Institution: **University of Strathclyde**

Unit of Assessment: 3

Title of case study: Automated assays for rapid mass screening and detection of bacteria and toxins in food, lead to economic and health benefits.

1. Summary of the impact (indicative maximum 100 words)

Professor William Stimson has led research into rapid diagnostic tests for the food industry from 1996 to the present day. These tests reduce the time for microbiological testing of food pathogens from 2-5 days to within a working day. The new technology is fully automated, uses less material and involves fewer manipulations than previously available kits, leading to a reduction in cost and time. A spin out company, Solus Scientific Solutions Ltd., has attracted €1.36M EUROSTARS funding for further Research & Development, and has created 24 jobs. Sales of testing kits produced revenue of £3.4 million by year end 2012, and have increased since this date.

2. Underpinning research (indicative maximum 500 words)

Context

The prevention of food poisoning is a major concern in every country, but poor food hygiene, bacterial infection and fungal mycotoxins are commonly regarded as far more of an issue in developing nations than diseases such as cancer or autoimmune disorders. In developed countries there is compulsory testing for food pathogens, mycotoxins and meat speciation, and the supply chain from producer to sales is strictly governed by regulations. In developing nations the lack of regulation and testing is compounded by lack of refrigerated food storage. Mycotoxins are present in around 25% of foods worldwide and are associated with many diseases and physiological disorders – one of the species, aflatoxin B1, is recognised as the most toxic naturally-occurring substance. Of the food poisoning bacteria, Salmonella and Listeria are the most recognised and cause millions of people to be ill every year. However, E coli 0157.H7 is now becoming a major concern, especially in meat products, and legislation is being introduced throughout the developed countries.

Key research findings

The original research concepts [1] aimed to develop an assay platform that was highly sensitive, stable, simple and inexpensive for bacterial detection. In the food industry, the microbiological regulations indicate the need to detect as little as one single organism in 25 grams food. In order to detect such low levels of contamination bacterial numbers must be grown to a detectable level. The more sensitive the assay, the less time is required for bacterial growth, and hence the overall time of diagnosis depends on both processes. Research conducted by Stimson led to a major step forward in reducing the overall assay time, while not increasing costs by making the following advances.

- Developing a novel broth that allowed bacterial growth at the fastest possible rate: Bacterial growth media were investigated systematically to understand precisely what each of the components did (some components had been introduced over almost a 100 years). It was found that many were unnecessary, their concentrations were sub-optimal and that some compounds actually inhibited the organism we wished to grow rapidly. Thus a single broth was developed (instead of the normal 2 broths required) that would grow even one injured organism up to our detection level of 500 bacteria in a few hours instead of 40+ hours, and would do this even in the presence of 10 million competing organisms [3-5].
- Providing highly selective monoclonal and polyclonal antibodies against specific sequences in the bacterial cell wall: Immunisation protocols have been designed using specific interferon subtype additives or pharmacological suppression that result in enhanced recognition of the carbohydrate sequences of importance. In addition, hybrid animals with hyperactive immune responses are also employed to respond to minor antigens. The origins of these protocols are recorded in [2, 5 and 6].
- Defining a detergent that reduced the bacterial cell wall into the smallest units possible, thus providing the greatest numbers of detection entities.
- Using a novel flash chemiluminescent molecule for the detection: This dioxitan derivative has enhanced stability and light output [1 and 4].

- Providing a dedicated luminometer at 10% the cost of existing instruments and adapting Dynex microplate automation systems for our assays.

This research supplied all the information to allow the mass microbiological screening of food products to be made achievable within the one working day (if required). This allows customers to obtain fresher foods and removes the need for expensive refrigerated holding facilities, which are required while waiting for assay results i.e. early release of product with a longer shelf life is obtained.

Key researchers: The research was carried out by William Stimson (Professor of Immunology at the University of Strathclyde during the period 1983 - 2013) and David Cowan (Optics and Instrumentation – Nephlar Electronics).

3. References to the research (indicative maximum of six references)

1. Stimson, W.H. Complying with food legislation through immunology: monoclonal antibodies and immunoassays, the next generation. In "Food Quality and Safety" (Sim, T.S. and Yeow, K.P., eds.), SSM & SIFST, Singapore (1993) pp. 7-32.
Note on quality: Invited Plenary Lecture, The Singapore Institute of Food Science and Technology (SIFST). This research output formed a part of the 1996 RAE submission for Immunology that gained a 5*.

