Submission to House of Commons Committee on Science and Technology Inquiry on Bridging the "Valley of Death": Improving the Commercialisation of Research:



Innovation Myths and Lead Customers: Game Changing Policies to Improve the Commercialisation of Research

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1. Background

- 1.1 This submission, and the specific, costed policy proposals it contains, are based on:
 - My 25 years' experience in the technology and venture capital sectors, including as cofounder and for many year Chief Executive of TTP Ventures, a Cambridge based VC fund backed by Siemens, Boeing and financial institutions and specialising in early stage science and technology based companies.
 - An extensive series of research programmes on the exploitation of academic research, the characteristics and funding models of Cambridge's most successful S&T companies and overseas innovation policy models. Much of this is in collaboration with colleagues at the Centre for Business Research/UK Innovation Policy Research Centre at the University of Cambridge.
 - Lessons learned from leading a six year campaign to get US style procurement based innovation policies adopted in the UK and EU and advising the UK Government on the introduction of the resulting Small Business Research Initiative.

Supporting publications are supplied with this submission and referenced in the text.

2. Innovation Myths

- 2.1 There have been for many years' three implicit assumptions underpinning the approach to UK innovation policy of successive UK governments:
 - (i) That academic research is the key source of innovation for new businesses
 - (ii) That venture capital is the key source of funding for new businesses
 - (iii) That multi-partner collaborative R&D programmes, involving industry and universities represent the best government mechanism for funding innovative R&D in companies
- 2.2 As the UK's most successful hi-tech cluster, Cambridge is an excellent "laboratory" in which to examine UK innovation policy. However, detailed research on the start-up strategies of its most successful companies suggests that all of these assumptions are in fact myths1.

Myth 1: Role of Academic Research

2.3 Over the last 30 years there have been few really successful new Cambridge companies built on university research in the physical sciences and engineering. All of Cambridge's four largest S&T companies: Arm, Domino Printing Sciences, CSR plc (Cambridge Silicon Radio) and

See Connell, D. and Probert, J. (2010), Exploding the Myths of UK Innovation Policy: How 'Soft Companies' and R&D Contracts for Customers Drive the Growth of the Hi-Tech Economy, Research Commissioned on Behalf of the East of England Science and Industry Council by the East of England Development Agency. CBR, University of Cambridge.

Autonomy (the "big four") are spin outs from existing firms and based on technology developed, and start-up teams built, within their parent companies. And whilst the parent companies were in each case founded by entrepreneurial Cambridge University alumni in their twenties, it was the challenge of solving customer problems in a business environment which in every case provided the stimulus for innovation. Only in the case of Autonomy, was the parent, Neurodynamics, established to capitalise on founder, Mike Lynch's research at Cambridge University.

- 2.4 The most successful Cambridge University spin outs of the last fifteen years Abcam and Solexa, are both essentially "Research Tools" companies whose products and services were developed to meet the needs of other scientists. Though both companies are still much smaller than the "big four", this category of company represents the "low hanging fruit" in terms of commercialising the science base and more could be done to capitalise on this opportunity².
- 2.5 Besides being intuitively attractive, the myth surrounding university spin-outs has been perpetuated as a result of premature celebration by government and media of high profile, VC-backed spin-outs when they are still at a pre-revenue stage, together with a tendency to incorrectly ascribe university research origins to successful Cambridge companies such as Arm and CSR.
- 2.6 There is no doubt that policies could be put in place to improve the commercialisation of academic science. However, the reality is that at Cambridge, just as at MIT, it is entrepreneurial university alumni rather than research results which play the key role in building successful new S&T companies³. This distinction is important as it has profound implications for policy.
- 2.7 In fact the most successful source of new product companies in Cambridge is the sub-cluster of technology "consultancies", whose business entails developing technology and products for other companies, mainly overseas based multinationals, on a fee basis. Besides employing some 1200 people directly, over the last forty years the four largest firms have created more jobs in "sponsored" product spin outs than the entire university. These are based on intellectual property developed within the parent, usually as a bi-product of funded projects for external clients. Surprisingly, the consultancies also make very little use of research results developed by university academics in their core businesses.
- 2.8 The role of demanding customer contracts as a stimulus to innovation is also evident in the US. For example, though it was venture capital backed, Intel's first single chip processor, and

² This argument is developed further in "Scientists are Customers too; How the SBRI can Help Research Councils Drive Economic Growth", David Connell, NESTA, March 2010.

