Photo: Biomedical Scientist performing Proclarix at the Center for Laboratory Medicine, St. Gallen, Switzerland

Fast & efficient implementation of Proclarix® in the workflow of a clinical laboratory

Introduction

The initial step to diagnose prostate cancer is PSA-testing in combination with a digital rectal examination (DRE). In case of a high PSA level clinical guidelines recommend a confirmatory prostate biopsy. However, elevated PSA can occur for many reasons and prostate cancer is only one of them. Currently, over 50% of biopsies with elevated PSA are negative or clinically insignificant. This means overdiagnosis and overtreatment. Unclear results cause patients anxiety and require both additional time spent on health care procedures and unnecessary biopsies.

Proclarix®

Proclarix® delivers clear and immediate answers for patients with unclear PSA results (2 to 10 ng/mL) and increased prostate volume to support physicians in deciding who needs a prostate biopsy. Proclarix® is a CE IVD blood test that can be done in any local clinical laboratory using the same samples as the PSA test. It comprises two quantitative Enzyme-linked Immunosorbent Assays (ELISAs) that measure the concentration of thrombospondin 1 (THBS1) and cathepsin D (CTSD) in human serum and the Proclarix® Risk Calculator software, which integrates the values for THBS1, CTSD, age, total PSA and

free PSA to calculate a Risk Score for high-grade (Gleason Score ≥7) prostate cancer.

While Proclarix® has been validated using manual processing of the ELISAs, the use on an automated system is preferred in clinical laboratories to reduce errors, improve throughput, manage testing workload and maximize efficiency. Here we describe the procedural steps for the implementation of Proclarix® in clinical laboratories taking the implementation at the Center for Laboratory Medicine (ZLM, St Gallen, Switzerland) as an example, showing the results of samples measured with the DSX® automated workstation and UniCel® DxI 800.

Material and Methods

Reagents

- Proclarix® THBS1 and CTSD ELISAs (Proteomedix AG, Schlieren, Switzerland)
- PSA tests: Access® Hybritech® PSA and Hybritech® free PSA (Beckman Coulter Inc, Brea, CA, USA)
- Samples: Eight quality control (QC) samples consisting of serum from healthy donors spiked with WHO international standard of seminal plasma-derived PSA-ACT + free PSA (NIBSC, Potters Bar, United Kingdom) and six patient samples

Instruments and Software

- DSX® workstation, with DSX Revelation® software and LIS-Link Software (Dynex Technologies Inc, Chantilly, VA, USA)
- PSA Analyzer UniCel® DxI 800 (Beckman Coulter Inc, Brea, CA, USA)
- Inlab Laboratory Information System (LIS) (developed in-house by ZLM, St. Gallen Switzerland)
- DSX Revelation (6.21 or newer) assay files (.asy files, Proteomedix, Schlieren, Switzerland)
- Proclarix® Risk Calculator (Proteomedix AG, Schlieren, Switzerland)

Test procedure and Proclarix® steps
See **Figure 1** and **Figure 2**.

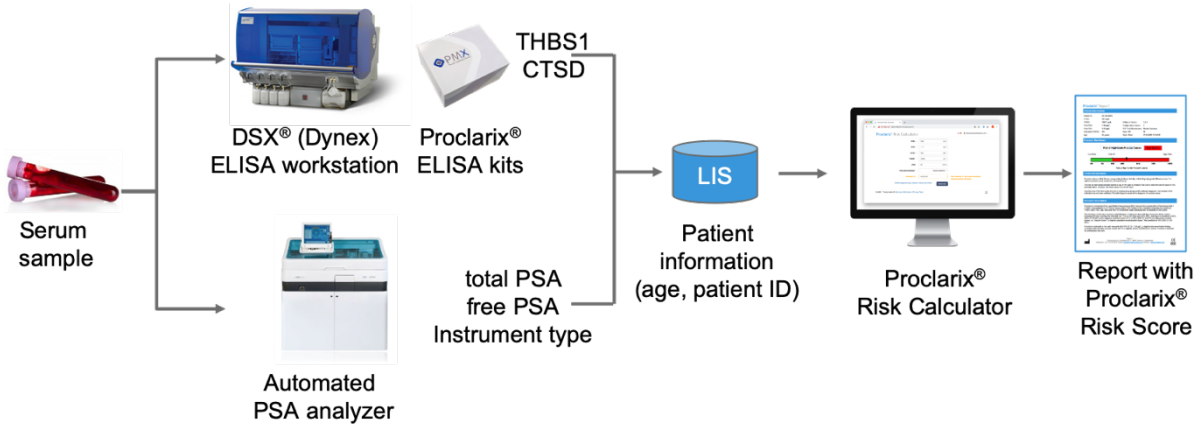

Figure 1. Workflow for the use of Proclarix® in the routine of a clinical laboratory.

