RSE-B

INSTRUCTIONS FOR USE

These Instructions for Use describe the RSE-B software product, RSE-B version 3.

Background

Stockholm3® is a blood-based test to estimate the risk of finding clinically significant prostate cancer in biopsy by combining information from protein markers, genotyping, and clinical patient data in an algorithm. RSE-B is a CE-marked software product used to calculate the Stockholm3 Risk Score.

Product Principle (product description)

RSE-B serves as an aid for physicians to assess the need for further diagnostic work-up, e.g., whether the patient should be referred to urologist due to an elevated risk of clinically significant prostate cancer (csPC), defined as Gleason Score ≥ 7, or when the next prostate cancer test should be taken.

RSE-B is a stand-alone software, automatically estimating the quantitative risk of having a csPC. The RSE-B product uses input data from a Stockholm3 test (several assays) and combines it with clinical patient data to produce a recommendation and an accompanying risk score value.

For proper function of RSE-B version 3, the chosen instrument platforms and assays shall generate input data fulfilling performance requirements defined in the **Input data requirements** section.

Intended use

RSE-B is a stand-alone software utilizing clinical data, data from protein analyses and genetic analyses of patient blood samples to automatically estimate a quantitative risk of having a clinically significant prostate cancer (csPC), defined as Gleason Score 7 or greater. RSE-B is intended to be operated by clinical laboratories to provide an aid for physicians in the diagnosis of csPC by providing an individualized re-test interval recommendation.

Intended medical indication

RSE-B supports the following indications for use:

- As an aid in the detection of csPC (1) (2) (3)
- As an aid to reduce unnecessary further procedures for men with abnormal PSA levels

Intended patient population

RSE-B's intended patient population are men aged 45-74 years with a PSA greater than or equal to 1.5 ng/mL.

Contraindications

RSE-B is not indicated for use in men:

- Outside the indicated age range [45-74 years]
- With a PSA less than 1.5 ng/mL
- Already diagnosed with prostate cancer
- For whom a digital rectal exam (DRE) has been performed one (1) week prior a blood sample is drawn

Intended User Profile

Table1: Users, level or training.

User/occupation	Level of training
Clinical laboratory IT technician	Training required: data handling and assay performance related to input data
Nurse	Read IFU regarding clinical data required for RSE-B
Physician	Read IFU regarding clinical data required for RSE-B and output provided
Installer/IT Engineer	Read Stockholm3 Lab Manual regarding technical description
Trainer/product specialist	Fully trained in implementing and using RSE-B
Maintenance/IT Engineer	Read RSE-B Use manual for Laboratory regarding technical description

For users with a stated training need, training shall be performed prior to the use of the product.

Product classification

RSE-B is an independent in vitro diagnostic medical device software classified as “general” according to the European Directive for in vitro diagnostic medical devices (IVDD), Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices.

Input data requirements

RSE-B requires input data from assays:

- **Biomarkers** total PSA, free PSA, KLK2 and PSP94 delivered as plasma concentration, ng/mL and GDF-15 delivered as plasma concentration, pg/mL
- **Genotypic profile** of the individual by analysing Single Nucleotide Polymorphisms (SNPs) in blood samples

  and clinical input data
- **Patient information** (age, family history, previous negative biopsy, use of 5-alpha reductase inhibitors)

Note: A detailed description regarding input data is provided in Stockholm3 Lab Manual (4).

Output

The outputs from RSE-B are:

- Risk Score
- Warning messages
- Risk class
- Prostate Volume Cutoff (when applicable, included in risk class)
- Input data
- Calculated Age
- Genetic score
- RSE-B SW version and related RSE-B IFU version
- Product label (URL-link)

Explanations:

The ***Risk Score*** is an estimate of the risk of having a csPC in biopsy and delivers a risk score between 3-99%.

Risk Class 1 is normal risk and Risk Class ≥ 2 are elevated risk.

Laboratory report

RSE-B output shall be formatted, and a laboratory report shall be generated to be communicated to a healthcare professional/physician. The laboratory can provide the laboratory report in any suitable format. At least the information listed in Table 2 shall be included, making sure that the information provided is clear and actionable. Based on local legislation, the laboratory can translate the content to the relevant language.

