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Hot from the press!

SWISS SYMPOSIUM in Point-of-Care Diagnostics at HES-SO Valais

Elsbeth Heinzelmann, Science + technology journalist

Abstract: When an innovative technology is going to be implemented in hospitals, medical practices or pharmacies, it often does not appear really new to researchers. It is the implementation itself and the domain where it is used that are at the core of innovation. That's why the SWISS SYMPOSIUM in Point-of-Care Diagnostics (POCD) brings together key stakeholders from research and industry to clinical settings and patient care to exchange knowledge and experience and to stimulate activities in POCD.

Chairman of the SWISS SYMPOSIUM at HES-SO in Sierre on 26 October 2017 was Professor ***Marc E. Pfeifer***, who organized the event with Dr ***Dieter Ulrich*** of CSEM. Pfeifer is head of the Diagnostic Systems research group at HES-SO Valais and, jointly with Ulrich, the driving force behind the Thematic Platform in-vitro Diagnostics (TP IVD) of the National Thematic Network (NTN) Swiss Biotech. Supported by the Commission for Technology and Innovation (CTI), this network is dedicated to enhancing knowledge and technology transfer between universities and business. Let's look back on the focus areas of the event:

Participants at the Symposium exchange views and experiences on issues of topical interest in POCD.

What Do General Practitioners Really Need?

"Describing the main features of the primary care setting in terms of epidemiology, functioning of general practitioners (GP) practices and main constraints serves to define the needs for POC in the GP domain", says ***Nicolas Senn***, Associate Professor of Medicine and Head of the Institut Universitaire de Médecine de Famille at the Policlinique Médicale Universitaire of Lausanne. In brief, GPs are working in a low-prevalence setting: most diseases are in fact rarely encountered. Furthermore, time spent with patients is limited. Lastly, the variety of possible diagnoses seen in clinical practice is large. "In such a context, it is more useful to have tests able to exclude diseases with good negative predictive values and to have tests that take little time to perform with long expiry dates", explains the renowned family doctor, who has a great deal of experience in tropical medicine and especially in malaria research (which he gained in Papua New Guinea). "POC should also focus mostly on diseases for which a quick medical decision is needed." In his presentation, Nicolas Senn used the example of the malaria POC rapid test to demonstrate the outcomes of interest in primary care. "Even if these tests are not yet perfect, they have shown very high levels of efficacy and safety when used in routine care."

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Progress for POC Testing Thanks to Microtechnologies

"POC devices require robust and reliable measurement, clinically relevant biomarkers with few steps and low invasiveness for the patient", declares Professor ***Philippe Renaud***, scientific director of EPFL's Center of MicroNanoTechnology (CMI). His current focus is on microsystems for handling, analysis and culture of biological cells. Miniaturization technologies have had a great impact on the development of POC devices due to their capacity to handle very small samples and to integrate multiple processing or measurement modalities in a compact system. "Despite the strong development of microfluidic and sensor technologies, their application to commercial products is not as easy as expected. The complexity involved in integrating all functions in one microsystem complicates delivery of the necessary reliability, accuracy and cost compatibility in line with market requirements. That's why most of the successful new POC devices are based on the smart use of simple technologies."

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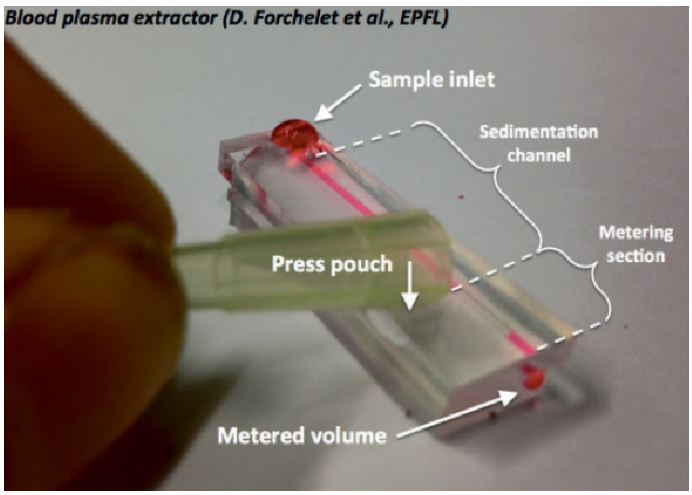

