IVD CAPSULE PSP - Instructions for Use (IFU)

REF P02.00026

English

Intended use

The **IVD CAPSULE PSP** is a single use, rapid in vitro diagnostic test for the quantitative measurement of pancreatic stone protein (PSP) in human capillary whole blood as well as in K_2-EDTA, K_3-EDTA and lithium heparin anticoagulated venous whole blood.

The **IVD CAPSULE PSP** is to be used with the **abioSCOPE** 2.0 in vitro diagnostic test system. The system is intended for professional use in clinical laboratory settings or point of care (PoC) locations including near-patient testing.

The **IVD CAPSULE PSP** is used in conjunction with other clinical assessments and laboratory findings to aid in the early recognition of sepsis in adults.

Summary

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection[1]. According to a recent study, an estimated **48.9 million incident cases of sepsis** were recorded worldwide in 2017, and **11.0 million sepsis-related deaths** were reported during the same period, accounting for approximately one death out of five [2]. Moreover, patients who survive sepsis often have long-term disabilities that result in impaired quality of life [3].

PSP is a small protein mainly secreted by the acinar cells of the pancreas that activates neutrophil granulocytes [4]. PSP levels allow to diagnose severe infection in adults [5]. In ICUs, PSP efficiently discriminates between sepsis and infection or inflammation whose aetiology is not related to infection [6]. PSP continuously increases during the three days preceding the clinical diagnosis of a sepsis [7]. Amongst septic patients, PSP demonstrates a high correlation with the prognosis of mortality[8,9].

Test principle

The blood sample is mixed with a solution composed of fluorescently labelled antibodies reactive to human PSP. The blood sample, now containing the PSP-antibody complex, is loaded onto the capsule of the kit.

Patient material is passively 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 antibodies immobilized on the capsule's read-out area.

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 instrument automatically calculates the concentration of each sample and displays it on the instrument screen in ng/ml.

Reagents

Each assay includes one vial containing 50 µl of the **abioMIX** reagent. The **abioMIX** reagent is composed of the fluorescently labelled anti-human PSP antibody, dissolved in a phosphate buffered saline solution supplemented with bovine serum albumin, Tween-20 and ProClin300 preservative (Table 1).

Ingredient	Concentration
Fluorescently labelled anti-human PSP antibody	4.00 µg/ml
Bovine serum albumin	0.1% (w/v)
Tween® 20 (CAS number 9005-64-5)	0.5% (v/v)
ProClin™300	0.04% (v/v)

Table 1| Composition of the **abioMIX** reagent.

Materials included

- 1x PSP capsule
- 1x vial of **abioMIX** reagent
- 1x capillary blood collector (**abioPIPETTE**)
- 1x desiccant bag
- 1 x printed Instructions for Use (IFU)

Not included Accessories

- IVD CAPSULE Control PSP (control material, REF P02.00040)

Sample collection and handling

Capillary whole blood is collected by pricking a finger. After puncturing the fingertip according to the product insert of the finger pricking device (e.g., a lancet), wipe away the first drop of blood. Then, form a droplet of blood on the finger while gently squeezing the finger near the puncture. Touch the droplet of blood with tip of the provided **abioPIPETTE** while holding it horizontally and let the capillary tip draw the blood inside. Repeat the formation of a new droplet and the **abioPIPETTE** filling procedure as needed until the blood reaches the white membrane (filling stops automatically when a metered volume of 50µl is reached). After filling, turn the plunger clockwise by one quarter to activate the **abioPIPETTE.**

Venous whole blood is collected in designated K_2- or K_3-EDTA or lithium heparin blood tubes by venous puncture and anticoagulated according to the manufacturer's protocol. Prepare a K_2- or K_3-EDTA or Li-heparin anti-coagulated blood tube. Turn the plunger clockwise by one quarter to activate the provided **abioPIPETTE**. Outside the test tube press on the **abioPIPETTE**'s plunger and maintain the pressure. Insert the **abioPIPETTE** into the tube. Release the plunger to completely fill the **abioPIPETTE** with blood and then remove it. 50µl of blood are loaded.

