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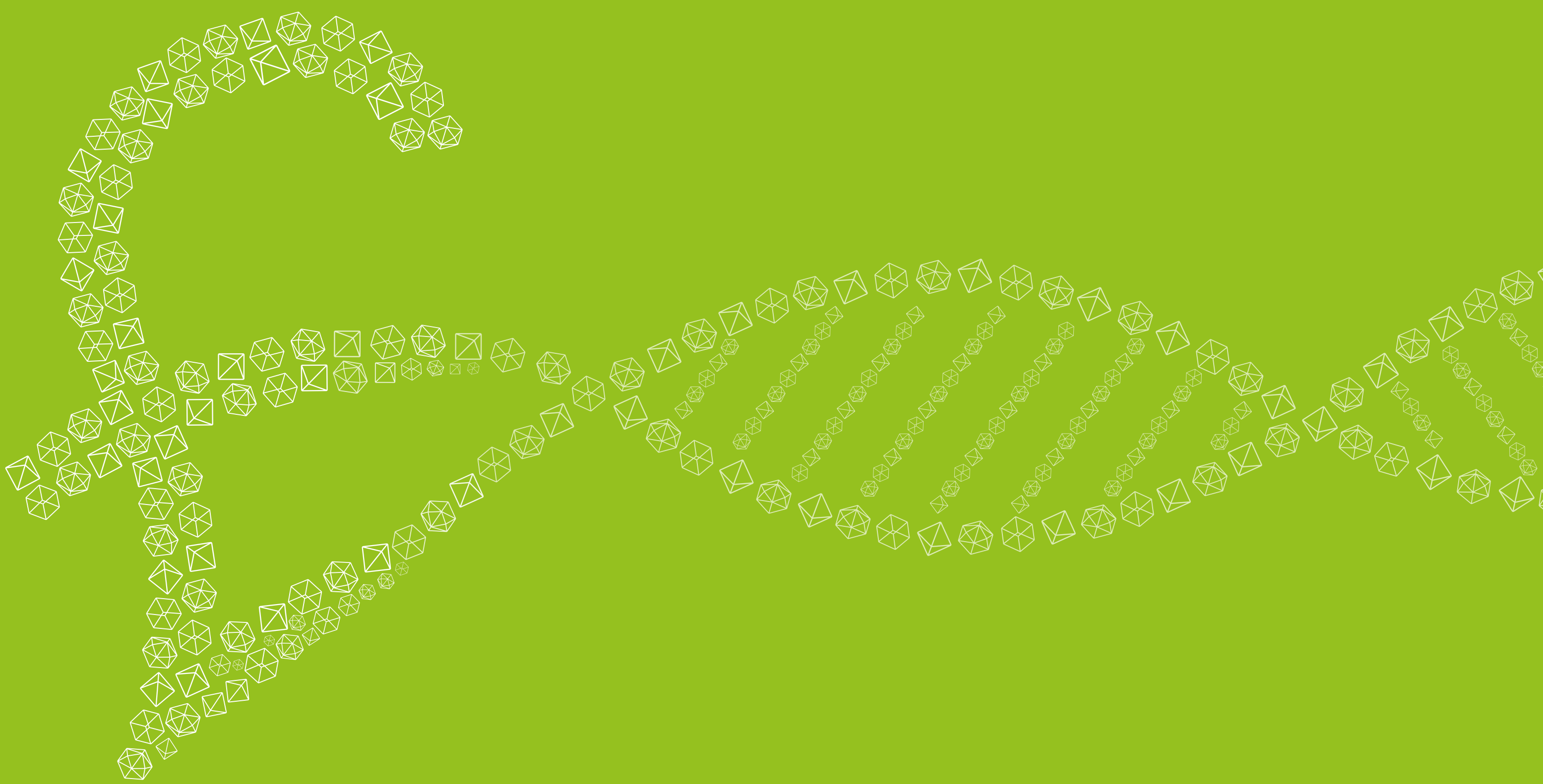
NESTA Making Innovation Flourish

Financing Industrial Biotechnology in the UK

Report prepared for NESTA by Technology Greenhouse Ltd



Financing Industrial Biotechnology in the UK

Foreword

Industrial biotechnology (biological processes used in industries apart from healthcare) has the potential to transform materials in amazing ways. It creates the opportunity to use alternatives to oil, to reuse waste, and to transform materials with low energy use. Oils secreted by microalgae can be harvested and used as biofuels, while sugar from beet and cane can be transformed into biodegradable plastics for food packaging.

Although what might be called the industrial biotechnology sector is small in the UK, it has the capacity to transform industries as varied as chemicals, waste treatment, energy production and plastics – industries with a combined value in the UK of £81 billion, and employing more than 800,000 people.[1]

Industrial biotechnology exemplifies the problems that companies who develop novel technology face – those with long and expensive development timelines, and who are dependent on large companies to put their products into action (as customers, acquirers, or by growing themselves). These companies need funding to develop and test the technology they have come up with. They need demonstrations to convince investors and large companies that the technology will work. They need to scale-up processes from the laboratory to the plant, usually in several stages.

The high degree of uncertainty and technical risk for these companies means they struggle for investment in a shrinking early-stage venture capital market. But the effects of this technology can be transformative – there are big prizes to be won for those who can make it work. And the results are not just in profits or cost savings, but in lower energy usage, less landfill and reduced greenhouse gases.

This report represents only a snapshot of the industry. While we believe the approach is representative of the industry as a whole, we would welcome feedback and further comments. The policy recommendations in this report are the first step towards a policy report we hope to publish in the coming months. Please comment, discuss and feed back to us what you think is needed to support this growing sector.

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October, 2011

1. Annual Business Survey 2009, revised figures for SIC codes 01, 10, 19, 20, 22, 35, 36, 37, 38

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Executive summary

Introduction

The UK Government has identified industrial biotechnology (IB) as a key driver of wealth creation in the 21st century and in November 2007 it established the Industrial Biotechnology Innovation and Growth Team (IB-IGT). In May 2009, the IB-IGT presented a major report to government ('IB-2025') which estimated that IB could add £4-12 billion per year to the UK economy by 2025. In order to capitalise on this opportunity, UK companies will need to raise finance to invest in the industrial and commercial development of IB products.

Building on the pioneering work of the IB-IGT, NESTA commissioned this research to examine the corporate funding environment for IB in the UK two years on. It involved an in-depth survey of selected participants working in this nascent sector. The output from the interviews is summarised into a series of common themes. Based on these themes, a number of conclusions were drawn regarding the current status of the UK IB sector and *ad hoc* recommendations developed for steps which could lead to an improved financing environment (Key Findings). In a final section, the Key Findings are synthesised into eight Principal Recommendations proposing practical measures for further improving the flow of finance required by the UK IB sector if it is to reach its potential.

At the broadest level of categorisation, biotechnology can be divided into 'Healthcare' and 'Industrial' segments. For the purposes of this research, the industrial biotechnology (IB) segment has been sub-divided by product into four categories: chemicals and materials, bioenergy and biofuels, waste to energy and waste remediation, and enhanced food production.

Current status of the IB sector

The leading country internationally in IB is the US. Within Europe, Germany is well ahead of all other countries. The UK competes in the next tier, most notably with Switzerland and Holland, which is an improvement on the position the UK has historically occupied. In Asia, both India and China are increasingly active. Brazil is also making significant progress, particularly where sugar is used as a feedstock.

The total number of significant and active UK participants in all components of the IB value chain comprises fewer than 100 organisations. Less than 30 of these are indigenous companies with a hands-on engagement in the practical commercialisation of IB and the majority of these indigenous companies employ fewer than 20 people. There are UK SMEs active in almost all relevant areas of IB but in almost no cases are these recognised as world leaders. A dysfunctional financing base which starves UK SMEs of capital has played a critical role in limiting the development of the UK's IB companies.

Several of the SMEs interviewed were set up initially as virtual entities – procuring all required services under sub-contract rather than having any direct employees. This is a lean and effective way to operate and, given the limited amount of seed money which it is possible to raise, many companies have no alternative but to operate in this way. The creation of a virtual company is facilitated by the availability of skilled technologists and experienced executives who have become surplus to the requirements of the UK's contracting (petro)chemicals manufacturing sector.

The UK academics working in IB command wide international respect. There is university research being undertaken in almost all relevant areas and in some cases the UK's research is leading the world. International companies are still funding research at UK universities despite their general perception that UK academic institutions have not established a track record in the collaborative applied research needed to commercialise these fundamental discoveries.

The number of UK SMEs spun out directly from universities is surprisingly small for an advanced technology-based sector. Out of the ten SMEs interviewed, only two fell into this category – in both cases coming from a chemistry department rather than a life sciences faculty or dedicated inter-disciplinary IB group.

Industrial research centres give rise to more spin-outs than academic institutions, but the predominant model was for companies to be set up by entrepreneurs released by large companies to target a particular market opportunity. This is probably because hands-on chemical engineering plant skills are vital in an IB company and these cannot easily be developed in a university environment.

There are no large and innovative chemicals companies with their headquarters and main R&D operations in the UK. If the IB sector turns out to thrive only in an industrial ecosystem which requires these mature companies (which have been compared to the tall trees in a forest) to be present, then it might have problems thriving in the UK. One obvious issue is that IB start-ups rely on recruiting employees who have already gained relevant post-graduate (practical) industrial experience. Without large established (bio) chemicals companies, it is difficult for such people to find somewhere to serve such an industrial apprenticeship.

Funding requirements and barriers to investment

There are three 'chicken and egg' situations that are acting as obstacles to investment in the UK IB sector. These are characterised as follows:

Multi-national 'tall trees' do not tend to invest in UK IB opportunities because such opportunities tend to be commercially under-developed and they remain so primarily due to a lack of investment: There is a lack of mature companies in IB that have the capacity and the strategic interest to invest in the UK IB sector. While the UK lacks industrial 'tall trees' in the chemicals and materials manufacturing sector altogether, this is not the case in the three other segments of IB, and particularly in fuels. Unfortunately, even in these segments, the nurturing provided by these mature companies in the form of research collaborations and corporate venturing appears to be rather limited.

UK VCs are reluctant to invest because historic returns on early-stage funds have been poor, but this may be because early-stage companies are starved of VC funding: Although the underlying techniques and science are advanced, the fuels, chemicals and foodstuffs produced by IB command prices in the low single-digit dollars per kilogram range. In order to recoup an investment in novel technology, annual sales of the resulting products need to be of the same order of magnitude as the sums invested in developing them. For IB, this requires industrial plants manufacturing hundreds of thousands of tonnes of product per year. The capital required to build and operate such plants is too high (£75-150 million) and the time it takes to develop them to the point when they become commercial (four to eight years) is too long for most UK investors, particularly Venture Capital (VC) funds to take the risk at the time such investment is needed. This stunts the development of UK IB companies and puts off international investors, who look for companies and markets with successful track records of growth. These problems are much more acute in the UK than in the US as US VC funds have a better track record of profitable exits from technology-based companies, but UK VC funds generally do not. These factors add to the observation that the investment climate for UK VC investment in technology based companies, of any sort, is not positive.

Generators of waste expect a company to have secured funding before awarding it a treatment contract but its financers expect to see signed contracts before investing: The waste treatment sub-sector of IB is somewhat different from fuels, chemicals and food. It is a more inherently distributed activity requiring a larger number of small, more local, facilities so an investment of £10 million would typically build a full-scale demonstration plant that was commercially viable. The main need in this case is for project finance and working capital to fund subsequent plants. Generators of waste expect a company to have secured such funding before awarding it a treatment contract but its potential financers expect to see signed contracts before investing because this is key due diligence input for them. That said, as the policy climate in the UK is forcing generators of waste to find ways of reducing waste (or better still recovering added value products from it) such organisations are, in principle, more engaged than most.

The financing picture for IB start-ups is not entirely gloomy. The funding market place is international and there is an emerging opportunity to attract VC investment from outside the UK and a detectable increase in interest from established multi-national companies in IB generally.

Unlocking early-stage opportunities

A healthy IB sector requires research collaborations between large corporates, SMEs, university labs and development facilities. Strong partnerships between SMEs and corporates provide the SMEs with funding for their research and the corporates with a degree of innovation that they are no longer able to source in-house. Such collaboration is made more difficult by the UK's lack of large domestic corporates relative to its main international competitors. UK IB SMEs would benefit from government support to facilitate these international contacts.

While there has been a lot of investment in the UK in science and facilities, there has been relatively little emphasis on identifying and developing IP that can be exploited commercially in IB. The Research Councils, as the academics' paymasters, have a role to play in improving the cultural alignment between the academic and entrepreneurial IB communities while the university technology transfer offices could help to transmit market pull through to the laboratory. For example, contract negotiation between universities and industrial sponsors could be simplified by the use of standard sets of terms and conditions such as the 'Lambert Toolkit' or similar standardised research collaboration agreements.

The use of friends, family and relatively unsophisticated local angel investors to provide seed money may be the only way to get a company started but a myriad of small shareholders diffuses control making it difficult to raise significant further VC funding to expand the business. Alternatively, virtual companies minimise the seed funding requirement but can face problems with bureaucracy and tax legislation. A simple tax template for treating contributions to technology start-ups made in return for equity would help by ensuring that tax only became payable on a liquidity event or disposal. There are also a number of practical ways in which Technology Strategy Board (TSB) project co-funding and R&D tax credits could be made more user-friendly for such companies. Several of the SMEs interviewed found R&D tax credits useful but the application process can be complex and bureaucratic with significant associated costs.

Grants are vital for funding early 'proto-start-up' companies and continue to be very important through the seed and VC rounds. Relative to early-stage equity funding, IB start-ups report that grant funding is more abundant, easier to access, easier to manage and highly attractive because it is non-dilutive. Grants from a respected agency provide reputational as well as financial leverage which can combine into a virtuous circle. The TSB and its directed IB calls have been hugely important to SMEs in this respect. EU funding, which tends to be directed at more established companies, has been much less so.

Unlocking growth-stage success

While start-up companies can be established for a few hundreds of thousands of pounds, if they are to grow into cash flow positive SMEs they will typically need funding two orders of magnitude greater than this. Such sums are generally provided by VCs but at present there is very little VC appetite for IB (or any other technology) investments in UK. There is little point in taking measures to promote start-up company formation if the prospects for follow-on funding are poor and there is thus an urgent need to improve the delivery of development capital to UK IB SMEs. Government procurement of demonstrators and other research outcomes could offer a more focused form of support than blanket R&D tax credits. It is worth noting that in the US, the relatively greater availability, longevity and scale of government funded development programme grants has encouraged private investors to take equity in SMEs that show the technical capability and the capacity for growth to deliver such programmes.

IB SMEs have particular difficulty funding sub-scale industrial demonstration plants. Once such a plant has served its purpose it quickly becomes obsolete. It therefore makes sense to rent time on a shared demonstration plant rather than to buy one outright and using an existing shared facility significantly shortens the lead time. The £12 million National Industrial Biotechnology Facility (NIBF) at the Centre for Process Innovation (CPI) was built in order to capture these benefits and is widely applauded as an excellent use of public funds.

While the NIBF was designed for maximum flexibility, a single facility cannot be reconfigured to meet every operational requirement nor located where the feedstocks exist across the UK. It is therefore important to expand the availability of shared-access facilities beyond the excellent precedent set by the NIBF. One possibility is to encourage the negotiation of *ad hoc* 'time share' arrangements for equipment that is surplus to requirement or not being fully utilised by its current owners. A central broker could be established to facilitate this, ideally on an international scale and the incorporation of the NIBF within the new High Value Manufacturing Technology & Innovation centre may help with this.

The banks are extremely reluctant to lend to early-stage IB companies even if they are trading profitably, thus restricting their growth. Loan guarantees could offer a partial solution to this problem and thereby play a role in unlocking revenue growth. It would be worth exploring a nationally administered scheme tailored specifically for strategically important industrial sectors.

Many IB processes are very energy-efficient while the feedstocks used are generally renewable. Government interventions aimed at promoting carbon reduction can recognise these benefits and at the same time support the nascent IB sector, but *ad hoc* schemes can distort the market and may not even result in an optimisation of the desired environmental outcome. Ideally a single accounting unit (e.g. tonnes of carbon saved or landfill diversion) can be developed, which will assist investors to estimate the strategic value of developing IB in the UK. It is recognised that developing such an accounting framework will not be simple.

Exits to unlocking returns

There are, in principle, three ways in which an investor may achieve an exit: initial public offering (IPO) on a stockmarket; tendering the shares to an offer made to buy the entire company (a 'trade sale'); or by a distribution of profits via dividends or share buy backs. The first of these is unlikely to be possible in the current market conditions. The last does not fit well with the VC investment model. It is therefore probable that the majority of UK IB SMEs will be sold to strategic buyers and, given the UK's lack of 'tall trees', these buyers are very likely to be foreign companies. Despite the current market conditions, the IPO route therefore offers the best long-term chance for UK IB companies to become 'tall trees' that assist the UK in rebuilding its manufacturing base and rebalancing its economy.

It was suggested that early-stage equity portfolio returns in the UK are disappointing mainly because conventional VCs exit too soon from the winning companies, meaning that these companies don't have time to create sufficient value to compensate for the inevitable failures in the portfolio. However, some individuals are bucking this trend (e.g. Neil Woodford at Invesco Perpetual) and pioneering a long-term (10-15 years) investment approach. If this approach demonstrates that taking longer term (and larger) bets can lift the historically disappointing returns on early-stage VC funds, then other money managers may be persuaded to put a small proportion of their assets into start-up companies. In addition to increasing the returns on funds that are desperately seeking improved yield, this would have a massive impact on creating new high technology manufacturing jobs.

Principal Recommendations

Policy recommendations that are specific to the IB Sector

Policy support can be used to assemble a coherent IB sector in the UK and to stimulate domestic and international investment into UK IB businesses. Our suggested recommendations are:

To improve strategic consistency:

1. A joint committee is formed consisting of representatives from government, industry and the finance sector to establish guidance

on which R&D goals are strategically important to the UK and standard metrics for assessing the relative strategic value to the UK of investing in specific IB development projects.

To improve collaboration:

2. Development funding is made available to encourage more active collaboration between corporates, SMES and the academic community. Such funding could lever in corporate investment and support measures such as:

   a. The facilitation of contacts between UK SMEs and multinational corporates. In addition to the work that the UKTI already does, this type of contact could be designed to attract 'tall trees' to UK by discussing plans for joint public and private sector investment in technology development programmes that are of strategic importance to the UK (see b).

   b. Technology development competitions requiring multiple participants to deliver strategically important results through open innovation to the mutual benefit of the parties involved. This would be an expansion of what TSB already does and the larger sums involved would be designed to attract international IB companies to come to UK to conduct their research in collaboration with UK SMEs and universities.

   c. If the measures described in bullets a. and b. are successful in generating a demand for more mid-scale (non-commercial) industrial facilities, a centralised pool of equipment and greater availability of shared demonstration facilities with links to business incubation services for hire to IB SMEs looking to industrialise processes developed in the lab could be considered.

Policy recommendations that are generic to technology development

There is a clear requirement for policy support to encourage technology development generally in the UK and to stimulate domestic and international investment into UK technology-based businesses.

Our generic recommendations are that:

To encourage growth:

3. Targeted measures to stimulate lending to those IB SMEs which have made considerable progress reducing technology risk and now need to invest in the elimination of scale-up risk. The criteria for assessing which companies qualified for such support would need to be specific to the technology concerned, but the support measure itself could apply across a variety of technologies. Such measures could include loan guarantee schemes and encouraging banks to offer debt facilities to venture lending funds.

To reduce start-up costs:

4. The tax system is modified to recognise the existence of virtual companies and to encourage the development of technology-based start-up companies by:

   a. Creating a virtual company legal and tax template in the same way that templates have been established for VCTs or EIS-qualifying businesses.

   b. Simplifying the administration of R&D tax credits.

These measures would need to be restricted to technology-based entities and they would need to deal with complexities relating to IP ownership, VC investment, valuation etc.

To encourage longer-term investment:

5. Ways are sought to encourage and replicate the investment strategy being pursued at Invesco Perpetual. This could include tax incentives for retail investors or preferential tax treatment for profits from such investments.

Observations that are relevant to the research community

There is a clear need for greater collaboration between the research, industry and finance communities to promote the commercialisation of IP. Our specific observations are that:

6. Research councils could consider encouraging more active collaboration between research and industry by funding more interdisciplinary and collaborative projects with the aim of developing IP that could be of commercial value.

7. Universities could consider encouraging greater project working by facilitating collaboration between traditionally separate academic fields such as chemical engineering, micro-biology etc. For IB, this could build initially on the existing centres at Manchester (CoEBio3) in the North and UCL in the South. These academic research centres should have close links to sources of business expertise, business incubation facilities and shared demonstration facilities. Most importantly, they should be funded with new money and not be simply a new organisational overlay on existing activity.

8. University technology transfer offices could consider facilitating closer ties with corporate funders by standardising forms of contract, thereby simplifying and shortening contract negotiations.

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From Technology Greenhouse the principal investigators were Philip Brain, Dr Jane Garnett, Dr Nick Goddard and Dr Garry Staunton. At NESTA, the project was managed by Louise Marston, Lead Policy Advisor for Growth Sectors, with input from Dr Robert Crawford, Director for Innovation, Investment and Growth, and Alex Hook of the VC investment management team.

NESTA and Technology Greenhouse Ltd wish to thank all the interviewees who very generously gave their time to participate in the survey reported herein. In the course of devising, commissioning and conducting the survey, valuable inputs were made by the following people to whom we are also most grateful: Iain Wilcock (Seventure Partners), Ian Shott (SCC), Nigel Gaymond (BIA), Dave Tapolczay (MRCT) and Carol Boyer-Spooner (CI KTN).

