Institution: University of Sunderland

Unit of Assessment: UoA3 Allied Health Professions, Dentistry, Nursing and Pharmacy

Title of case study: Commercialisation of analytical technologies: rapid and specific quantification of airborne actives in the manufacturing environment

1. Summary of the impact

Analytical methods and nanotechnology developed and patented since 1994 by the University of Sunderland, for healthcare, forensic and environmental monitoring applications have been exploited for their commercial and healthcare benefits. The patents were out-licensed to a University spin-out company for the production of a 'sniffer' device to detect raw material air contamination in a manufacturing environment. The proof of concept project resulted in significant commercial benefits, such as inward investment, new industry, specialist training, and >20 new jobs for a range of skilled workers, both in the UK and overseas, development of health and welfare protection, exploitation of technology to meet new industry regulations, and improved efficiency in the manufacture of active pharmaceutical ingredients and products for household goods.

2. Underpinning research

In the 1990s, new environmental Health and Safety (H&S) legislation was driving changes to manufacturing methods and standards. Professor Fred Rowell at the University of Sunderland responded to the need for technology to support implementation of the strict H&S requirements by developing devices for substance measurement in collaboration with industries, such as Unilever, Proctor and Gamble, Monsanto and Glaxo-Wellcome.

From 1994 innovative research conceived and led by Prof Rowell investigated the use of ELISA and other immunoassay-based methods for the detection and monitoring of solvents, active pharmaceutical ingredients (APIs) and enzymes as airborne substances that can cause chemical sensitisation and ill-health to employees during manufacturing processes. The research at the University initially focused upon the specific interactions possible between a monoclonal antibody and a target molecule, in collaboration with Dr Rob Cummings (University of Teesside) and industrial partners. Fourteen patents resulted from this work; five are held by the University of Sunderland. Prof Rowell set up two spin-out companies, one of which proceeded to commercialise the technology based on the out-licensed intellectual property. Although he left the University in December 2005 to pursue the commercial opportunities, he maintains his relationship with the University as an Emeritus Professor.

Under the leadership of Prof Rowell, eight research associates and PhD students based at the University developed immunoassays for a series of target molecules, such as enzymes and APIs. [1,2,3] When coupled with a collection sampler device, also developed by the Rowell research group, the immunoassays were shown to accurately and reproducibly quantify specific airborne molecules. [4,5] To meet new H&S regulatory requirements (culminating in COSHH Council Directive 98/24/EC), the quantification of airborne substances was necessary to limit exposure in the workplace and to improve the protection of workers, preventing ill-health and loss of commercial productivity as a result of over-exposure to toxic and sensitising agents.

The initial work concentrated on the development of the assay techniques; in particular, ELISA methods using specific polyclonal antibodies to the analyte under investigation were developed for the detection of the airborne pharmaceutical agents ceftazidime and ondansetron. [1] Assays were subsequently developed for the detection of airborne biochemical ingredients in the household commodities industry, such as alcalase, serine proteases, protease and proteolytic enzymes, as found in washing powders and liquid detergents. [2] These assays had evolved considerably and now allowed for 2 airborne enzymes to be detected and quantified concurrently in a flow-cell system, through the use of different fluorophore-bearing substrates that would be acted upon by

the airborne enzymes to release the relevant fluorophores, which could be measured independently. [3,4]

Subsequently, the focus turned to the incorporation of assays into devices for air-sampling. This was achieved through an air-sample open loop system with flow injection analysis (FIA). [5] Over the space of twelve years, the work resulted in the development of systems that allowed for:

- rapid analysis of air in the manufacturing environment;
- appropriate sensitivity and continuous monitoring;
- portable devices for personal use;
- a 'real-time sniffer', based on a cyclone air sampler and fluorimetric quantification of enzyme contaminants;
- devices that were cost effective.

Through the monitoring of airborne concentrations of solvents, APIs or enzymes in order to prevent over-exposure, this work has also directly informed the protection of employees involved in the manufacture of API and enzyme-based products. To realise the market potential of these devices, a spin-out company, Analytical Nano Technologies (ANT) Ltd, was established in 2002 and continued to invest in research and development, producing devices for monitoring air quality in a manufacturing environment, until the end of 2009.

Eight PhD students and post-doctoral fellows were engaged on this project while it was based at University of Sunderland: Dr Colin Farrell (1992-1996), Dr Dale Herczuk-Hirst (1993-1999), Dr Zhi Feng Miao (1995-2002), Dr Ioanna Nitescu (joint with Teesside University; 1992-1996), Dr Lian Xiang Tang (joint with Teesside University; 1993-1997), Dr Brendan Theaker (2000-2005), Dr Jay Trigg (2005-2009), and Dr Latha Sundar (2003-2005 and 2011-2012).