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Test procedures

1. Use the **abioPIPETTE** filled with 50 µl of (capillary or venous) whole blood that was collected according to "**Sample collection and handling**".
2. Pick up the **abioMIX** vial and flick it to move the **abioMIX** down to the bottom before use. Pierce the cap with the tip of the filled **abioPIPETTE** without pushing the plunger and insert it fully into the vial. Next, push on the **abioPIPETTE**'s plunger to dispense the entire blood sample into the **abioMIX** reagent vial. Hold the pressure on the plunger of the **abioPIPETTE** and remove the **abioPIPETTE.** The plunger can be released outside of the vial.
3. Tap the vial at least 10 times on a hard surface to mix thoroughly the blood-**abioMIX** solution and proceed immediately to the next step (***note**: a well-mixed sample will have a homogenous color*).
4. Outside the vial, push down the plunger completely and hold the pressure. Insert the **abioPIPETTE** as far as possible into the vial. Release the plunger to completely fill the **abioPIPETTE** with the mix and remove the **abioPIPETTE**. Press the plunger gently to deposit the mixture evenly on the entire surface of the membrane (white area) in the center of the capsule. The mixture should be dispensed slowly to allow the solution to wick into the capsule. Ensure that the pipette tip does not scrape the membrane.
5. Fold the lid over to close the capsule. Hold the capsule only by the edges. Be careful not to touch the bottom side of the capsule.
6. To start the measurement, touch the button "measure" on the **abioSCOPE** reader. The tray will open automatically.

   Place the capsule onto the tray according to the guided capsule position on the screen, then touch the button "close tray".

To measure the sample, refer to the **abioSCOPE 2.0** User Manual.

Storage and stability

Store at 2-8 °C until the expiry date printed on the label. Allow the **IVD CAPSULE PSP** and the **abioMIX** to equilibrate to room temperature before opening and use immediately after. The maximum stay at room temperature after opening must not exceed 3 hours.

The blood sample mixed with the **abioMIX** reagent should be immediately loaded onto the PSP capsule and the filled capsule immediately measured.

Sample stability

It is preferred to analyse the samples as soon as possible, but EDTA anticoagulated whole blood is stable for 24 hours at room temperature (20 to 25 °C).

Traceability and calibration

IVD CAPSULE PSP is calibrated by the manufacturer using a purified preparation of recombinant human PSP based on the mass (concentration) of the analyte present in K_3-EDTA anticoagulated venous whole blood matrix. Each lot of **IVD CAPSULE PSP** is calibrated using a weighted 5 parameter logistic curve fit data reduction method. The instrument automatically reads in the lot-specific calibration data that are embedded within the capsule's chip, eliminating the need for calibration by the user. PSP values assigned to controls and calibration materials are directly traceable to a master lot of calibrators.

Quality control

For quality control, use the **IVD CAPSULE Control PSP.** Follow the applicable local regulations and guidelines for quality control.

The control intervals should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined target range. Each laboratory should establish corrective measures to be taken if values fall outside of the defined ranges.

Warnings and precautions

- For in vitro diagnostic use.
- The **IVD CAPSULE PSP** must be kept refrigerated until use.
- Do not freeze.
- Make sure that all packaging is intact. Do not use the test if the blister packaging is visibly damaged.
- Patients suffering from acute pancreatitis have increased levels of PSP.
- Allow the **abioMIX** reagent vial to reach room temperature before use.
- This product requires the handling of human specimens. It is recommended that all human-sourced material be considered potentially infectious. Universal precautions that apply to the user's facility should be applied for handling and disposal of materials during and after testing [10].
- Do not use reagents after the expiry date printed on the box.
- Incubation of the specimen in the **abioMIX** for more than 5 minutes may impact test results.
- If the whole blood sample is not immediately analysed, it is important to homogenize the sample (i.e., ensure the resuspension of the blood cells) before performing the test.