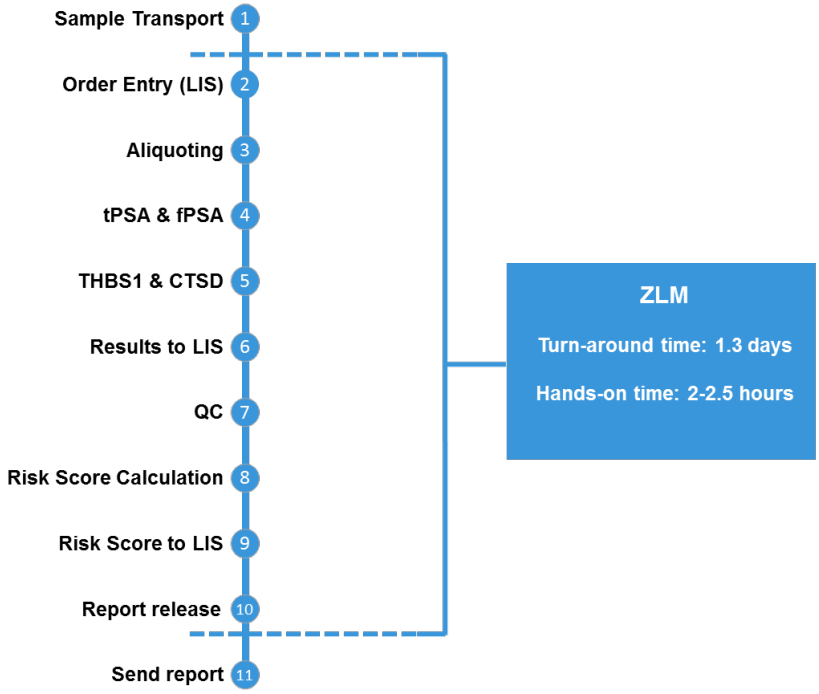

Figure 2. Steps of the procedure to determine the Proclarix® Risk Score.

Implementation of Proclarix® in ZLM clinical laboratory

In order to implement a new test in the laboratory, the first step is to define the test in the laboratory information system (LIS). According to the Standard Operating Procedure (SOP) of ZLM a form containing product-related information needs to be filled. Relevant data are then entered into the LIS. **Table 1** shows information that are usually required by laboratories to define Proclarix® in their LIS and laboratory workflow. Next, the DSX® was set up to run the Proclarix® THBS1 ELISA and CTSD ELISA according to the Proclarix® Instructions For Use (IFU) using the DSX Revelation assay files provided by Proteomedix. Additionally, connection between DSX® and LIS was established using the LIS-Link Software.

As a last step, a Proclarix® Risk Calculator user account was created through an easy online registration step, which is described in the Proclarix® IFU and takes approximately five minutes.

Name of parameters	Proclarix® Risk Score, THBS1, and CTSD
Product code	PCLX
Rounding and units	Proclarix® Risk Score: rounded to two decimal places, unit %
	THBS1: rounding to integer, unit ng/mL or µg/L
	CTSD: rounding to integer, unit ng/mL or µg/L
Reference ranges	Proclarix® Risk Score: 0.48% - 72.80%
	THBS1: 8333 - 165700 ng/mL
	CSTD: 124 - 1009 ng/mL
Lower limit of quanitification (LLoQ)	THBS1: 2174 ng/mL at 1:861 dilution
	CSTD: 62 ng/ml at 1:21 dilution
Upper limit of quanitification (ULoQ)	THBS1: 282285 ng/mL at 1:3321 dilution
	CSTD: 1385 ng/ml at 1:81 dilution
Minimal / Standard / Maximal Dilution	THBS1: 1:861 / 1:1681 / 1:3321
	CSTD: 1:21 / 1:41 / 1:81
Order of parameters in the laboratory report	tPSA, fPSA, THBS1, CTSD, Proclarix® Risk Score
Sample material	Serum
Controls	THBS1: two controls: low and high
	CTSD: two controls: low and high
Targeted sample volume	1.5 mL (total), 1 mL for both ELISA and 0.5 mL for tPSA/fPSA measurement
Minimum sample volume	0.7 ml (total), 0.25 mL for both ELISA and 0.45 mL for tPSA/fPSA measurement
Collection tube	Serum collection tubes containing clot activator
Reference cut-off value (Proclarix® Risk Score)	10.00%
Interpretation of Proclarix® Risk Score (to be added to laboratory report)	> 10.00%, high-risk of high-grade prostate cancer; <10.00%, low-risk of high-grade prostate cancer
Recommended text for addition to the Proclarix® laboratory report	Proclarix® returns a Risk Score corresponding to the probability of detecting high-grade (Gleason score 7 or higher) prostate cancer based on a prostate biopsy. The risk for high-grade prostate cancer is low in men with a Proclarix Risk Score below the cut-off value of 10.00% and high with a Proclarix Risk Score above the cut-off value. Incorrect use of the test carries the risk of unnecessary testing and/or delayed diagnosis. Use outside of the indication has not been validated. Prostate biopsy is required for diagnosis of prostate cancer.

Table 1. Proclarix® implementation-related information.