2. See: www.technologygreenhouse.co.uk

Contents

Financing Industrial Biotechnology in the UK

Part 1: Introduction

This report summarises the feedback and key conclusions from a survey of a cross section of the participants in the UK's nascent industrial biotechnology (IB) sector. The work was carried out on behalf of the National Endowment for Science, Technology and the Arts (NESTA) by Technology Greenhouse Ltd.

The background and objectives for the project are described in Part 2 while its remit in terms of the particular focus on IB is discussed in Part 3. The survey was based on 32 in-depth telephone interviews conducted by scientifically qualified senior consultants, all of whom also have a background in the commercialisation of advanced technologies. The interviews took place in July and August 2011. Details of the interviewees and other aspects of the survey methodology are summarised in Part 4 and Appendix 1.

A synopsis of the responses from across the entire set of interviews is presented under various headings and the implications of these in terms of prospects, challenges and recommendations for financing the creation and growth of innovative IB companies in the UK (the 'Key Findings') are explored in Parts 5-9. The total of 16 Key Findings set out in Parts 5-9 are summarised in Part 10. Finally, in Part 11, the Key Findings are synthesised into eight Principal Recommendations proposing practical steps which could be taken to improve the financing of the UK IB sector.

The interviewees were encouraged to speak candidly in the interests of developing an authentic picture of current attitudes within the sector. Because of this, many of their comments have been summarised and reported anonymously herein. This is indicated by the use of "inverted commas", which therefore do not necessarily imply a verbatim quotation. Where necessary to provide a context for certain remarks, the type of organisation making them is indicated in [square brackets]. In some cases the interviewees have given approval for certain comments to be attributed and these are indicated either by naming them in the text or using [square brackets] at the end.

As discussed at the beginning of Part 5,[3] the IB sector in the UK is small and relatively immature. We estimate that the total number of significant and active participants in all components of the IB value chain comprises slightly less than 100 organisations. On this basis, we believe that the programme of 32 interviews was sufficient to provide a balanced and statistically significant view of the entire sector. However, it should be noted that the remit of the work carried out was to report and summarise the personal opinions of sector participants rather than to prepare a comprehensive landscape study of IB in the UK. Resources were not made available to validate or contextualise the comments made. The result should therefore be viewed as a 'collective subjective' view of the sector rather than an exhaustive, independent and objective evaluation.

3. See Key Findings F1 and F2.

Part 2: Background and objectives

Industrial biotechnology has been identified by many commentators as being a key driver of wealth creation in the 21st century. Indeed, it has been suggested by some that if chemistry was the pre-eminent driver of industrial development in the 19th century and physics in the 20th century, then we have now entered the 'Century of Biology'. While this may be over-simplistic (steam power was pretty important in the 19th century and could reasonably be claimed to depend more on physics than chemistry) it is true that, going forward, industrially applied biology will have a key role to play that goes beyond simply picking up the baton of wealth creation.

The human race is now facing unprecedented challenges in securing sufficient food, energy and water to support the growing global population, all of which have to be met without doing irreversible ecological damage. These 'existential' challenges have been added to, rather than replaced, the expectation which has operated ever since the beginning of the industrial revolution that technology can deliver ever-greater levels of prosperity. One of the respondents to this survey noted that *"biotechnology – the use of biological systems for the development of sustainable products and processes – is key to a future knowledge-based bio-economy"* [Croda]. Its use of renewable resources is an obvious response to the exhaustion of finite natural resources, most notably oil and gas.

The importance of IB to a successful modern economy is starting to be more widely recognised in the UK. In November 2007, the then Department for Business Enterprise and Regulatory Reform (BERR) established the Industrial Biotechnology Innovation and Growth Team (IB-IGT) tasked with looking at opportunities for IB in the UK, barriers and obstacles for realising these opportunities, and strategies and mechanisms for accelerating progress. Among the most important outputs to date from the IB-IGT was a report to government in May 2009 on 'Maximising UK Opportunities from IB in a Low Carbon Economy'.[4] This report, often referred to as 'IB-2025', estimated that IB could add £4-12 billion per year to the UK economy by 2025. It set out 21 recommendations aimed at preparing the UK to capitalise on this opportunity.

The government response to IB-2025, published by the Department for Business, Innovation and Skills (BIS) in June 2009,[5] accepted all of its recommendations. Since then, BIS has set up the IB Leadership Forum (IBLF) co-chaired by Ian Shott, Chair of the IB IGT, and Mark Prisk MP, Minister of State for Business and Enterprise. It has also provided £12 million to establish the National IB Facility (NIBF) at Wilton and launched three funding rounds of £2.5 million each via the Technology Strategy Board (TSB).[6] The TSB has also established an Industrial Biotechnology Special Interest Group (IB-SIG) which will operate across its networks to implement the IB-2025 recommendations. In September 2009, the Biosciences KTN (Knowledge Transfer Network) was formed by the amalgamation of three predecessor bodies – it is part-funded by the TSB. Like all KTNs, its mission is to put companies and innovators in contact with the knowledge and funding that they need to bring new products and processes to market.

The IB-IGT and the activity which it has helped to catalyse at the TSB are concerned mainly with the need and opportunity for IB (the industrial 'demand side'). The 'supply

4. IB-IGT (May 2009) 'IB 2025 Maximising UK Opportunities from Industrial Biotechnology in a Low Carbon Economy.' Available at: http://www.bis.gov.uk/files/file51144.pdf
5. BIS (June 2009) 'Government Response to the Industrial Biotechnology Innovation and Growth Team Report to Government.' Available at: http://www.bis.gov.uk/files/file51891.pdf
6. The most recent call for proposals, under the heading 'Producing high-value chemicals through industrial biotechnology', was announced on 7 September 2011.

side' of this equation is the development of novel enabling biology-based technologies. In January 2010, the Biotechnology and Biological Sciences Research Council (BBSRC) published a strategic plan for 2010-2015 entitled 'The Age of Bioscience'[7] which identified IB as one of three high level strategic priority areas. A subsequent report, 'BBSRC support for bioenergy and industrial biotechnology: the use of science and technology to support energy chemicals and healthcare industries', presented recommendations for specific actions to reflect this. The first of these was that BBSRC should increase the size of its IB portfolio as a proportion of its total budget. The BBSRC's current delivery plan includes an intention to increase industrial biotechnology funding from £20 million to £30 million by 2014-2015.[8] In January 2009, it established the BBSRC Sustainable Bioenergy Centre (BSBEC), a £24 million investment aimed at increasing UK bioenergy research capacity. Working with the Engineering and Physical Sciences Research Council (EPSRC) and a consortium of leading companies, it has also established the Integrated Biorefineries Initiative (IBTI Club). This is a £6 million, five-year initiative aimed at developing biological processes and feedstocks.

Alongside the inventors and exploiters of IB, the third vital ingredient of wealth creation is the finance required by companies to invest in the industrial and commercial development of IB products. Building on the pioneering work of the IB-IGT, NESTA commissioned the present work, in order to examine the current corporate funding environment within the UK IB sector. The specific objective is to make recommendations which could improve the availability of funding for UK companies in this sector. The results from the work, reported herein, and a related internal study on the historic pattern of VC investment in the sector, will inform NESTA's on-going work on innovation policy for economic growth.

7. BBSRC (2010) 'The Age of Bioscience: Strategic Plan 2010-2015.' Available at: http://www.bbsrc.ac.uk/web/FILES/Publications/strategic_plan_2010-2015.pdf
8. BBSRC Delivery Plan 2011-2015. See: http://www.bbsrc.ac.uk/web/FILES/Publications/delivery_plan_2011_2015.pdf

Part 3: What constitutes industrial biotechnology?

Biotechnology may be described as the practical application for commercial purposes of fundamental scientific discoveries made by biologists or interdisciplinary teams focused on projects defined by biologists (e.g. biomechanics, bioinformatics). More specifically, it is usually taken to mean advances made during the past 60 years or so, over which period biological processes have come to be understood at the fundamental molecular level.

At the broadest level of categorisation, biotechnology can be divided into 'Healthcare' and 'Industrial' segments. The healthcare segment is more advanced and includes drug discovery programmes focusing on large molecules (new biological entities or 'NBEs'), gene therapy, drug delivery, tissue engineering, cell therapy, prosthetic and other implants and various devices for assisted living. Industrial biotechnology (IB) – which is sometimes referred to as 'white biotechnology' – essentially captures all commercial applications of biology that do not fall into the healthcare segment.

Because IB generally uses renewable raw materials and produces biodegradable and/or recyclable outputs, it is a very environmentally friendly approach and is therefore a key 'green' or 'clean' technology. In addition to being sustainable in terms of feedstocks, the biologically-mediated processes take place at, or relatively close to room temperature and pressure, reducing energy consumption. IB is therefore an important 'low carbon' technology and can play a key role in reducing emissions of greenhouse gases (GHGs). Biological routes are particularly attractive if chiral (stereo) specificity is required in the end product.[9]

The use of labels such as 'clean', 'green' 'sustainable' or 'low carbon' can have practical consequences in establishing national and international research agendas, highlighting new market opportunities and attracting funding – these issues are discussed further in Part 6. Indeed, the commercial viability of many IB processes depends on some financial value being assigned to their superior environmental impact. Biofuels are a good case in point: these are generally not cost-competitive with fossil fuels unless a value can be allocated to the resulting carbon savings.

The TSB follows the EuropaBio definition of IB as the use of enzymes and micro-organisms to make bio-based products in sectors such as chemicals, food and feed, detergents, paper and pulp, textiles and bioenergy (notably biofuels and biogas). However, for the purposes of the current study we have adopted a less nebulous definition of IB based on the following four end-use sectors:

- **Food production** – the use of modern biotechnologies to develop improved plant and animal strains, cultivation techniques (e.g. pest control strategies) and processing technologies to improve the primary yield, processing economics and distribution chain utilisation of food (e.g. by increasing shelf-life to reduce wastage). Genetically modified (GM) crops are the best known (and most controversial) example but many other technologies exist. In this report, we are concerned only with food for basic nutrition: active foods or 'nutraceuticals' intended to promote health are considered to fall into the healthcare biotechnology segment.

- **Biofuels** – these may be solid (e.g. charcoal or biochar), liquid (e.g. bioethanol

9. That is control of the mix of stereoisomers produced – molecules whose spatial arrangements are mirror images of one another.

produced by fermentation or oils secreted by microalgae) or gas (e.g. biomethane produced by anaerobic digestion). The key objective is to use photosynthesis to convert atmospheric CO_2 into biomass which is then converted into a fuel and combusted; releasing the CO_2 back into the atmosphere, but making no net addition to total atmospheric carbon levels (at least from the combustion process itself).

- **Biomaterials and manufacturing** – the use of biological processes in the extraction and/or synthesis of materials. Biodegradable polymers, for example polylactic acid, can be produced from biological precursors. There is renewed interest in fibres made from cellulosic precursors (the original being rayon). Enzymatic catalysis can be used to promote energy-efficient reactions at low temperatures and pressures. Simple organisms are being studied for 'bio-mining' and 'bioleaching' – extracting and concentrating metals from low grade ores.[10]

- **Waste treatment** – organic waste can be converted into fuels via 'waste to energy' routes such as anaerobic digestion. In particular, the use of synthetically produced enzymes has opened up the possibility of using lignocellulosic and other hard to treat organic waste. This simultaneously reduces the demand for landfill and the GHG emissions from the decomposition process, while providing a source of biofuels. Remediation of contaminated soil or water (including marine oil spills) can be achieved by biological processes.[11]

There are now various technologies being developed on the fringes of IB which do not directly harness biological discoveries, agents or processes, but are inspired by an understanding of the natural world. The most advanced is probably 'biomimetics' – the development of synthetic materials or structures which mimic certain aspects of those observed in nature. The underlying philosophy is that these structures have been optimised over millions of years of evolution and are therefore worth copying. Examples include 'shark skin' coatings to reduce drag, textured surfaces to combat bio-fouling and various structural composites. More recently, biological sensors and actuators have been developed, in some cases for use in biomimetic robots and other cybernetic applications. While offering long-term potential, such technologies are at an early stage in their development and are not currently associated with large end-use markets of the sort described above. They have therefore been excluded from the current study.

10. These are examples of a technology sometimes referred to generically at biohydrometallurgy. Where the extraction is by plants the technology is called phytomining.
11. Where this is carried out by plants it is referred to as phytoremediation.

Part 4: Survey methodology

As already noted in Part 1, the survey was based on 32 carefully targeted telephone interviews conducted by scientifically qualified senior consultants, all of whom have a background in the commercialisation of advanced technologies. The in-depth interviews typically lasted from 30 to 60 minutes, although in some cases more extended discussions or follow up calls took place. The qualitative output from the interviews is summarised into a numbered series of common themes, which deal with respectively the industrial characteristics of the UK IB sector and its funding environment.

In order to provide an element of quantitative output, at the end of most interviews the interviewee was asked to indicate their level of agreement with the following eight statements:

1. The UK IB sector is currently getting the funding it needs.

2. Growth of the UK IB sector is currently constrained by a lack of available funding.

3. Even the best quality companies are finding it hard to raise the necessary funds.

4. It is harder to fund IB companies in the UK now than it was five years ago.

5. Overall, investors in UK IB companies have to date had disappointing returns.

6. A healthy IB sector is important for the broader competitiveness of UK industry.

7. Hard-headed investors are right to be sceptical of the potential returns from IB.

8. Today's IB SMEs have the potential to become the IB multi-nationals of tomorrow.

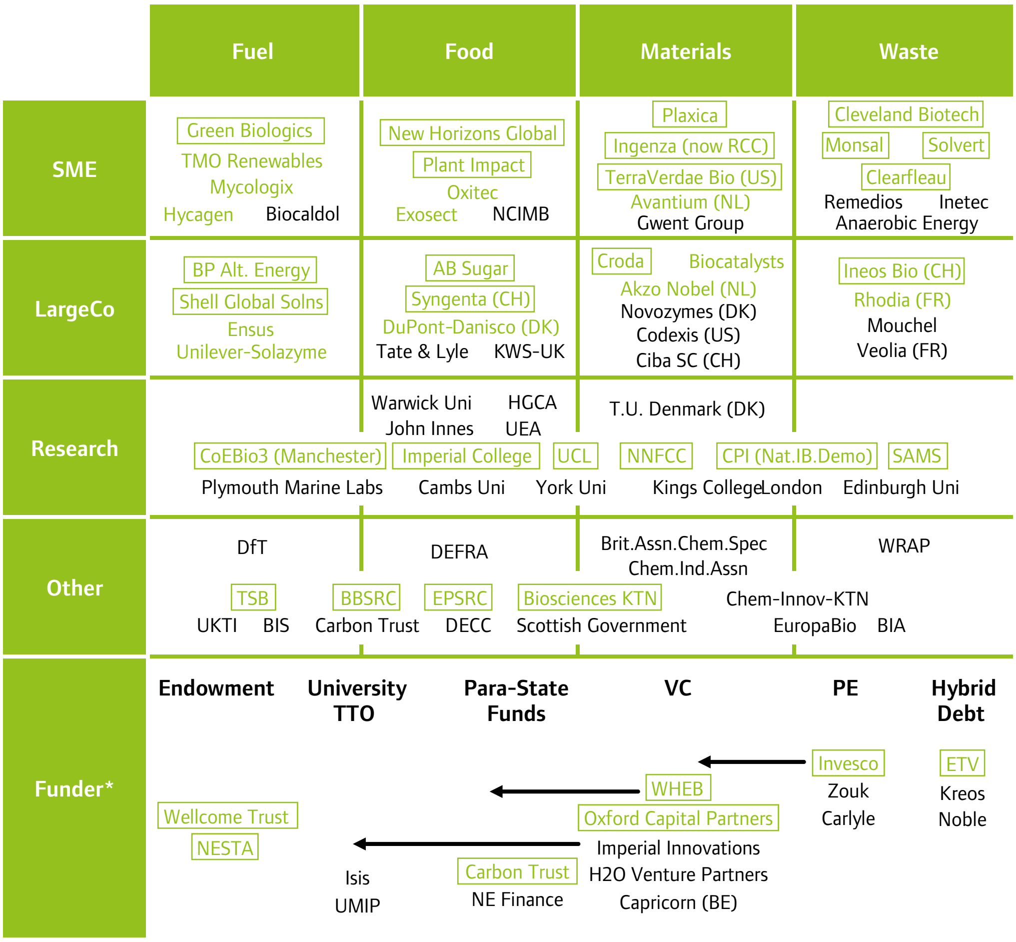
The answers to these quantitative questions are summarised and discussed in Part 6.

Based on the common themes from the survey, a series of conclusions were drawn regarding the current status of the UK IB sector and recommendations developed for steps which could lead to an improved financing environment. These numbered Key Findings are presented in Parts 5-9, which deal successively with the creation and early-stage funding of new IB companies; ensuring their commercial development and associated revenue growth, and; providing an eventual exit/return for their investors. The Key Findings are summarised in Part 11 and distilled into eight 'Principal Recommendations' listed in Part 11. Two of the Principal Recommendations relate specifically to the IB sector while another three are more generally applicable to UK technology start-up companies and a further three are observations on how the academic community could improve the chances of commercialising IP.

A list of survey participants is provided in Appendix 1.

In Figure 1, the 'long list' of 90 IB sector participants is shown mapped by type and industry segment. The 45 short-listed participants are shown in red with the 32 actually interviewed indicated by a box around their name.

Figure 1: Mapping of interviewees



* 'Funder' refers to company funding as opposed to research funding.

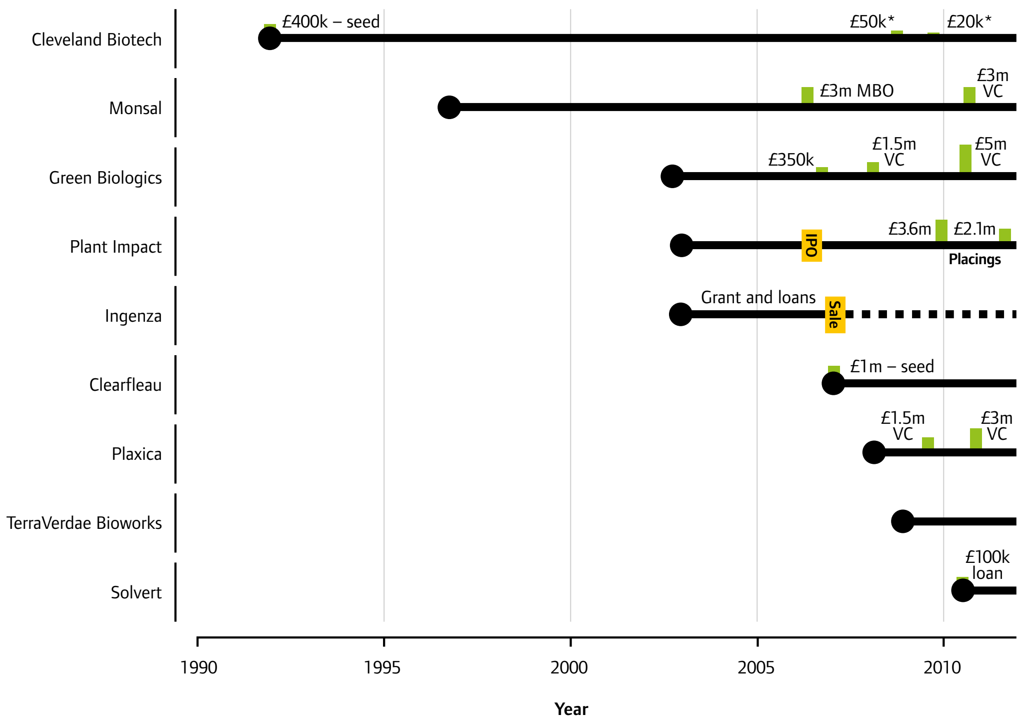
12. This is taken roughly to have its vertices at Cambridge, London and Oxford, the location of the UK's three highest ranked universities. It contains the majority of successful UK technology SMEs, although clearly there are some very successful companies located elsewhere.

13. See Key Finding F13.

In addition to the broad two-dimensional mapping shown in Figure 1, the interviewees provided a range of more specific experiences. The ten SMEs were founded over a period spanning 20 years and have made varying amounts of progress raising funding, as illustrated in Figure 2. They are also employing various distinct business models including a virtual company funding the extra-mural development of intellectual property (IP), companies developing IP in-house with a view to licensing it to manufacturing partners and those developing products which they intend to manufacture and sell.

