Institution: Cardiff University, School of Engineering
Unit of Assessment: UoA 15
Title of case study: Q Chip Ltd – Micro Technology for Injectable Therapeutics
1. Summary of the Impact

Economic impact is claimed through the growth of the biopharmaceutical spin-out company Q Chip Ltd. During the REF period, this has created 19 new jobs, £7.5M investment, a new Dutch subsidiary (Q Chip BV), and staged-payment, six figure contract sales to four major international pharmaceutical companies.

Q Chip has generated over £928K in contract sales from the pharmaceutical industry from 2008–2012, with further sales of over £1M projected in 2013–14.

Originally established by Professor David Barrow in 2003 from his micro technology research, Q Chip has developed new processes and miniaturised equipment to encapsulate materials, including drugs, within uniform polymeric microspheres as injectable therapeutics.

2. Underpinning Research

Since 1995, Barrow has led the specialist research field of microchip-based, multiphase-microfluidics, at Cardiff University, focused on precision polymeric microsphere production. Specific research undertaken by Barrow (Professor since 2000) and co-workers between 1998–2002 resulted in the development of a new manufacturing technology that creates uniform microspheres within planar microfluidic ducts (Fig. 1). Two phases of grants from EPSRC (GR/M29634, July 1999, £105k; GR/M73026, May 2000, £293k) and TSB (TI NCBT, 6/25 May 2002, £50k) resulted in two patents, now assigned to Q Chip [3.1], [3.2]. The co-workers were post-doctoral staff Dr. Nicola Harries and Dr. Kostas Bouris, and PhD research associate Mr Tyrone Jones, all employed at Cardiff University between 1998-2001.

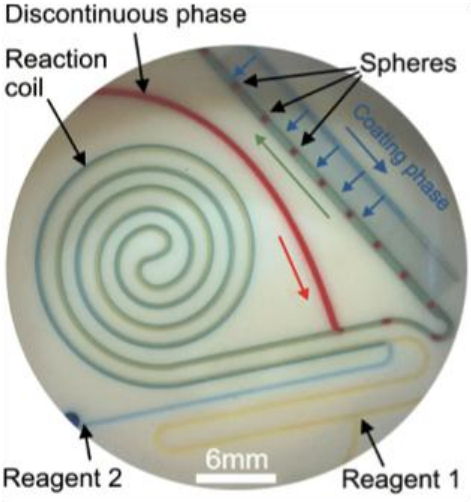

Figure 1: **Microsphere production chip**. Reagents 1 and 2 are precision delivered through flat capillaries, in which they are incubated within a reaction coil. After this they are interfaced with an immiscible discontinuous phase, thus causing the formation of droplet microspheres, which are then coated.

The first phase focused on the method of generating ideal fluid mixing conditions required to produce uniform fluidic droplets (shown in Fig. 2), initially by modelling [3.3] and then by experiment [3.4]. This research discovered and characterised the many inter-related microfluidic geometries for the generation of segmented flow streams, and their manipulation to engineer uniform microspheres. A key advantage of this particle manufacturing technique is the rapidity, purity, and uniformity of products, the low-shear aseptic environment (thus preventing damage to living cells), and the ability to undertake precision, serial chemical operations on individual microspheres. It had not been possible to achieve these features using traditional manufacturing techniques. At that time, only a few other scientists were investigating similar phenomena. Since then, the area of multiphase microfluidics using planar chip-based substrates has developed rapidly and is now heavily researched and is used in diverse applications. Subsequent related research by Barrow and new co-workers has continued, with new inventions such as the liquid phase separator [3.5].

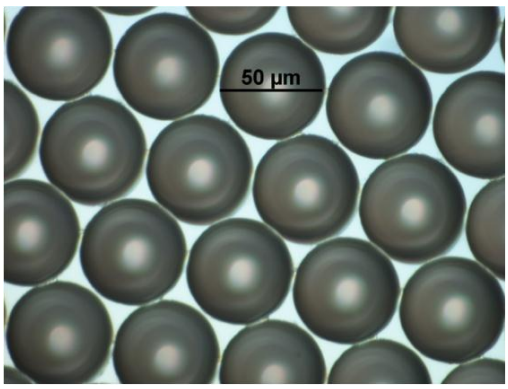

Figure 2: **Polymeric microspheres**, with a highly uniform diameter of 50 microns.