³ Two thirds of entrepreneurial MIT alumni attribute the ideas for their new enterprises to industry work experience and only ten per cent to research. *Entrepreneurial Impact: The Role of MIT, Edward. B Roberts and Charles Eesley, MIT Sloan School of Management; publ. Kauffman Foundation.*

⁴ The term "sponsored" implies that the parent retained a shareholding in the spin out and actively supported its formation. Many other jobs have been created in start-ups created by ex employees without the parent firm's involvement.

⁵ The largest firms are TTP Group plc (The Technology Partnership), Cambridge Consultants, PA Technology and Sagentia plc; see *Myths......*, op. cit.

the basis of its subsequent success, was a side project developed under a paid contract for a Japanese calculator firm. The Federal Government has played a similar role in relation to many other technologies.

- 2.9 The role of academic research in creating successful new life sciences companies is less clear and there are prima facie reasons to believe that academic science can play a greater role in this sector than in engineering, physics and materials based start-ups. Cambridge Antibody Technology, the UK's most successful biotech start up to date, was based on research by Sir Greg Winter at the MRC Laboratory of Molecular Biology. CAT was acquired by Astra-Zeneca in 2006.
- 2.10 Nevertheless, no Cambridge biotech company has ever employed more than a few hundred people. Indeed a league table published in 2007 of the 100 largest global biotech companies by revenue includes only three UK firms⁶. The largest, Acambis, ranked 46 with 285 employees and revenues of \$57m, was acquires by Sanofi-Aventis in 2008. Given the emphasis placed on the biotechnology industry as a jobs generator by recent governments, this is deeply disquieting. Though the Government's Strategy for UK Life Sciences, announced in November 2011, contains some important new initiatives, the detail of these is still unclear and the overwhelming focus continues to be on strengthening *research* in universities and the NHS.

Myth 2: Role of Venture Capital

- 2.11 The second assumption, that venture capital is the key source of finance is also a myth. The dominant source of early stage funding for the most successful firms in Cambridge, measured in terms of sustained profitability and number of employees, is customer funding, especially through R&D contracts⁷. Venture capital tends to come in later or not at all. This "Soft Start Up" strategy is common in technology companies everywhere. It contrasts with the better known "Hard Start-Up" strategy in which the development of standard products starts immediately, financed by venture capital, and revenues and profitability can be delayed for many years. Other examples of soft start-ups include Research in Motion (RIM, maker of the Blackberry), Microsoft, Logica and Wolfson Microelectronics, Scotland's most successful new technology firm. Vodafone was a spin out from Racal, a classic soft start-up.
- 2.12 The soft start up model has many benefits, including enabling new entrepreneurs to learn their management skills on the job, before moving to a higher growth model, and gain a better understanding of their technology and potential markets before committing to developing a proprietary product. This reduces business risk.
- 2.13 Venture capital is predominantly about building new product lines for other companies to acquire. In the UK the acquirer will usually be a corporation based overseas, leading to dispersal of the entrepreneurial team and truncation of further employment growth in the UK. Soft start-up strategies make it easier for the entrepreneurial team to remain in control of a

⁶ *Top 100 Biotechnology Companies*, MedAdNews, June 2007.

⁷ Myths...., op. Cit.

company's destiny and pursue a strategy with much greater economic impact over the long term.

2.14 This does not mean that the UK does not need a strong venture capital sector; for businesses needing to grow fast against competitors it is essential. However, venture capital cannot alone do the job of investing in high risk, long lead time technologies that policy makers currently expect of it. The problem is underlined by the rates of financial return, currently averaging around zero per cent per annum over the life of UK VC funds. Average returns in science and technology orientated UK VC funds have for twenty years been too far below that of other asset classes to make them attractive to pension funds and other investors in private equity funds⁸. There is no reason to believe that co-investment in VC funds by government, the current policy, will change this position significantly. To build a viable UK venture capital industry, complementary policies are needed that will help create more VC-ready firms and make them more likely to succeed. These are discussed below.