The 32 interviewees were distributed across most regions of the UK, as shown in Figure 3. There has been some discussion about clusters of IB companies forming in the old industrial heartlands, however, just over half of the interviewees were nonetheless located in the prosperous 'Golden Triangle' of SE England.[12] If only SMEs are considered (marked in green in Figure 3), then the position is somewhat more balanced, with 70 per cent lying outside of the Golden Triangle. The existence and potential significance of IB clusters is discussed in Part 8.[13]

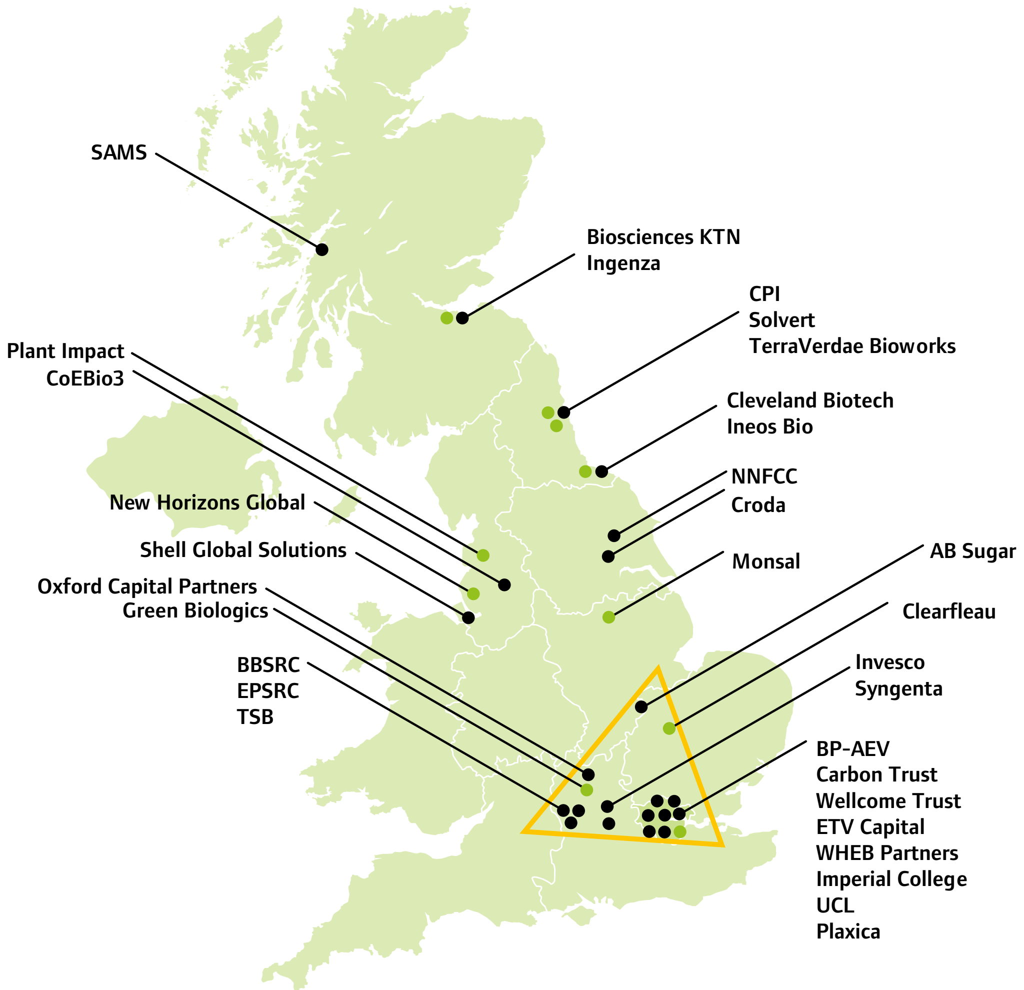
Figure 2: Corporate finance status of SME interviewees



Note: Almost all the SMEs have benefitted from grants but this is marked only for Ingenza to underline the point that it did not raise significant equity funding.

* Share buy-backs

Figure 3: Geographical distribution of interviewees



Note: Green dots represent SME companies.

Part 5: Current status of the IB sector in the UK

F1. IB is not yet a true sector but rather a tool used across a range of industries.

The sense of identity within the sector was found to be somewhat patchy, possibly because IB captures a very broad spectrum of activities. *"'IB' is a useful shorthand term, but not always a fully understood one"* [EPSRC]. *"It is used elastically and when the definition is so broad it might begin to lose coherence"* [UCL]. While some participants clearly viewed themselves as members of the IB community, others were almost surprised to be included in the survey, some even being unfamiliar with the term 'industrial biotechnology'.

"Failure to categorise IB activity correctly could inhibit the flow of funding: gaps could emerge between BBSRC and EPSRC programmes through which important topics and areas might fall" [Research]. *"There has to be a clear definition if the funding of research is to be coordinated across the various funders. Until the BBRSC and EPSRC strategies are fully in step there will remain some concern that calls will not be fully aligned"* [Research].

"Most academics are so specialised that biologists are unlikely to find themselves working with chemical and process engineers, unless tasked by a third party (such as a funding body) to deliver a specific project" [Research]. The BBSRC is now encouraging plant scientists developing non-food crops to work alongside engineers to ensure traits are selected for improved processability as well as for desirable molecular end products.

A better idea of the true size of the sector could be achieved in the short term by identifying activities which fall within the 'IB' remit but are not normally labelled as such. It is, for example, not easy to pull out IB projects from within the Research Councils UK (RCUK) database since relatively few will use obvious IB designators. An academic noted that *"some of the university researchers who could fall under the IB umbrella do not see themselves in this category"*. It is of some concern that there may be work going on that is relevant to IB, but not 'badged' in this way. EPSRC felt that there is a need to build a wider profile of IB as a topic area.

Croda saw 'IB' as *"a tool rather than an industrial sector in its own right"* while the NNFCC refers to it as *"a set of tools in a toolbox rather more than a classic industrial sector"*. Drawing such activity more closely under the 'IB' umbrella would not simply constitute cannibalistic growth – it would have practical benefits in expanding the network effect and bringing in new blood. However, if available research funding did not expand commensurately there would be a risk of more mouths to feed from the same budget.

"Some players in the food sub-sector may consciously avoid being labelled as 'biotechnology' because of its association in the public mind with genetically modified organisms (GMOs)" [Industry]. *"The IBLF are addressing this with public engagement"*. *"In the biofuels sub-sector, there is a perception among some people that using crops for fuel drives up food prices and is therefore somehow unethical, although the actual correlation is less clear"*. *"The real cost of food is still less than in 1972."*

The interviewees were asked if the label 'IB' confered a 'halo effect' of the kind associated at one time with 'dotcom', 'nanotechnology' and 'biotech' (in its original healthcare context – now undergoing something of a rehabilitation). One SME reported that there is some halo effect in the sector. Another found that describing itself as an IB company tended to ensure greater interest than the equally valid description as a plastics or polymer company. However, two other SMEs felt that labels such as 'cleantech', 'greentech', 'sustainable', 'low carbon' and 'renewable energy' all conveyed a more useful positioning with customers and investors than 'IB'.

With regard to end-users of IB products, one commentator could not see anyone paying an appreciable premium for 'IB Inside'. However, another believed that people may well be persuaded to do so if IB is clearly defined and comes to be accepted as a 'good thing'. An inclusive and 'fuzzy' definition of IB makes it hard for end-users (particularly consumers) to know whether or not they are purchasing an IB product, and if so what benefit this brings with it.

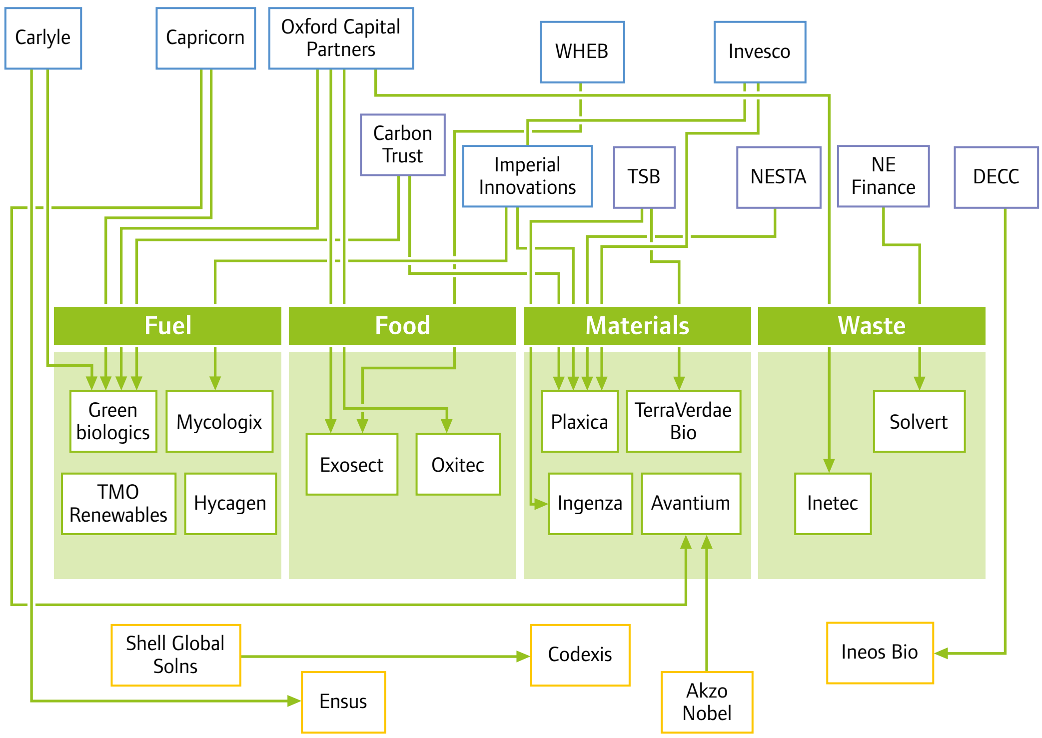
The UK IB sector is small and multiply-interconnected, and it is also widely perceived to be 'fragmented' (see Figure 4). *"There are too many government departments and agencies trying to develop a sector, which consists of a relatively small number of companies, most of which are SMEs"* [Industry]. *"There are too many networks and industry associations"* [Industry]. *"The IB space is not vast and a smaller number of relevant networks that can drive the link between commercial needs and academic research would be more useful"* [Industry].

"The UK needs joined-up leadership in IB" [Industry]. *"The UK IB sector does not have a clear and powerful voice. There are three KTNs active in the area and at least three industrial groups (not including professional bodies in the underlying technologies such as the Royal Society for Chemistry (RSC))"* [Other]. *"The IBLF is a useful forum to have and is playing a valuable role in bringing the various players together. Nonetheless, the UK really needs a national centre for IB that gives a single point of entry to UK capability – a single front door to knock on"* [Research].

One of the SMEs noted that it had found the BioIndustry Association (BIA) and other trade bodies to have been useful. Another was positive about the IB IGT, noting that under the leadership of Ian Shott and Mark Prisk MP[14] it is doing a very good job of cohesifying the sector.

14. Minister of State for Business and Enterprise.

Figure 4: Funding links between some members of the UK IB community



F2. The UK has fallen behind many other countries in IB.

As noted in Part 1, we estimate that the total number of significant and active UK participants in all components of the IB value chain comprises slightly less than 100 organisations. However, this includes any foreign company which has at least some IB activity in the UK. There are probably less than 30 indigenous companies with a hands-on engagement in the practical commercialisation of IB. The remaining players are carrying out academic research, developing policies or providing finance and professional services. Less than half of these 30 companies employ more than 20 people.[15]

The UK's IB community therefore probably comprises no more than 1000 individuals who spend a significant proportion of their time working 'at the coal face'.[16] Not surprisingly, these are well-networked with one another both at the commercial and the professional level. While networking is to be encouraged, it is of little benefit if it only occurs because the community is isolated and sub-scale. Hence there is a challenge if the UK IB sector is to maintain the benefits of its close networking while attracting new entrants.

15. Note that we have taken a relatively narrow definition of 'significant and active' companies and have considered only those capable of 'practical commercialisation' rather than, for example, very narrow contract R&D projects. In its IB 2025 report the IB-IGT identified 44 'core' IB companies (excluding 'end-user' companies) of which 37 were SMEs. In 2010, BIS reported 55 IB companies operating in the UK industrial biotechnology sector, 37 of which were SMEs (BIS (2009) 'Strength and Opportunity; The Landscape of the Medical Technology, Medical Biotechnology and Industrial Biotechnology Sectors in the UK.' London: BIS.).
16. But note that the Biosciences KTN has over 2,500 members.

Few UK IB companies are recognised as world leaders

There are UK SMEs active in almost all relevant areas of IB and this may contribute to the sector's struggle to reach a critical mass. However, unlike fundamental academic research, in almost no cases are these recognised as world leaders. *"As an industrial sector, IB is much less mature than most other science based sectors in the UK"*. *"Agricultural applications of biotech are 10-15 years behind pharmaceutical applications"*. *"The entire UK IB sector is lagging very far behind the other major developed nations"* [SMEs].

As a result, UK SMEs are generally playing catch up with their competitors in the rest of the world. A good illustration of this is New Horizons Global which, with revenues of ca. £175k, is among the leading UK producers of biotechnology-derived food additives. One of its main competitors is Martek Biosciences a company spun out of Martin Marietta in 1985 in the US, undertook a successful IPO in 1993, achieved $300 million of revenues by 2010 and was acquired by DSM for just over $1 billion in 2010.

The large companies tend to agree with this analysis. One considered most UK start-ups to be *"not very impressive: they have young, unconvincing, management who lack commercial nous and tend to focus on technology-push rather than market pull"*. When Syngenta set up a corporate VC arm it was based in the US and subsequently in Switzerland. Another large company views the UK IB sector as so fragmented that it wouldn't know where to start looking for partners and therefore looks at more viable markets such as the US.

One academic suggested that while Europe is clearly second to the US in terms of biofuels technology, this is largely in terms of cash rather than technology *per se*. Others agreed that under-funding has played a critical role in limiting the development of the UK's IB companies. *"The problem is a dysfunctional financing base which starves UK SMEs of development capital"* [SME]. *"The UK is behind because we are investing less"* [Industry].

The global leaders in IB are the US, Germany and Holland. The UK falls into a second division comprising other European nations plus Brazil, India and China. Almost all interviewees agreed that the UK IB sector lags behind the world's leading players and almost everyone identified the US as being in first position. *"On the West Coast there is a virtuous circle of engagement between academics, VCs and spin-out companies which we have been unable to replicate in the UK"* [Industry]. *"Among the large US companies, Dow and DuPont are particularly active."*

Behind the US come the leading European players with a general consensus that Germany is in second place globally. *"German companies really 'get' IB: BASF is looking at developing entire plants using IB whereas the ambitions of UK companies do not seem to extend beyond putting IB into one process step"*. However, BP-AEV noted that components are easier to integrate into existing facilities than whole processes. *"In anaerobic digestion, the UK is 10-20 years behind Germany"* [SME].

In next place after Germany interviewees mentioned Switzerland, Holland and there was one mention of Austria. In the chemicals/materials sub-sector there was also some mention of multi-nationals based in France and Italy making extensive use of IB. The ranking of the UK was felt by some to be roughly equivalent to these other (i.e. non-German) European players. One academic said that the

UK had recently overtaken Holland to gain second place. Another felt that it is still an open race for second place in Europe between the UK, Holland and Italy which can be taken as evidence that recent investment in IB capability is beginning to produce returns.

If this is true, then the collective view of those interviewed would be that the UK is simultaneously way behind the leaders in IB but still manages, on aggregate, to be one of the three leading players worldwide. The answer may be that *"the UK's strength lies at the small/medium scale and tends to focus on adding value to more speciality/fine chemicals"* leaving us a long way behind the large foreign-owned bulk chemicals companies but still a respectable player. Consistent with this view, one interviewee noted that the leading IB countries are those with large and innovative chemical industries – essentially Germany, Japan and the US. This list (with the inclusion of Japan) highlights that any ranking which puts the UK in third place globally behind the US and Germany ignores the claims of non-European (and notably Asian) players.

In Asia, more interviewees mentioned China and India than Japan. *"Indian IB has focused on pharma and high value chemicals, but they have the plant, processes, skills and capital and could relatively easily refocus on, say, fuels"* [Industry]. *"Brazil is up and coming, not just because of its emerging superpower 'BRIC'*[17] *status, but because of its key role in sugar-based bioproducts"* [Industry].

There is likely to be a long-term IB skills shortage in the UK, offset temporarily by experienced staff being shed from contracting chemicals and pharma companies. The potential for an IB skills shortage was widely recognised. One large company reported that the supply of fresh graduates is not a problem but getting people with ten years relevant experience is much harder. *"There are good graduates around but getting them with two to five years of relevant experience is when it gets challenging"* [SME]. Another SME agrees: it is challenging to get hold of people in the UK with the right experience (i.e. exposure to relevant post-education practical work). *"There is a secular shortage of genuine biotech expertise and experience"* [Industry].

Somewhat paradoxically, the contraction of the UK chemicals sector has provided a temporary and partial solution to the long-term skills shortage which is likely to cause the nascent IB sector problems. One SME reported that it can find recruits at the moment, but they tend to be an older generation, surplus to the requirements of the pharma and chemicals industries. The company is not sure how easy it will be when these people finally retire to replace them from among new graduates. Monsal has not so far found a problem recruiting people with the right skills, while Green Biologics has managed to access executives from a range of backgrounds without too much difficulty.

There are also some causes for longer-term optimism regarding the skills situation. Students coming out of CoEBio3 have good employment prospects. An increasing number of them are choosing to stay in IB and are finding jobs in the sector. Within five years, these will have served their industrial apprenticeship in the IB sector itself. Medical biotech has had a higher profile and has been seen as 'sexier' and has in the past therefore attracted many of the most able students [Imperial, CoEBio3]. However, the pharmaceuticals industry is closing a number of large research, development and pilot plant facilities in the UK, and this should encourage graduates towards IB.

The skills shortage can also be addressed by recruiting good people from related disciplines (e.g. chemists) and then adding biotech skills [SME]. UCL suggested that there will be considerable demand for Masters degree courses able to add bioscience to engineering graduates and *vice versa*, a route successfully taken by regenerative medicine at Manchester, Loughborough and Newcastle universities. The education and skills mix required by the IB sector is being looked at by the BBSRC strategy panel (membership of which is about one half from industry). BBSRC are also looking to develop DTPs (Doctoral Training Partnerships) as a way of developing people with the level of skills required for multidisciplinary working. Industrially sponsored CASE PhD studentships now have a level of management training built into them.

F3. The UK lacks indigenous large companies to support its SMEs with investment, partnering, training and credibility – the 'tall trees' of a healthy industrial ecosystem.

Several interviewees discussed the sort of industrial 'ecosystem' necessary in order for the IB sector to thrive. Two possible

17. Brazil, Russia, India, China.

pictures emerged – 'savannah' and 'forest'. In a savannah the plants grow up quickly to a relatively low height and are regularly replaced by new plants – often on a seasonal basis. In a forest a few of the plants (the tall trees) grow to a great height and live for hundreds of years. The presence of the tall trees is essential for the functioning of the entire ecosystem because they provide shade, shelter, leaf mould, soil stabilisation etc. A 'savannah' industry would consist entirely of SMEs growing up quickly to a medium size and then disappearing (by attrition or acquisition) to be replaced by others. A 'forest' industry would also have the majority of SMEs growing up and dying away, but in order to do so they would in some way depend on the 'canopy' of the 'tall trees' – the large established companies (possibly themselves once SMEs) which endure from generation to generation.

The 'savannah' and 'forest' industrial models are both viable but one or the other may be much more suited to a particular industrial sector. The relevance of the analysis is that the UK does not have its fair share of domestic 'tall trees' in the chemicals industry. If the IB sector turns out to thrive only in a 'tall tree' ecosystem, then it might have problems thriving in the UK. One multi-national company, headquartered overseas but with a significant presence in the UK, noted that *"There is no equivalent of BASF, DuPont-Danisco-Genencor or Novozyme with its headquarters here. Even the smaller Dutch economy has DSM – a global science-based company active in health, nutrition and materials which is particularly well positioned to commercialise generic IB technologies. In this respect the demise of ICI was not good for the UK"*.

The nearest that the UK has to an indigenous 'tall tree' in the chemicals sector is arguably Croda, which itself incorporates some of the ICI legacy activities. The company was established in 1925 and acquired Uniqema from ICI in 2006. It currently has a turnover of ~£1 billion and manufacturing facilities throughout the UK and mainland Europe, North and South America, India, Singapore, South Korea, Indonesia and Japan. In January 2005, it established the Enterprise Technology Group to drive forward the company's interests in new technologies. Operating as Croda Enterprises Ltd, a separate legal entity within Croda International plc, it can be best described as a corporate research group working within an internal venture capital model. It has been tasked to identify new technologies for the global Croda network while focusing on Croda's existing markets. However, Croda is not of the same scale as really 'tall trees' such as BASF which has revenues around 50 times greater.

Two of the VCs were in agreement that the UK's lack of large/mature corporates with a strong IB presence has the following impacts:

- Less institutional funding available to support VC investments.
- Perception that 'trade sale exits' could prove challenging.
- A poorer understanding of the benefits of IB amongst the UK's corporate community and by association the political and finance communities.
- Less technical knowledge, both directly within the corporate community and indirectly through leakage from the corporate community to the finance sector.

The SMEs tended to emphasise the last of these points. The practical plant skills required by IB companies cannot be learnt at university and IB SMEs therefore rely on recruiting employees who have already gained relevant post-graduate industrial experience. Without large established chemicals companies, it is difficult for such people to find somewhere to serve their industrial apprenticeship. One academic agreed that it can be difficult for graduates to get the couple of years of practical experience most employers require. *"If the 'tall trees' are missing, then the work force has to be mobile – working in different SMEs, and overseas, to gain the experience needed by new IB start-ups"* [Solvert].

Multi-national 'tall trees' do not tend to invest in UK IB because it is commercially under-developed and it remains under-developed primarily due to a lack of investment – the first 'chicken and egg' problem besetting the sector. While the UK lacks industrial 'tall trees' in the chemicals and materials manufacturing sector, this is not the case in the three other segments of IB, and particularly in fuels. Unfortunately, even in these segments, the nurturing provided by the 'tall trees' in terms of research collaborations and corporate venturing appears to be rather limited.

BP Biofuels invests in IB research via an agreement to provide $500 million over ten years to the Energy Biosciences Institute (the University of California Berkeley and its partners, the University of Illinois, Urbana Champaign and the Lawrence Berkeley National Laboratory). There is no similar arrangement with UK universities. Another large company does not fund UK research. It *"does not need inventions, it needs process innovations: it funds the applied technologies which emerge from the R&D pipeline"*.