3. References to the research

There are too many publications to list here that provide evidence of the quality of this research; a few of the key outputs are listed below. For each output, Prof Rowell was the PI for the project; the international citations of each publication indicate the global significance of this research.

1. R. Cumming, C. Farrell, I. Nitescu, **F.J. Rowell**, L.X. Tang. Environmental analysis in the workplace; development of airborne monitoring systems for potentially harmful pharmaceuticals: an improved rapid ELISA for ceftazidime, *Analytica Chimica Acta,* 1995*,* **311**, 377-382. *This initial research led to the antibody-based ELISA that specifically measured the amount of airborne ceftazidime for application to the manufacturing workplace. It was presented at a conference and subsequently developed into this full paper.*

2. **F.J. Rowell**, R.H. Cumming, I. Nitescu. Environmental-analysis in the workplace – development of a rapid, sensitive ELISA for monitoring airborn alcalase, *Analytica Chimica Acta*, 1995, **316**(2), 247-252. *The ELISA analysis of different airborne species, such as alcalase, that could cause a threat to the health of manufacturing employees was also developed and shown to be significantly better than any other tests at that time.*

3. L.X. Tang, **F.J. Rowell**, R.H. Cumming. Development of near real-time monitoring systems for some serine protease enzymes in the industrial atmosphere, *Ann. Occup. Hyg.,* 1996, **40**(4), 381-389. *Using a flow-cell based assay with fluorescence detection, the quantification of airborne serine proteases was significantly improved.*

4. **F.J. Rowell**, D. Sykes, L. Grieveson, B. Theaker, L. Sundar, R.H. Cumming. A near real-time system for continuously monitoring airborne subtilisin-type enzymes in the industrial atmosphere, *Journal of Environmental Monitoring*, 2007, **9**(1), 33-43. *Further development of the enzyme and API-detecting technology led to its optimisation into a system that allows continuous monitoring of potential airborne contaminants.*

5. Patent: Method for monitoring enzymes, L.X. Tang, **F.J. Rowell**. Patent Number WO 97/21831, 19th June 1997; followed up with Method and Apparatus for Monitoring Enzymes

Mixtures. **F.J. Rowell** and L. Sundar, Patent Number US 20070184510 (09/08/2007). *The patents describe the inventions and intellectual property relating to the detection of enzymes and APIs in the air of manufacturing environments and form the basis of the commerce outlined in this impact case study.*

The research carried out at the University leading to the impact described was funded from a variety of sources. Between 1993 and 2010, Prof Rowell received more than £1.9 million in research and investment funding, managed by the University of Sunderland. Of this, over £1.625m was awarded through UK Government Grants, such as ONE North East, ERDF, and NorthStar Equity Investors, and Research Council funding from EPSRC; the remainder was mostly industrially-sourced funding. Additional funding was awarded directly to ANT Ltd, e.g. late in 2007, ANT Ltd received an order from Unilever of £750,000 for the production of several 'sniffer' detectors for their manufacturing establishments.

4. Details of the impact

The primary impact delivered by this research is on commerce, through establishment of a spin-out company, creation of jobs, and new products. Since 2008 the impact measures have been:

- further establishing, and improving the viability of, ANT Ltd in the sector;
- attracting considerable investment into research from industry and other investors;
- commercialising a new product for the adoption of new technology by several manufacturing industries;
- acquisition of other companies to improve the performance of all businesses involved; and,
- creation of jobs for highly skilled individuals taking specialised roles.

The new technology impacts upon health and welfare by preventing damage to the health of employees in the manufacturing industries, such as those engaged in the manufacture of enzyme-containing household products.

Since 1994, nanotechnology has been developed at the University of Sunderland using ELISA methods to detect and quantify specific biochemical substances of relevance to the manufacture of pharmaceuticals, chemicals, plastics, health care products, breweries, tanneries and bakeries; these industries form over 5% of UK industry, employing over 500,000 staff, contributing to global revenues of £110.5b for the sector (2011 data: ReportLinker.com). The initial patent on the invention was filed in 1997 and Prof Rowell established Analytical Nano Technologies (ANT) Ltd as a spin-out company in 2002 (initially as Sandco777 Ltd, becoming ANT Ltd in 2005), out-licensing the technology from the University. The first products were small portable systems, such as dipsticks and personal monitors, which could measure airborne active ingredients in real time and detect biochemical leaks in 15-20 minutes. The economic argument was strong: the galley test system took >150 hours and £64 per test, while the ANT dipstick test took 4 hours per test and cost £30. The spin-out company, ANT Ltd, employed 5-6 staff at this time, to continue the product development; this initial impact was in the form of a new commercial venture and new products, with inward investment and new jobs created.