The second parallel phase of research identified combined manufacturing mechanisms and materials required to create the microfluidic chips for fluidic processing [3.1]. The mechanism involved novel, deep plasma-etching of microfluidic structures on bioinert, solvent-resistant, fluoropolymer substrates (shown in Fig. 3). This enabled highly-regular microparticle formation, without the undesired use of surfactants, some of which are toxic. This novel wafer-processing method favoured solvent-resistant polymers and is compatible with processing equipment already used in industry for silicon (like silicon-based, high-aspect-ratio structures; for example, airbag sensors and accelerometers).

Pilot manufacturing studies, initiated by Barrow in 2001, established a desk-top manufacturing microPlant for the production of microspheres [3.6]. This has been employed for payload delivery in multiple industries, such as biopharmaceuticals, neutroceuticals, cosmetics and smart paints. An independent commercialisation report from Biolauncher Ltd. (contact Rowan Gardener, Biolauncher Ltd., www.Biolauncher.com) proposed that significant revenues would be obtained by focusing product development on high-value, low-volume markets (including pharmaceuticals delivery) and this strategy has since been followed.

With initial Welsh Assembly Government support (*Q Chip exploitation roadmap*, Education and Learning Wales Ref. 112; 01/08/02), and working with Entegris and Victrex corporations, Barrow produced a platform [3.6] for bespoke microsphere production to demonstrate the technology to potential investors and supply chain partners.

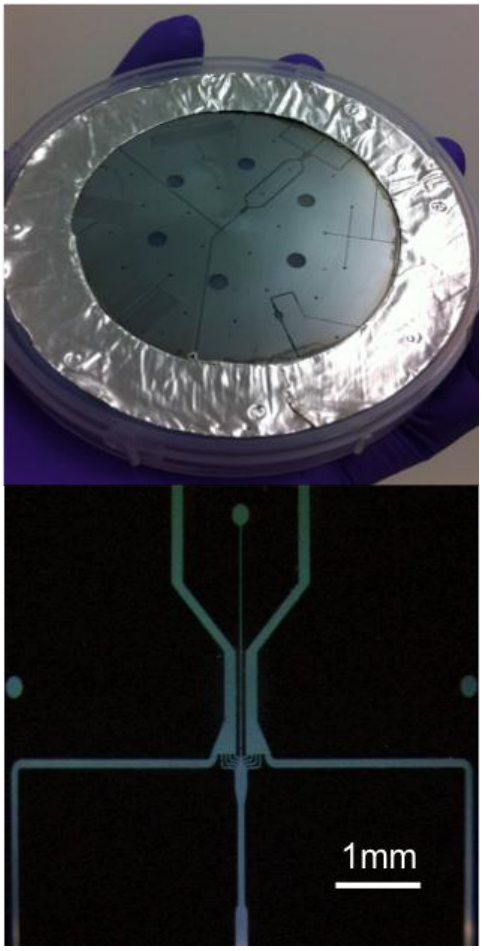

Figure 3: **A four inch PTFE wafer**, with a metal mask, showing deep-etched microfluidic ducts (top). Fine detail of the microfluidic duct system on this wafer is also shown (bottom).

The market potential for the Cardiff University research was supported by Barrow, as inventor, patent author, pre-seed development leader, Q Chip co-founder, and Q Chip Chief Scientific Officer. He exemplified the initial prospects through exploratory work from 1999–2000, for Unilever UK, by demonstrating pectin fibre production for hair-care products (Hugh.Clare@liv.ac.uk, at Liverpool University, previously at Unilever).

Q Chip Ltd. was founded in 2003 by Prof. Barrow, Mr Mark Barry and Dr Jo Daniels (Dr Nick Bourne, Cardiff University, Bourne@cf.ac.uk, and documents kept therein). The company secured first round funding from the E-Synergy investor syndicate (lead investor John Moulton), with a corresponding second closing IP-equity swap with Cardiff University.