A number of explanations were put forward to explain this situation. *"Most large UK-based corporates with significant activity in IB, base this in the US on the grounds that it provides the best environment for innovation. A discovery made in the US has a better chance of being commercialised"* [Industry]. *"The fact that the UK does not have its fair share of large/mature corporates with a strong IB presence adds to the tendency for those multinationals that are in UK to invest where all the other multi-nationals invest (i.e. the USA)"* [Industry]. *"Corporates with a culture of investing in start-ups tend not to be UK-based, but rather American, Japanese or based in European countries noted for their emphasis on technology development such as Germany, Sweden, Denmark, The Netherlands and Switzerland"* [Finance].

It would thus appear that a 'chicken and egg' situation has developed in which the 'tall trees' do not tend to invest in the UK IB sector because it is commercially under-developed and it remains under-developed primarily due to a lack of investment.

F4. Universities are generating high quality research but not companies

The BBSRC believes that there is very good work being done in the UK in the science underlying IB and sees a good flow of highly-rated grant applications. There is university research being undertaken in almost all relevant areas and in some cases (e.g. cell libraries) the UK is a world leader. International companies are still funding research at UK universities. Syngenta, headquartered in Switzerland, has collaborations in the UK with Manchester University on the use of sensors in agriculture, and with Imperial College, building predictive models for biological systems. *"The quality of research in the UK is second only to the US (because of their scale and commercial focus)"* [Industry].

Two people working for large industries said that the UK has a good research base, but no real track record of commercialising research when compared to the US and some other EU countries. *"The underpinning research is up there with the best but as you go downstream the picture becomes less positive"* [Other]. *"University technology transfer offices are often poorly resourced and tend to focus on filing patents rather than building the relationships between academic and commercial partners necessary to secure a commercial return"* [Research].

Various explanations were put forward for the UK's comparative weakness in IB applied research. This included; conversion of the polytechnics to universities placing an over-emphasis on academic learning, rather than practical or vocational learning; undervaluing of applied research when compared with fundamental research due to the system whereby academics are rated purely on the number and academic quality of publications produced rather than their ability to commercialise technology, and; poor pay for engineers.[18]

The importance of fundamental discoveries and associated patents is in any case less in IB than in the healthcare segment of biotechnology. One large company stated that it has *"a culture of innovation in tiny increments generating know-how rather than patentable IP: the company has a miniscule IP portfolio"*. It noted that chemicals manufacturing in the UK has always been based upon know how around the plant and processes. One SME believes that its competitive advantage does not come from proprietary high tech design features, but rather from operational excellence and intellectual know-how. Similarly, improvements in its designs are likely to come from tweaks and iterations based on extensive operational experience in the field rather than new discoveries in the laboratory.

The food segment of IB is perhaps an exception to this general rule. The market for patented crop protection products is worth ca. $35-40 billion per year. About a quarter of these revenues are derived from products that are about to come off patent. This provides a patent expiry problem for the major players, similar to that of 'big pharma'. Like the pharma majors, they may well look to biotech companies to replenish their on-patent product pipeline. In view of this, Plant Impact has devoted considerable attention to developing its patent portfolio and now has nine worldwide patents on six major technologies.

18. It is interesting that the interviewee cited poor pay for engineers rather than a shortage of engineering graduates. Recent research by Prof. Emma Smith of Birmingham University found that 54 per cent of engineering graduates are lost to the profession within six months of graduating.

The number of UK IB SMEs originating via the 'classic' route of being spun-out or licensing their technology directly from universities was surprisingly small for an advanced technology-based sector. Out of the ten SMEs interviewed, only Ingenza (Edinburgh University) and Plaxica (Imperial College) fell into this category – in both cases coming from the chemistry department rather than a life sciences discipline. Industrial research centres appear to give rise to more spin-outs than academic institutions. TerraVerdae Bioworks was set up by an industrial technologist to commercialise technology developed in a Canadian National Research Centre. CPI has invested in a number of SMEs and generated a number of spin-out companies.

Nor were there many examples of companies being spun-out directly from corporate research laboratories. The closest to this model were three SMEs (New Horizons Global, TMO Renewables (not interviewed) and Green Biologics) which acquired the assets of failed companies and raised fresh funding to move the research forward. Instead, the predominant model was for companies to be set up by business executives and entrepreneurs to target a particular market opportunity with technology and technologists drawn in as and when required. Clearfleau was formed by a group of high-net-worth-individuals while New Horizons Global and Plant Impact were set up by non-technical entrepreneurs. Cleveland Biotech was set up by a microbiologist with experience in industry and academia, an engineer and a management professional. Solvert was created by one of the UK's very few 'serial entrepreneurs' in IB. Solvert offered a possible explanation for this trend. The technology may come from a university, but hands-on chemical engineering plant skills are vital and these cannot be developed in a university environment. Therefore, unlike some of the high technology physics based industries (e.g. manufacturing photovoltaic cells), IB companies need to have a majority of industrial technologists in the founding team.

In addition to not coming *from* universities, most SMEs also tend not to go to universities in order to develop their technology further. Some felt that the full economic cost (FEC) now charged by UK universities is prohibitively expensive and poor value for money as *"academics generally make poor industrial consultants"*. Monsal does not work closely with universities, although it does participate in a JIP with BHR Ltd, a spin-out from Cranfield University.

However, this attitude was by no means universal. Green Biologics views its links to universities as very important, but sees these as extending well beyond the UK. In addition to collaborations with Nottingham and Manchester, it has also established links to Chinese and US universities which it sees as a way of supporting the introduction of its technology into foreign markets. New Horizons Global worked with Hull University to develop an optimised algae strain. UCL has worked with TMO renewables.

Part 6: Funding requirements and barriers to investment

F5. IB is different from other technology investments because of the investments in heavy plant needed

The end-products from the various high technology industrial sectors have huge differences in their 'value density'. Software, which can be distributed over a data network, is effectively weightless and therefore arguably has an infinite value density in terms of price per delivered kilogram. The price of therapeutic drugs is very variable, but for on-patent molecules can readily be $10k-100k per kilogram. ICT hardware ranges quite widely in price – a high specification smartphone costs $1-2k per kilogram and a flat screen television $30-60 per kilogram. The fuels, chemicals and foodstuffs produced by IB are generally at the extreme end of the spectrum, all tending to command prices in the low single-digit dollars per kilogram range. The total variation in price per kilogram between these sectors is thus at least five orders of magnitude.

The investments needed to develop new products in these sectors do not vary by anything like the same amount. The range may be from low tens of millions of dollars to low hundreds of millions – one order of magnitude. Furthermore, and as discussed in detail below, IB tends to be at the more expensive end of this range. A defensible 'rule of thumb' is that in order to recoup any investment in technology, annual sales of the resulting products need to be of the same order of magnitude as the sums invested in developing them. For the sectors discussed above, this means annual product sales worth tens (and preferably hundreds) of millions of dollars.

For software, this could be delivered from a single relatively small server. For a drug, this would necessitate manufacturing no more than a few tonnes of active ingredient per year, which could be done on a small developmental plant. For IB, it would require an industrial plant manufacturing hundreds of thousands of tonnes per year. Another 'rule of thumb' is that the capital cost of an industrial process plant is at least $1,000 per tonne of annual output capacity. In order to recoup an investment in IB, it will therefore be necessary to build plants costing around $100 million each. Smaller plants would not only generate insufficient revenues to repay the initial investment in R&D, but would also lack the manufacturing economies of scale needed to achieve a commercially viable cost of production. As one industrial interviewee noted, *"the end products of IB have not been expensive enough or there hasn't been sufficient demand for them to create an industrial process to manufacture them"*.

Other interviewees confirmed this analysis. TerraVerdae Bioworks would need at least $100 million (£65 million) to build a full-scale plant for its process, Green Biologics agreed that a global scale manufacturing facility can easily come in at $100 million, while Solvert estimated that it would need £150 million ($240 million) for a full-scale plant with profitable economies of scale. Of course, no new process moves straight from the laboratory to a plant producing hundreds of thousands of tonnes per year. Solvert, founded by a serial IB entrepreneur with very extensive plant operational experience, has estimated that it will require £250k for business planning and devising its process model, £1.5 million for lab-scale proof of concept demonstration and £3.5 million for a pilot plant demonstration before its novel waste treatment process has been validated.

While a pilot plant demonstration will eliminate many of the technology risks, there remains an engineering risk in the scale-up process. Scale-up is not just a question of dimensions and volume; there is also often a fundamental difference in approach. *"Scientists tend to want to intervene manually with their laboratory processes in order to get the best results, but this tends not to be advisable (or even possible) for an automated industrial process"*. Many chemical engineers believe that that there is a limit to the increase in output that should be targeted for any single scale-up step and this is likely to apply to IB as well. One interviewee suggested that this should be no more than a 20-fold volumetric increase in output while another suggested a maximum of up to 50-fold might be possible in some cases, particularly for processes taking place at room temperature and pressure.

This tends to suggest that a demonstration pilot plant producing a few hundreds of tonnes of output per year should be followed by a sub-scale industrial plant producing a few thousands of tonnes before moving to a full scale plant producing >100 ktpa.[19] An intermediate scale plant of this kind is likely to cost in the region of £10-20 million to build.[20] The overall picture is hence that for a typical IB start-up the investment requirements will be £1-3 million for laboratory research, £3-5 million for a pilot plant demonstration facility, £10-20 million for a sub-scale industrial plant and £75-150 million for a full-scale commercial production plant.

The challenge for the IB sector is that its position at the higher end of the development cost spectrum and the lower end of the product value density spectrum does not fit well with any existing VC funding model. IT software development, which has probably been the consistently most profitable sector for VC investors, doesn't require the same degree of investment to move from small-scale to large-scale demonstration [Finance]. The timescales are also shorter. The software development cycle of one to three years fits well with the time horizons of many VC funds. The development cycle for IB is at least twice as long. AB sugar would take a technology through a new pilot plant in three to five years. BP invests in opportunities with potential to exit within five to seven years. The Biosciences KTN considers the IB commercialisation timeframe to be six to eight years.

Therapeutic biotech has capital requirements and development timescales that more closely resemble IB. It is also a sector which has made, on average, lower returns than software for VCs – perhaps because of these differences. However, the therapeutic biotech sector is nonetheless still more 'user friendly' for VCs than is IB. There are more stage-gates on the drug development path (in vitro laboratory screening experiments, animal models, Stages I-III of clinical trials), a much wider choice of contract research organisations (CROs) to support the development process and a relatively liquid market for early-stage investors to sell out after each stage-gate. *"Early-stage investors in IB companies face the prospect of very heavy dilution further down the development track without an interim exit opportunity"* [SME].

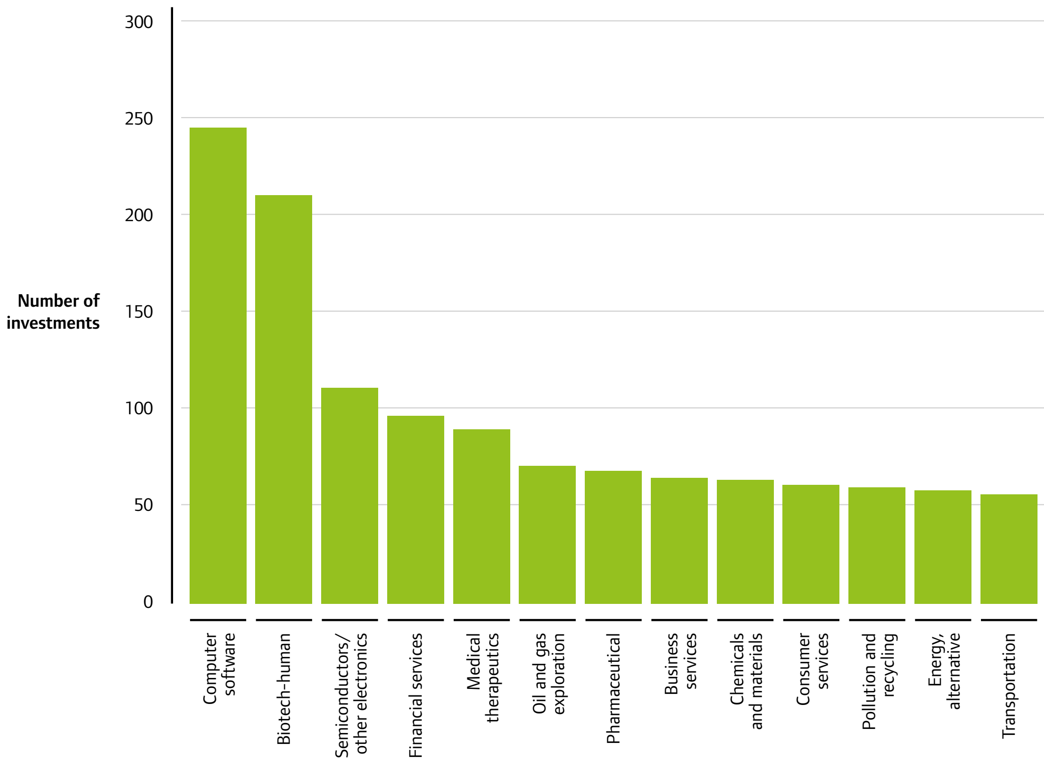
The fact that IB start-ups do not fit very well with familiar UK and European VC investment paradigms probably explains why many of them report difficulties securing such funding. There are particular problems associated with the £10-20 million required for the sub-scale industrial plant, which tends to 'fall between two stools'. Outside the US, this is a large sum for the VC market and would represent an unacceptably big bet (i.e. concentration of risk) for most European funds. Of the US funds investing in 'expansion' rounds of biotech companies in the last five years, the average fund size was £150 million. There are only 16 VC funds with £150 million or more in the UK, compared to 66 in the US.[21] There are 12-15 UK VC funds that are bigger than £150 million and have made investments in biotech or pharma since 2000. Over 75 per cent of these funds were raised before 2005.

VCs in any case don't like buying fixed assets such as steelwork; they are much more comfortable investing in IP [SME]. One VC noted that: *"the most challenging step to fund is when companies need to move out of the lab and into a demonstration facility of sufficient scale to show that the technology can be reproduced commercially"*.

Sums of this magnitude and purpose might normally be raised from the project finance debt market. However, because the resulting plant is still sub-scale it may not be able to sell its output profitably in order to service this debt. One SME noted that UK investors simply do not like investing in demonstrators. *"Finding finance to build such facilities is difficult because they are generally not large enough to be commercial"* [Other]. However, a contrary view was expressed by BP which tends to invest at the $20-$25 million scale into early-growth

19. Ktpa = kilotonnes per annum.
20. It should be noted in this discussion of investment steps that plant output will not scale linearly with cost.
21. Source: Thomson Reuters.

Figure 5: Other sectors invested in by those funds investing in industrial biotechnology



Data source: Thomson One, Reuters.

stage companies which have proven their science and need investment for scale-up. They see the final scale-up step (requiring $100 million+) as being the crunch point for IB companies.

Access to shared demonstrator facilities (renting the steelwork rather than buying it) can be an extremely attractive option for an IB company that is having difficulty raising sufficient VC funding.

One large company noted that *"VCs may understand technology but they are poor at understanding scale-up. In other words, VCs might employ scientists but not experienced chemical engineers"*. The perspective of the SMEs was summarised by one as *"business needs investors with deep pockets, long-term horizons and an understanding of the sector. Most of the existing VC investors have shallow pockets, short-term horizons and a poor understanding of what they are investing in"*. Eventually, a newly emerging technology sector (IB) might lead to the creation of its own VC investment paradigm with a more sophisticated understanding of the need for sub-scale industrial demonstration plants. However, even the more visionary end of the VC market considered it unlikely that there will be any specialist VC funds focused on the IB sector for the foreseeable future.

Two VCs believed that IB is at such an early stage, and the investment opportunities are so few, that IB investments are much more likely to form part of a broader technology portfolio than to be the sole focus area for a VC fund. *"Some of the funds which have been investing in cleantech are now considering IB propositions"* [Other]. *"This has a certain logic because IB has good cleantech credentials while heavy renewables (e.g. large scale wind and marine generators) generally require even greater levels of investment than IB at a similar stage in the technology's development"* [VC]. The Wellcome Trust has observed that a number of US VCs that have traditionally only invested in healthcare and pharmaceuticals are now investigating IB.

F6. The UK has a specific funding problem, linked to poor historic returns

Many of the interviewees commented that the difficulty in finding VCs with the capability and vision to make meaningful investments in IB is very much more severe in the UK (and Europe in general) than in the US. UK VCs tend to be generalists who do not possess the specialist technical knowledge required to make early-stage investments in IB. They manage relatively small funds (only a handful can invest more than £10 million in a single deal) and so prefer to invest in technology companies only when they've demonstrated that they can manufacture their product commercially (i.e. *after* the sub-scale industrial demonstration plant has been successfully built and operated).

This desire to minimise technology risk is not such a dominant factor in US VC funds, which tend to have access to many times more capital and therefore are able to specialise at a level that is significant. For example, they might employ in-house experts to do their due diligence and to look actively for companies offering promising technologies [VC]. Amyris, Genomatica and Solazyme, all of which are in the US, are examples of companies which have successfully raised significant ($100 million+) sums of VC money, making them credible industrial partners [Industry].

The large scale of US funds was felt to be more significant than their greater level of in-house technical expertise (UK funds could, if they so wished, buy-in this expertise – if need be from the same consultancies as US VCs). *"When US investors talk about seed investment, they are talking about a scale of investment different from UK and EU based VCs"* [Finance]. *"A UK VC will invest, say £3 million, when the company wants £5 million and then the company struggles to meet its targets, 'fails' and the VC leaves. In the US the company asks for $5 million and the VC will often offer $7-10 million and then the company has enough resources to succeed"* [Industry].

The main reason why UK VCs lack funds is because institutional investors are not prepared to entrust large sums of money to them. In the UK, pension funds only allocate 2 per cent on average to VC investments, but in the US this is 5 per cent [Wellcome Trust]. Neil Woodford of Invesco Perpetual, one of the very few large fund managers in the UK who is increasing his exposure to early-stage VC investments, believes that *"most UK equity investors are structurally and culturally conditioned to short-termism and that regulation now reinforces this behaviour. Long-term investing has come to be the preserve of fixed income investors"*.

Somewhat perversely, UK VCs can also prove unresponsive to companies seeking relatively small sums of money, believing that small deals are not worth the effort (i.e. transaction costs) required for due diligence and subsequent management of the investment. One SME set out to raise £1.5 million of corporate development capital from local VCs with no success. The company is now using an advisor and has increased the round size to £5 million. It would appear that the early stages of the typical IB funding journey can also fall between two stools – being too large for seed or angel funds but too small for mainstream VCs.

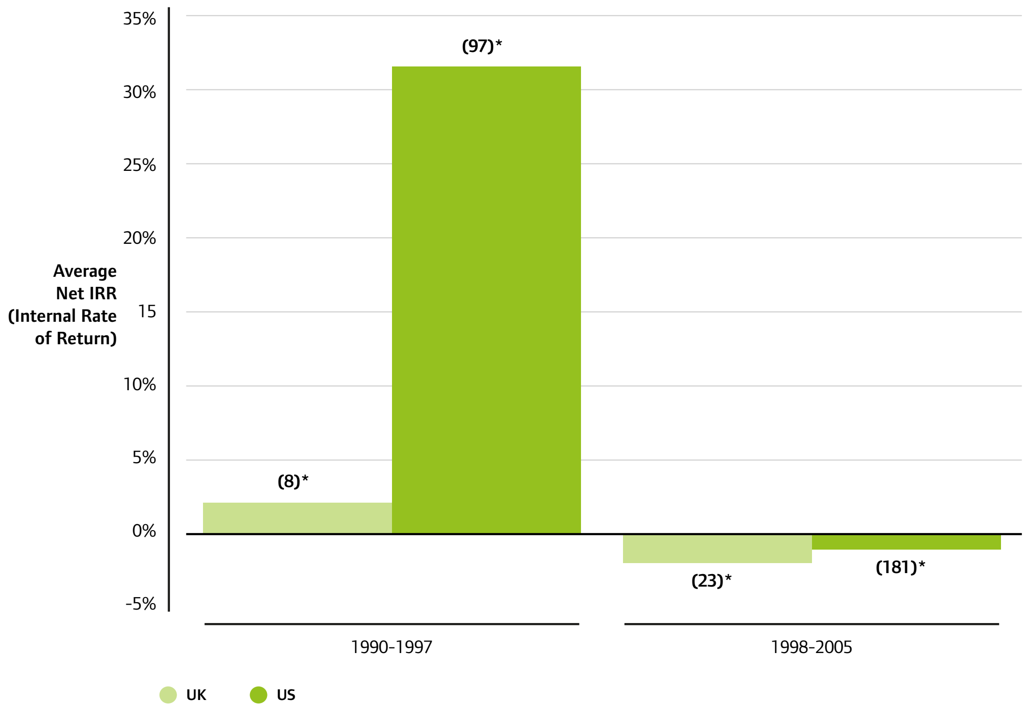
UK VCs are reluctant to invest because historic returns on early-stage funds have been poor, but this may be because early-stage companies are starved of VC funding – the second 'chicken and egg' problem besetting the sector. There tends to be an implicit assumption that the shortage of VC funding in the UK represents a systematic failure by the finance sector. An alternative narrative would be that fund managers prudently limit the funds they provide to UK technology companies because the investment opportunities they present are often of low quality. One VC advisor noted that *"the quality of investment proposals in the UK is generally very poor. UK academics tend not to mix well with either industry partners or with the investment community, so few academics have the skills and experience necessary to produce good quality investment proposals"*.