Reagent deterioration

The following observations indicate reagent deterioration, and this kit should not be used:

- Presence of turbidity in the **abioMIX** vial.

- Consistently high or low values from assay kits from the same batch.

Limitations

- Test results should be interpreted within the complete clinical picture. Definitive diagnosis and/or clinical decision should not be based solely on the results of any single diagnostic test but made after all clinical and laboratory findings are evaluated.
- Clinically elevated total protein level may interfere with test results.
- Grossly haemolytic, icteric, or grossly lipemic specimen may interfere with test results at clinically elevated concentrations.
- All assay materials are single-use and cannot be re-used or transferred to another kit.

The user shall report any serious incident that has occurred in relation to the device to the manufacturer and the relevant national competent authority.

Expected values

The normal PSP concentration [ng/ml] range in adults was determined by the manufacturer on an adult population. Results are provided in Table 2.

Mean	44 ng/ml
Median	42 ng/ml
5-95% percentiles	27 – 61 ng/ml
Lowest / Highest value	23 / 74 ng/ml

Table 2| Normal PSP values. Values are from 40 healthy donors (Male/Female (%): 50/50, Caucasian/African American /Hispanic (%): 57/35/8).

Normal PSP values are not influenced by age, gender or ethnicity/race. It is recommended that each laboratory establishes its own expected reference range for the population it serves.

Measuring range: 20 - 600 ng/ml

The linear range of the assay was determined by diluting a pool of samples with clinically elevated PSP level in a PSP-depleted sample to obtain concentrations spanning the entire assay range (24 to 670 ng/ml of PSP). Regression analysis demonstrated that the assay response was linear with an R^2 value of 0.98, a slope of 0.99 and an intercept of 6.37 in this range. The analytical sensitivity study demonstrated a limit of blank (LoB) of 2.6 ng/ml, a limit of detection (LoD) of 9.4 ng/ml and a limit of quantification (LoQ) of 17.0 ng/ml.

PSP concentrations below 20 ng/ml are reported as "< 20 ng/ml", and values above 600 ng/ml are reported as "> 600 ng/ml".

Linearity was established in accordance with the recommendation of the CLSI document EP06, 2nd edition [11], and the LoB, LoD and LoQ with EP17-A2 [12].

The **IVD CAPSULE PSP** showed no high-dose effect ("prozone effect", "Hook effect") at concentrations below 10'000 ng/ml (this was the highest tested PSP concentration) for K_3-EDTA anticoagulated whole blood.

Precision

The between-run, between-day and repeatability were measured with 2 runs of two replicates per day, for 20 days, with 8 samples covering the assay reportable range of the **IVD CAPSULE PSP** on the **abioSCOPE** 2.0 (Table 3).

PSP level	Mean value [ng/ml]	Between-run CV	Between-day CV
Level 1	46	0 %	3 %
Level 2	62	2 %	5 %
Level 3	131	2 %	0 %
Level 4	173	2 %	3 %
Level 5	217	1 %	2 %
Level 6	392	3 %	0 %
Level 7	404	5 %	0 %
Level 8	463	0 %	6 %

Table 3| Summary of the 20 days precision study.

In another study performed in the ICU with trained healthcare professionals, the between-site and between-user precision variance components have been determined in a 3 x 5 x 5 scheme, where "3" is the sites or users, "5" the days and the replicate measurements per day. This study was performed on 3 samples with low, intermediate, and high PSP concentration (Table 4).

PSP level	Mean value [ng/ml]	Between-users CV	Repeat-ability CV	Mean value [ng/ml]	Between-sites CV
Level 1	72	6%	13 %	72	5%
Level 2	235	0%	11 %	245	5%
Level 3	669	8%	18 %	646	0%

Table 4| Between-users, repeatability and between-sites precision determined in the ICU.

All the precision studies were designed, executed, and analysed in accordance with the recommendations of the CLSI document EP05-A3 [13].

