

## Valipro

### Prototype development, validation and production of a TIRF based protein chip system for diagnosis of sepsis

In VALIPRO ([www.valipro.eu](http://www.valipro.eu)) we develop and validate a fully automated total internal reflectance fluorescence (TIRF) based biochip system. The compact and cost-efficient system diagnoses sepsis fast and accurate by use of multiparameter assays. New methods for self-calibration lead to highly accurate, precise and reliable diagnostic reports meeting point-of-care requirements and clinical regulations. The system can also be adapted for the use of other sets of parameters and applications.

The sepsis chip is a simple and low cost cartridge offering an easy and hygienic handling. The cartridge is consisting of two injection moulded parts being merged with common connection technology:

- The microfluidic chip or cover chip with channel structure manufactured by injection molding and
- The optical chip with prism for light coupling containing the array of protein spots for biomarker detection.

The optical chip is made of an excellent optical polymeric material of high transparency and low autofluorescence at the excitation and detection wavelengths of interest.

Onto the optical chip the capture molecules for biomarker detection are deposited. Each spot (about 100  $\mu\text{m}$ ) is arrayed in triplicate. In addition, guide dots, positive and negative controls are spotted.

The biomarkers targeted comprise the inflammation markers C reactive protein (CRP), Interleukin-6 (IL-6) and procalcitonin (PCT), specific for bacterial infection. Though the relevant concentration ranges are extremely different, e.g.  $\mu\text{g/ml}$  for CRP, while  $\text{pg/ml}$  for IL-6, they can all be measured with the same biochip system using a single platform and no multiple tests and other detection systems are necessary.

The microfluidic part includes channels for sample transport, a waste chamber and a blood/plasma separation unit. The image shows the optical chip (25x75 mm) and the microfluidic chip which laser-welded together form the chip cartridge.



For each measurement a new such cartridge is required.

The biochip system also includes pre-analytical tests like the measurement of bilirubin.

The sepsis chip system works with serum, plasma and whole blood. One drop of blood is sufficient for biomarker measurement. Each chip is self-calibrated. The time required for a complete multiplex assay from sample injection till data read-out is 20 min.

Specifications	
Chip cartridge	Disposable Flow-through Optical and microfluidic part
Sample	Whole blood (integrated separation unit) Serum Plasma
Assay time	20 min
Pre-analytics	Bilirubin
Biomarkers	C reactive protein (CRP) Interleukin-6 (IL-6) Procalcitonin (PCT)
Calibration	Chip self-calibration
TIRF detector	Laser excitation CCD camera Sensitivity comparable to commercial high-end laser scanners

#### Consortium Partners:

1. AIT Austrian Institute of Technology GmbH  
Project coordination, assay development, validation
2. Fraunhofer Institute of Physical Measurement Techniques  
System and fluidic developments, chip design
3. micro resist technology GmbH  
Surface chemistry development
4. Payer International Technologies GmbH  
Injection molding, connection technology, chip design
5. MVZ Labor Seelig  
Clinical specifications, pre-analytics, validation