3. References to the Research

3.1 **Barrow D.A., Harries N., Jones T.G.** and **Bouris K.** (2004) Method for the bulk machining of fluoropolymer substrates, *Patent Numbers: WO2004044655; UK0226688.0*, filing date 11/11/2002. http://www.google.com/patents/WO2004044655A1?cl=en

3.2 **Barrow D.A., Harries N., Jones T.G.** and **Bouris K.** (2004) Microfluidic device and methods for construction and application, *Patent Numbers: UK GB2395196B, Worldwide CA2545205, UK0226691.4*, filing date 11/11/2002. http://www.google.com/patents/US7802591

3.3 **Barrow D.A., Harries N.,** Burns J.and Ramshaw C. (2003) A numerical model for segmented flow in a microreactor, *International Journal of Heat and Mass Transfer,* Vol. 46 No. 17 pp. 3313–3322, http://dx.doi.org/10.1016/S0017-9310(03)00120-0

3.4 **Ahmed B., Barrow D.A.** and **Wirth T.** (2006) Enhancement of reaction rates by segmented fluid flow in capillary scale reactors, *Advances in Synthesis and Catalysis*, Vol. 348 No. 9 pp. 1043-1050, ISSN 1615-4150 10.1002/adsc.200505480

3.5 **Castell O.K., Allender C.J.** and **Barrow D.A.** (2009) Liquid–liquid phase separation: characterisation of a novel device capable of separating particle carrying multiphase flows, *Lab Chip,* Vol. 9 pp. 388–96, 10.1039/b806946h (this is output *Barrow 3*)

3.6 Velten T., Ruf H.H., **Barrow D.A.,** Aspragathos N., Lazarou P., Jung E., Malek C.K., Richter M., Kruckow J. and Wackerle M. (2005) Packaging of bio-MEMS: strategies, technologies and applications, *IEEE Transactions on Integration and Packaging,* Vol. 28 No. 4 pp. 533–546, 10.1109/TADVP.2005.858427

4. Details of the Impact

Impact summary: During the REF period, employee numbers at Q Chip increased from 10 to 29 (up 180%), there were 5 patent filings and there was £7.5M of new investment (75% of the total company investment) over 6 funding rounds [5.1],[5.2]. Access to new miniaturised industrial bioprocessing equipment and new drug delivery techniques (currently under trials) were sold to top pharmaceutical companies for improved quality of life through cancer treatment. Revenues from four, staged payment, six-figure value contracts [5.1],[5.2] have risen from £17k in 2010, £297k in 2011 to £578k in 2012.

Company growth: During the REF period Q Chip has developed a bio-encapsulation and drug delivery platform that enables companies to extend product life cycles and deliver complex bio-therapeutics [5.3]. It currently manufactures drug-loaded microspheres, mainly for pharmaceutical industries. Q Chip aims to improve patient compliance and experience, and improve therapeutic performance through the development of long-acting, injectable therapeutics using its proprietary platform, Q-Sphera™ [5.3]. This breakthrough microsphere manufacturing and formulation system is compatible with small molecules, peptides and complex biologicals.

With its commercial client partners, and with guidance from its scientific advisory board (on which Barrow sits), Q Chip is developing point-of-care clinical data with three different molecules encapsulated within drug-eluting, polymeric microspheres. Q Chip is licensing the microsphere production and sale via these client partners who, through their own existing global marketplace presence, are taking the products to market. Q Chip has five injectable, encapsulated drug formulations in its therapeutics pipeline, including Q-Goserelin and Q-Leuprolide for the treatment of breast and prostate cancer, Q-Insulin for diabetes therapy, Q-Octreotide for acromegaly, and a new formulation of monoclonal antibodies for a confidential application [5.1]. All have substantial existing markets. For instance, Leuprolide and Octreotide products achieved annual sales of around $1800M and $1200M in 2010; this is out of a total global market for injectable therapeutics of $49B. During 2011, Q Chip signed four separate multi-year R&D deals with international pharmaceutical companies [5.1]. Two of these contracts are with those in the top five global pharmaceutical industries. Q Chip has developed a contractual relationship with leading biotechnology/pharmaceutical company, ARTES Biotechnology GmbH [5.4], for the sustained release of therapeutic protein interferon alpha 2 (using microspheres) to treat chronic hepatitis B and C. A third contract is with a UK pharmaceutical company, a fourth with a mid-sized European pharmaceutical company [5.1] (contractually, other company names cannot be disclosed).

Further technical development: During the REF period Barrow has continued to be instrumental in determining the on-going evolution of the technology developed through the underlying research into Q Chip's expanding range of products. He has also supported the company as chair and co-chair of Q Chip's Scientific Advisory Board. His involvement has enabled access to his TSB funded metaFAB facility for HPLC-MS and femtosecond laser micromachining, and has enabled additional two-way development contracts between the University (Professor Steve Dunnet, Dr. Peter Kille) and Q Chip. The latter contracts developed cell-encapsulation capabilities for the company, using its core microsphere production technology.

