study was conducted to establish equivalent performance of IVD CAPSULE PSP assay for both venous and arterial K2-EDTA whole blood sample types. Matched venous and arterial K2-EDTA whole blood sample pairs were collected from 33 patients. The samples from each donor were tested in triplicate using one lot of IVD CAPSULE PSP and four abioSCOPE 2.0 devices. The Pearson correlation coefficient for arterial K3-EDTA whole blood was found to be 0.99 (slope = 1.04 (95% CI: 0.98-1.14); Intercept = 0.33 (95% CI: -11.82 – 8.59)) in comparison to venous K3-EDTA whole blood.

Overall, the data from the matrix equivalency studies was found acceptable to support equivalent performance of claimed sample types (i.e., use of venous and arterial K2-EDTA anticoagulant whole blood samples and venous K3-EDTA anticoagulant whole blood samples).

## C Clinical Studies:

1. Clinical Sensitivity:

The clinical performance of the IVD CAPSULE PSP assay was evaluated in a multicenter, blinded, observational, prospective clinical study (Clinicaltrials.gov identifier: NCT04105699) across 6 different sites in the U.S. The primary objective of this study was to validate the ability of the IVD CAPSULE PSP assay when performed on the first day of a participant's ICU admission to correctly identify those with sepsis, manifesting within the first three days of testing. For the comparator, patients were identified as having sepsis based on external independent review committee (EIRC) assessment (i.e., physician adjudication). In this analysis, experts were blinded to procalcitonin (PCT) values.

A total of 497 patients admitted to the ICU were enrolled in the study based on the following inclusion and exclusion criteria:

Study inclusion criteria were as follows:

1. Provision and understanding of signed and dated written informed consent by patient or legally designated representative prior to any mandatory study-specific procedures, sample collection, or analysis.
2. Male or female, aged ≥ 18 years
3. Admitted to ICU on the day of screening, with expectation that patient will require ICU management for a minimum of 24 hours.

Study exclusion criteria were as follows:

1. Expected to die within 24 hours no matter what therapy is given, from the time of screening.
2. Suffering on ICU admission or study entry from or known acute or chronic pancreatitis or pancreatic cancer.
3. Admitted to ICU due to elective cardiac surgery with an uncomplicated stay anticipated.
4. Patients having a valid Do Not Resuscitate order.
5. Previous ICU admission during this hospital stay.
6. Confirmed COVID-19 as reason for ICU admission.

Tables 8 and 9 below summarize the subject demographics of the study population (N = 497). Of the 497 subjects in the study, 220 (44.3%%) were females and 277 (55.7%) were males. The mean age of subjects was 59.7±16.38 and ranged between 18 and 100 years. Most subjects were white (83.3%), followed by black or African American (11.3%). The most common reason for ICU admission was observed to be respiratory failure (16.3%). Based on the comparator of physician adjudication, 241 (48.5%) of subjects were diagnosed with sepsis. Age, sex and race were comparable between those adjudicated with sepsis and those without sepsis.

**Table 8: Clinical Study Cohort Demographic Distribution**

| | **Total Population N = 497** | **Physician Adjudication Result** | |
|---|---|---|---|
| | | **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) |
| 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 | 0.0% (0/497) | 0.0% (0/241) | 0.0% (0/256) |

| | | | |
|---|---|---|---|
| Islander | | | |
| 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) |
| **Ethnicity** | | | |
| Hispanic or Latino | 4.2% (21/497) | 5.4% (13/241) | 3.1% (8/256) |
| Not Hispanic or Latino | 88.7% (441/497) | 90.0% (217/241) | 87.5% (224/256) |
| Unknown/Not Reported | 7.0% (35/497) | 4.6% (11/241) | 9.4% (24/256) |
| *Subjects could report more than one race so numbers may be greater than the total. | | | |