Myth 3 Role of Collaborative R&D

- 2.15 The third implicit assumption, that funding multi-partner R&D collaborations involving industry and universities is the best way for government to fund innovative R&D projects in companies is also flawed, particularly as regards SMEs. This is the overwhelmingly dominant approach to R&D funding used by both the Technology Strategy Board and European Commission.
- 2.16 Start-ups and SMEs do not find the collaborative grant model attractive⁹. It does not support the single-minded championship needed to build new businesses and projects tend to be too far from market for small firms to participate. As they usually require matched funding, collaborative projects are inappropriate for the majority of start ups and SMEs which do not have venture capital or significant cash reserves. Firms need to be able to choose their partners, sub contractors and consultants freely, and to change them if things do not work out. A "collaboration" that ticks the boxes in the application form just to get the money can end up being a distraction.
- 2.17 Fully funded R&D contracts with lead customers, the commercial mechanism which drives the soft start-up model, are much more appropriate. The SBRI scheme, based on the successful US Small Business Innovation Research (SBIR) programme, mirrors the private sector process that has helped make the Cambridge Cluster successful, as it funds the development of technologies and products the public sector itself needs, either as customer or specifier¹⁰. It also enables companies to keep the IP generated so they can go on to build product businesses. Collaboration with a university is in both cases at the option of the SME, not an artificial requirement which must be met just to get funding.

⁸ See British Venture Capital Association and European Venture Capital Association investor return statistics. There is a range of returns around the average, but asset allocations by pension funds and other institutional investors are made largely on the basis of average returns.

⁹ Myths, op cit

¹⁰ Secrets, op.cit.

3. Challenges of Commercialising Academic R&D

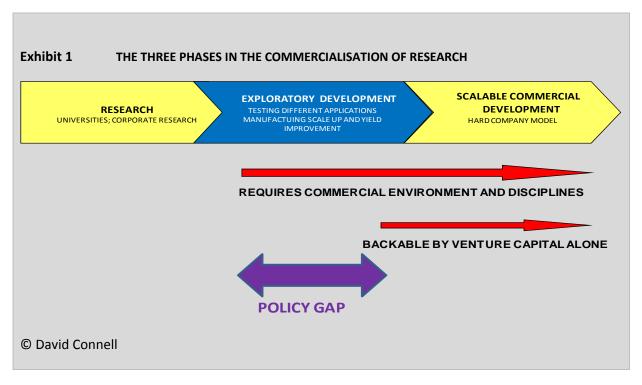
- 3.1 In recent years, a good deal of emphasis has been placed on trying to modify the university model to make it easier to spin out companies. Alongside the strengthening of university technology transfer offices, academics have been strongly encouraged to work more closely with companies in the research they undertake. However, EPSRC funded research carried out by the author, Dr Andrea Mina and Professor Alan Hughes¹¹ has shown that there are major challenges in trying to accelerate commercialisation in a conventional university research settings:
 - (i) Most externally funded research projects in universities are undertaken by teams staffed by PhD students and post-docs who tend to move on quickly. As a result it is very hard to retain competence in depth or build the core technology team required to create a spin out business. This is exacerbated by the dominance of short term grants and employment contracts
 - (ii) The time that must be devoted to writing publications, teaching, supervisions and giving papers at academic conferences means that R&D during a preventure stage can only be advanced in fits and starts
 - (iii) IP is often not managed throughout a project. Past leakages of various kinds and competitor positions may only become apparent when commercialisation is being considered. The problem is particularly acute for the long lead time technologies which typify much academic research as there may be an accumulation of IP over successive projects involving many different individuals and corporate partners.
 - (iv) The pressure on academics to collaborate with industry, coupled with changes in personnel, means that exploitation rights are not always properly thought through or managed over the long term. Poorly negotiated agreements with industrial sponsors can restrict the potential for later spin-offs or licensing deals.
 - (v) It is very difficult to accelerate the pace of R&D prior to the stage when a technology becomes ripe for exploitation. As a result any competitive advantage can be eroded at this critical stage.
 - (vi) Universities are not normally equipped with the expertise or resources to take technologies to the demonstrator stage required to attract investment or customer interest
- 3.2 It is difficult to see how these issues could be addressed within a conventional UK university research setting.
- 3.3 The challenge for innovation policy is compounded in the UK because in many areas of technology the natural industry collaborators are foreign companies with little inclination to

¹¹ The Role of TICs in Rejuvenating British Industry; Submission to House of Commons Committee on Science and Technology Enquiry on Technology Innovation Centres Submission to House of Lords Enquiry on Technology Innovation Centres, December 2010 David Connell, Professor Alan Hughes and Dr Andrea Mina, Centre for Business Research, Judge Business School, University of Cambridge.#

commercialise in the UK. Start-ups must therefore play a disproportionate role if there is to be significant economic benefit to the UK.