Organization and functioning of a blood plasma extractor developed in the labs of Professor Philippe Renaud at EPFL. (Source D. Forchelet et al)

Breakthrough in Molecular POC Testing

The privately owned company GenePoc, which is affiliated to the Debiopharm Group, is opening up new horizons with accurate and cost-effective molecular solutions to detect pathogen genes. "The need to simplify processes and accelerate molecular testing at lower cost is revolutionizing molecular diagnostics. Advanced Polymerase Chain Reaction (PCR) methods and emerging disruptive technologies based on microfluidics are driving low-cost, 'sample-to-result', miniaturized device development, providing ground-breaking platforms for applications in infectious disease POC testing", explains CEO Dr ***Patrice Allibert***, who has over 25 years of experience working in biomedical industries all over the world. "Our solution is REVOGENE, a compact, fully automated and stand-alone instrument well suited to on-the-spot molecular diagnostic testing." REVOGENE uses real-time PCR technology and offers unique flexibility, allowing the labs to run 1–8 samples simultaneously for an optimal testing workflow. "We are now launching two CE-IVD (*in vitro* diagnostic) assays on the market: GenePOC CDiff for the detection of toxigenic *C. difficile* DNA in liquid or soft stool specimens, and GenePOC GBS DS for the screening of group B streptococcus directly from a vaginal/rectal swab at intrapartum. Both assays showed very good performance when tested by several labs and hospitals across Europe."

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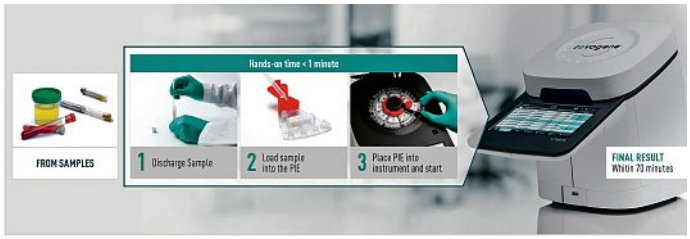

GenePoc Workflow Revogene: From samples to final results within 70 minutes. (Source: GenePoc)

New Avenues with Smartphone-based Self-monitoring

BÜHLMANN Laboratories AG is a leading IVD company that offers the broadest calprotectin product range with its automatable BÜHLMANN fCAL® ELISA, the quantitative Quantum Blue® Calprotectin rapid test and the new high-throughput immunoturbidimetric BÜHLMANN fCAL® turbo assay. As Dr ***Jakob Weber*** says, immune-mediated inflammatory diseases have a major impact on patients with such chronic disabling conditions in terms of physical suffering and pain leading to diminished quality of life and work-related productivity. "Regular testing of inflammatory biomarkers such as calprotectin or C-reactive protein in a patient's stool extract or serum increases the need for rapid tests that can be performed by the patients themselves", states the specialist in immunology, endocrinology, chronobiology and biotechnology. BÜHLMANN developed a smartphone-based home testing platform called IB*Doc*®, which delivers real-time information about inflammatory processes in the gut to both patients and clinicians. The IB*Doc*® consists of a stool collection and extraction device and an immune-chromatographic calprotectin rapid test which uses a smartphone app controlling the phone's camera. Once the test has been performed, the result is sent to a secured webserver allowing the treating physician immediate access. Jakob Weber takes stock: "IB*Doc*® is the first such test system to have achieved the CE-IVD mark for self-testing in March 2015 by a notified body. We now have to think about expansion and application of this platform to other medical and therapeutic fields."