2. Ferro, V.A. and Stimson, W.H. Immunoneutralisation of gonadotrophin releasing hormone: a potential treatment for oestrogen-dependent breast cancer. European Journal of Cancer, 33, 1468-1478 (1997).
Note on quality: This is a high impact cancer journal (5.1)

3. Stimson, W.H. and Taravati, M. Characterisation of anti-*Escherichia coli* monoclonal antibodies for use in diagnostic assays. Food and Agricultural Immunology, 11, 61-73 (1999).
Note on quality: This is unique journal dealing almost exclusively with antibody-based assays in the food industry.

4. Ronald, A. and Stimson, W.H. The evolution of immunoassay technology. Parasitology, 117, S13-S27 (1998).
Note on quality: A special edition of this highly rated journal. An invited, peer-reviewed article.

5. Rahman, S. and Stimson, W.H. Characterisation of monoclonal antibodies with specificity for the core oligosaccharide of *Shigella* lipopolysaccharide. Hybridoma, 20/2, 85-90 (2001).
Note on quality: Peer reviewed paper that is commonly cited as prior art in responses to patent applications claiming specific anti-bacterial antibodies.

6. Khan, M.A.H., Ferro, V.A. and Stimson, W.H. Use of a highly specific monoclonal antibody against the central variable amino acid sequence of mammalian gonadotrophin releasing hormone to evaluate GnRH-1 binding sites in adult male rats. American Journal of Reproductive. Immunology., 48, 1-10 (2002).
Note on quality: Journal ranked 7th in all reproductive biology with a 3.4 impact factor.

Additional evidence for quality of research

The research has led to a granted patent - Compositions and methods for the rapid growth and detection of microorganisms. W.H.Stimson. International Patent Application PCT/GB2009/051161 WO 2010/029360. A patent 'Compositions and methods for the rapid growth and detection of microorganisms. W.H.Stimson. United Kingdom 2463369' has been granted.

4. Details of the impact (indicative maximum 750 words)

Process from research to impact

The Company Solus Biologicals Ltd. was initiated in 2007 by Stimson and Cowan, supported by a SMART grant award from Scottish Enterprise to produce prototype instrumentation for the assays based on the prior research conducted by Stimson. During its second year of life Anglo Scientific, a UK investment group, took a particular interest in funding the developing technologies and in 2009

Solus Scientific Solutions Ltd. evolved to take these to market, with a Physics graduate of the University of Strathclyde as Chief Executive Officer.

Types of impact

- The impact of this research has been initially economic, with expansion of the original spin out company, investment leading to employment and product development, and profit to the company from sales of testing kits.
- The food testing kits offer significant advantages to the producers, wholesalers and supermarkets supplying food in the UK, over previous testing systems.
- The final impact is on the health of the public due to improved testing for mycotoxins, and other products which will detect food spoilage.

Commercially successful spin out company

The food sector represents the largest market segment within the industrial microbiology market and represents almost 50% of the total market for food pathogens such as Listeria, Salmonella and E.coli. Europe is a substantial market for food microbiology testing. With a population of more than 500 million (2009), the 27 countries of the European Union (EU) performed an estimated 275 million food micro tests in 2011 [Sources A and B]. In mid-2011, Solus Scientific Solutions absorbed a significant sales and marketing diagnostic company, RayAl Ltd, to initiate full production and sales of its products on a wider basis. RayAl sells extensively in the UK, France and Denmark. [Source C] The products marketed by this company are assays for Salmonella, Listeria, E coli 0157.H7, meat speciation and a number of mycotoxins tests, as well as the broths essential for bacterial culture. The Solus-developed test-kits and antibodies were all developed from the Strathclyde research and account for significant sales and projections, based on current levels suggest they will account for 65/70% of the turnover of this company by 2014.

Investment into assay development

A Scottish Enterprise SMART grant for £100,000 was awarded in May 2010 to assist in the development of the rapid (20 hour) *Listeria monocytogenes* test, which is expected to be the first to comply with present EU legislation. An initial Eurostars grant of €1.36million was awarded in July 2011, to fund the full development of the 5 hour abattoir assay and assist its uptake throughout the EU, by the introduction of the appropriate legislation. The system incorporates Salmonella and E. coli 0157.H7 assays into a robot-based process that will automatically test beef, pork and sheep carcasses before release to the public. Trials of the robotic system, based on the principle of the automated cow milking system, are reaching an end-point in abattoirs in France and Denmark (July 2013). However, it will take time to assist the EU in accepting individual carcass meat testing legislation.