Two VCs agreed that, whatever the underlying explanation, it is certainly true that US VC funds have a better track record of profitable exits from technology based companies than UK VC funds (see Figure 6).[22] There is danger of this becoming a repeat of the 'chicken and egg' situation noted in Key Finding F3 regarding the general failure of 'tall trees' to make industrial investments in the UK IB sector. It would seem that the UK's IB SMEs could fail to make returns for their investors because they are starved of VC funding, but investors will not provide them with adequate VC funding until they have demonstrated a track record of making profits.

One way to break out of this vicious circle would be to find ways of leveraging the limited funding that UK VCs *are* prepared to offer, thereby providing at least some UK SMEs with the critical mass of funding needed in order to establish a return on investment track record. A good starting point may be somehow to associate or otherwise lump together the limited VC funding with the limited industrial (i.e. 'tall tree') funding. One VC noted that *"large corporates with a track record of investing in R&D and a strategic interest in*

22. The exception was during the inflation of the dotcom (and broader technology, media and telecoms, TMT) bubble in the late-1990s when, for a short while, VCs everywhere made seemingly effortless profits from early-stage technology sector investments.

Figure 6: Data on venture capital fund returns from biotechnology investments: 1990 to 2005



Data source: Preqin, NESTA.
* Number of funds

23. Pierrakis, Y. and Mason, C. (2008) 'Shifting sands: The changing nature of the early stage venture capital market in the UK.' London: NESTA.

developing a particular technology could be a useful source of early-stage leverage for UK VC funds, but they tend not to be UK-based and they all want someone else to take the first step". A large company did not envisage Asian or US companies wanting to invest in UK start-ups.

Quasi-governmental or charitable investment funds (e.g. those managing money from the ERDF, EIB or UK Government) can invest alongside private sector VCs to increase their funding capacity [Wellcome Trust]. However, EU State Aid law constrains the percentage of funding that can come from the public purse. Furthermore, *"the people managing public sector funds tend to be conservative and therefore invest in lower risk later stage technologies"* [Finance].

NESTA research indicates that where public VC funds do invest in higher-risk technologies, they are often sub-scale and unable to follow-on with later funding rounds, and so get diluted down to very small holdings.[23]

Quantitative views on the UK investment climate

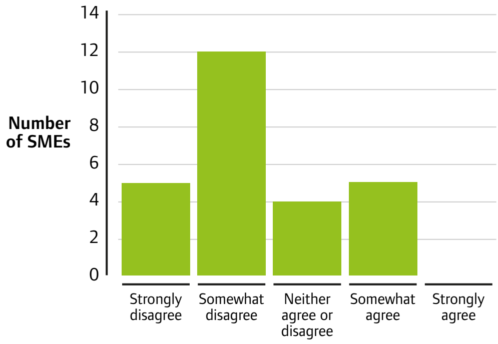
Results from the eight quantitative questions asked at the end of most interviews are summarised in Figure 5 (note that the vertical scales on the various bar charts are different).

Most interviewees believe that it is becoming increasingly difficult to raise funding for IB companies but a significant minority apparently see the companies themselves as partly to blame. Less than 20 per cent of interviewees agreed in any way with *"the UK IB sector is currently getting the funding it needs"* (Question 1) and nobody strongly agreed. There was an even greater consensus that the funding climate has deteriorated over the past five years. Only three respondents disagreed in any way with *"it is harder to fund IB companies in the UK now than it was five years ago"* (Q4). Interestingly, none of the dissenters came from a finance background suggesting that those working in finance are prepared to acknowledge that financing mechanisms are currently not functioning effectively for IB companies.

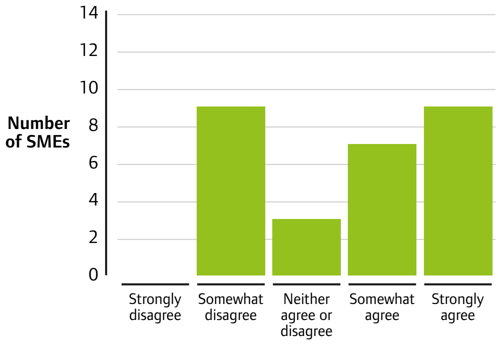
However, a more significant minority appear to believe that the generally acknowledged shortage of finance is not causing significant harm to the IB sector. This can be seen from the answers to the somewhat related questions #2 and #3. The first asked if growth of the UK IB sector is currently constrained by a lack of

Figure 7: Summary results of quantitative questions

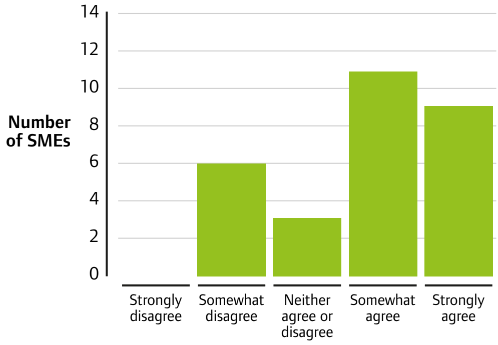
1. The UK IB sector is currently getting the funding it needs (three declined to answer)



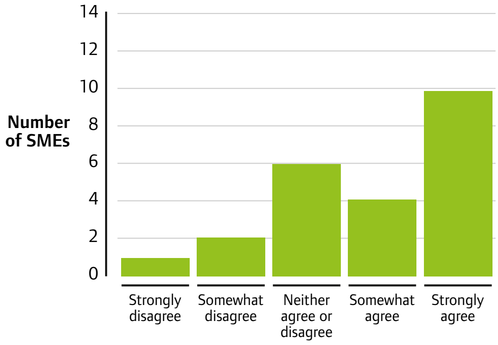
2. Growth of the UK IB sector is currently constrained by a lack of availible funding (one declined to answer)



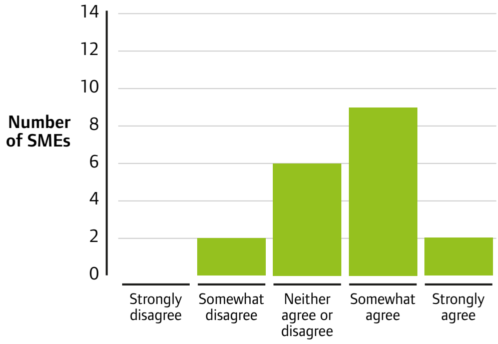
3. Even the best quality companies are finding it hard to raise the necessary funds (none declined to answer)



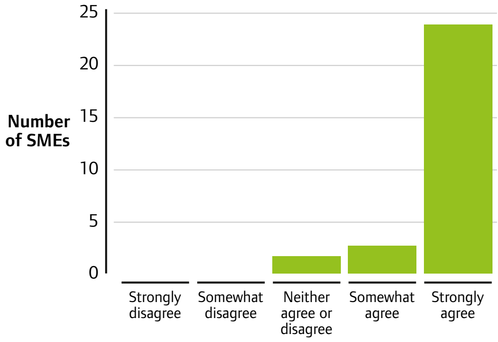
4. It is harder to fund IB companies in the UK now than it was five years ago (six declined to answer)



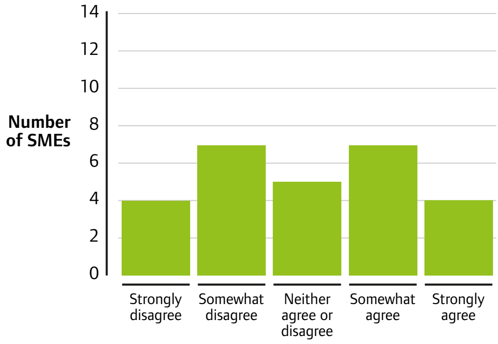
5. Overall, investors in UK IB companies have to date had disappointing returns (ten declined to answer)



6. A healthy IB sector is important for the broader competitiveness of UK industry (none declined to answer)



7. Hard-headed investors are right to be sceptical of the potential returns from IB (two declined to answer)



8. Today's IB SMEs have the potential to become the IB multi-nationals of tomorrow (two declined to answer)

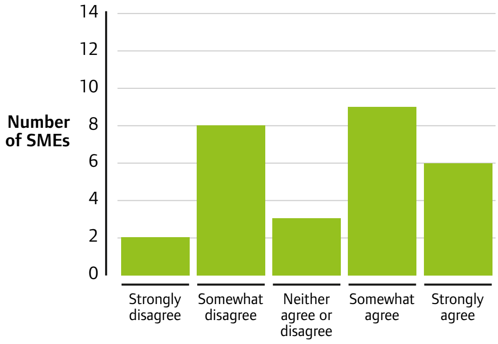
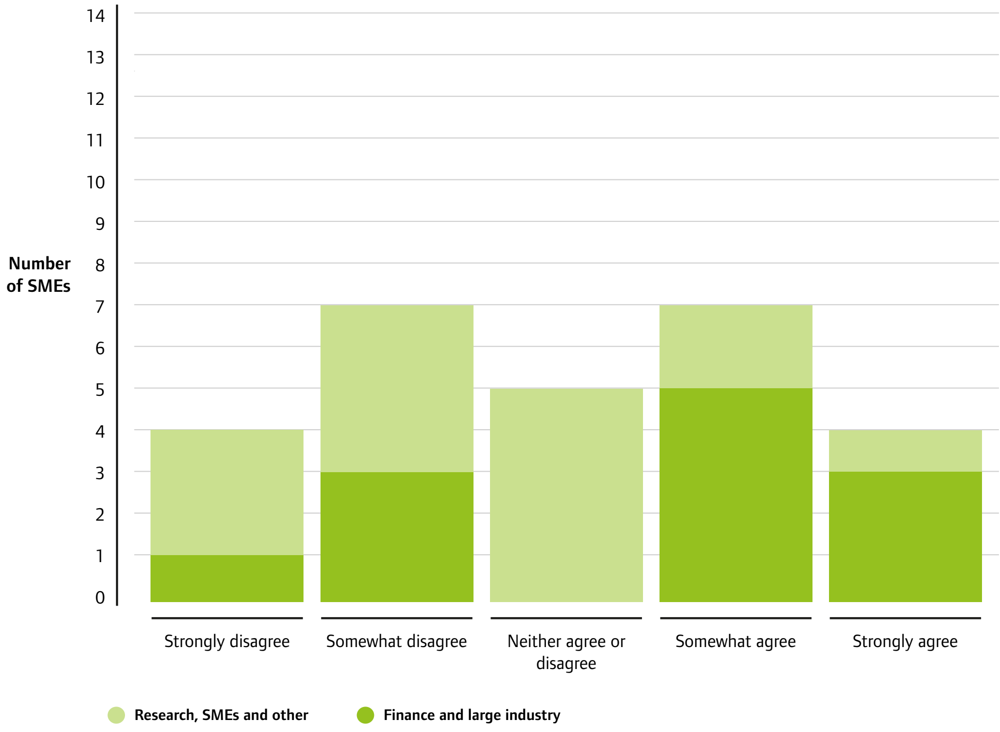
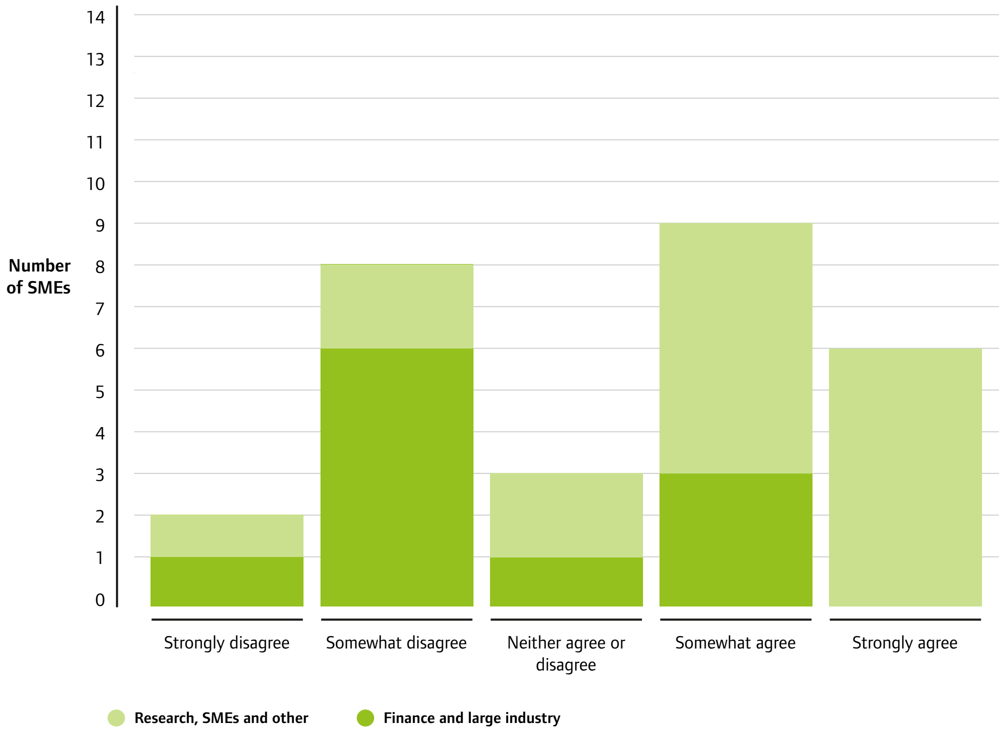


Figure 8: Responses to questions #7 and #8 plotted by constituency

7. Hard-headed investors are right to be sceptical of the potential returns from IB (two declined to answer)



8. Today's IB SMEs have the potential to become the IB multi-nationals of tomorrow (two declined to answer)



available funding while the second asked if even the best quality companies are finding it hard to raise funds. Disagreeing with these statements would imply a belief that, while funding is indeed in short supply, the best quality companies can still get the investment they need and that it is these companies which will drive most of the sector growth. In other words, those companies finding difficulty in raising funds are themselves partly to blame because they are not of the very highest quality: what is not being funded will not be greatly missed.

It might be thought that this view would be espoused particularly by the finance interviewees, since it exonerates them to some extent from the accusation that they fail to recognise and fund even good quality companies. However, the finance community is not in fact disproportionately represented among those disagreeing with questions #2 and #3.

It is possible to believe that the IB companies themselves are not to blame for failing to attract investment but that such investment nonetheless does not make financial sense. Rather than ask the interviewees directly if they had confidence in the UK IB sector at the macroeconomic level, three somewhat more oblique questions were asked. These were: #5 (*"have investors in UK IB companies had disappointing returns to date"*), #7 (*"are hard-headed investors right to be sceptical of the potential returns from IB"*) and #8 (*"do today's IB SMEs have the potential to become multi-nationals"*).

There was a general agreement that historic returns have indeed been disappointing) but note that this had the highest number of non-responders (ten) because many interviewees felt that they did not have any knowledge on which to base a response. The responses to questions #7 and #8 provide perhaps the most interesting charts in Figure 7, with a classic 'twin peaks' pattern between those whom agree and disagree. It is hard to see how anyone who agrees that historic returns have been disappointing, does not think that today's IB SMEs can grow into large companies and is therefore sceptical of future investment returns from IB is saying anything other than that the UK IB sector is flawed at the macroeconomic level.

To see if this 'sceptical' view correlated with particular groups of interviewees the responses to questions #7 and #8 were divided into two groups. The first comprised 'hard-headed' executives working for financial institutions and large industries. The second comprised other players in UK IB from the SME, research and 'Other' segments [see Figure 1]. The results are shown in Figure 8. It can be seen that the specialists are much more inclined to believe that UK IB SMEs can grow into large companies and that investors are therefore wrong to be sceptical. Hard-headed executives show precisely the reverse correlation.

F7. Bank finance and venture debt are not filling the gap

The traditional way to leverage equity investments has been by using debt. It has already been noted briefly that funding for the sub-scale industrial demonstration plant, particularly problematic for VCs, could perhaps be secured instead in the form of debt finance.[24] The specific problem here is that such demonstration plants are not large enough to be fully commercial propositions: it is not clear if they should be viewed as a very expensive experiment or a loss-making production facility.

There are, in fact, much more generic problems with early-stage technology companies raising any sort of debt finance. In response to the global economic crisis, banks and other providers of debt finance have sought to reduce their risk profiles whilst building up their capital reserves. This makes it very difficult for early-stage companies to raise unsecured bank loans – two of the SMEs pursuing very promising business opportunities reported difficulties finding lenders. *"Even if loan facilities are offered, they are prohibitively expensive. There usually has to be an existing relationship with the bank and some sort of cross-guarantee"* [SME].

Raising unsecured loans was not particularly easy for SMEs even before the credit crunch. The natural source of working capital and project finance for commercial plant installations ought to be asset-backed borrowing. However, asset-backed finance is not easy to access until the technology is proven – if the plant does not work once it is installed then the 'collateral' held by the bank has little value. *"Tanks for an anaerobic digestion plant that would cost £1 million to fabricate and install would have a scrap value of only about £10k. Banks are reluctant to incur due diligence (DD) costs and will prefer to fund a bundle of three to*

24. See Key Finding F5.

five projects worth £25-30 million, doing one due diligence exercise on the whole lot. This is a disadvantage to SMEs funding their first projects" [SME].

In healthcare biotechnology, venture lending has played an important part in leveraging the equity investments of VCs and allowing SMEs to diversify their source of funding. The venture lending model was developed in Silicon Valley in the 1980s for semiconductor start-ups which faced challenges because of the high capital intensity of their development programmes relative to software. It is now a widely recognised asset class in the US, providing up to $2 billion per year of development capital. Some estimates suggest that around 70 per cent of US start-up companies have included an element of venture debt in their funding strategy.

Venture lending comprises a loan made to a company in return partly for interest and partly for an equity-based consideration. It evolved to address the well known 'vicious circle' in which companies at relatively high risk of default are charged high interest, but the high interest actually adds to the risk of default. By taking some of its return as equity, the lender can charge lower levels of interest than would otherwise be the case, hopefully breaking the vicious circle. For the borrower, the attraction of venture debt is that while there is some equity dilution this is much lower than for 100 per cent equity (i.e. VC) funding. For a VC fund (most of which in the UK know their portfolio companies need more money than they can provide), it allows expansion of the available funding without the need to syndicate the equity deal and share control.

A typical time to use venture debt would be when a company is approaching a value-enhancing milestone but needs additional funds to achieve it. The venture debt provides a bridge to an equity round after the milestone at a higher valuation (and/or greater ease of closing) than could be achieved for an equity round in advance of the milestone being achieved. Larger and later-stage private equity funds might provide such debt themselves. VC funds are not only smaller, they also generally don't employ any debt experts.

ETV Capital, interviewed in this survey, is one of the three leading players in Europe providing venture lending to technology sector SMEs. The other two are Kreos and Noble. Over the past decade, venture lending has fed about £500 million into European start-ups, about half of it in the UK. ETV alone has lent £260 million to 190 companies over this period, many of them in the healthcare segment of biotech. The venture lending model is recognised as being a valuable catalyst to wealth creation (some of ETV's capital was provided by the EIB) and has generated better returns over the past ten years than many early-stage healthcare biotech equity funds.

Despite its successful track record, venture lending has suffered more dramatically than VC funding during the credit crunch as banks have developed a blanket aversion to what they perceive to be 'sub-prime' lending. One of the banks providing funds to ETV has, as a matter of policy, withdrawn from what it views as sub-prime lending and this has led to the termination of ETV's entire borrowing facility. At a time when funds such as ETV should be expanding from healthcare biotech to IB, many are being wound up.

The feedback regarding financing IB start-ups was not entirely gloomy. The funding market place is international and if UK investors do not recognise the merits of IB then it is possible that more sophisticated overseas investors might take their place. UK research effort is reported to be attracting more interest from overseas partners [BBSRC]. There is an emerging opportunity to attract VC investment to UK IB from outside the UK [Wellcome Trust]. At least one SME is seeing more international money flowing in to the sector and has been able to secure investment in China. One VC thinks that Asian or US players of all kinds are more likely to invest in UK IB companies than European VCs.

On a global scale, the level of investment in IB by established companies also seems to be picking up, despite the poor economic climate. In fact, the search for growth in mostly stagnant markets may actually be driving a renewed interest in IB. *"Some pharmaceutical companies seem to be looking at their biotechnology assets and seeing if these can be applied to the fine chemicals sector"* [UCL]. *"Companies such as BASF and GSK are moving back into IB, reversing the trend of the past 10-15 years"*. [CoEBio3]. One of the SMEs agrees that *"some of bigger industrial players who stopped investing in IB a decade ago are now starting to get back into the game"*. *"The market place is international – companies such as Shell, Total and BP are investing across the globe"* [Industry].

The chemicals industry sees sustainable manufacturing as increasingly important; companies *"are no longer paying lip service"*. The inherently green credentials of IB are seen to be a way of making intermediates more environmentally friendly while energy prices make the cost savings from low temperature processes more attractive [Other]. One SME agreed that *"the business environment has improved in the last 18 months"*. Another felt that *"it is easier to get people interested in the IB proposition now than it was 12 months ago"*. *"Large companies will adopt IB – they cannot afford not to be doing this"* [Industry]. It has yet to be seen to what extent UK SMEs will benefit from this increased interest from corporates with most of their R&D and existing IB activities based overseas.

F8. Even with increased funding, on balance it remains unlikely that any of today's UK SMEs will develop into the 'tall trees' of tomorrow

In the software sector, most of today's corporate 'tall trees' trace their origins back to relatively recent start-ups – many are still run by their founders. The higher funding intensity required for IB process development poses the question of whether IB SMEs can ever grow into tomorrow's multi-national companies (MNCs). *"It must also be remembered that much of the current research into IB is being carried out by existing multi-nationals in order to maintain their competitive position and avoid losing market share to upstart new entrants"*. Internet start-ups initially faced much less competition from incumbent software and services players.

