

Rapid Biosensor Systems

Portable breath analyser for rapid TB detection

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Rapid Biosensor's Breath Analyser is able to detect the presence of TB bacilli in a cough deposited onto a biochemically coated sensor. TB can be indicated in only two minutes compared with hours or days for existing methods. Such rapid detection is of immense help in reducing infections from spreading and for starting treatment much earlier especially in the most 'TB-burdened' Third World countries.

Key facts/data:

Rapid Biosensor Systems Ltd

Technology: Breath analyser for rapid disease detection at the point-of-care

Established: 2002

Type: Startup

Location: Cambridge

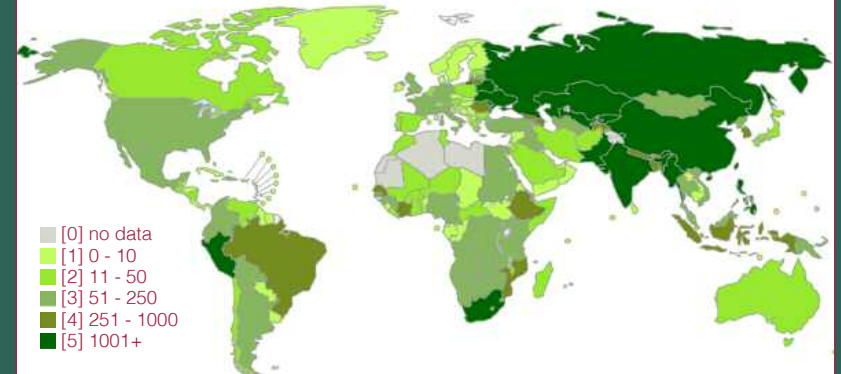
Employees: 5

CEO/Co-Founder: Dennis Camilleri

Dennis Camilleri has held directorships and senior commercial roles with SMEs such as Melles Griot (photonics), Willett International (industrial inkjet) and Leica Microsystems. After establishing his own consultancy in 2001 he helped spin out companies from UK Universities, notably Midaz Lasers (Imperial College), and Oxtox (Oxford University) where he was also CEO. He started his career in the fibre optic telecoms industry with STC having graduated with a Masters degree in Applied Optics from Reading University.



Diagnosis and notification of multi-drug-resistant TB
Notified 2013 MDR-TB (absolute numbers) 2013



Copyright – WHO 2015. Source: www.who.int/tb/data

TB background

Tuberculosis (TB) is spread through the air by an infected cough, sneeze or spit. According to statistics published by the World Health Organization (WHO) there are 8.8 million active cases of TB diagnosed each year – and almost 2 million of those infected die. Despite effective drugs against tuberculosis, it remains one of the world's most serious public health problems killing more adults than any other single infectious disease. The problem has been made worse because new strains of Multi-Drug Resistant TB have added further pressure on healthcare systems.

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TB Screening and Diagnosis

Having accurate and very rapid diagnosis enables health workers to identify the correct course of treatment faster saving time and valuable resources. As TB is most prevalent in the poorest countries, such screening needs to be low-cost and to require minimal training. However, current tests are slow, require specialist facilities and are only effective for detecting advanced disease.

The Mantoux tuberculin skin test is most widely used for screening and fails to meet any of these requirements, says Rapid Biosensor's CEO, Dennis Camilleri. It involves a health worker injecting testing fluid (tuberculin) under the skin of the patient's arm, and waiting between 48 and 72 hours for a reaction (swelling on arm) that indicates the presence of TB.

The type of reaction is influenced by such factors as the patient's health and age, thus calling for expert assessment and a degree of subjective interpretation. As a result, it can take up to two weeks for a qualified assessment.

A chance discussion

Dr Nicol Murray, a specialist Trauma Surgeon and Pathologist, who also has particular expertise in life-threatening communicable diseases, happened to explain the problem of slow TB detection to Dr Elaine McCash who at the time was working as a chemical physicist consultant at Sentec Ltd, one of the many specialised consultancies in Cambridge. Trained at the Cavendish Laboratories, she was interested in how she could use her specialist knowledge of surface physics, spectroscopy and chemistry to solve the problem.