Table2: Content in Laboratory report

Type of information	**Possible outcome**
LABORATORY	
Physician reference	
Patient related data	
Sampling related data	
Warnings	"*No warning*" Warning example: "*Age '43' is out of validated range [45-74]*".
Risk score	3 – 99%
Risk class	1-7
Patient age	Calculated, based on input of date of birth and date of sampling.
Reference how to access the latest approved version of the IFU	https://a3p.com/IFU Example: IFU RSE-B version 3

Recommendations for PSA < 1.5 ng/mL

For PSA values below 1.5 ng/mL, a risk score cannot be calculated since this area is outside the Intended use of RSE-B and not validated.

Warnings and precautions

When using RSE-B it will be assumed that the patients have not undergone a DRE (digital rectal exam) one (1) week prior a blood sample is drawn, since DRE has an impact on PSA-levels.

If RSE-B is used to analyze patients outside the indicated age range [45-74 years], for which the performance is not validated, there is a risk of obtaining an understated or overstated risk score.

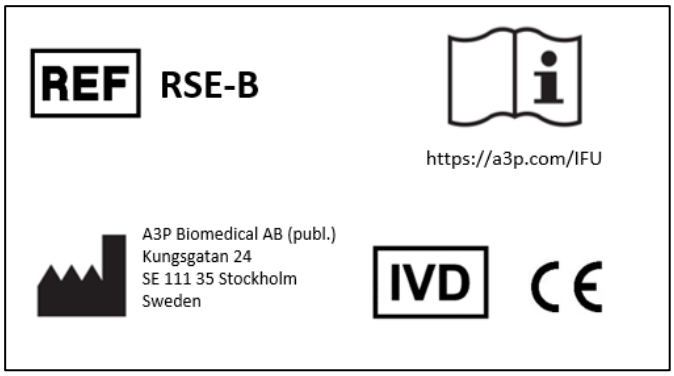
Limitations

The results from RSE-B should be used in conjunction with the patient's medical history, clinical examination, and other findings.

The risk score is not intended to substitute for prostate biopsy, US, MRI or diagnosis of prostate cancer.

PRODUCT LABEL

The product label is available on https://www.a3p.com/en/product-label/. RSE-B provides this URL as part of the output.



Explanation of Symbols used:

CE	**CE marking of conformity:** The manufacturer declares on his sole responsibility that the products conform to all applicable essential requirements of the IVD Directive EU In Vitro Diagnostic Directive 98/79/EC and other legal requirements.
	Manufacturer: Indicates the device manufacturer.
REF	**Catalogue number:** Indicates the manufacturer's catalogue number so that the medical device can be identified
IVD	**In vitro diagnostic medical device:** Indicates a medical device that is intended to be used as an in vitro diagnostic medical device
	Consult instructions for use or consult electronic instructions for use: Indicates the need for the user to consult the instructions for use.
A→文	**Translation:** Indicates that the original medical device information has undergone a translation which supplements or replaces the original information.

MANUFACTURER

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Address:
A3P Biomedical AB (publ.)
Kungsgatan 24
SE 111 35 Stockholm
Sweden

www.a3p.com

customersupport@a3p.com

REPORTING OF SERIOUS INCIDENTS

Any serious incident occurred in relation to the device must be directly reported to A3P Biomedical AB and to the competent authority of the Member State where the user and/or patient is established.

Contact information to A3P Biomedical AB can be found in section MANUFACTURER.

BIBLIOGRAPHY

1. *Prostate Cancer Diagnostics Using a Combination of the Stockholm3 Blood Test and Multiparametric Magnetic Resonance Imaging.* Grönberg H. et al. 6, 2018, Eur Urol., Vol. 74, pp. 722-728.

2. *Effects of replacing PSA with Stockholm3 for diagnosis of clinically significant prostate cancer in a healthcare system - the Stavanger experience.* Viste et al., E. 3, 2020, Scand J Prim Health Care, Vol. 38, pp. 315-322.

3. *Nordström et. al Prostate cancer screening using a combination of risk-prediction, MRI, and targeted prostate biopsies (STHLM3-MRI): a prospective, population-based, randomised, open-label, non-inferiority trial.* s.l. : Lancet Oncology, 2021.

4. *Stockholm3 Lab Manual (Master doc. 08-0097-01).*

5. *European Urology Association, [Online]. Available: https://uroweb.org/guideline/prostate-cancer/.*