The growth challenges facing today's IB SMEs are particularly marked in the UK with its problematic funding environment. At present, it appears that the UK has mainly small and large industrial enterprises with little or nothing in between. One SME suggested that this is because *"UK start-ups do not grow into larger businesses – either because they fail commercially or are acquired by their competitors while still small"*. A VC manager believed that although some companies may grow into large corporates and float on a stock market, this was unlikely to happen in UK, where the most likely outcome would be for a company to be acquired by a corporate. The problem of UK SMEs selling out too soon (as they have no other option to finance growth) is discussed in Part 9.[25]

Another SME felt that overall it was unlikely that today's SMEs would develop into tomorrow's MNCs. *"Like the pure-play drug discovery companies in healthcare biotech, companies with a process development business model will eventually sell out completely or license their technology to the existing large companies. However, the exception is that companies dedicated to manufacturing what are today niche chemicals (e.g. biopolymers) might be able to remain independent and grow to become large companies as the markets for those products also grow"*. CPI felt that companies which develop technologies that are applicable to multiple processes (e.g. feedstock production) are more likely to become large independent companies in their own right, but this will depend more on their financing journey than their technology development journey.

There were some more broadly optimistic opinions expressed. One SME believed that at least some of today's IB SMEs will go all the way and become sector 'tall trees'. Neil Woodford of Invesco believes that the basic science in the best UK companies is every bit as good as in US companies, so if UK fund managers will only provide a level playing field by committing large amounts of capital over a long timeframe (10-15 years), then he sees no reason why it should not be UK companies that grow into the next generation of sector success stories. Further insights into this are provided by the answers to quantitative question #8 (see Part 6).[26]

Failure to raise sufficient funds to finance a sub-scale industrial demonstration plant may mean that an SME has no option other than to license its technology to a larger industrial partner after completing tests on its pilot plant proof of concept facility. Ironically, a course of action dictated by an inability to raise adequate funding from VCs may make those very same VCs reluctant to invest what little money they might otherwise have made available. *"The licensing model is generally not attractive to VCs because the returns are much smaller and the licensees are difficult to control (e.g. sometimes the licensee will buy the licensor and bring the company in house, causing the VC to exit prematurely)"* [VC]. Two large industries agreed that licensing tends to put off VC investment. *"A licensing model is unlikely to give the equity growth that VCs want but in-house production assets have too high a price tag for European VCs"* [SME]. Angel investors, on the other hand, *"tend to like licensing business models as the risks and the costs are*

25. See Key Finding F16.
26. See Key Finding F6.

lower" [VC]. However, their funding capacity is even lower than the VCs.

There may be technical as much as commercial reasons to adopt a licensing business model. One interviewee noted that *"many academics and SMEs make the mistake that lab-scale processes are automatically suited to industrial processes and base their business projections on vastly over-ambitious extrapolation of results produced in the laboratory. It is more likely that the technologies and processes that are developed will form a small part of an existing industrial process and that the overall operator of that process will acquire or license the innovative technology"*. New products and processes may be safety critical and need to be introduced to an industrial process with care. It may be essential to work with the existing suppliers and contractors to a corporate end-user, in order to facilitate the introduction of novel solutions to that end-user. It is the need to have staff that understand, and can respond to the implications of such transitions that underpins the desire of IB companies to appoint people with 5-10 years of experience.

The SMEs seem to be in two minds over the merits of a licensing business model, early or otherwise. In the long run it reduces financial returns and also undermines the autonomy of their business. *"There is a risk that shortage of funds will lure companies into granting exclusive business partnerships prematurely".* One SME noted that while licensing is seen as being the obvious initial business model, it recognises that getting into an asset based business (i.e. one owning its own manufacturing plant) is desirable in the medium term. *"Some SMEs may use a couple of licence deals to provide the cash to invest in taking a product to market – using licensing as a step to manufacturing"* [Other]. Green Biologics aims to develop initially through licences, but to use this to generate sufficient revenue to take a future proposition down the asset path.

All of the foregoing analysis on funding requirements applies particularly to the biofuels and chemicals sub-sectors of IB. In the food sub-sector the production of food itself will be somewhat similar because the value densities lie in the same low single-digit dollars per kilogram range. However, food additives and health promoting 'nutraceuticals' (not strictly within the remit of this survey) can command much higher prices. There will also be some products in the agricultural supply chain which are effectively therapeutic drugs for animals and plants. The funding dynamic in this sector will be closer to that of healthcare biotechnology, and therefore more compatible with conventional VC models.

The waste treatment sub-sector is different again, not least because the disposal of waste is a service rather than a product. Obviously one way to effect this disposal is to turn the waste into a useful by-product (energy or chemicals). However, this differs from conventional manufacturing because it is often possible to charge a 'gate fee' for the in coming waste – effectively a negative raw material cost. Waste treatment is also a more inherently distributed activity than chemical or fuels manufacture, requiring a larger number of smaller, more local, facilities. UK waste policy drivers mean that all parties know that this gate fee will rise.

This reduces the typical plant size and associated funding requirement. Technology development and demonstration for a novel process still costs £3-5 million but, taking AD as an example, a full-scale plant will process 30-40 ktpa and will cost £8-12 million. Assuming that the buyer contracts directly for the civils,[27] the AD equipment supplier will have to undertake a contract worth £6-8 million. Hence a £10 million investment would comfortably build a demonstration plant that was commercially viable. The main need in this case is for project finance and working capital.

However, several companies working on the treatment or conversion of waste noted that yet another 'chicken and egg' problem is operative here. *"Customers expect them to be able to demonstrate secure sources of funding before they will grant them waste treatment contracts, but potential investors expect them to have secured contracts before they will offer funding (securing the contracts is viewed as a key due diligence comfort factor)"* [SME]. In this respect, the investment in Monsal by the Waste Resources Fund is very interesting because it included an equity investment in the company itself and a project finance debt facility to enable it to secure customer contracts.

27. Civil engineering requirements – the foundations, fences, access roads, utilities etc.

Part 7: Unlocking early-stage opportunities

F9. Academic work needs a closer connection to industry if it is to produce commercialisable outcomes

"While there has been a lot of investment in the UK in basic science and facilities, there has been relatively little emphasis on identifying and developing IP that can be exploited commercially" [SME]. The two largest companies interviewed both agreed with this SME. *"The IB sector hasn't progressed a great deal in 25 years due to the over-promise of results from lab-based enzyme research"* [Industry]. This may be because attitudes to IB within universities are being shaped by scientists rather than engineers. BP is particularly conscious that IB requires chemical and process engineers to be involved in the innovation process from the outset if commercial solutions are to be developed. It could be helpful for the UK to develop a national R&D strategy aimed at achieving business-defined strategic goals. This is particularly the case where the early application of IB takes the form of a single stage or process within a large scale, integrated, chemical plant.

One academic admitted that *"the academic community's engagement with the commercial sector is generally very poor. This is primarily for cultural reasons as different relative values are often placed on measures of performance against time, cost and quality. Academics don't always understand the need to develop long-term business-style relationships with those able to commercialise their work. They need to engage more with industry to encourage a commercial focus to their research. However, companies also need to be more flexible in their attitudes to procuring contract research, for example by allowing interesting discoveries which have a commercial application to be pursued outside the original focus of a project"*.

One large industry interviewee agreed that attitudes found among the UK's academic community can be unhelpful. They saw pull from along the commercial value chain as important in changing these attitudes. *"University technology transfer organisations (or their fully commercial successors) such as Imperial Innovations, Isis and UMIP have a key role in communicating this market pull to researchers"*. It is interesting that, as discussed in Part 5,[28] more IB SMEs have been spun out of non-university research laboratories than the universities. *"This is perhaps because contract research laboratories derive a significant proportion of their revenue from the private sector and are therefore more attuned to its needs"* [Other].

Shell has in the past facilitated the interface with universities by participating in programmes such as the EU FP7 funded Marie Curie researcher exchange programme, where a Post-Doctoral Research Assistant (PDRA) parented to a top EU university spends two years in Shell's labs and one year in an equally prestigious UK university, whilst maintaining links to their original university.

One VC commented that *"neither academics nor industrialists generally make ideal entrepreneurs, but rather this is a particular and distinct type of person who is in short supply in the UK. As already noted, academics are too technically focused to have the perspective needed, but industrialists are often too risk-averse and comfortable in their salaried positions to venture into the uncertain world of founding a technology start-up company"*.

28. See Key Finding F4.

Another VC suggested that *"the UK needs a means of providing a facilitation/co-ordination function to communicate between the universities and SMEs on one hand and the corporates on the other. This would help to translate the corporate needs into problems for the academics/SMEs to solve. Corporates should be taking the lead, but getting them engaged is a long, slow process. The chemical/agriculture industries are innately conservative. They realise that they need good innovative applications to solve processing issues but do not know how to access the universities"*.

The paymasters of most university research recognise the need for better cultural alignment with industry. BBSRC plans to be more strategic with the allocation of training resources and to increase the size of its training portfolio in IB. In particular, BBSRC seeks to ensure that a significant proportion of training in IB is industrially relevant. It will promote collaborative approaches and facilitate the creation of cross-disciplinary research teams with industry to develop programmes of industrially-relevant research. An ideas factory-style approach may help to bring together the relevant teams while the use of industrial facilitators would ensure that the resulting research proposals tackled industrially relevant questions. CoEBio3 has a dedicated knowledge transfer fellow who is funded by EPSRC and tasked with helping to improve the dialogue a cross the 'academic – commercial divide'.

"The UK university sector is not viewed as very user-friendly in terms of contract R&D projects. Contracts have to be negotiated on a piecemeal basis with different universities demanding different terms and conditions and acting more or less aggressively. It can take up to 12 months to reach an agreement" [Industry]. The stance of a university can depend more on the personality and attitudes of an individual TTO officer than commercial reality. Potential stumbling blocks include: arguments over who owns the technology; agreeing the value of foreground IP, and; the suitability of individual academics to carry out collaborative research with industrial partners. Shell Global Solutions suggested that *"it would be helpful if there were a single standard set of terms and conditions (similar to those used in the construction industry) which formed part of academic contracts"*. In fact, there has been a previous attempt to create standard model research collaboration agreements which have been published as the 'Lambert Toolkit'[29] but none of the interviewees made any reference to this.

F10. Virtual companies could help with seed investment, incorporating only when the technology can attract investment

Several of the SMEs were set up initially as 'virtual entities' – procuring all required services under sub-contract rather than having any direct full-time employees, permanent premises or facilities. This is a lean and effective way to operate and given the limited amount of seed money which it is possible to raise, many companies have no alternative but to operate in this way. Even if seed money is offered, the 'soft start' option of a virtual company has certain attractions. It is less time consuming (distracting) to set up, leaves freedom of self-determination and avoids prohibitive dilution (>50 per cent of the equity must often be given away for the first £250k).

Solvert, for example, has operated as a virtual company, putting together a business plan using a team of individuals contracted on a consultancy basis. This will continue for the next phase of its development when a proof of concept study will be undertaken with the experimental work being carried out at the NIBF at CPI.[30] As a result, cash burn has been modest and the company had funded itself through a convertible loan from the NE Finance Proof of Concept Fund. TerraVerdae Bioworks initially followed a similar model, funded by its founder, and also plans to use the NIBF to carry out its preliminary experimental work.

"The creation of virtual companies is facilitated by the availability of skilled technologists and experienced executives who have become surplus to the requirements of the UK's contracting (petro)chemicals manufacturing sector". *"The emergence of 'proto-clusters' of IB companies in South Wales, NE and NW England and Scotland (Edinburgh) may well be driven by the redeployment of skilled people who have been shed in these locations"*[SME]. When New Horizons Global acquired a facility in Liverpool that was being closed down by the US gums and hydrocolloids company CP Kelco, it was able to recruit a team of technically qualified ex-Kelco employees. The capability underpinning CPI's role in the sector is based on people who came through ICI and where equivalent training and development will come from in the future is far from clear.

The use of friends, family and relatively unsophisticated local angel investors to provide seed money may be the only way to get a company started but can lead to difficulties

29. The Lambert Review on Business-University Collaborations chaired by Richard Lambert, former editor of the Financial Times and Director General of the CBI, and also formerly a member of the Monetary Policy Committee at the Bank of England, reported in December 2003. For a guide to the model agreements see: www.ipo.gov.uk/lambert
30. This is discussed further in Key Finding F13.

in the later stages of its development. The seed funding of one SME left it with a myriad of small shareholders, none of whom want to exit (the company has tried offering share buy-backs). This diffuses control and makes it difficult to raise significant further VC funding to expand the business. Another SME was similarly funded by high-net-worth-investors and as a result, the shareholder base is now quite diffuse and not particularly technically sophisticated. It has also reached the limit of the funding capacity/appetite of its original shareholders, presenting the challenge of finding new sources of funds.

Although a number of government-endorsed schemes have been devised to improve the flow of early-stage equity funding, these did not appear to have been widely used in the IB sector. One SME had received an investment from a Venture Capital Trust (VCT) to fund an MBO – its willingness to provide a combination of debt and equity was attractive. However, two other SMEs commented that VCTs are not offering an obvious avenue for funding SMEs.

Three of the SMEs mentioned that the Enterprise Investment Scheme (EIS) allowing tax relief on seed investments had been useful and one of the VCs also endorsed this view. However, many more of the interviewees found grant funding helpful during the early stages of their development.[31] One SME mentioned that Enterprise Management Incentive (EMI) share option schemes are important to attract, incentivise and retain the management team.

Technologists who have independent means of support (perhaps having retired early or taken redundancy, voluntary or otherwise, from a large industrial company) are often prepared to work initially for a new start-up unpaid, being rewarded instead with shares in the company created. However, if these shares are taken to be income they have to be valued and PAYE tax and National Insurance paid in cash by both the company and the executive. The majority of start-ups fail, which means that the shares usually turn out eventually to be worthless. The net effect *ex post facto* would then be that the executive has not only spent time working for the start-up unpaid, but has also paid out a cash sum to the government for the privilege of doing so.

The actual situation is very much more complicated than just described, but that very complexity and ambiguity is a major disincentive to resourcing a virtual company in this way. Even where discounted valuations can be negotiated on the grounds that there is no liquid market for the shares, or tax efficient share schemes put in place, the professional advice needed to do this is often prohibitively expensive. It would be helpful if there was a simple tax template for treating contributions to technology start-up companies in return for founder equity which ensured that tax only became payable on a liquidity event (providing a meaningful valuation for the shares) or disposal.

As discussed below,[32] TSB funding is an important source of non-dilutive funding and particularly attractive for very early-stage companies. However, there is a 'Catch 22' that an applicant cannot be approved for TSB support unless it demonstrates that it has secured the matched funding, but the providers of matched funding (e.g. seed investors) often won't commit until they know the TSB grant is in place. This is partly because award of the TSB grant is an important due diligence input for investors who may lack the sophistication to assess the quality of the technical opportunity themselves. It would be helpful if the TSB, and other grant awarding bodies, could make time-limited provisional offers subject to finding matched funding within, say 12 months, although it has to be recognised that EU state aid laws can also complicate the position.

More importantly for virtual companies, the TSB will not support the costs of extensive sub-contracts (they have to be <20 per cent of the total project budget). This does not work for a virtual company where almost all the costs appear as sub-contracts. There is a somewhat similar problem with R&D tax credits. Virtual companies don't qualify because these are paid via relief on PAYE contributions and as a virtual company they don't make any significant PAYE payments.

F11. Grants and R&D tax credits are complementary in early funding

Relative to early-stage equity funding, IB start-ups report that grant funding is more abundant, easier to access, easier to manage and highly attractive because it is non-dilutive. Many of the SMEs interviewed believed that without grant funding they would never have been founded. *"Grants provide reputational as well as financial leverage which can combine into a virtuous circle. In the US, getting picked to work on high profile collaborative projects for respected government agencies*

31. See Key Finding F11.
32. See Key Finding F11.

or programmes raises a company's profile, provides an important credentialisation and is used by VCs as part of their due diligence" [SME]. Another SME pointed out that *"grants can be a good way of funding research to one side of a company's critical IP or business development pathway, thereby keeping alternative options open (keeping the Plan B's alive)"*.

When selecting SMEs for interview no prior reference was made to any list of successful applicants for TSB grant funding, but nonetheless a high proportion of the interviewees turned out to have received funding from this source. This serves to illustrate the current importance of this scheme to the growth of successful companies now that many other sources of funding are unavailable. According to the TSB, the rough split of the funding allocated is:

- 30 per cent to lab scale projects to assist early-stage companies demonstrate proof of concept and feasibility;
- 50 per cent to 'hardened SMEs' that have existed for more than five years and need support to demonstrate that their technologies can be scaled-up; and
- 20 per cent to medium-scale companies that need funding to demonstrate that their technologies can be scaled up and remain commercial.

An academic now working for a start-up company considered that TSB feasibility grants of £100-150k were 'great' for helping to fund the first step out from the academic funding environment. Green Biologics used TSB grants to leverage its seed money. It found these grants to be *"well targeted and of a scale that fitted well with the needs of its business"*. Ingenza received a TSB Collaborative R&D Award of £500k, three more TSB grants and a Scottish Enterprise SMART feasibility study award and, as a result, was able to fund itself without recourse to equity investors. In September 2009, Plaxica was awarded a High Value Manufacturing TSB grant and in 2010 received a second grant from the High Value Chemicals call. TerraVerdae Bioworks applied successfully to the same call and reported that *"the TSB were impressive throughout the application process. The grant has been hugely important to the company's development"*.

TSB grant funding has obviously been of considerable importance in taking many ideas forward. *"However, such funding pre-supposes that the applicant has already undertaken some proof of concept demonstration, and the problem for some companies is funding themselves to the point of becoming eligible for TSB funding. A BBSRC programme which gave out awards at the proof of concept stage of up to £250k without needing matching funding was particularly useful, though may no longer be available"* [Research].

There are a number of other schemes which complement the pervasive TSB funding. Clearfleau used grant funding from the Environmental Transformation Fund (ETF) and the Waste and Resources Action Plan (WRAP). The grant helped to finance a successful demonstration of their AD waste treatment technology (at DB Dairy in Dorset) and this subsequently led to exclusive deals with Nestlé and Diageo. Grants have been important to Cleveland Biotech to help fund its product development programme. It received a GRD and consultancy support via the RDA (One NorthEast) and laments the abolition of the RDAs. The relocation to Liverpool by New Horizons Global was carried out with help from The Mersey Partnership (TMP) and Knowsley Council.

Relatively few interviewees had received any funding from European programmes (e.g. the multi-billion Euro Framework 7) or even made mention of this possibility. One SME had led a successful European grant application in 2009 which brought in €300k. Another commented that *"European money is an attractive source of development funding, but the UK does not seem as sophisticated as other European countries at putting together winning consortia"*. A third SME reported the under-whelming experience of applying for ERDF and other RSA (Regional Selective Assistance) money.

Large companies can also benefit from grants, which can be an important influence on their investment decisions. The £3.5 million feasibility study for a bioethanol and bioenergy plant at the Seal Sands site in the Tees Valley carried out by Ineos in 2009 was supported by a £2.2 million grant from the Regional Development Agency (One North East) and the Department for Energy and Climate Change. The feasibility study informed an investment decision in 2010 to proceed with planning for a commercial plant which will receive a further £7.3 million of support from the same sources.

R&D tax credits are another source of government support for early-stage companies. Several of the SMEs interviewed found them 'useful' while one said that they had made 'an important difference'. One SME has not yet applied for any R&D tax credits, but their VC is now encouraging them to explore this option. WHEB Partners confirmed that VCs view them as useful non-dilutive leverage.

One SME reported that applying for R&D tax credits is a *"complex and bureaucratic process with significant associated costs, reducing the net benefit"*. The problems for virtual companies have already been discussed previously.[33] It was noted that *"in the US, procurement of technology demonstrators and development projects by the Department of Defence (DoD) and other government agencies effectively subsidises corporate R&D – this does not seem to happen to the same extent in the UK"* [SME]. Procurement could offer a more focused form of support than blanket R&D tax credits. For example, the government could take the lead in powering its road vehicle fleet with sustainable second generation biofuels produced from waste and procure these as a means of stimulating the development of candidate processing technologies.

F12. Collaboration plays a key role in unlocking early-stage funding

A healthy IB sector requires research collaborations between large corporates, SMEs, university laboratories and development facilities – 'open innovation' [Industry]. *"Strong partnerships between SMEs and corporates allow the SMEs to focus on their research and provide the corporates with a degree of innovation that they are no longer able to source in house"* [CPI]. One large industry interviewed does not do any in-house R&D but instead relies on collaborations. Corporate venturing deals tends to be done between companies that have developed mutually beneficial relationships from working on earlier projects, often co-funded by government grants [CPI]. Indeed, *"IB is distinct from healthcare biotechnology more in its scale-up and route to market than in the basic skills and technologies involved. The key collaboration for IB SMEs is with chemical and process engineers rather than medical researchers; these are two profoundly different constituencies"* [Industry]. Collaboration is even more important for funding corporate growth and is discussed in more detail in Key Findings F12 and F15.

Part 5 introduced the concept of 'tall trees' in an industrial ecosystem – large corporates with a significant domestic presence which can provide funding and nurturing to SMEs.[34] The UK has a shortage of such 'tall trees' relative to its main international competitors. This will not make it impossible for the UK to compete in IB, but its SMEs will need to work that much harder to collaborate with 'tall trees' based overseas. Canada, for example, does not have any domestic chemical giants but still has some worthwhile IB activity [TerraVerdae Bioworks]. Alternatively, some of the functions of 'tall trees' – such as industrial training – could be partially replaced by a consortium of smaller companies provided with a small amount of co-ordination funding.