4. The Commercialisation Process and Industry Differences

4.1 The process by which academic research is converted into businesses and jobs is unpredictable and non-linear, but it can usefully be divided into the three phases shown below.



- 4.2 The initial, *Research Phase* is typically carried out in universities, and sometimes in government funded laboratories and the laboratories of some large corporations. It typically concludes with the discovery of a new material, phenomenon, device, process, algorithm or methodology and a laboratory proof of principle demonstration.
- 4.3 The final *Commercial Development Phase* encompasses the work of completing the development of commercial products and bringing them to market. This is the domain of companies particularly start-ups, together with new ventures within existing companies.
- 4.4 New companies are usually in competition with others addressing the same customer need, and the size and homogeneity of the US market means that companies based there can grow revenues much more quickly than UK firms. This enables them to spend more on R&D and marketing as markets mature, and to make acquisitions earlier to consolidate their position. The time taken to make the first sale is a critical factor in how successful a firm is ultimately, as this makes it easier to make every subsequent sale, as well as to attract investment. Policies to encourage lead customers therefore have an important role to play in reducing the width of the "valley of death".
- 4.5 In between the *Research* and *Commercial Development* phases is the process of *Exploratory Development*, during which potential applications of the research are conceived, demonstrated, turned into prototype products and trialled with lead customers.

- 4.6 In the case of software and some information technology hardware this process can be quite short as there is minimal technical risk. Facebook, Google and Cisco, formed by undergraduates, doctoral students and university computer services managers respectively, illustrate this. In each case successful, large scale product demonstrators, involving real, university users, were produced in just a few months. The venture capital backing that enabled the businesses to be scaled rapidly followed later.
- 4.7 However, in the case of the physical and biological sciences, the exploratory development phase can take years or decades. The most important opportunities are generally based on new technology "platforms", with multiple commercial applications. To define and evaluate them involves working with a range of potential users, in an exploratory manner, progressively focusing on those that look most promising. Blind alleys are common. Lead customers, prepared to pay for initial feasibility studies and the development and trialling of new technologies and products again play a crucial role.
- 4.8 Work to scale up production, improve quality and incorporate the complementary technologies needed to create a commercially viable product or process often takes place in parallel. Dependence on advances in other technologies means that progress takes place in fits and starts. This can take many years and be spread across continents. Only in very few cases, mainly pharmaceuticals, is the "inventor" able to secure sufficiently strong patent protection to ensure significant royalties at the end of this process. In most cases an accumulation of IP and know-how takes place over many years as the process progresses, with many parties involved. In the case of liquid crystal displays, in which UK academics played an important early role, the lead in developing the technology passed to RCA Corporation in the US and later to Sharp in Japan, before LCDs appeared in consumer products.¹²
- 4.9 Large corporations are increasingly hungry for new business opportunities and operate open innovation strategies with a global reach. Intermediate research laboratories like the Fraunhofer Institutes in Germany, ITRI in Taiwan and SRI in the US are constantly searching for academic research findings to help build their own internal, more mission orientated, long term R&D programmes¹³. This process makes it inevitable that research undertaken in UK universities will mainly be exploited by overseas organisations. And the longer the lead time involved the greater the chances that this will be the case.
- 4.10 To increase the probability of the UK drawing an adequate return from its investment in academic research, where it has an outstanding record, it must be more effective at points in the innovation process which are closer to market.

5. The Policy Challenge and Lessons from Other Countries

- 5.1 The critical Exploratory Development Phase must be undertaken, not in a university, but in a mission orientated R&D environment, working to commercial standards and with strong management of IP and commercialisation rights. The challenge for policy makers is that the risks and timescales associated with this phase are too great for venture capital backing.
- 5.2 Two successful policy responses to this dilemma are practised in other countries.

¹² Sharpe, S., A. Cosh and D. Connell, (2009), *Funding Breakthrough Technology: Final Report to the CIKC*; CBR, University of Cambridge, Cambridge.