A final investment round to raise £800k was closed successfully in January, 2013. This is being used in part to develop 8 mycotoxin assays for food and crop monitoring using immunoassays and lateral flow devices. – the latter are particularly useful for assessing risks associated with lorry deliveries of grain where tests should be completed in 15 minutes to allow rapid unloading. The monoclonal antibodies for these have already been produced in Strathclyde University and have been licenced to Solus Scientific Solutions Ltd.

Sales

Solus Scientific Solutions Ltd converted its market for the major Enzyme-Linked Immunosorbent Assays (ELISA) for Salmonella and Listeria to the Strathclyde research based products in July 2013. This followed the successful completion of 2 full AFNOR Accreditation Trials for both products in June 2013. [Source D]. Association Française de Normalisation (AFNOR) is the French national organisation for standardisation. AFNOR is the EU body that provides certification for the food industry and conducts rigorous audit of any product before it can be marketed [Source E]. The E. coli assay is currently on trial (June 2013) to be completed by the end of the year.

From 2011, with the acquisition of RayAl Ltd. food testing kits were sold across UK, France and Denmark. The market share available to Solus products was 2.5m test kits in 2011, and growth is expected. Solus is currently in discussions to provide tests to countries such as India (with plans to

set up a sales office), where food safety is of particular importance. Revenue received by Solus Ltd was £1.1 m for the first quarter of 2013, representing a 43% increase over same time period (January-March) 2012. Sales of testing kits produced revenue of £3.4 million by year end 2012. Sales have increased since this date and the figure is predicted to be £5.1 million by end 2013.

Public Health and Consumer Benefits

By July 2013 the companies utilising the Solus assays based on Strathclyde research included Eurofins, Marks and Spencer, RHM, Cargill, Iceland, Premier Foods and Alcontrol. Eurofins, for example, is the world leader in food and feed testing [Source F], offering a comprehensive range of state-of-the-art analytical techniques to global food suppliers, including the rapid diagnostic testing for salmonella [Source G]. The other companies listed are distribution and marketing companies with global reach. Cargill is an international producer and marketer of food, agricultural, financial and industrial products and services. This company employs 140,000 people in 65 countries [Source H]. Other companies have extensive reach throughout the UK (Marks and Spencer, Iceland). These companies conduct rigorous testing of their own food product ranges, or are companies which conduct testing on behalf of other companies to meet hygiene standards. Their testing, based on Strathclyde research, will have direct health benefits to consumers throughout the UK, Europe and globally.

Employment

24 jobs have been created from Solus start-up in 2007 to July 2013, and will increase as sales expand.

Reduced costs and increased efficiency

The assays developed from the Strathclyde research are constructed closely on systems that have formed the basis of modern immunoassays. Hence, little additional user training is needed and no expensive additional assay materials are required other than those available 'off the shelf' – thus, this can be reflected in a very competitive selling price resulting in a percentage cost reduction of around 50% from existing high sensitivity testing products. Additionally, the assays may be fully automated using Dynex machines (these are leased to customers) and can assay up to 200 food samples per hour. These improve quality control of testing as well as reducing the staff numbers required and the need for highly trained scientists. In addition, the standard test for Listeria takes 2-5 days, whereas the rapid test produced by Solus is completed in 22 hours.

5. Sources to corroborate the impact (indicative maximum of 10 references)

A. http://www.researchandmarkets.com/reports/1071788/food_microbiology_2008_to_2013.pdf market report titled "Food Micro – 2008 to 2013", the worldwide rapid testing food microbiology marketing in 2008 represented over 738 million tests with a market value in excess of $2.06 billion.
B. http://www.strategic-consult.com/product/food-micro-sixth-edition-europe/
Europe is a substantial market for food microbiology testing. With a population of more than 500 million (2009), the 27 countries of the European Union (EU) performed an estimated 275 million food micro tests in 2011**.**
C. http://solusscientific.com/ Solus Scientific Solutions Ltd. website.
D. http://solusscientific.com/about-solus-scientific/latest-news/2013/07/04/solus-secures-iso-16140-approval---june-2013 AFNOR accreditation for Solus Ltd Salmonella and Listeria assays
E. http://www.afnor.co.uk/uk/ and http://www.afnor.org/. AFNOR (Association Française de Normalisation) website. AFNOR is the premier organisation in Europe for the validation and certification of food diagnostic assays.
F. http://www.eurofins.co.uk/food-testing.aspx Eurofins website
G. http://www.eurofins.co.uk/media/4375335/salmonella_pathatrix_sp10_01.pdf Rapid food testing for Salmonella by Eurofins
H. http://www.cargill.com/company/glance/index.jsp Information on the size of Cargill.