Large companies take an international perspective and most would be perfectly happy to collaborate with UK SMEs even though being foreign-owned and perhaps having only a very limited UK presence. However, it is not always easy for the UK SME to indentify and make contact with potential 'tall tree' partners overseas. Facilitating overseas contacts by SMEs far too small to be truly multinational would be a very valuable form of support.

Within Europe, trade associations such as EuropaBio can be useful – it has a specific focus on IB.[35] The UK Trade & Investment (UKTI) department is another potential source of assistance. Its Overseas Market Introduction Service (OMIS) helped one SME to expand overseas by providing detailed research on export markets, as well as identifying potential customers and distributors. TerraVerdae Bioworks became aware of CPI, with which it now collaborates, through a presentation given by UKTI at the British Consulate in Boston.

33. See Key Finding F10.
34. See Key Finding F3.
35. See: http://www.europabio.org/Industrial_biotech/

F13. Shared demonstration facilities play a critical role in corporate development and are particularly valuable in an uncertain VC funding environment

It was noted in Part 6 that the UK's IB SMEs have particular difficulty in sourcing the £10-20 million needed to build a sub-scale industrial demonstration plant.[36] Once this plant has served its purpose and demonstrated that an IB process works at the next level of scale-up it will quickly become obsolete and be superseded by a full-scale (and therefore commercially viable) industrial plant. In view of this, it can make sense to rent time on a shared demonstration plant rather than to buy one outright, particularly if funding is difficult to come by.

A shared facility not only reduces the cost of the industrial demonstration phase but also significantly shortens the lead time and reduces the risks associated with introducing an IB step into an existing integrated industrial facility. *"If a company raises, say, £15 million to build its own plant then up to two years will necessarily elapse between banking the investment and starting the experiments, during which time the plant is designed, contracted and built. This means that it will be up to three years before any results are obtained – stretching the patience of the VCs and reducing their internal rate of return (IRR) on whatever value uplift results from the process demonstration"* [SME].

Recognition of the potential benefits of a shared demonstration facility lay behind the decision to fund the £12 million National Industrial Biotechnology Facility at CPI. It forms part of SUSPROC – the UK's Sustainable Processing and Advanced Manufacturing Centre – which helps companies and organisations test, develop and scale-up sustainable processes and energy solutions. In addition to the NIBF, SUSPROC comprises the Anaerobic Digestion Development Centre together with major activities in smart chemistry and sustainable engineering. In March 2011, BIS announced that the facilities at CPI would form part of the High Value Manufacturing Technology and Innovation Centre (TIC) – the first of six to eight planned TICs with a total budget of £200 million. Further details regarding how this will impact on the way CPI/NIBF operate are expected to emerge in October 2011.

The large number of interviewees who made reference to the NIBF all expressed favourable opinions. The TSB provided funding because it believed that shared industrial scale facilities are crucial to the development of IB companies and technologies. Croda saw it as *"a very important means for the university sector to prove its research and enable technology transfer"*. *"As the NIBF becomes more mature, its alumni will start to become dispersed throughout the UK, helping to address the skills shortage in IB"* [Research]. The Biosciences KTN believed that it was something which had been *"desperately needed for a number of years"*. *"The use of TSB and other funds to help people gain access to the facility is a good and joined up piece of thinking"* [Other]. AB Sugar stated simply that SUSPROC was *"the best money spent by government"*.

Attitudes to the NIBF are also very positive among its principal target customer group of SMEs. Plaxica has used NIBF1 and may use the larger NIBF2 facility in a few years assuming that it is cheaper than a pilot plant. *"Bespoke facilities would be ideal, but the more generic*

36. See Key Finding F5.

facility at Wilton is much less expensive". NIBF2 will also be 'vital' to Solvert's plans.

The world class facilities of NIBF are being recognised internationally. CPI is seeing increasing interest from US-based SMEs wanting to access shared development facilities at a fraction of the cost of building and operating their own. This is confirmed by the US-based TerraVerdae Bioworks which has set up a subsidiary in the UK specifically so that it can carry out trials at the NIBF.

The CPI facility complements a smaller scale laboratory proof of concept facility at the CoEBio3 in Manchester. *"SMEs can carry out their preliminary R&D here and then move seamlessly to the CPI facility for scale-up"*. UCL also has a test rig that can be used to perform scale-up work and could act as stepping stone to NIBF. UCL and CoEBio3 have collaborated in pushing their combined capability as an Innovation and Knowledge Centre (IKC) – a designated 'national centre of excellence'.

While everyone was positive about the NIBF there was a note of caution sounded by some people that it cannot provide a universal panacea. *"Companies should not be lured into thinking that they can squeeze the cost of their pilot plant work too far: two to three runs on a shared plant do not constitute a good basis for a decision on a £100 million+ full-scale plant"* [SME]. One VC agreed that *"while trials at the NIBF are a good start, most companies will still need to scale-up further before non-specialist UK VCs will take an interest in them"*. Furthermore, in the waste treatment sector a demonstrator at a fixed location in the UK may be of limited use. Clearfleau found that it needed to have a portable demonstration unit allowing it to take its technology to the source of the industrial waste.

One SME expressed the concern that *"the NIBF may soon become over-booked, introducing a bottleneck into development of the UK sector"*. While the NIBF was designed for maximum flexibility it is unreasonable to expect that a single facility can be reconfigured to meet every operational requirement. There are many SMEs located in regions remote from NE England which would find it difficult to manage test programmes at a distance. It is therefore important to consider ways for expanding the availability of shared-access facilities beyond the excellent precedent set by the NIBF.

CPI itself suggested that *"the cost of accessing industrial facilities could be subsidised by an agency (presumably government) issuing tokens for the use of capital equipment (i.e. an approach somewhat analogous to 'R&D voucher' schemes), with right of first use going to the receiver of the token and a duty to sell this equipment to a shared facility afterwards. In the long-term, this might migrate to a simple hire model once there was sufficient equipment in the system"* [CPI]. Another suggestion was *"to encourage the negotiation of ad hoc 'time share' arrangements for equipment that is not being fully utilised by its current owners"*. One large company has considered renting facilities to its partner companies. Another interviewee noted that *"such time share arrangements are only likely to happen when the companies concerned already have a strategic and commercial relationship as the risks to the host operator are often greater than the immediate financial rewards"* [Finance].

"In some cases a facility closed down by one company can be resurrected relatively cheaply by another" [VC]. One example of this is New Horizons Global. In 2009 it took the opportunity to acquire a large fermentation facility at Knowsley in Liverpool which was being closed down by the US gums and hydrocolloids company CP Kelco (part of J.M. Huber Inc). The facility was originally set up by Tate & Lyle in 1978 and acquired by Kelco in 1981. Green Biologics has found it possible to retro-fit its equipment to existing facilities that are no longer being used. This allows the company to demonstrate production at an industrial level but at considerably reduced cost. It could be useful to establish a central broker or agent for such relationships, ideally on an international scale.

Much has been written elsewhere about the benefits of clustering for promoting wealth creation by technology start-up companies. The specific application of this to the IB sector is outside the scope of the present survey, but the interviewees were invited to make general comments on clustering. The BBSRC considers clusters to be important, but does not believe that any have yet reached a critical mass. One of their reasons for moving towards their 'longer and larger' (LOLA) investment in IB is to promote this. CoEBio3 echoes this view and *"does not yet see anything it would call a fully developed cluster. There are some clear regional strengths in the North East, the North West and Scotland which could well develop into future clusters"*. Another academic identified pockets of activity in Scotland, South Wales and the North East. *"Key to this has been One Northeast support for CPI and*

Scottish and Welsh Government support for the other groupings". The Wellcome Trust clearly believes that the creation of IB hubs such as that envisaged in their unsuccessful Olympic Park legacy bid could play an important role in promoting knowledge transfer and reducing investment risk.

F14. Government interventions aimed at promoting positive environmental outcomes can also support the nascent IB sector, but there is a need for more joined-up thinking

Many IB processes are very energy-efficient while the feedstocks used are generally renewable. Companies commercialising these processes may therefore benefit from government interventions aimed at reducing GHG emissions – either in the form of subsidies or regulations mandating the deployment of sustainable or energy-efficient technologies. The two IB sub-sectors most likely to benefit from this are the manufacture of biofuels and the treatment of waste (especially where this is converted into heat or power). The UK Renewable Transport Fuels Obligation (RTFO), for example, mandates minimum levels of biofuel in commercial road transport fuels.

The fuel mandate has stimulated investment in advanced manufacturing and supply chains that both use and produce renewable feedstocks. It is acting as a spur to innovation and further investment supported by a highly skilled workforce, whose capabilities will also underpin the development of bio-based chemicals and the IB sector as a whole. However, this support also distorts the market and may not even result in an optimisation of the desired environmental outcome. For example, *"there is strong support for turning biomass into biofuels but not for turning it into chemicals, even though the GHG savings can be just as great. The result is that biofuel plants get built in preference to chemicals plants"* [Industry]. *"There is a similar situation in the US where the key focus is on biofuels and everything has to be wrapped in that banner. Thus many of the IB companies set up to exploit algal biomass were really based on the production of a broad suite of biogenic products but had to present themselves as biofuel companies to attract funding"* [SME].

There is a similar ambiguity in the UK Government's attitude to AD of waste to make methane compared to fermentation to make chemicals. *"If the former can claim subsidies via schemes such as the Renewable Heat Incentive (RHI) or Renewables Obligation Certificates (ROCs) which are not open to the latter, then they will be in a privileged position when it comes to competing for organic waste feedstock, even if their environmental impact is no better"* [SME].

Two SMEs reported that there are also specific regulations relating to waste disposal which can create complexities for anaerobic digestion companies. There are, for example, some uncertainties about the regulations relating to discharge of the final residue to fields. This can only take place during certain months, necessitating additional hold up storage on site. Permission depends on the phosphorus and nitrogen contents which introduces a project risk as it is difficult to know in advance what these will be. The alternative is to de-water the residue and use the resulting cake for compost even though this might reduce the net greenhouse gas savings.

In the food sub-sector, one SME noted that *"if its product is classed as a 'novel food' (which seems likely) then EU certification takes a minimum 12 months, can take three to four years, and is very costly. By comparison, the US has relaxed the need to seek FDA approval and now allows commercial sales based on a 'Self Affirmed GRAS' (Generally Recognised as Safe) status"*.

There was a general feeling that the plethora of schemes all attempting to achieve the same environmental outcomes created unnecessary complexity. For example, it has been proposed that from 2012 Feed in Tariffs (FiTs) will no longer be allowed alongside other investment incentives such as EIS or if the project is supported by another government grant. Similarly, *"if an AD project is supported by WRAP it cannot qualify for FiTs, which may swing the economics back towards manufacturing chemicals"* [SME]. It must surely be possible to develop a single accounting unit (e.g. tonnes of carbon saved or landfill diversion) which can apply across the board.

Government interventions in the UK lack the coherence displayed some of its key IB competitors. Brazil, for example, has mandated ethanol/bioethanol (from sugarcane) for many years and as a result has seen its industry become a world-leader. *"The lack of strategic direction over a long-term investment time frame does not encourage corporates to invest in developing IB in the UK.[37] This is exacerbated*

37. Just two examples are the policy on new nuclear and changes to the PV feed-in-tariffs. Closer to home, there appears to be deliberate ignorance of the predictions surrounding the global supply of biomass and the UK's ability to procure the share it will need to support a commercially viable IB sector. For example, no Government funding is directed towards securing commercial sources of sustainable biomass for the UK and yet the same Government continues to spend R&D grants and encourage knowledge sharing in the belief that this will assist in the development of a healthy IB sector.

by the fact that European legislation takes so long to put in place and that different countries (including the UK) then interpret it in their own way" [Industry].

F15. Collaboration plays a key role in unlocking revenue growth opportunities

"Partnering is an extremely important market entry strategy but is not very well executed in the UK" [Industry]. *"SMEs often don't have the expertise and industry contacts (particularly overseas) needed in order to tailor their research to meet market needs while the corporates are often not aware of what technologies are being developed"* [Other]. There is a need for more match-making between SMEs and large corporates to promote this. *"Utilising shared facilities such as the NIBF encourages contact between SMEs and larger corporates, making CPI well positioned to provide such a service"* [CPI].

From the SME perspective, Green Biologics see partnering as very important, especially with regard to accessing plants and markets. Its foray into China was very much driven by this. Another SME noted that *"small companies need partnerships; it is their only route to a market where the customers are global"*. Plant Impact has licences in 25 countries and development programmes with four of the top ten agricultural companies. Its partnership with Arysta LifeScience Corporation, the world's largest privately-held crop protection firm, has been secured by an equity investment. A third SME agreed with this approach – *"swapping licenses for partnership deals is seen as a good opening gambit in negotiations, especially when there is the prospect of an equity investment or trade sale further down the line"*.

Part 9: Exits to unlock returns

F16. VC reluctance to invest in IB is based partly on disappointing historic returns from early-stage investments: this may be caused by a culture of exiting too soon

While some VCs have questioned the 'investible' quality of many UK start-ups, most avoid getting into a 'blame game' and simply point out that, for whatever reason, historic returns in the UK from early-stage technology funds have been very disappointing. Private sector VCs will not be cajoled into making more money available to IB SMEs if they remain unconvinced of the returns that can be made. Funds linked to the public sector are too small to fill the gap and are anyway constrained by State Aid rules. A more effective approach would be to discover why historic returns from private sector investors have been so poor and to identify a remedy.[38] If a profitable investment paradigm can be demonstrated then there should be no problem attracting private capital which is searching for high-yield opportunities in a low interest rate environment.

There is a school of thought that portfolio returns in the UK are disappointing mainly because the VCs exit too soon from the winning companies, meaning that they don't have time to create sufficient value to compensate for the inevitable failures in the portfolio. For example, if a portfolio comprises ten investments, each of £10 million, and only one company is successful, then the VC needs to make £100 million from that company just to recover its initial investments. To ensure a reasonable rate of return on the fund, it would ideally need to make £200 million from the one successful investment. Given that the VC will not own 100 per cent of the equity, this company will need a valuation considerably greater than £200 million when the VC makes an exit – probably above £500 million. The reality, however, is that many UK VCs exit from successful companies once their value has reached about £100 million.

The reasons behind this are complex and outside the scope of the present survey. An over-optimism regarding portfolio success rates may be to blame, perhaps exacerbated by a timing factor (successes may become apparent sooner than failures). One SME noted that *"VCs don't have a long-term vision of growing the business and will tend to want to 'cash in their chips' once they have hit a hurdle return, even if to management the best years still seem to be ahead. Business is seen as a means to the end of growing money, rather than money as a means to the end of growing business"*.

Another SME suggested that a failure by lending banks to pick up the corporate funding baton from VCs means that VCs face a choice of either selling out too early or leaving their portfolio companies starved of cash. The SME in question has a £1 million turnover, a £5 million order book and cannot negotiate a £250k overdraft. *"In Germany the regional Landesbanks support regional family-run companies which as a result develop long term into bigger businesses"* [SME]. Whatever the reasons for it, exiting prematurely may be helping to starve the SMEs of their growth capital while at the same time denying VCs their profitable returns.

It will not be possible to attract the necessary investment into UK IB unless there is a credible and tangible prospect of an attractive return on that investment. Given the risks involved, the rate of that return will need to be much

38. For a fascinating critique of early-stage VC funding see: www.foundersfund.com/the-future

higher than the investor's cost of capital. Most early-stage investors would view 20 per cent per year as at least an aspiration, if not a firm target. For purely financial investors (as opposed to corporates which might make strategic investments) this return will at some point need to be monetised by an exit from the original investment – an acquisition or floatation. To date there have been few, if any, high profile and clearly profitable exits from IB investments in the UK. This lack of precedents is deterring further investment in the sector. The flow of investment funding can be viewed as a pipe: if the exit is blocked eventually further liquidity stops flowing into the front end. This provides a further feedback loop, whereby investors will not make investments if there are no precedents for successful exits, but there cannot be exits without a pipeline of previous investments.

There are, in principle, three ways in which an investor may achieve an exit. The first is an initial public offering (IPO) on a stockmarket which provides a 'liquidity event' by opening up a liquid market for the company's shares. The investor can then sell down its stake over whatever timescale appears to offer the most attractive total return. The second is to tender the shares to an offer made to buy the entire company. The buyer will usually be a corporate acquiring the company for strategic reasons (a 'trade buyer') but may sometimes be another private equity fund (a 'secondary buy-out'). A third option, which is rarely seen, is for the company to start paying a dividend out of its profits, or to buy back some of its shares, in either case returning the investors' original investment while leaving them with a residual stake in the company which they may choose to hold indefinitely to provide an annuity income.

Only one of the SMEs surveyed had undergone an IPO and this was more properly a liquidity event rather than an 'exit', although a number of company executives have experience of taking non-IB companies down this route. Plant Impact was floated on the AIM stockmarket in 2006, about three years after being founded and before the collapse of investor confidence precipitated by the credit crunch. It then raised £3.59 million gross (£3.32 million net) through share placings undertaken in July 2009 and March 2010. In May 2011, Arysta LifeScience Corporation, the world's largest privately-held crop protection firm, invested £2.1 million in the company in return for a stake of around 9 per cent.

One of the SMEs had already been acquired by a trade buyer. Ingenza was acquired by the US speciality chemicals company Richmond Chemical Corp approximately four years after being founded as a university spin-out. This provides the company with access to customers, worldwide marketing and distribution, thereby accelerating the commercialisation of its technologies. However, the new owners have not injected significant fresh capital and Ingenza is now seeking to raise £2-3 million to fund a bespoke manufacturing facility.

The oldest of the SMEs surveyed had returned the capital of its seed investors without them exiting from the equity. Cleveland Biotech originally funded itself via *ad hoc* sales of shares to friends and family, raising about £400k in total. It took about ten years before the company started to trade profitably, but today its *annual* profits are approaching the level of the total cash invested in setting it up.

The sample of ten SMEs surveyed therefore included one example of each of the possible exit mechanisms described earlier. In current market conditions it is very unlikely that any other early-stage UK start-ups will be able to achieve IPOs for the foreseeable future. Return of capital via dividends or share buy-backs is very rare for start-up companies, particularly if backed by VCs rather than private individuals. It is therefore likely that the majority of the IB SMEs in the UK will be sold to strategic buyers and, given the UK's lack of 'tall trees', these buyers are likely to be foreign companies.

All the interviewees who expressed an opinion agreed with this analysis. One SME felt that a trade sale was by far the most likely exit for its VC investors in the current financial climate. Its timing is likely to be dictated by the investors deciding that their rate of return is starting to plateau or tail off.

If all of the UK's IB SMEs are sold to foreign buyers then none will grow into domestic 'tall trees' which, as discussed in Part 5,[39] are important for a healthy industrial ecosystem. Furthermore, precedent suggests that UK investors also tend to sell out prematurely. The result is that many of the current crop of SMEs will not even have time to grow into foreign owned but UK-based 'saplings'. Instead, their IP will simply be absorbed into the existing IB operations of the buyer, most of which will be based overseas. This will do little to help rebuild the UK's manufacturing base and rebalance the economy. It seems likely that

39. See Key Finding F3.

this impatience on the part of investors is also damaging their own narrow financial interests.

A culture of exiting too soon could very well be responsible for the disappointing historic returns from most UK early-stage VC funds. Neil Pitcher of ETV Capital suggested that the UK does not have a worse company failure rate than the US in percentage terms, but simply sells out its winners too soon and too cheaply, before they can create enough wealth to compensate for the losers. Neil Woodford of Invesco Perpetual put forward a similar analysis. He also believes that UK companies are given insufficient funding to compete effectively with better-funded competitors, particularly in the US. He is happy to take bigger bets – for example putting ca. £50 million into a recent therapeutic biotech company (Circassia). This overcomes any potential problem of 'dropping the funding baton' between the early-stage VCs and later-stage bank lending.

Neil Woodford's early-stage VC investments are held in the same income funds as his large positions in quoted equities. These are open-ended funds, meaning that he does not experience the same short-term pressure to exit as a VC – he would be happy to hold the shares for up to ten years. His current exposure (>£300 million including direct stakes and indirect exposure via a holding in Imperial Innovations) is less than 2 per cent of his total assets under management, meaning that there is not the same focus on short-term marking up or down of valuations as there would be in a separate fund consisting solely of VC investments. This makes it easier to take a long-term view. It is worth adding that Neil's previous exceptional track record also means that investors are prepared to back his judgement over the long-term – he has earned the right to be a patient investor.

The success of Invesco's approach could be of critical importance to the UK economy. If taking larger and longer term bets can lift the historically disappointing returns on early-stage VC funds then other money managers may be persuaded to put a small proportion of their assets (2-3 per cent) into start-up companies. In addition to increasing the returns on funds that are desperately seeking improved yield, this would have a massive impact on creating new high technology manufacturing jobs.

Part 10: Summary and conclusions

An in-depth survey has been carried out to canvass opinions from ca. 30 per cent of the most active players in the UK's nascent IB sector regarding the prospects for financing strategically important further investment in the current climate. The feedback obtained has not been verified for factual accuracy, objectivity or context. Rather it has been drawn together into a number of common threads and presented as the 'collective subjective' view of the IB community. In this report, the output from the survey has been divided into 16 'Key Findings' (F1 to F16) which describe what the UK IB sector is like and present lessons which could potentially improve the financing of IB in the UK.

Part 5: Current status of the IB sector in the UK

F1. IB is not yet a true sector but rather a tool used across a range of industries:

- The sense of identity in IB is patchy – the UK sector could be expanded by bringing more existing activity under the IB umbrella.
- Despite its small size the UK sector is fragmented and lacks clear leadership.