Since Q Chip's inception, there has been significant process development and intellectual property protection, through five patents, based on its collaborative research programme. Microspheres are produced using a hybrid of the original IP with new geometries and sub-systems. This happens at

a greater rate, with less solvent waste, using automated, industry-ready bespoke equipment, also manufactured by Q Chip. The Q-Sphera manufacturing process leads to environmental improvements and is now much 'greener' than current methods because (i) it operates without Class II halogenated/hazardous solvents (e.g. dichloromethane/chloroform), (ii) it uses >80% aqueous solvents (so waste may be recycled to remove Class III solvents such as DMSO, alcohols), (iii) it is far more efficient than current methods since there is no need for size-fractionation (no wastage of intermediary product since there is none), and (iv) the unique, highly miniaturised, production-on-demand processing equipment (manufactured by Q Chip) sits on a desk, rather than occupying a building [5.1]. In 2011, through a £3.6M external investor round, the Q Chip BV European manufacturing subsidiary was founded as a cGMP sterile pharmaceutical production facility at Geleen, near Maastricht, with initially three FTE staff [5.5]. In 2012, the company was awarded a TSB grant of £250k towards the cost of developing its innovative, scaled-up, sustained-release pharmaceutical manufacturing process and production equipment [5.1].

Company investment: To provide context to the company investments **during the REF period**, it is valuable to know that **before the REF period**, the business secured first round funding from the E-Synergy investor syndicate in 2004 (lead investor John Moulton), with a corresponding second closing IP-equity swap with Cardiff University, which now holds about 3% equity. Since its incorporation in 2003, Q Chip has attracted investment of £10.4M over 12 funding rounds from angel and institutional investors, has over 57 shareholders, with 29 FTE staff who have contributed to employment in Wales [5.6].

During 2011–12, existing shareholders, including Disruptive Capital Finance and Finance Wales, were joined by venture capitalist Jon Moulton (founder of Better Capital) [5.7] and industrial entrepreneur Sir Harry Solomon, in two £5.6M Series C financing rounds led by Limburg Ventures and Nedermaas Hightech Ventures [5.7],[5.8]. Q Chip uses these funds to increase production by scaling-up manufacturing development of encapsulated drugs for prostate cancer and acromegaly.

Finally, in 2011-12 EPSRC undertook a healthcare economic IMPACT Study on Q Chip, since its origins were based on EPSRC-funded research (IMPACT summarised in [5.9] and [5.10]).

5. Sources to Corroborate the Impact

5.1 Confirmation of employment generated, investment and contracts achieved and that Q-Chip developed 5 injectable microsphere formulations on company contracts from Chief Operating Officer Q Chip Ltd.

5.2 Confirmation of turnover from audited (Ernst & Young) annual company reports (Companies House Company No. 04929486).

5.3 Confirmation of Q Chip's specialist drug delivery mechanisms and their benefits at http://www.q-chip.com/downloads/0723_Inside_Technology_article.pdf.

5.4 Confirmation of a contractual relationship with leading biotechnology/pharmaceutical company, ARTES Biotechnology GmbH http://www.artes-biotechnology.com/news.jsp. Article on 29.04.2010.

5.5 Confirmation of investment and establishment of Dutch manufacturing subsidiary http://www.growthbusiness.co.uk/news-and-market-deals/fundraising-deals/1625353/jon-moulton-backs-q-chips-series-c-financing-round.thtml.

5.6 Confirmation from the (then) Welsh Assembly Government Minister, Mr Andrew Davies, of economic (including employment) impact of Q Chip.

5.7 Confirmation of £3.6M investment raised http://www.walesonline.co.uk/business-in-wales/business-news/2011/06/14/q-chip-raises-3-6m-more-to-expand-91466-28871341/

5.8 Confirmation of £2M funding from external investors in 2012 http://www.insidermedia.com/insider/wales/81880-2m-funding-q-chip/index.html.

5.9 Confirmation of original EPSRC funding from: "EPSRC Pioneering Healthcare Technologies for the UK Life Science Sector", [No 3 on page 5]. One of four IMPACT case studies selected for this EPSRC publication.

5.10 Confirmation of economic impact from 'EPSRC Research Performance and Economic Impact Report 2011/12' [Page 13] at: (*paste hyperlink into google address bar on macs*): http://www.epsrc.ac.uk/SiteCollectionDocuments/Publications/corporate/ResearchPerformanceAndEconomicImpactReport2011-12.pdf.