Proclarix® measurements and Proclarix® Risk Score calculation

Once the set up was completed, 8 QC samples and 6 patient samples where measured in 6 runs on different days to determine the Proclarix® Risk Score. Proclarix® THBS1 and CTSD ELISAs were performed on DSX®. Total PSA and free PSA were measured using the same samples with assays and analyzers already validated by the laboratory. Precisions of THBS1 EISA and CTSD ELISA were 3.1% and 5.9%, respectively (**Table 2**) and similar to data reported in the IFU for manual execution. The Proclarix® Risk Score varied little (**Figure 3**), with average CVs of 5.0% and 7.8% for QC samples and patient samples, respectively.

Parameter	Total precision, CV (%)	
	Average of 8 QC samples	Average of 6 patient samples
THBS1	3.1	5.8
CTSD	5.9	11.4
total PSA	2.7	4.1
free PSA	5.6	4.2
Proclarix® Risk Score	5.0	7.8

Table 2. Total precision (six different measurements on different days) of individual markers and the Proclarix® Risk Score.

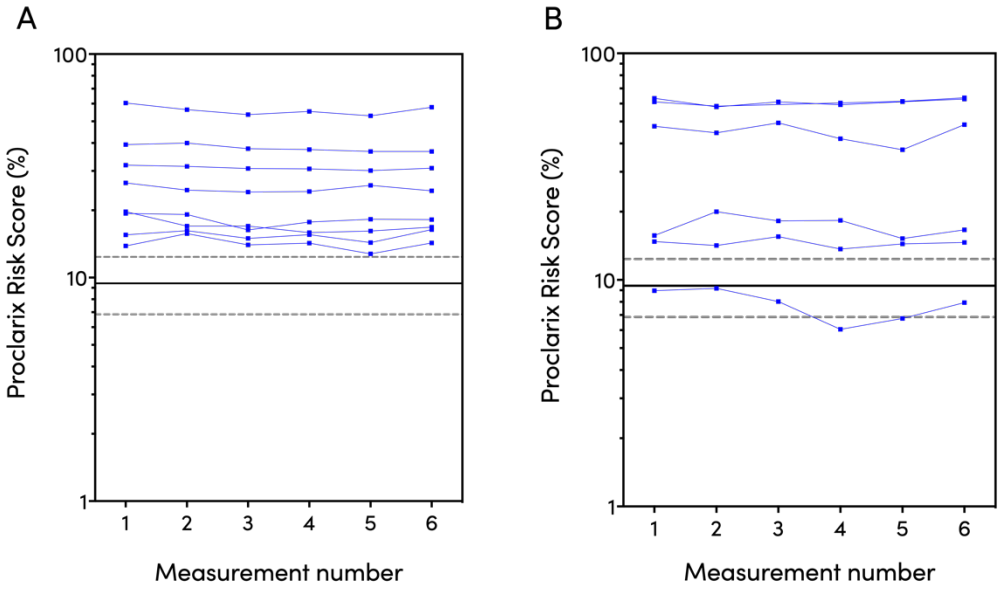

Figure 3. Proclarix® Risk Score of eight QC samples (A) and six patient samples (B), each measured in six different measurements. The solid line at 10% represents the cut-off between low risk and high-risk for high-grade prostate cancer and dotted lines represent the 95% confidence interval of the cut-off.

Conclusion

Proclarix® is an innovative CE IVD test that returns a Risk Score to aid in discriminating between high-grad and low-grad prostate cancer and thus helping physicians and patients to decide whether a prostate biopsy is needed.

"Proclarix addresses an important medical need and the implementation at the Center for Laboratory Medicine was unproblematic and fast"

(Prof. Dr. med. Wolfgang Korte, CEO and Medical Director, Center for Laboratory Medicine, St. Gallen)

The implementation of Proclarix® at ZLM was unproblematic and fast. The test was easily automated on the DSX® workstation, allowing high-throughput measurements of Proclarix® THBS1 and CTSD markers with as little as 30 min hands-on time. Variation of the Proclarix® Risk Score was low (total precision CV < 10%) and results from different runs were reproducible.

Based on this experience at ZLM, with the provided DSX Revelation assay files and information in **Table 1**, the set up in other clinical laboratories is expected to be straightforward, with an overall hands-on time of 2-4 hours. Once the test is established, the use of Proclarix® at ZLM showed that the determination of the Proclarix® Risk Score from samples can be completed within 1.3 days and requires an overall hands-on-time of 2-2.5 hours.

Further information

To find out more about Proclarix®, visit www.proclarix.com. For technical details or support in relation to procedures described in this document, please contact Proteomedix by email at contact@proteomedix.com or phone +41 44 733 40 90.

Acknowledgements

ZENTRUM FÜR LABORMEDIZIN

Frohbergstrasse 3
Postfach 1217
CH-9001 St.Gallen
Switzerland

We thank Prof. Dr. Wolfgang Korte, Carolin Thurnher and Jana Jentsch for their support