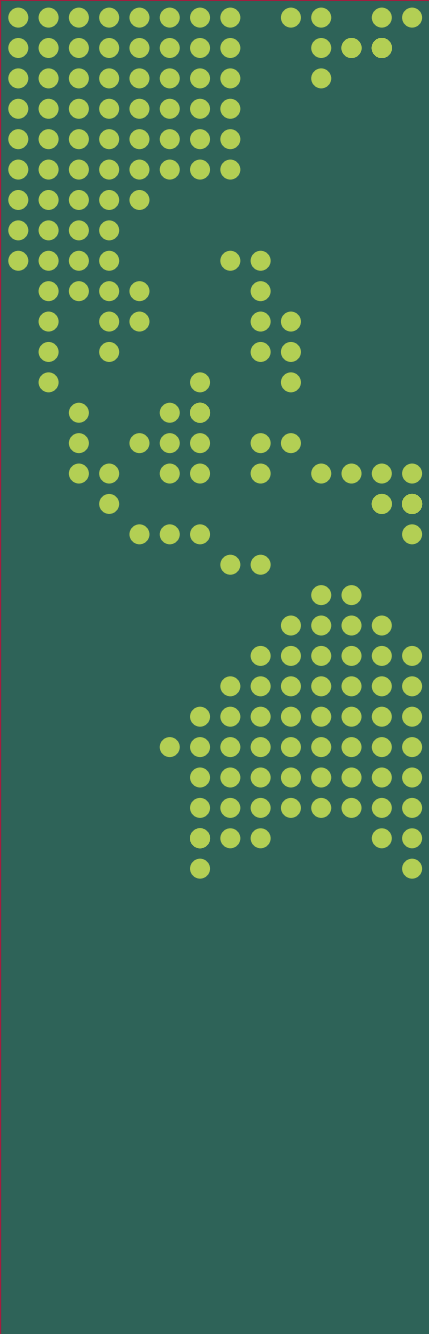
Sentec

The two agreed that the best solution to detect TB rapidly would be to use a breath test since TB is a pulmonary disease. At first McCash worked on the problem inside Sentec, but after a few months it was decided to establish it as a standalone business. Dennis Camilleri was approached by Sentec to join as CEO due to his experience in optics and successful management experience. The three then formed the start up as Rapid Biosensor Systems Ltd (RBS) with Sentec as a major shareholder, and the IP owned by Rapid Biosensor Systems Ltd.

Start up years

The founders decided to take a 'lean and mean' approach to the business says Camilleri – using grants and other soft finance and their own professional networks. They established the Company at the Babraham Research Campus which gave them access to research expertise and facilities. "We wanted to have a viable and robust product before we looked for venture capital". The Founders also had other business commitments so were not working full time on the company's business (Camilleri for example had his consultancy and was also CEO of Oxtox from 2013 to 2014).

At first they considered manufacturing the breathalyser themselves but decided to follow a technology licensing model which enabled the team to focus on their experience and skills in R&D and business development. Clement Clarke International (CCI) based in Harlow, a medical device manufacturer, joined at this stage and brought much needed investment as a Corporate Partner. Clement Clarke continues to be a loyal shareholder in the Company.



Breathalyser's USPs

Between 2002 and 2008, the founder team worked on developing the TB Breathalyser using grants from the WHO and UK research bodies together with funding from the business angel community. Their aim was to create the following 'USPs' says Camilleri:

- fast – screening test that outputs a result in minutes and far exceeds the speed of other competing technologies
- accurate – sensitivity and specificity exceeding WHO requirements
- portable – to use in the field away from health centres, so suitable for poor countries
- disposable – for convenience
- affordable – for developing countries
- simple to use – no expert intervention needed
- scalable – for high volume manufacture

The result is a Breathalyser that can be used in places without access to health facilities, without electricity or running water, making it particularly suitable for use in developing countries where low screening costs are also essential.

How it works

The TB Breathalyser unit comprises a single-use disposable cough (aerosol) sample collection tube in which the sample is made up of the fine liquid droplets produced by coughing. After being nebulised using a 0.9% saline solution, the patient coughs into the collection tube, at the bottom of which is a bio-optical sensor with a patented bio-chemical coating formulated to react with the TB bacilli. A push-and-twist action seals the aerosol sample in the tube causing the droplets to collect on the bio-sensor.



Disposable cough sample collector.