**Table 9: Clinical Study Cohort: Reason for ICU admission**

| Reason for ICU Admission | Total Population N = 497 | Physician Adjudication Result | |
|---|---|---|---|
| | | Sepsis N = 241 | No Sepsis N = 256 |
| Alteration in mental status | 6.4% (32/497) | 8.7% (21/241) | 4.3% (11/256) |
| Hematologic problems | 3.6% (18/497) | 0.8% (2/241) | 6.3% (16/256) |
| Hemodynamic disorders | 4.0% (20/497) | 4.1% (10/241) | 3.9% (10/256) |
| Hepatic problems | 0.8% (4/497) | 1.2% (3/241) | 0.4% (1/256) |
| Infection | 7.0% (35/497) | 12.4% (30/241) | 2.0% (5/256) |
| Investigator decision | 0.4% (2/497) | 0.4% (1/241) | 0.4% (1/256) |
| Mechanical ventilation | 1.4% (7/497) | 2.1% (5/241) | 0.8% (2/256) |
| Metabolic problems | 2.0% (10/497) | 0.8% (2/241) | 3.1% (8/256) |
| Need for telemetry | 0.4% (2/497) | 0.4% (1/241) | 0.4% (1/256) |
| Neurological problems | 3.4% (17/497) | 1.7% (4/241) | 5.1% (13/256) |
| Refeeding survey | 0.0% (0/497) | 0.0% (0/241) | 0.0% (0/256) |
| 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) |
| Surgical complications and/or wound care | 3.0% (15/497) | 2.9% (7/241) | 3.1% (8/256) |
| Vasopressor support | 3.8% (19/497) | 7.5% (18/241) | 0.4% (1/256) |
| Voluntary drug intoxication | 0.2% (1/497) | 0.0% (0/241) | 0.4% (1/256) |
| Other | 36.6% (182/497) | 33.2% (80/241) | 39.8% (102/256) |
| Missing | 0.0% (0/497) | 0.0% (0/241) | 0.0% (0/256) |

The clinical study results indicate a statistically significant association between the IVD CAPSULE PSP assay result and the increasing probability of sepsis across each PSP concentration bin. The Likelihood Ratios (LR) in were calculated using the standard definition where LR equals the probability that an individual at risk of developing sepsis has the test result divided by the probability that an individual without the risk of developing sepsis has the test result. This formula was applied to each PSP concentration bin separately.

The predictive values of IVD CAPSULE PSP test results depend upon the prevalence of sepsis in the patient population. Laboratories and other users should establish their own

reference intervals for their patient populations using the IVD CAPSULE PSP test considering other potential sources of variability, such as patient gender, race, and age.

**Table 10: Clinical Performance Summary: Association of IVD CAPSULE PSP results with Sepsis Risk**

| PSP concentration | Physician Adjudication | | | Risk (PV) | Percent of results | Likelihood ratio | Lower bound of 95%CI | Upper bound of 95%CI |
|---|---|---|---|---|---|---|---|---|
| | Sepsis | No Sepsis | Total | | | | | |
| **≥300 ng/mL** | 103 | 44 | 147 | 70.10% | 29.60% | 2.49 | 1.83 | 3.38 |
| **100-299 ng/mL** | 88 | 71 | 159 | 55.30% | 32.00% | 1.32 | 1.02 | 1.71 |
| **<100 ng/mL** | 50 | 141 | 191 | 26.20% | 38.40% | 0.38 | 0.29 | 0.49 |
| **Total** | 241 | 256 | 497 | Prevalence =48.5% | | | | |

**Table 11: Interpretation of Sepsis Risk Based on PSP Concentration**

| PSP Concentration | Result Interpretation |
|---|---|
| ≥300 ng/mL | Increased risk |
| 100-299 ng/mL | Slightly increased risk |
| <100 ng/mL | Decreased risk |

**Table 12: Stratification of Assay Results Compared to Physician Adjudication by Patient Demographic Group**

| Race | N | PSP concentration Bin | | | | | |
|---|---|---|---|---|---|---|---|
| | | <100 ng/mL | | 100-299 ng/mL | | ≥300 ng/mL | |
| | | Sepsis | No sepsis | Sepsis | No sepsis | Sepsis | No sepsis |
| **Asian** | 5 | 1 | 1 | 0 | 1 | 1 | 1 |
| **Black** | 56 | 6 | 18 | 8 | 5 | 11 | 8 |
| **White** | 414 | 40 | 117 | 76 | 60 | 87 | 34 |
| **Hispanic or Latino** | 21 | 1 | 3 | 3 | 3 | 9 | 2 |

**Table 13: Stratification of Assay Results Compared to Physician Adjudication by PCT Measurements**

| PCT values (ng/mL) | N | PSP concentration Bin | | | | | |
|---|---|---|---|---|---|---|---|
| | | <100 ng/mL | | 100-299 ng/mL | | ≥300 ng/mL | |
| | | Sepsis | No sepsis | Sepsis | No sepsis | Sepsis | No sepsis |
| **<0.5** | 258 | 25 | 111 | 26 | 56 | 18 | 22 |
| **0.5<PCT<2.0** | 87 | 9 | 20 | 18 | 7 | 22 | 11 |
| **>2.0** | 151 | 16 | 10 | 44 | 7 | 63 | 11 |
| **Total** | 496 | 50 | 141 | 88 | 70 | 103 | 44 |

7. Clinical Specificity:

See Section VII.C Clinical Sensitivity above.

8. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

A generally healthy adult population including 211 subjects representative of the U.S. demographics was enrolled in a study to determine the reference range interval of PSP values measured using the IVD CAPSULE PSP assay(Clinicaltrials.gov identifier: NCT04409561 and NCT05849935). The inclusion and exclusion criteria for the prospective study are listed below:

Study inclusion criteria were as follows:

1. Male or female, aged ≥ 18 years.
2. Apparently healthy as determined by a subject questionnaire.
   Note: there were no special preanalytical factors to consider before the study procedure (i.e., no need of fasting or rest period before sample collection).

Study exclusion criteria were as follows:

1. Current diagnosis, or history, of any underlying major medical condition determined by the investigator, including but not limited to:
   a. renal disease
   b. Stroke
   c. Liver disease
   d. Pancreatic disease (including diabetes)
   e. Chronic obstructive pulmonary disorder
   f. Hypercalcitoninemia
   g. HIV AIDS
   h. Receiving antibiotic therapy
   i. Suspected infection
   j. Immunosuppression
   k. Heart disease
   l. Heart failure
   m. Bleeding disorders
2. Underwent procedures related to sepsis, or diagnosed with sepsis, within the last 12 months
3. Current diagnosis of uncontrolled:
   a. Hypertension,
   b. Hypotension, or
   c. Diabetes
4. Diagnosis of bacterial, fungal, or malaria infection within the last 3 months that required antimicrobial treatment
5. Experienced severe trauma, surgery, cardiac arrest, or severe burn within the previous 3 months requiring medical care
6. Diagnosis of cancer within the last 12 months
7. Received immunotherapy to stimulate or inhibit cytokines within the last 12 months
8. Hospitalization for more than 24 hours within the last 1-3 months

9. Reported as currently pregnant or nursing a child
10. Unable or unwilling to provide the required blood sample for testing
11. Any other criteria that, in the opinion of the investigator, would render the participant unsuitable for inclusion in the trial. For instance, if the investigator did not consider the patient as relatively healthy.

**Table 14: Reference Range Study Population Demographics**

| | **Study Population N = 211** |
|---|---|
| **Age, years** | |
| Mean ± SD (N) | 49.3 ± 16.33 (211) |
| Median (Min, Max) | 52.0 (18.0, 88.00) |
| **Age Group** | |
| <60 | 67.8% (143/211) |
| >60 | 32.2% (68/211) |
| **Gender** | |
| Male | 34.6% (73/211) |
| Female | 65.4% (138/211) |
| **Race*** | |
| American Indian or Alaska Native | 0.5% (1/211) |
| Asian | 7.6% (16/211) |
| African American | 14.7% (31/211) |
| Native Hawaiian or Other Pacific Islander | 0.0% (0/211) |
| Caucasian | 77.3% (163/211) |
| Other | 0.5% (1/211) |
| Unknown | 0.5% (1/211) |
| **Ethnicity** | |
| Hispanic or Latino | 2.8% (6/211) |
| Not Hispanic or Latino | 94.3% (199/211) |
| Unknown | 2.8% (6/211) |
| *Subjects could report more than one race so numbers may be greater than the total. | |

According to the CLSI guideline EP28, lower limit of the reference interval corresponds to the 2.5th percentile and the upper limit corresponds to the 97.5th percentile. The reference interval for the PSP concentration in blood samples of generally healthy adults representative of the U.S. population was found to be 28.7 ng/mL (90% CI: 25.8 - 31.9) and the upper limit of the reference interval was found to be 228.3 ng/mL (90% CI: 204.7 - 255.4), with mean and median values of 96.8 ng/mL and 81.0 ng/mL, respectively.

Overall, PSP values exhibited a variability of less than 10% across different ethnicities and genders, suggesting that these factors did not significantly contribute to differences between subgroups. However, when considering age, PSP values were higher in the 60+ age group compared to the younger age group (median PSP value ≥ 60 Years of Age: 93.5 ng/ml vs Median PSP value < 60 Years of Age: 69.0 ng/ml).