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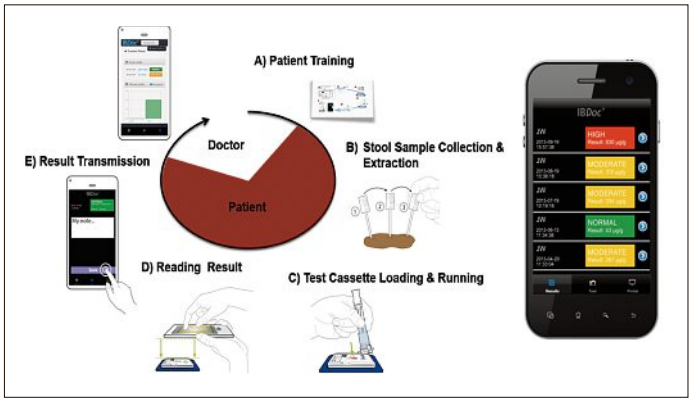

IB*Doc*® is the first self-testing application for fecal calprotectin in IBD subjects, based on BÜHLMANN's long experience with calprotectin assays. CALEX® Valve has been developed for simple and easy-to-handle stool extraction. The CalApp® smartphone application, which is available for iOS and Android phones, transforms smartphones into a test cassette reader. (Source: BÜHLMANN Labs)

From the Laboratory to the Hospital Bed

Already in 2001, the management of Inselspital Berne organized a 'Work Group POCD' and appointed a quality manager to satisfy growing quality assurance requirements. Today, ***Franziska Amiet*** is head and co-ordinator of the POCD unit at this Center for Laboratory Medicine, which provides competent care on an outpatient and inpatient basis. "The choice for POCT (point-of-care testing) depends on many factors", she says, and sums up the requirements as follows: "It should be easy to handle, safe, cheap, give comparable results with the laboratory devices and be connectable to established IT systems." She is very concerned about the integration of POCT in the hospital environment: "Results should be rapidly available without media breaks and be shown together with all other important patient related data on the patient data monitoring system. Then, POCT can be the missing piece in the puzzle and bring key benefits to all involved parties."

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Let's Take a Look at the Costs

Dr ***Michèle Fleury-Siegenthaler***, who works at the Federal Office of Public Health (FOPH), points out the regulatory aspects governing the reimbursement of laboratory analyses in the context of compulsory health insurance. The FOPH is responsible for public health in Switzerland, develops national health policy and works to ensure that the country has an efficient and affordable healthcare system in the long run. "Compulsory health insurance (CHI) covers the costs of medical care needed to diagnose or treat a disease and its consequences. It also covers the costs of certain tests aimed to detect diseases in time, as well

With the patient data monitoring system (PDMS) at Inselspital Bern, it is possible to check laboratory and POCT results together with other clinically relevant data. In the example shown here, POCT data (glucose plus insulin and energy data) are visualized as trends over a period of seven days. (Source: Inselspital Bern)

as certain preventive measures for insured persons at particular risk. The medical care provider must limit his care to the measure required by the patient and the aim of the treatment. Healthcare coverage is based on closed and open lists of health technologies. To be covered by the CHI, health technologies have to fulfil the legal criteria of effectiveness, appropriateness and economic efficiency. Decisions for coverage are taken by the Federal Department of Home Affairs (FDHA), or the FOPH for drugs, based on the recommendations of the advisory commission. - The FDHA publishes a list of analytical tests with tariff. The latter are applicable to outpatient care and are the maximum amounts admitted.

Analyses can only be covered by the CHI if they are performed in medical laboratories in accordance with the Health Insurance Ordinance.

Finally, concerning diagnostic tests, it is stated in the preamble to the list of analyses that a diagnostic test must make it possible with an acceptable probability to decide whether a treatment is necessary – and, if so, which one –, to reorientate the medical treatment applied hitherto, to redefine the needed tests or to give up other tests to explore symptoms, after-effects or typically expected problems.