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Rapid detection method

The tube with the sample collected on the biosensor is inserted into the reader where light from a laser diode directed from underneath the sample detects the change in fluorescent light emitted from the biochemical coating. This technique is called a 'displacement assay' because the TB antigen displaces

fluorescently-coated analogues and bonds more strongly to antibodies, causing a reduction in the fluorescent signal after excitation by the laser. The laser detects the signal change if the TB antigen is present. The whole operation takes only two minutes. The sample tube is destroyed after use.

Advantages

Smear microscopy, like the Mantoux Test, remains the main method for diagnosing TB. It is lab-based, so it requires trained microscopists, and not everyone can produce (cough up) sputum so it has significant disadvantages. Furthermore, it has a low specificity of 10% and a sensitivity of up to 85% (the WHO's guidelines for TB screening are 60% and up to 95% respectively). The Rapid Biosensor TB Breathalyser on the other hand has specificity and sensitivity in excess of 95%. In addition, unlike the Mantoux test, it is not compromised by the presence of any other infective agents, so other respiratory tract conditions are discounted and only early stage TB and actively infectious TB are recognised.



Rapid Biosensor Systems TB Breathalyser is designed to be small, robust, simple to use and low cost.



Above and beyond this, there is no other TB test currently available which delivers an almost instant response at the point of care, says Camilleri. The relatively new PCR technology still takes three hours to produce a definitive result, as it requires a blood test and fairly complex analysis (also PCR readers are expensive, he adds).

A second patent, 'Bioassay and Peptides for use therein' (WO2007/072063) covers the biochemistry of the assay system used to detect TB. This has been granted in Australia, Russia, South Africa and USA; accepted for grant in Canada; grant is pending in the EU.

Ortho Clinical Diagnostics Inc

Ortho Clinical Diagnostics Inc became interested in Rapid Biosensor's technology in 2010 following discussions between Camilleri and Ortho's commercial management in America. This led to an exclusive licensing agreement and funding so that Rapid Biosensor could develop a pre-production beta model of the system to test in field conditions. Within 18 months it developed a portable version [see next page] using an outside consultancy to undertake the electronics and mechanical integration.

Field testing

Following on from earlier trials in India, the company carried out a series of field trials in Ethiopia. In total just under 1,000 patients were screened in five different hospital environments as part of five different trials. One trial was carried out under the supervision of the London School of Hygiene and Tropical Medicine. The final trials were independently conducted by medics at a university hospital in Ethiopia. The tests validated that the breathalyser could achieve >95% specificity and sensitivity.

The TB Breathalyser Key Features:

- Detects TB early stage infection before sputum smear/X-ray, with sensitivity and specificity of >95%+
- limit of detection estimated at ~ 25-75 bacilli
- results correlate with X-ray, sputum smear & clinical examination
- results are unaffected by other conditions, HIV, URTI, cancer etc
- can diagnose patients who do not produce sputum (~50% of total)

Patented technology

The system, comprising the Breathalyser collection method, sample types and optical Reader interrogation method, is patented in patent filing 'Biological Measurement System' (PCT WO 02/084266 A2) covering the concept, device and methodology, as well as a wide range of potential sample types and detection methods. It has been granted in Australia, Canada, Japan, Korea, Mexico, South Africa, USA (& Divisional). The grant is pending in Brazil, EU and India.

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Re-start

There was a set back in 2014 when Johnson & Johnson, which owned Ortho Clinical Diagnostics, decided to sell its subsidiary to the Carlyle Group. Thereafter, the exclusive Agreement with Rapid Biosensor expired which has opened the way to find one or more licensees.

2015 plans

The company is confident of securing licensing partners and is now undertaking a larger fund raising of £2.5m. Under the guidance of its well-connected chairman, John Reynolds, the valuation has been increased by nine times since the previous round; the higher valuation reflects in particular the potential of the R&D pipeline.

R&D Pipeline

The ability of the technology to analyse liquid as well as aerosol samples has significantly broadened the range of applications. In particular, Rapid Biosensor has identified new market opportunities for: sputum-based TB diagnostic testing; testing for bovine TB; and testing for bacterial pneumonia; all of them major markets. Once funds are raised it will recruit life scientists to accelerate the work on the product pipeline; it will also hire personnel with experience in electronics hardware design and testing. The final goal is an IPO unless a more attractive offer comes first. ■

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Cough sample collector being used in field trials in India.