In 2008, ANT continued to grow and contribute to the economy of the region; the research results and intellectual property, underpinned by further patents, improved the existing business and staff base. In response to the order from Unilever, the company further developed a real time air analyser, a 'sniffer' system, which drew air to be sampled into a cyclone, through which fluid was passed; this removed any substance, such as enzyme, from the sampled air and carried it into a bioreactor, where the enzyme reacted with a specific substrate to release a fluorescent marker. Measurement of the fluorescence gave a quantifiable signal proportional to the amount of enzyme present. This new system further decreased the test time to 0.1 hours at a cost of £1.50 per test.

Acquisition of Newton Instruments followed early in 2008, adding to the performance of both businesses. Their galley sampling equipment was ideal as a vehicle for delivering a new real time analyser or 'sniffer' system into the relevant manufacturing industries and resulted in world-leader status in static airborne industrial enzyme monitoring. In April 2008, now with 18 employees and renamed, ANTNano acquired a specialist electrochemical sensor company, Microarray Ltd, to develop specific detectors for infectious diseases, such as MRSA and avian flu, and secured

approximately £4m from Singapore industry to further develop the research in collaboration with Nanyang Technological University in Singapore. By June 2008, ANTNano had established its viability by generating revenue that gave it sufficient credibility to be launched as ANTNano (UK) Plc, which bought the Limited company and was then listed on the PLUS markets (open exchange) with tradeable shares. The customer base had expanded to include other manufacturers, such as Johnson Diversey Ltd and Novozymes.

In the period from June 2008 – Dec 2009, the technology developed at Sunderland supported considerable commercial impact upon ANTNano (UK) Ltd, providing the fundamental science upon which the existing dipstick and personal monitors were based, and enabling the development of the new 'sniffer' detection system. As a result, two sniffer systems were commissioned for manufacture and evaluation by Proctor & Gamble and Unilever, where they provided evidence of their success and reliability in detecting airborne particles and protecting employees from over-exposure in the manufacturing environment. Their excellent performance resulted in orders for a further 4 systems targeted at detecting and quantifying additional detergents. Prof Rowell attracted about £4m in investment for ANTNano (UK) Plc and set up a consortium to deliver the components required for the sniffer systems: dipstrip manufacture, nanotechnology, direct air sampling, and miniaturisation. However, issues from the pipeline software providers caused a fatal financial blow to ANTNano (UK) Plc and the company ceased trading in Dec 2009.

Since 2012, the patents underpinning the technology have again been out-licensed from the University of Sunderland and are starting to show evidence of impact, with the registration of a new company, Air Analytics Ltd, in 2011 and 3 new employees, thus supporting the creation of new business. There remains no comparable industry or product in the European air-monitoring market. This research is again attracting interest from industry for the development and production of new products to be adopted by the household commodities industry: Air Analytics Ltd aims to re-launch its innovative products to protect the health and welfare of manufacturing industry employees.

5. Sources to corroborate the impact

Although ANTNano Plc ceased to trade in 2009, there remain websites that provide information to corroborate the impact:

- News article reporting order from Unilever for 'sniffer' devices to protect the health of manufacturing workers; it also corroborates the research collaborations with Unilever, Proctor & Gamble, Genecor, and Novozymes, Jan 2008 [accessed 4th Nov 2013]: http://www.thefreelibrary.com/RBS+in+association+with%3A+Inventors+scent+a+lifesaving+market.-a0173701823;
- Acquisition of Newton Instruments, Feb 2008 [accessed 4th Nov 2013]: http://www.nanowerk.com/news/newsid=4649.php;
- Acquisition of Microarray Ltd: April 2008: http://www.marketwire.com/press-release/Analytical-NanoTechnologies-UK-Plc-PLUS-Company-Exclusive-Licensing-Agreement-Acquisition-LSE-ANAP-843169.htm [accessed 4th Nov 2013];
- Business and financial position at October 2008 [accessed 4th Nov 2013]: http://www.crmz.com/Report/ReportPreview.asp?BusinessId=10771233;
- Liquidation of ANTNano, Mar 2010 [accessed 4th Nov 2013]: http://www.nebusiness.co.uk/business-news/latest-business-news/2010/03/25/bioscience-firm-antnano-is-forced-to-leave-stock-market-51140-26103965/

The background to ANTNano, and to the science upon which its products are based, were presented by CEO Dr Allan Syms to CONNECT North East in April 2009 [accessed 4th Nov 2013]: http://www.slideshare.net/CONNECTNorthEast/ant-nano-presentation-to-connect-north-east-conference-09.

Air Analytics Ltd does not yet have a website, although it is listed on several business websites (e.g. www.companiesintheuk.co.uk/ltd/air-analytics) and returned financial assets of £115,250 in 2012; however, Prof Fred Rowell can corroborate the information provided here.