¹³ Mina, A, Connell, D. and Hughes, A. (2009), *Models of Technology Development in Intermediate Research Organisations*, CBR Working Paper No. 396, Centre for Business Research, University of Cambridge: Cambridge

Procurement Based Innovation Policies

- 5.3 The first is for public sector agencies to fund the development of demonstrators as lead customers, based on their own requirements for innovative technologies as users or specifiers. This enables start-ups and other innovative companies to operate more easily during the exploratory development phase.
- 5.4 US support for R&D in companies is largely based on this model, using pre-commercial procurement contracts to provide significant funding. Contracts cover 100% of project costs and enable the contractor to retain any intellectual property. This enables start-ups and other SMEs to operate more easily during the exploratory development phase. Key programmes are the Small Business Innovation Research Programme (\$2.5 billion per annum) and DARPA (\$3 billion). The total is considerably more than this, with probably \$5-8m going to SMEs directly each year¹⁴.
- 5.5 SBIR projects are phased to manage risk and concentrate funding on the best projects. DARPA projects are also strongly milestone driven. This, and the fact that projects are funded by informed customers, helps reduce the risks associated with trying to "back winners".
- 5.6 The UK Small Business Research Initiative mirrors closely the US SBIR programme and has proved highly successful since it was launched in 2009. However, it is still only worth around £20m per annum and it has proved difficult for the Technology Strategy Board to persuade spending departments to increase funding levels.

Intermediate Research Laboratories

- 5.7 The second approach is to construct R&D institutions specifically designed to conduct the kind of mission orientated work needed during the exploratory development phase. These are typically not-for-profit organisations funded through a mixture of public and private sector R&D contracts, sometimes with some core government funding. Examples include the 60 German Fraunhofer Institutes, ITRI in Taiwan and a diverse range of US organisations, including Battelle and SRI International, originally the Stanford Research Institute¹⁵. SRI's most recent spin-out is Siri, which sells the voice control software used in the Apple iPhone4S. Like SRI's other more successful spin outs, Nuance and Intuitive Surgical, its technology was developed on the back of a large DARPA project.
- 5.8 To be successful Intermediate Research Laboratories need contracts from informed lead customers, just as early stage private sector R&D companies do.
- 5.9 The Cambridge technology consultancies operate in a very similar way to the Fraunhofer Institutes on which the Technology Strategy Board's new "Catapult Centres" are based, but with two differences. First, the Cambridge consultancies have had little or no government funding or development contracts and have therefore operated closer to market; and second,

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¹⁴ Further federal R&D funding flows to small US companies as subcontractors to larger firms. "Secrets" of the World's Largest Seed Capital Fund: How the United States Government Uses its Small Business Innovation Research (SBIR) Programme and Procurement Budgets to Support Small Technology Firms; David Connell, Centre for Business Research, University of Cambridge, July 2006.

¹⁵ Models of Technology Development in Intermediate Research Organisations, op.cit.

they have been much more successful in generating jobs in product spin-out companies. Government innovation policy has much to learn from these businesses.

6. Policy Proposals

Lead Customer Programmes

- 6.1 The most important thing Government can do to improve the effectiveness with which the science base is exploited is to increase the number and value of public and private sector lead customer contracts available to innovative companies. This includes early stage technical feasibility and design studies, as well as demonstrator and prototype development, and β site testing by users. This could be achieved by:
 - (i) Increasing the UK SBRI programme in steps from around £20m per annum currently to £250m per annum. This is a sum broadly equivalent to the US SBIR programme given the relative sizes of the two economies. All major government departments and agencies should be asked to participate, including the Research Councils through a Research Tools programme¹⁶. The Technology Strategy Board should be funded to provide half of the funding for each competition, with Departments funding the remainder and owning the topics.
 - (ii) Adding an equivalent sized budget for larger scale demonstration projects (above the £1m SBIR Phase 2 ceiling)
 - (iii) Establishing a similar programme to encourage more private sector organisations to act as lead customers for new technologies developed by SMEs. This could be achieved within EU State Aid Regulations by adapting the TSB's multi-partner collaborative R&D grant mechanism to fund bilateral partnerships between SME suppliers and large company customers. SME support levels (i.e. the percentage of total project costs funded) should be at EC norms rather than the less generous levels normal for TSB programmes. Further details of this proposal are available on request. After piloting this programme, the aim should be to increase funding projects to £100m a year.
 - (iv) Encouraging the European Council and European Commission to include a significant "pre-commercial procurement"¹⁷ element within Horizon 2020, the successor to the FP7 R&D programme which is currently being developed by the Commission. To match the scale of the US SBIR, the author has called for the EC to commit €1 billion per annum to match fund national SBIR programmes on a 50:50 basis. ¹⁸
- 6.2 Lead customer programmes would help move policy from a technology push to a more demand pull model. It would provide funding for the exploratory development stage and, by accelerating first customer purchases, reduce the width of the "valley of death". By helping firms adopt a "softer" start up model it would enable firms to remain independent for longer, thereby increasing their economic impact in the UK. It would also improve the flow of "VC ready" firms for those that need venture capital investment, thereby increasing average financial returns and attracting more investors into UK VC funds

¹⁷ Pre Commercial Procurement is the European Commission term for this kind of government activity

¹⁶ Proposals for a Research Tools SBRI are discussed in: *Scientists are Customers Too*, op. cit.