F2. The UK has fallen behind many other countries in IB:

- The significantly active core of the UK IB sector comprises a closely linked network of about 30 indigenous companies, most of which are SMEs.
- UK start-up companies have been formed in all major IB segments but very few are recognised as world leaders.
- The global leaders in IB are the US, Germany and Holland. The UK falls into a second division comprising other European nations plus Brazil, India and China.
- There is likely to be a long-term IB skills shortage in the UK, offset temporarily by experienced staff being shed from contracting chemicals and pharmaceutical companies.

F3. The UK lacks indigenous large companies to support its SMEs with investment, partnering, training and credibility – the 'tall trees' of a healthy industrial ecosystem:

- Multi-national 'tall trees' do not tend to invest in UK IB because it is commercially under-developed and it remains under-developed primarily due to a lack of investment – the first 'chicken and egg' problem besetting the sector.

F4. Universities are less important than other sectors as a source of new companies:

- UK academic institutions are excellent at fundamental research but very poor at the applied and collaborative research necessary to commercialise IB discoveries.
- Few IB start-up companies originate as university spin-outs, possibly because hands-on chemical engineering plant skills cannot be developed at university.

Part 6: Funding requirements and barriers to investment

F5. IB is different from other technology investments because of the investments in heavy plant needed:

- Because IB products cost much less per kilogram than IT or healthcare biotech they have to be commercialised in large plants costing £100 million+ each to build.
- The characteristic investment quanta needed in IB do not fit well with VC models developed for IT and healthcare biotech.
- There is a particular problem sourcing VC funding of £10-20 million for a sub-scale industrial demonstration plant.

F6. The UK has a specific funding problem, linked to poor historic returns:

- Difficulty in securing VC investment is much more severe in the UK than the US due to systematic failures in the UK market.
- UK VCs are reluctant to invest because historic returns on early-stage funds have been poor, but this may be because early-stage companies are starved of VC funding – the second 'chicken and egg' problem besetting the sector.
- Most interviewees believe that it is becoming increasingly difficult to raise funding for IB companies but a significant minority apparently see the companies themselves as partly to blame.
- Approximately half the interviewees expressed views which could be construed as implying that there are rational reasons for not investing in the UK IB sector.

F7. Bank finance and venture debt are not filling the gap:

- Banks are not prepared to lend early-stage IB companies money to leverage the limited VC funding that is available.
- Venture lending can play an important role offering technology companies a hybrid between debt and equity, but is itself a casualty of the credit crunch.
- While the current funding environment is very gloomy, there are early signs that the situation is starting to improve.

F8. Even with increased funding, on balance it remains unlikely that any of today's UK SMEs will develop into the 'tall trees' of tomorrow:

- Companies which cannot raise sufficient funding to complete their scale-up path may be forced to license their technology prematurely.
- The scale-up path in the waste treatment sub-sector requires less investment because the plants are smaller and more distributed.
    - Generators of waste expect a company to have secured funding before awarding it a treatment contract but its financers expect to see signed contracts before investing – the third 'chicken and egg' problem besetting the sector.

Part 7: Unlocking early-stage opportunities

F9. Academic work needs a closer connection to industry if it is to produce commercialisable outcomes:

- R&D in the UK has a poor record of producing commercialisable outcomes. The UK should develop a national R&D strategy targeting business-defined goals.
- The academic and entrepreneurial IB communities need to become more closely engaged with each other to promote to a better alignment of their cultures.
- Contract negotiation between universities and industrial sponsors needs to be improved to promote a better alignment of their economic interests.

F10. Virtual companies could help with seed investment, incorporating only when the technology can attract investment:

- It can be beneficial to form a start-up company initially as a virtual entity which procures all its required services on a contract basis.

- Unsophisticated seed investors may cause a company problems later on.

- Government initiatives to improve early-stage equity funding have been only partially successful.

- Virtual companies minimise the seed funding requirement but can face problems with bureaucracy and tax legislation.

F11. Grants and R&D tax credits are complementary in early funding:

- Grants are vital for funding early 'proto-start-up' companies and continue to be very important through the seed and VC rounds.

- R&D tax credits are a useful complement to grant funding but could be improved.

F12. Collaboration plays a key role in unlocking early-stage funding:

- Collaboration is made more difficult by a lack of large domestic corporates.

Part 8: Unlocking growth-stage success

F13. Shared demonstration facilities play a critical role in corporate development and are particularly valuable in an uncertain VC funding environment:

- Ways and means should be explored of increasing the quantity and variety of shared demonstration facilities available in the UK.

- Shared demonstration facilities can be useful in nucleating IB clusters.

F14. Government interventions aimed at promoting positive environmental outcomes can also support the nascent IB sector, but there is a need for joined-up thinking.

F15. Collaboration plays a key role in unlocking revenue growth opportunities.

Part 9: Exits to unlock returns

F16. VC reluctance to invest in IB is based partly on disappointing historic returns from early-stage investments: this may be caused by a culture of exiting too soon:

- The lack of precedents for profitable exits from UK IB investments is deterring further investment but there cannot be exits without a pipeline of previous investments.

- The most likely form of exit for investors in the UK is a trade sale to a large corporate buyer which will very probably be a foreign company.

- Trade sales by impatient investors to foreign buyers do little to help rebuild the UK's manufacturing base and rebalance the economy: they may also be damaging to the investors themselves.

Reminder: the 'three chicken and egg' problems

1. Multi-national 'tall trees' do not tend to invest in UK IB because it is commercially under-developed and it remains under-developed primarily due to a lack of investment (F3).

2. UK VCs are reluctant to invest because historic returns on early-stage funds have been poor and there is no track record of successful exits, but this may be because early-stage companies are starved of VC funding (F6 and F16).

3. Generators of waste expect a company to have secured funding before awarding it a treatment contract but its financers expect to see signed contracts before investing (F8).

Part 11: Principal Recommendations

The 16 Key Findings listed in Part 10 vary in their degree of specific relevance to IB; many would be true of any technology-based UK start-up company while others are focused on particular IB sub-sectors. They also vary in their scope, timescale and feasibility of deliverability in the current economic climate. In this final section we have synthesised the Key Findings to produce eight Principal Recommendations for practical steps which could, with a certain degree of courage and energy, be taken to improve the financing of the UK IB Sector. Some are endorsements of ideas already being explored elsewhere while others may be rather more novel. In our opinion, all are worth pursuing.

In discussing the real and substantial financing issues facing the IB sector in the UK it can be difficult to distinguish between those associated with the wider prevailing (challenging) business and economic climate and those particular to the IB sector. However, it does appear that the IB sector faces a range of specific issues, but these may be at least in part counter-balanced by the scale of the future prize on offer.

11.1 Policy recommendations specific to the IB Sector

There is a clear requirement for policy support to assemble a coherent IB sector in the UK and to stimulate domestic and international investment into UK IB businesses. Our suggested recommendations are that:

To improve strategic consistency:

1. A joint committee is formed consisting of representatives from government, industry and the finance sector to establish guidance on which R&D goals are strategically important to the UK and standard metrics for assessing the relative strategic value to the UK of investing in specific IB development projects. This would go some way to addressing the issues raised in Key Findings F1, F4, F9, F12 and F14.

To improve collaboration:

2. Development funding is made available to encourage more active collaboration between corporates, SMES and the academic community. Such funding could lever in corporate investment and support measures such as:

    a. The facilitation of contacts between UK SMEs and multinational corporates. In addition to the work that the UKTI already does, this type of contact could be designed to attract ‘tall trees’ to UK by discussing plans for joint public and private sector investment in technology development programmes that are of strategic importance to the UK (see b).

    b. Technology development competitions requiring multiple participants to deliver strategically important results through open innovation to the mutual benefit of the parties involved. This would be an expansion of what TSB already does and the larger sums involved would be designed to attract international IB companies to come to UK to conduct their research in collaboration with UK SMEs and universities.

    c. If the measures described in bullets a. and b. are successful in generating a demand for more mid-scale (non-commercial) industrial facilities, a centralised pool of equipment and greater availability of shared demonstration facilities with links to business incubation services for hire to IB SMEs looking to industrialise processes developed in the lab could be considered.

Such measures would go some way to addressing the issues raised in Key Findings F1-F5, F9, F12-F15.

11.2 Policy recommendations that are generic to technology development

There is a clear requirement for policy support to encourage technology development generally in the UK and to stimulate domestic and international investment into UK technology-based businesses. Our generic recommendations are that:

To encourage growth:

3. Targeted measures to stimulate lending to those IB SMEs which have made considerable progress reducing technology risk and now need to invest in the elimination of scale-up risk. The criteria for assessing which companies qualified for such support would need to be specific to the technology concerned, but the support measure itself, could apply across a variety of technologies. Such measures could include loan guarantee schemes and encouraging state-controlled banks to offer debt facilities to venture lending funds. This would go some way to addressing the issues raised in Key Findings F5-F8.

To reduce start-up costs:

4. The tax system is modified to recognise the existence of virtual companies and to encourage the development of technology-based start-up companies by:

    a. Creating a virtual company legal and tax template in the same way that templates have been established for VCTs or EIS-qualifying businesses.

    b. Simplifying the administration of R&D tax credits.

These measures would need to be restricted to technology-based entities and they would need to deal with complexities relating to IP ownership, VC investment, valuation etc. However, were such measures introduced with the associated complexities resolved, they would go some way towards addressing the issues raised in Key Findings F10 and F11.

To encourage longer-term investment:

5. Ways are sought to encourage and replicate the investment strategy being pursued at Invesco Perpetual. This could include tax incentives for retail investors or preferential tax treatment for profits from such investments. This would go some way to addressing the issues raised in Key Findings F5-F8 and F16.

11.3 Observations that are relevant to the research community

There is a clear need for greater collaboration between the research, industry and finance communities to promote the commercialisation of IP. Our specific observations are that:

6. Research councils could consider encouraging more active collaboration between research and industry by funding more interdisciplinary and collaborative projects with the aim of developing IP that could be of commercial value. This would go some way to addressing the issues raised in Key Findings F4 and F9.

7. Universities could consider encouraging greater project working by facilitating collaboration between traditionally separate academic fields such as chemical engineering, micro-biology etc. This could build initially on the existing centres at Manchester (CoEBio3) in the North and UCL in the South. These academic research centres should have close links to sources of business expertise, business incubation facilities and shared demonstration facilities. Most importantly, they should be funded with new money and not be simply a new organisational overlay on existing activity. This would go some way to addressing the issues raised in Key Findings F4, F9 and F13.

8. University technology transfer offices could consider facilitating closer ties with corporate funders by standardising forms of contract, thereby simplifying and shortening contract negotiations. This would go some way to addressing the issues raised in Key Findings F4 and F9.

Appendix 1: Survey Participants

Based on a preliminary survey, 90 representative participants were identified as playing various roles in the UK's IB sector. Of these, 45 were selected as being particularly influential or as having a perspective or personal experience which it would be valuable to capture. Preliminary contact was made with all 45 candidate interviewees, following which a final list of 32 were selected for interview. At the request of NESTA, the main focus was on industrial participants. The breakdown of the 32 interviewees by category was as follows:

Industry	16
Finance	6
Research	6
Other	4

The target interviewees were carefully selected to cover a matrix of industry segments and types of participant. The industrial companies included both established large companies (six interviews) and SMEs (ten interviews). The SMEs were selected in order to include those having reached different stages on their corporate development and funding journeys and pursuing a range of different business models. Research organisations included both university groups and contract research organisations. Those engaged in providing finance spanned the spectrum from early-stage venture capitalists (VCs) to later-stage equity and debt providers. The 'Other' players were targeted from government and quasi-governmental organisations involved in the funding and co-ordination of IB research and the dissemination of results. Brief details of each interviewee are given below.

In order to provide an element of quantitative output, at the end of most interviews the interviewee was asked to indicate their level of agreement with the following eight statements:

1. The UK IB sector is currently getting the funding it needs.
2. Growth of the UK IB sector is currently constrained by a lack of available funding.
3. Even the best quality companies are finding it hard to raise the necessary funds.
4. It is harder to fund IB companies in the UK now than it was five years ago.
5. Overall, investors in UK IB companies have to date had disappointing returns.
6. A healthy IB sector is important for the broader competitiveness of UK industry.
7. Hard-headed investors are right to be sceptical of the potential returns from IB.
8. Today's IB SMEs have the potential to become the IB multi-nationals of tomorrow.

The required responses were: strongly agree/somewhat agree/neither agree nor disagree/somewhat disagree/strongly disagree. The interviewees were allowed to decline to answer a question if they felt they lacked the necessary background knowledge or insight. The 'neither agree nor disagree' category therefore implied sometimes agreeing and sometimes disagreeing, rather than "I don't know".

Industry – SME (ten interviews)

Clearfleau develops innovative anaerobic digestion (AD) technology to generate renewable energy from industrial effluents. It focuses on treating municipal waste and trade effluents and co-products from the food, dairy farming and beverage processing sectors. The company was founded in 2005 by a group of high-net-worth-individuals (HNWIs) and is based in Cambridge.

Cleveland Biotech supplies microbial agents which are able to digest grease and other organic waste, providing an environmentally friendly method of cleaning drains and other pipework. The company, which was founded in 1992, now employs 14 people and has traded profitably for more than a decade.

Green Biologics develops advanced fermentation biotechnology for the production of renewable butanol and other chemicals from waste and agricultural by-products. It was formed in 2003 when the CTO (Edward Green) acquired the assets of a failed previous venture (Agrol).

Ingenza is a biocatalyst and bioprocess development company founded in 2002 as a spin-out from the School of Chemistry at the University of Edinburgh. It applies engineered microbes to produce chiral amines and unnatural amino acids. It was acquired by Richmond Chemical Corporation (a US fine chemicals company) in 2007.

Monsal is one of the UK's leading anaerobic digestion and integrated biogas-to-energy businesses, having installed over 220 AD systems in the last 14 years. In 2007, the CEO led an MBO backed by £3 million from a Matrix Group VCT. In July 2010, the company raised £3 million from the Waste Resources Fund, a large international investor.

New Horizons Global produces 'Omega-Vie' oil derived from algae biomass for human and animal feed supplements, pharmaceuticals and cosmetics. In 2009, it acquired a large fermentation facility in Liverpool which was being closed down by a US company. So far, the company has raised £5 million and is now seeking a further £2 million.

Plant Impact develops crop nutrition and crop protection products which improve crop yields by reducing plant stresses caused by temperature, salinity, drought and light. The company sells its products directly and through licensing agreements with international agrochemical companies. It floated on AIM three years after being founded in 2003.

Plaxica was spun out of Imperial College in 2008 to commercialise fermentation and chemical processing technology for synthesising carefully controlled combinations of the two stereoisomers of lactic acid. This creates a feedstock which addresses many of the problems associated with current generation polylactic acid (PLA) biopolymers.

Solvert is developing a fermentation process to produce industrial chemicals from organic waste. The company was founded in July 2010 by a highly experienced chemical engineer and IB technologist. Since then it has operated as a virtual company, putting together a business plan using a team of individuals contracted on a consultancy basis.

TerraVerdae BioWorks is a Canadian-based start-up company developing a novel biorefinery concept for the manufacture of biopolymer precursors, using technology from a range of sources including the National Research Council (Canada). The pilot plant work is being carried out in the UK (at CPI) with support from the TSB. To date, the company has been funded mainly by grants – it is now seeking to raise a $10 million VC equity round.

Industry – large (six interviews)

AB Sugar is one of the world's largest sugar producers. In addition to the original British Sugar business, it now has operations in Africa, China and Europe following international acquisitions. It is seeking to commercialise novel technologies for the extraction of sugars and their conversion into added-value products, including bioethanol.

BP Alternative Energy Ventures (BP-AEV) is a corporate venturing operation of the oil major with offices in London and the US. Its main interest in IB relates to alternative transport fuels based on biomass feedstocks. Of the $130 million invested in 20 cleantech companies so far, five could be construed as IB, all focused on developing biofuel and biochemical technologies or processes.

Croda International is a global leader in speciality chemicals. Its Croda Oleochemicals subsidiary employs a variety of 'traditional' chemical processes to convert natural based raw materials (mainly vegetable oils and fats) into fatty acids and glycerol, and then further refines and process them via biotechnology into a range of functional specialities.

Ineos, founded in the UK but now headquartered in Switzerland, is the world's third largest chemicals group and a leading manufacturer of petrochemicals, speciality chemicals and oil products. Ineos Bio was set up in 2008 to commercialise a process for converting organic waste into bioethanol via a syngas intermediate.

Shell Global Solutions is the engineering and technology arm of the oil major. The 'Biodomain' group sits within the Projects and Technology section (11,000 people). It focuses on biological sciences, and specifically IB, linked to first and second generation liquid transport biofuels, chemicals and related enabling technology developments.

Syngenta was formed in 2000 from the agribusinesses of Novartis and AstraZeneca. The company spent $1 billion on R&D in 2010 on eight core technology platforms, including basic plant sciences. Its Agricultural Research Station at Jealott's Hill was opened in 1928 by ICI. The Syngenta Ventures Group operates from Basel.

Investment, has a long-term interest in the biotech sector. He invests directly in early-stage companies, often alongside Imperial Innovations in which Invesco has a 46 per cent stake.

Oxford Capital Partners is a specialist investment manager focused on growing international technology businesses. Its investor clients include institutions and high-net-worth individuals. About a third of the fund is invested in sustainable/clean technologies, of which a half is invested in IB companies.

The Wellcome Trust is a global philanthropic organisation with a budget of over £600 million per year dedicated to improving human and animal health. It invests the returns on a fund set up as a bequest by the founders of the Wellcome Foundation Ltd. It proposed setting up a life sciences innovation centre as a legacy to the 2012 Olympic Park.

WHEB Partners began as a clean technology incubator and corporate finance boutique in 1995 before focusing on private equity fund management. It provides both venture and growth-stage equity funding and has assets under management of £130 million. In 2005, WHEB raised the UK's first broad-based clean technology fund.

Finance (six interviews)

CT Investment Partners (CTIP) is one of the leading UK cleantech investors, advising and managing around £70 million of investments for the Carbon Trust, EIB and ERDF. The CITP team have been investing since 2003 and have made 25 early-stage investments in the broad cleantech sector, typically investing between £250k and £4 million in any individual opportunity. Two companies within this portfolio are in the IB sector (Green Biologies and Plaxica).

ETV Capital is one of the leading players in Europe providing venture lending to technology sector SMEs. Over the past decade it has lent £260 million to 190 companies, many of them in the healthcare segment of biotech, generating better returns than most early-stage biotech VC funds.

Invesco Perpetual is one of the UK's largest independent investment managers, offering a broad range of products including VCTs and pension funds. Neil Woodford, Head of

Research (six interviews)

The Centre for Process Innovation (CPI) is a contract R&D company based on the old ICI site at Wilton which develops novel chemical processes. It hosts the National Industrial Biotechnology Facility (NIBF), first opened in 2007 and expanded in 2010 to allow increased throughputs and upstream processing. CPI/NIBF is expected to become part of the High Value Manufacturing Technology and Innovation Centre which will be supported by BIS (through TSB).

CoEBio3, the Centre of Excellence for Biocatalysis, Biotransformations, and Biocatalytic Manufacture, is a consortium between the Universities of Manchester, Strathclyde, York and Heriot-Watt. The Centre has a dedicated biomanufacturing pilot facility which is available on a contract basis to academic and industrial groups.

Imperial College London is one of the world's leading science and technology universities with a strong track record of commercial research collaborations. It has given rise to a large number of spin-out companies, many of them funded by Imperial Innovations plc. In the IB space this includes Plaxica and Mycologix.

The National Non-Food Crop Centre (NNFCC) is co-located with the University of York. It supports companies, government and other organisations in projects aimed at developing biorenewable energy, fuels and materials. It does this by undertaking work sponsored directly by government and commercial consultancy projects.

The Scottish Association of Marine Science (SAMS) is one of the UK's leading marine science research organisations, and one of the oldest oceanographic institutions in the world. It is a Collaborative Centre of the Natural Environment Research Council (NERC) and currently employs ca. 140 staff based at the Scottish Marine Institute near Oban.

University College, London (UCL) operates the Bioconversion-Chemistry-Engineering Interface Programme which brings together academics from three UCL faculties interested in synthesising the next generation of complex chemicals through better integration of chemical and biocatalytic routes.

Other (four interviews)

The Biotechnology and Biological Sciences Research Council (BBSRC) invests public funding in bioscience research and training in universities and strategically funded institutes. Its aim is to further scientific knowledge for the benefit of the UK and beyond. Its budget for 2011-12 is ca. £445 million. It recently identified IB as a new council-wide high level strategic priority research area.[40]

40. Further information on this is given in Part 2.

The Biosciences KTN (Knowledge Transfer Network) is part of the '_connect' network managed by the TSB and co-funded by various government and EU bodies. It was formed in September 2009 and incorporated three existing organisations; the Bioscience for Business KTN, the Food Processing KTN and Genesis Faraday.

The Engineering and Physical Sciences Research Council (EPSRC) is a sister body to the BBSRC, and its budget for 2011-2012 is ca. £834 million. Its interest in IB stems from the necessary contribution that engineering and physical sciences and especially chemistry and chemical engineering makes alongside the biological sciences. It co-funds BBSRC's Integrated Biorefining Research and Technology Club.

The Technology Strategy Board (TSB) is the UK's national innovation agency. It is the main funder of the Knowledge Transfer Networks (with ERDF, DEFRA and the EU), Technology Innovation Centres (TICs – with industrial partners and other sources of public funding) and runs competitions for grants to promote R&D in the UK.

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