If it is clear at the time of the request that an analysis will not meet at least one of the four criteria listed above, its costs will not be covered.

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Diagnostic Biochips – Swiss Innovation for POCD

Let's go back to the HES-SO labs, where Professor ***Jean-Manuel Segura*** and a team of experienced scientists want to push out the boundaries of what is possible in novel POCD technologies. The latest innovation of this specialist in biophysics and bioanalytics is in the field of therapeutic drug monitoring (TDM) and has been developed within the 'diagnostic biochips' research program. TDM allows for personalized dosage, which is mandatory for anticancer and anti-infective drugs and for organ transplants. As the TDM process is currently subject to a number of limitations, Segura and his team have been looking for a point-of-care solution based on fluorescence-polarization immunoassays (FPIA). "FPIA can be downsized with a reduced blood sampling requirement – only 1 µL – and a reduced number of steps, yet without compromising assay reliability. Thus we integrated it successfully within paper-like micro-chambers", explains the former EPFL researcher. "The final TDM point-of-care test requires minute amounts of blood and minimal handling steps (see Figure).

Jean-Manuel Segura and his team developed a point-of-care solution based on fluorescence-polarization immunoassays. This FPIA can be downsized with reduced blood sampling requirements and a reduced number of steps, yet without compromising assay reliability. The final TDM point-of-care test requires minute amounts of blood and minimal handling steps. (Source: HES-SO)

In the second part of his presentation, he addresses cases where single measurements are not sufficient – such as during cancer chemotherapies, where patients have to endure high doses and long-term administration of drugs lasting up to several days. "Ideally, drug doses should be continuously adjusted to keep blood concentrations within the therapeutic range, "says Jean-Manuel Segura. "This requires regular blood tests, typically every 15 to 30 minutes. With our innovation we are aiming at an autonomous monitoring system able to continuously measure drug concentrations in blood – a novelty on the medical market!"

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Science Helps to Kick-start Computer Tomography

At the Centre Médicale Universitaire of Geneva University (UNIGE), Professor ***Jean-Charles Sanchez*** explores – among other things – mild traumatic brain injury (mTBI) patients with

possible trauma-induced brain lesions. Here there is a tough nut to crack: computer tomography (CT) scans should identify the risk of developing brain lesions, yet most of them are CT-negative. As an alternative, single blood biomarkers in mTBI patients have been widely studied as a CT decision tool, but they have not been satisfactory to date. However, Jean-Charles Sanchez has a keen grasp of proteomics: he knows that combining several biomarkers into diagnostic panels enhances classification performance and this is arousing increasing interest in many different disease fields. "We evaluated 15 different proteins individually and in combination for their capacity to differentiate between patients with and without a brain lesion according to CT results. Three European sites enrolled cohorts of patients diagnosed with mTBI, and each patient gave a blood sample at hospital admission and underwent a CT scan." Patients were dichotomized into CT-positive and CT-negative groups for statistical analysis. Single markers and panels were first evaluated for the whole cohort with sensitivity set at 100%. "Three proteins were present at significantly higher levels in CT-positive patients", declares the scientist who founded the start-up ABCDx that has exclusive rights to Geneva University's intellectual property in mTBI. At the end of October 2017, he and his team received the Innovation Academy Award for their work.

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Linnea Lagerstedt and Prof Jean-Charles Sanchez, head of the Translational Biomarker Group at the University of Geneva and co-founder of ABCDx SA, at the 11th Innovation Day in Geneva at the end of October 2017. (Source unknown)

Non-invasive Diagnostics in Focus

At CSEM, scientists are realizing – amongst other topics – low volume tests for POCD on behalf of the pharma industry. Research activities encompass different solutions for diagnostics developed on a modular approach. On the one hand this entails sample collection and preparation: based on different microfluidic designs that allow the collection, sampling, loading and processing of different body fluids, such as urine, saliva and sweat. Simple pre-concentration approaches have been successfully tested. On the other side there is the detection unit: according to specific targets and requirements, engineers are developing colorimetric, fluorescent or electrochemical sensors that are integrated into cost-effective systems. Last but not least, the scientists are developing data acquisition, analysis and exchange. Together with the detection unit, the researchers are also working on the necessary electronics, power management and data management tools to realize a fully integrated system. "We have proved that the sensors could be integrated in wearable solutions – sweat analysis – or be used for saliva and urine diagnostics", says Dr ***Samantha Paoletti***, CSEM Business Development Manager. "An important focus of our work is the usability of the new device by untrained personnel in clinically challenging situations and in remote areas."