**Table 15: PSP value and Reference Interval**

| | Study Population N = 211 | |
|---|---|---|
| | **Mean Value** | **95% Reference Interval** |
| PSP Value | 96.8 | 88.8 - 104.8 |
| | **Median Value** | **Q1, Q3** |
| | 81.0 | 60.0, 114.0 |
| | **Reference Interval** | **90% CI** |
| Lower Limit of Reference Interval | 28.7 | 25.8 - 31.9 |
| Upper Limit of Reference Interval | 228.3 | 204.7 - 255.4 |

**Table 16: PSP value Distribution by Race (Reference Range Study)**

| | Study population N = 211 | |
|---|---|---|
| **Asian** | **Mean Value** | **95% Reference Interval** |
| PSP Value | 70.4 | 54.2 - 86.6 |
| | **Median Value** | **Q1, Q3** |
| | 67.5 | 43.5 - 90.5 |
| | **Reference Interval** | **90% CI** |
| Lower Limit of Reference Interval | 24.7 | 18.5 - 35.4 |
| Upper Limit of Reference Interval | 167.8 | 117.5 - 218.5 |
| | | |
| **African American** | **Mean Value** | **95% Reference Interval** |
| PSP Value | 90.2 | 67.0 - 113.4 |
| | **Median Value** | **Q1, Q3** |
| | 67.0 | 54.0 - 112.0 |
| | **Reference Interval** | **90% CI** |
| Lower Limit of Reference Interval | 20.2 | 15.4 - 28.7 |
| Upper Limit of Reference Interval | 248.0 | 171.3 - 359.9 |
| | | |
| **Caucasian** | **Mean Value** | **95% Reference Interval** |
| PSP Value | 100.3 | 91.0 - 109.5 |
| | **Median Value** | **Q1, Q3** |
| | 84.0 | 61.0 - 124.0 |
| | **Reference Interval** | **90% CI** |
| Lower Limit of Reference Interval | 30.3 | 27.2 - 34.2 |
| Upper Limit of Reference Interval | 233.4 | 205.5 - 264.1 |
| | | |
| **Other/Unknown*** | **Mean Value** | **95% Reference Interval** |
| PSP Value | 86.3 | -40.0 - 212.6 |
| | **Median Value** | **Q1, Q3** |
| | 59.0 | 55.0 - 145.0 |
| | **Reference Interval** | **90% CI** |

| | | |
|---|---|---|
| Lower Limit of Reference Interval | N/A | N/A |
| Upper Limit of Reference Interval | N/A | N/A |
| *Analysis for American Indian/Alaska Native, Other, and Unknown race groups combined together. | | |

**Table 17: PSP Value Distribution by Age (Reference Range Study)**

| | Study Population N = 211 | |
|---|---|---|
| **<60 Years of Age** | **Mean Value** | **95% Reference Interval** |
| PSP Value | 90.7 | 80.8 - 100.5 |
| | **Median Value** | **Q1, Q3** |
| | 70.0 | 55.0 - 110.0 |
| | **Reference Interval** | **90% CI** |
| Lower Limit of Reference Interval | 24.5 | 21.8 - 28.2 |
| Upper Limit of Reference Interval | 219.9 | 188.6 - 254.8 |
| | | |
| **60 Years of Age or Older** | **Mean Value** | **95% Reference Interval** |
| PSP Value | 109.8 | 96.3 - 123.2 |
| | **Median Value** | **Q1, Q3** |
| | 97.0 | 69.0 - 127.5 |
| | **Reference Interval** | **90% CI** |
| Lower Limit of Reference Interval | 39.6 | 34.9 - 46.2 |
| Upper Limit of Reference Interval | 230.4 | 193.4 - 273.3 |

## D Clinical Cut-Off:

The following IVD CAPSULE PSP interpretation tables are supported by the results from the prospective observational multi-site clinical study (specifically Tables 12 and 13 above).

**Table 18: Recommendations for Interpretations of IVD CAPSULE PSP Values**

| PSP concentration | Sepsis Risk Interpretation | Bin Sepsis Prevalence | Percent of results | Sepsis Likelihood ratio | Lower bound of 95%CI | Upper bound of 95%CI |
|---|---|---|---|---|---|---|
| **≥300 ng/mL** | Increased Risk | 64.90% | 29.60% | 2.49 | 1.84 | 3.39 |
| **100-299 ng/mL** | Slightly Increased Risk | 54.20% | 32.00% | 1.32 | 1.02 | 1.71 |
| **<100 ng/mL** | Decreased Risk | 26.20% | 38.40% | 0.38 | 0.29 | 0.49 |
| | | Study Sepsis Prevalence = 48.5% | | | | |

## E Expected Values/Reference Range:

See Clinical cut-off. Predictive values depend on the likelihood ratios and the prevalence of disease. It is recommended that each laboratory using the IVD CAPSULE PSP test establishes

their own reference intervals based on the clinical practice as well as potential sources of variability in the population it serves, such as patient gender, race, or age.

### F Other Supportive Instrument Performance Characteristics Data:

Not applicable.

## VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

## IX Conclusion:

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