For practical reasons, these studies were performed with K_2-EDTA plasma samples. The within device precision of K_2-EDTA anticoagulated whole blood and matching plasma has been verified and found to be similar.

Analytical selectivity

The substances listed below were tested for interference. Each substance was tested at a clinically elevated concentration, on three PSP samples covering the low, intermediate (near the medical decision point) and high range of the assay. Analytical selectivity was established in accordance with the recommendation of the CLSI document EP07, 3rd edition [14] and its supplement EP37, 1st edition [15].

No interference was observed at these concentrations (the mean bias across the three PSP samples was within +/- 10%) (Table 5).

Substance	Concentration
Acetaminophen	1.56E+01 mg/dl
Acetylsalicylic acid	3.00E+00 mg/dl
Ascorbic Acid	5.25E+00 mg/dl
Azithromycin	1.11E+00 mg/dl
Caffeine	1.08E+01 mg/dl
Cefotaxime	5.28E+01 mg/dl
Celecoxib	8.79E-01 mg/dl
Cetirizine HCl	4.35E-01 mg/dl
Dextromethorphan	1.56E-03 mg/dl
Dobutamine	1.21E-01 mg/dl
Dopamine	6.21E-02 mg/dl
Doxycycline	1.80E+00 mg/dl
Epinephrine	1.00E-05 mg/dl
Ethanol	6.00E+02 mg/dl
Fentanyl	3.00E-02 mg/dl
Furosemide	1.59E+00 mg/dl
Heparin	3.30E+02 Units/dl
Ibuprofen	2.19E+01 mg/dl
Imipenem	3.39E+01 mg/dl
Levofloxacin	3.60E+00 mg/dl
Loratadine	8.70E-03 mg/dl
Nicotine	9.69E-02 mg/dl
Norepinephrine	5.07E-05 mg/dl
Oxymetazoline	1.26E-04 mg/dl
Phenylephrine	3.00E-03 mg/dl
Prednisolone	1.20E-01 mg/dl
Salmeterol	2.73E-05 mg/dl
Tiotropium	4.80E-06 mg/dl
Vancomycin	1.20E+01 mg/dl
Albumin, human	6.00E+00 g/dl
Bilirubin, conjugated	4.00E+01 mg/dl
Bilirubin, unconjugated	4.00E+01 mg/dl
Haemoglobin	1.00E+03 mg/dl
Triglycerides	1.50E+03 g/dl

Table 5| Test substances (exogenous and endogenous) and their concentrations.

Only a high total protein content was found to bias test results by more than 10% (Table 6).

Substance	Concentration
Total protein	1.50E+01 g/dl

Table 6| Substance that showed a significant bias at the tested concentration.

Rheumatoid Factor (RF) and Human anti-mouse antibodies (HAMA) solutions were prepared by adding concentrated rheumatoid and HAMA solutions to human whole blood samples. No bias outside the +/- 10% acceptance limit was found at 3.50E-02 mg/dl of HAMA and 100 IU/ml of RF.

Although precautions have been taken to minimize interference caused by heterophilic antibodies, erroneous results caused by interferences can be observed. For diagnostic purposes, the results should always be compared to the patient's medical history, clinical signs, and other findings.

Diagnostic performances

The association of PSP with the development of sepsis has been demonstrated in a multicentric, prospective, observational clinical study (AB-PSP-001; NCT03474809) [6].

In this study, the diagnostic sensitivity, specificity and accuracy at the time of the clinical diagnosis of sepsis were found to be 0.74, 0.67 and 0.75, respectively. In this study, in which the prevalence of sepsis was 22%, the positive and negative predictive values were 0.39 and 0.90, respectively. The PSP cut-off for the diagnosis of sepsis estimated in the cohort of the clinical study AB-PSP-001 is 290 ng/ml.

It is recommended that each laboratory determines its own cut-off based on the population it serves.

References

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The Summary of Safety and Performance (SSP) can be found under: https://ec.europa.eu/tools/eudamed.

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Near-patient testing.