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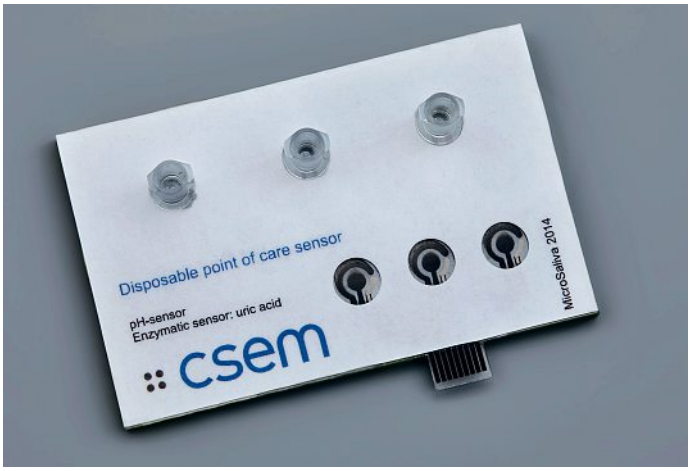

Disposable point-of-care sensor for non-invasive diagnostics. (Source: CSEM)

How Nanofluidics Bring Diagnostics Closer to the Patient

Abionic SA, a company located near Lausanne, does research at the intersection point between medical technology, biotechnology and nanotechnology. Committed to improving medical diagnosis, it has created a rapid *in vitro* diagnostic platform based on a revolutionary nanotechnology. "We developed the abioSCOPE®, an innovative point-of-care platform based on nanofluidic biosensors assembled into disposable cartridges", explains CSO Dr ***Fabien Rebeaud***. "Nanofluidic channels strongly influence the diffusional behaviour of biomolecules and increase molecular interactions. In addition, the high surface-to-volume ratio greatly enhances the interaction of biomolecules with the surfaces, making nanofluidic systems an excellent way to improve IVD performance."

To illustrate the potential of nanofluidics, the CSO of Abionic presents the development and performance of abioSCOPE®

Abionic's abioSCOPE is a medical device that provides rapid diagnostic test results. It is composed of a fully automated fluorescent microscope and a mounting plate onto which is placed a single disposable IVD capsule. The abioSCOPE can be used by any healthcare professional and does not require extensive training. (Source: Abionic)

testing based on the pancreatic stone protein (PSP), a novel biomarker that assists in the early identification and clinical management of sepsis. "As biomarkers currently available in clinical laboratories for sepsis diagnostics are neither sufficiently specific nor sensitive, and turnaround times of these tests are not suitable for most emergency situations, the development of a PSP test at the point-of-care represents a logical approach", says Dr Rebeaud, a biologist who joined Abionic four years ago. "We are convinced that the combination of PSP and nanofluidics will substantially improve the way sepsis is diagnosed and treated. The World Health Organization recently highlighted the need to identify sepsis earlier to improve survival – and our technology is perfectly positioned to fulfil this key challenge."

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www.hevs.ch/poc-symposium provides access to the presentation slides and videos.

Please don't miss…

…the continuation of this article in the January-February 2018 issue, which features an interview with Professor Georg M. Whitesides, the famous American chemist and Harvard professor who was awarded the Paracelsus Prize of the Swiss Chemical Society in 2004 – plus a look ahead into the future of POC diagnostics by Professor Marc E. Pfeifer.

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