¹⁸ Speech to member state economy ministers at the European Competiveness Council Meeting, Budapest, 13th April 2011.

Catapult Centres

- 6.3 The creation of *Catapult Centres* is an important and necessary initiative for technologies with very long lead times. This programme should draw lessons from the Cambridge technology consultancies, whose experience in other areas of technology offers a valuable role model. The first Centre in High Value Manufacturing is really a partnership spread over seven existing locations, most of which are university based. To realise the potential of the Catapult programme, it is important that Centres are based on a single site and managed outside the university system. Capital and annual operating budgets are still unclear and need to be studied carefully to ensure the success of the programme is not compromised by underfunding.
- 6.4 Public sector R&D organisations easily become sleepy, so the aim should be for each to be privatised after ten to fifteen years, so that new Centres focused on emerging areas of technology can be created.

Universities

6.5 Excellent research universities are a vital part of any innovation cluster, but the most important way of exploiting that research is through their alumni, not the research results per se. The excessive pressure on university researchers to collaborate with industry and spin out new ventures has created unrealistic expectations and may even, in some cases, have been counter-productive. The focus must now switch to complementary policies to create demand pull through lead customers, private sector companies and intermediate R&D institutes. For those academics that do have technologies they believe could form the basis of an immediate spin out, a competitive grant scheme should be put in place to enable them to employ technologists from industry for one to two years to develop the proposition during a preventure stage¹⁹.

How These Policies Could Be Funded

6.6 Given the pressure on Government finances, the funding for these programmes could come partly from improving the cost effectiveness of the UK R&D tax credit programme.

6.7 Since its introduction in 2000 this has increased government funding for R&D in firms generally by around 600 per cent, dwarfing other policies²⁰. Three quarters of this money goes to large companies. This increase in R&D funding has been strongly welcomed by the business community, but there are many question marks over whether it represents the best way of using the money. R&D tax credits work by returning a percentage of a firm's total expenditure on R&D many months later, thereby increasing its profitability. There is no reason to believe that most firms will do anything other than spread the extra cash received across their full

¹⁹ Eight-19, a photovoltaic spin out from the Cambridge Cavendish Laboratory, was made possible by a scheme of this kind, funded by the Carbon Trust. It emanates from one of a number of technical projects being tracked over a 6 year period by CBR under the EPSRC funded Cambridge IKC.

²⁰ This refers to funding from generally available programmes and policies and excludes expenditure through departmental procurements or launch aid for aerospace projects, for example.

- range of expense items, from marketing to dividends. R&D tax credits are therefore best seen as providing a **subsidy to firms that do R&D** rather than an incentive for them to do more.
- 6.8 Although there is no requirement for firms to increase their R&D, it seems likely that the scheme has encouraged R&D to be reported which firms did not previously treat as such, aided by eligibility extensions by HMRC. For example, the 2009 R&D Scoreboard published by BIS indicated that three of the top 25 companies by R&D expenditure were UK banks (Royal Bank of Scotland, HSBC and Barclays, up 25%, 30% and 13% on the year respectively) with a total recorded R&D expenditure of £1.4 billion. HSBC and RBS were ranked 6th and 7th respectively, just above Rolls Royce and BAe Systems. A forth company, Tesco, reported R&D expenditure of £192 million, an increase of 50% on the previous year. In 2005 none of these four companies reported sufficient R&D (i.e. more than £1m) to be included in the top 750 UK R&D spenders.
- 6.9 For most established firms the majority of their R&D expenditure goes on incremental product and process developments with relatively little risk. As such it represents part of the cost of staying in business. Policies that focused government support for R&D on higher risk projects, particularly in firms spending a high proportion of turnover on R&D, would appear to offer greater additionality and better value for money.

Conflicts Declaration

I am a Director of TTP Capital Partners Ltd and a minor shareholder in a number of medium and small science and technology companies including TTP Group plc, TAP Biosystems, Knowledge Solutions (UK) Ltd, ZBD Displays Ltd, TeraView Ltd and Argenta Therapeutics.